ABSTRACT BOOK

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DDC1

Fulminant Non-ADEM Encephalitis ¿MOGAD without MOG-IgG?

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Objectives

Autoantibodies against MOG-IgG have been described in both children and adults with acquired demyelinating syndromes, including ADEM, but also in other autoimmune encephalitis cases without predominant white matter involvement, further expanding the MOGAD spectrum and confirming autoimmune pathogenesis in these cases as well. On the other hand, around 40-50% of ADEM patients are negative for these antibodies. Furthermore, it is not clear whether patients with other encephalitis conditions, lacking MOG antibodies, might present clinical and radiological patterns similar to those of non-ADEM MOG-positive encephalitis. Here, we present a case of fulminant non-ADEM encephalitis with typical MOGAD features without antibodies identified.

Content

We present the case of a 12-year-old patient who developed severe encephalopathy with ataxia and acute urinary retention lasting 24 hours. An extensive study revealed mild pleocytosis in the cerebrospinal fluid (CSF) with negative PCR results for viruses and bacteria. Brain MRI showed confluent hyperintense lesions on T2/FLAIR in the cortical-subcortical areas, basal ganglia, brainstem, and extensive longitudinal myelitis. Laboratory analysis of blood/CSF for MOG, GlyR, GFAP, and AQP4 both in serum and CSF was performed. The patient was treated with broad-spectrum antimicrobials and antivirals along with first-line immunotherapy (steroids), which showed slight improvement in focal neurological deficits. However, 48 hours after onset, the patient experienced sudden deterioration with cardiorespiratory arrest and no signs of increased intracranial pressure, which did not respond to rescue measures, resulting in death. Anatomopathological examination showed extensive demyelinating lesions in the brainstem with perivenular lymphocytic infiltrates, without signs of herniation, suggesting death due to brainstem dysfunction. The findings are suggestive of a demyelinating pathology associated with anti-MOG antibodies.

Conclusion

We describe a case with a poor evolution despite early immunomodulatory treatment due to brainstem dysfunction from demyelinating lesions. The clinical-radiological pattern resembles that of MOGAD patients presenting with cortical encephalitis but without the presence of antibodies. It is currently unknown whether these represent the same disease, but the negativity might be due to sensitivity issues with current cell-based assays or other antibodies might be involved. Studying these patients is essential to guide specific treatment and avoid outcomes like the one described.

DDC2

Could lasting headache in first patient have the same etiology as the second presenting neck pain and upper limb weakness

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Objectives

Lyme disease is an infectious disease transmitted to humans through the bite of a tick infected with the spirochete Borrelia burgdorferi. If untreated in the early stages, patients may develop neurological complications in the weeks or even months following the tick bite. Neuroborreliosis is classically characterized by a triad, including a painful radiculoneuritis, cranial nerve involvement, and lymphocytic meningitis, which may occur together or separately. Lyme disease can be effectively treated with antibiotics if diagnosed in time. But diagnosis requires accurate reporting of the clinical history and clinical evaluation. We are reporting here two cases in which some clinical observations were lacking, leading to a missed early diagnosis.

Content

1: A 12-year-old patient has been presented with headaches lasting for 3 months, which were relatively intense and repetitive. The patient had been regularly taking analgesics. Initial tests were negative, except for a positive serology for mononucleosis. The clinical and neurological examinations were reassuring, with the only finding being slight hesitation during the Romberg test. Since mononucleosis does not typically present with headaches, further investigations were carried out, including a COVID PCR test, blood tests, an EEG, and an MRI. A lumbar puncture later confirmed the diagnosis of Lyme disease. 2: A 13-year-old patient consulted for diffuse complaints of neck pain, as well as migratory shoulder pain, associated with muscle weakness without sensory loss in the upper limbs. On neurological examination, we noted neck stiffness and a positive Lasègue sign, as well as a slight drop of the left arm during the Barré test. After performing a cervical and brain MRI, which excluded muscular and spinal hypotheses, blood tests and a lumbar puncture were carried out, leading to the diagnosis of Lyme disease. Retrospective history later revealed that the young patient had been bitten by a tick at a scout camp the previous summer. Both cases have progressed well under antibiotic treatment.

Conclusion

Lyme disease should be part of the differential diagnosis in cases of neurological involvement. We want to emphasize the importance of clinical examination and accurate recording of patient history. This is especially true given that the chronological symptomatology of Lyme disease is rarely observed in its entirety. We typically encounter symptoms that appear at a certain stage of the disease's progression, without knowledge

of possible earlier manifestations. Furthermore, the initial tick bite is often forgotten, and the erythema migrant is reported in only a minority of patients with neuroborreliosis.

DDC3

The Chameleon Effect: when a rare disease hides in plain sight

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Objectives

Pediatric Onset Multiple Sclerosis is a rare condition, accounting for 3-10% of all MS diagnoses. Onset before the age of 10 is considered exceptional and poorly documented in the literature. According to McDonald criteria, alternative diagnoses for POMS in children under 11 years of age should be carefully considered. We present a case of a child with MS onset before the age of five.

Content

A 4-year and 8-month-old healthy girl, with normal psychomotor development, was brought to the emergency department of Buzzi Children's Hospital due to the acute onset of left lower limb monoparesis. Brain MRI revealed a lesion in the right central white matter and unilateral optic neuritis. Cerebrospinal fluid (CSF) analysis showed normal cellular content, protein, and glucose levels, and oligoclonal bands were negative. A neuro-ophthalmological examination documented papilledema, severe visual acuity deficit, slowed conduction, and reduced amplitude of the visual evoked potential. Somatosensory evoked potentials (SSEP) showed increased central conduction time in the right upper limb and bilaterally in the lower limbs. MOG and AQP4 antibodies in both serum and CSF were negative. Intravenous methylprednisolone (IVMTP) led to complete recovery of motor symptoms, but not of visual deficit (monocular severe visual acuity deficit). Four months later, a fine intention tremor during spontaneous activity and fine bilateral dysmetria were observed. The MRI showed an oval lesion in the right parietal region with the CVS sign, a multilobulated lesion in the right thalamocapsular region, with minimal contrast enhancement of the medial geniculate body, and a lesion in the anterior limb of the left internal capsule with contrast enhancement. Clinical signs disappeared after further treatment with IVMTP. At this point, a diagnosis of POMS was established.

Conclusion

Despite its rarity, our patient meets the diagnostic criteria for Multiple Sclerosis (ECTRIMS 2024). In line with what is generally observed in children, the initial clinical presentation—apart from the severe and persistent visual impairment—was very mild, as was the relapse. However, the lesion burden is significant, and the child experienced a relapse just a few months after the first event. These cases, although exceedingly rare, present numerous challenges in terms of management and long-term therapy.

CO01

Altered dopamine metabolism and response to treatment with levodopa/carbidopa in AHDS/MCT8 deficiency syndrome: preliminary results

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Objectives

MCT8 deficiency, also known as Allan-Herndon-Dudley Syndrome (AHDS), is a rare X-linked leukoencephalopathy caused by pathogenic variants in SLC16A2 gene, which encodes the MCT8 protein, a membrane transporter responsible for the active transport of thyroid hormones (TH) at the blood-brain barrier. An impairment of MCT8 transporter results in thyroid hormones deficiency in the central nervous system (CNS) from early fetal development, where these hormones are critical for normal brain development, particularly for the basal ganglia. The AHDS clinical picture is characterized by severe psychomotor delay/intellectual disability, epilepsy, axial muscular hypotonia, and pyramidal and extrapyramidal signs. The latter include a combination of dystonic movements, paroxysmal involuntary movements, and parkinsonian features, which are severe and often dominate the clinical presentation. The pathophysiology and clinical presentation strongly suggest an impairment of dopaminergic circuits. Therefore, this study aims to investigate dopamine metabolism alterations and evaluate the response to levodopa (L-DOPA) treatment in a group of AHDS patients. Retrospective data collection included patients' medical history, clinical features, genetic profiles, and instrumental findings. All patients underwent lumbar puncture to measure cerebrospinal fluid (CSF) neurotransmitter (NTR) metabolites. A standardized neurological and neuromotor assessment, including video recordings, was performed before initiating levodopa/carbidopa trial and after titration to 10 mg/kg/day.

Content

In all patients, the clinical phenotype was characterized by severe psychomotor delay/intellectual disability, limb spasticity, and infantile parkinsonism, predominantly presenting as muscular hypotonia, hypomimia, bradykinesia, and low reactivity and responsiveness to environmental stimuli. CSF NTR analysis showed reduced dopamine

metabolite (HVA, 5-HIAA) levels in 2/6 patients and values at the lower limit of normal in 4/6. Administration of levodopa/carbidopa (7-8 mg/kg/day) led to an improvement in hypomimia, bradykinesia, and hypo-reactivity, with enhanced responsiveness to environmental stimuli and better motor initiative (documented through video contributions) in the currently reassessed patients.

Conclusion

The pathophysiology of movement disorders in AHDS is complex, multifactorial, and not yet fully understood. Thyroid hormones are key factors for dopaminergic differentiation of neuronal stem cells in animal models and human embryonic stem cells in vitro. Clinical and biochemical data, alongside partial responsiveness to levodopa, confirm the involvement of the basal ganglia and dopaminergic system in AHDS patients. In vivo assessment of the dopaminergic system's integrity in these patients using nuclear medicine techniques imaging could further elucidate the underlying pathophysiological processes, particularly by distinguishing between pre- and postsynaptic defects or a combination of both. This could guide the therapeutic use of levodopa or other dopaminergic drugs.

CO02 Genetic epidemiology of congenital and very-early-onset ataxia

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Objectives

To describe the genetic epidemiology of congenital and very early onset ataxia in a cohort of 810 patients referred to our reference center on Cerebellar Malformations and congenital diseases from 2015 to 2024.

Content

All patients were ataxic and presented clinical cerebellar symptoms before the age of two years. We excluded patients whose ataxia was clearly progressive at the time of inclusion, patients whose brain MRI results were suggestive of a specific diagnosis, (Joubert, Poretti-Bolsthauser, or Dandy-Walker syndromes, tubulinopathies, VLDLR mutations, and acquired cerebellar damage), and patients with cerebellar atrophy without clinical ataxia (intellectual deficiency without motor trouble, severe encephalopathies with very poor development). We carried out a systematic genetic exploration in these patients that has evolved over the years and technological developments, from Sanger sequencing to high-throughput sequencing. Three successive NGS genes panels were designed and allowed to reach a total yield of diagnosis of 35%. A part of the patients without a genetic diagnosis underwent a pangenomic analysis, mostly exome trio and genome trio for a few. We will present our results, the genetic epidemiology in congenital and very-early onset ataxia in our center, and a tentative correlation between genotype and phenotype.

Conclusion

Like in previous studies, we observed that ITPR1, CACNA1A, were among the most frequent genes. We were able to identify several patients affected with a metabolic disease with a very insidious onset mimicking a congenital ataxia. Exome sequencing allowed to identify new genes, but regarding the relative high yield of the panel, WES was not used at first-line to avoid incidental findings. As validation of the variants generated by NGS is now the main challenge, we are developing RNAseq analysis routinely in our laboratory.

CO03 Atypical ADCY5-related movement disorders: highlighting adolescent/adult-onset cervical dystonia

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Objectives

ADCY5-related movement disorders are known to be paroxysmal and/or permanent hyperkinetic movements. Nocturnal paroxysmal dyskinesia (PxD), facial or perioral dyskinesia are suggestive of this genetic diagnosis. Next generation sequencing has enabled an expansion of the ADCY5- related phenotype. The aim of our study was to report atypical phenotypes.

Content

We describe 12 patients from 8 different families, of which 10 had adolescent/adult-onset head and upper limb tremor followed by permanent cervical dystonia without PxD. We report three novel ADCY5 variants in these patients, located in the catalytic domains, close to previously reported variants. Caffeine was ineffective for the 2 patients who tried the treatment, and botulinum toxin therapy seemed to be the most effective treatment. We also describe 2 patients with spontaneous remission of pediatric-onset PxD before adulthood.

Conclusion

We highlight an adolescent/adult-onset phenotype with head tremor and cervical dystonia, broadening the clinical spectrum of ADCY5-related movement disorders.

CO04 Acute ataxia in children - from onset to outcome

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Objectives

Background: Acute ataxia is an uncommon complaint in children. It is characterized by impaired coordination and balance, with children manifesting an unsteady gait or refusal to walk. In the present study, authors aimed to provide an overview of the approach to acute ataxia in children, from presentation to diagnosis and follow-up.

Content

Methods: Authors conducted a single-center retrospective chart review of all pediatric patients hospitalized with acute ataxia in a Level II Center between January 2015 and November 2024. Authors evaluated the patient's demographic features, primary complaint, physical examination findings, laboratory and imaging results, as well as final diagnosis, treatment and follow-up. Results: A total of 26 cases were included, with a mean age at onset of symptoms of 7,5 years (min. 8 months; max. 17 years) with male preponderance (14 vs 12). On the physical examination, almost all children presented with ataxia at the emergency room. The associated symptoms reported were mostly fever, vomiting and other neurologic symptoms. The mean length-of-stay was 6,6 days. Among the 26 cases, eight cases (31%) were classified as cerebral acute ataxia, seven (27%) were related to medication ingestion, five with post-infections conditions and one due to a vestibular cause. In 5 individuals, a more severe diagnosis was identified (ADEM, Guillain-Barré syndrome, Miller-Fisher syndrome and Multiple Sclerosis), with need of intensive care.

Conclusion

Ataxia is a clinical manifestation rather than a single disease and encompasses a wide spectrum of disorders, ranging from benign to life-threatening conditions, with different prognosis. Early diagnosis and intervention are pivotal in optimizing outcomes. This study highlights the diverse etiologies of ataxia in pediatric patients and the need to consider alternative diagnoses.

CO05

Unraveling the phenotypic spectrum of TMEM63A-Related Disorders

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Objectives

Transmembrane proteins (TMEM) are proteins located within cell membranes, that pass through the phospholipid bilayer. They are integral to cell membranes and facilitate various cellular processes including molecular transport, enzymatic activity, and cell communication. TMEM63A is recognized as a mechanically activated ion channel crucial for central nervous system development, mainly involving sodium currents. Pathogenic variants in TMEM63A are associated with "Infantile-onset Transient Hypomyelination"(HLD-19). In the original description, patients typically present with early-onset neurological symptoms such as nystagmus and motor delay, alongside profound brain and spinal cord hypomyelination on MRI. However, these abnormalities usually remain stable until childhood, as in classical hypomyelinating leukodystrophies, but then regress or improve, often resulting in normal motor and cognitive abilities. We describe the clinical and neuroradiological picture of four unreported exemplary case studies and define the diverse clinical presentations and outcomes of TMEM63A-related leukodystrophy, while also exploring and analyzing the cases already reported in literature.

Content

While some patients exhibit significant improvement in both neurological symptoms and myelination, others experience persistent and profound developmental delay, and often present cerebral and cerebellar atrophy in addition to hypomyelination at brain MRI. An intermediate phenotype may also be observed, while an adult-onset form has been described in literature. In addition, we describe a shared clinical feature consisting in focal epileptic seizures at disease onset, that consistently improved with administration of sodium channel blockers.

Conclusion

This study broadens the phenotypic spectrum of TMEM63A-related leukodystrophy and defines the four main presentations, that have never been clarified before. The early onset

of epilepsy may suggest potential primary neuronal involvement in TMEM63A-related disorders. Enhanced knowledge in this area could aid in early diagnosis and tailored management strategies for affected individuals.

CO06

Three cases of Mycoplasma pneumoniae neurological complications

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Objectives

Mycoplasma pneumoniae is mainly responsible for respiratory diseases and can lead to neurological complications either directly or through a post-infectious immune response. We report a case of encephalitis, optic neuritis, and acute demyelinating encephalomyelitis (ADEM) following Mycoplasma pneumoniae infections.

Content

Case 1: A 3-year-old boy presented with ataxia, nystagmus, action tremor and somnolence, preceded by three days of rhinorrhoea. Toxicology screening was negative. Magnetic resonance imaging (MRI) was unremarkable, electroencephalography showed mild diffuse slowing of baseline electrogenesis. Cerebrospinal fluid (CSF) revealed pleocytosis and decreased glucose levels. Etiological work-up revealed positive serology for M. pneumoniae, suggesting M. pneumoniae-associated encephalitis. He was treated with ceftriaxone, azithromycin and acyclovir, achieving full recovery. Case 2: A 13-year-old male was admitted with bilateral eye pain, reduced visual acuity, altered colour perception, photophobia, headache, and vomiting. Six weeks prior, he had an upper respiratory tract infection. The physical exam showed decreased visual acuity and papilledema. MRI revealed T2 hyperintense optic nerves and optical coherence tomography showed bilateral retinal nerve fibre layer deficits. Serum myelin oligodendrocyte glycoprotein (MOG) antibodies were detected, suggesting MOG-associated optic neuritis, with M. pneumoniae as the likely trigger (positive IgM and IgG serology). Treatment with azithromycin and methylprednisolone pulses, followed by oral prednisolone, led to full recovery within two months. Case 3: A 14-year-old male presented with intense headache, photophobia, phonophobia, confused speech, temporal disorientation, ataxia, vomiting, urinary retention, somnolence and progressive decreased level of consciousness. He had a respiratory infection and an acute otitis media a week before. CSF revealed decreased hypoglycorrhachia, increased protein levels and pleocytosis and intrathecal IgG synthesis. Brain and medulla MRI suggested ADEM. He received methylprednisolone pulses, followed by oral prednisolone, and intravenous Immunoglobulin (IVIG), with significant improvement, despite minor memory and movement deficits. Serology and nasopharyngeal PCR were positive for M. pneumoniae, suggesting ADEM following M. pneumoniae infection. Aquaporin-4 and MOG antibodies were negative.

Conclusion

Neurological complications of M. pneumoniae can be severe and cause long-term sequelae. We present three rare cases that occurred during a recent rise in high M. pneumoniae infections in 2024. The latency between respiratory and neurological symptoms might help distinguishing direct infection of the central nervous system (CNS) from immune-mediated CNS damage. Prompt diagnosis and treatment are crucial to reduce mortality and morbidity.

CO07

Neurovisual impairments in individuals affected by Aicardi-Goutières syndrome: correlations with clinical severity

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Objectives

Aicardi-Goutières syndrome (AGS) is a monogenic type-I interferonopathy characterized by diverse neurological and extra-neurological manifestations. Ophthalmological findings, such as glaucoma and nystagmus, have been reported in affected individuals. This study aimed to assess the neurovisual profile of individuals with AGS and explore potential associations between visual impairments and related motor, cognitive and adaptive deficits.

Content

Forty-four individuals (25 males, 19 females; mean age 9.87 ± 7.19 years, range 8 months – 31 years) diagnosed with AGS were enrolled in the study. Clinical history was reviewed, and neurological examination was conducted, including evaluations of gross motor (Gross Motor Function Classification System) and fine motor skills (Manual Ability Classification System), and the degree of neurological impairment (AGS Severity Scale). Cognitive profile was assessed using age-appropriate tools (Griffiths Mental Developmental Scales-III or Wechsler scales) and adaptive functioning using the Vineland Adaptive Behavior Scales. All participants underwent a comprehensive assessment of ophthalmological, oculomotor, and basic visual functions. Additionally, a visual total score was calculated as the sum of the impaired visual items, ranging from 0 to 13. All individuals exhibited visual impairments, primarily characterized by a variable combination of refractive errors, ocular fundus abnormalities, strabismus, alterations in fixation, smooth pursuit and saccadic movements, and/or reduction in visual acuity, contrast sensitivity and visual field. Correlation analyses revealed significant relationships between the degree of motor impairment and strabismus (gross motor $p<0.01$, fine motor $p=0.03$), unstable fixation (fine motor $p=0.03$), discontinuous smooth pursuit and saccadic abnormalities (gross motor $p=0.05$, fine motor $p=0.01$), reduced visual acuity and contrast sensitivity deficits ($p<0.01$). We also documented a correlation between the presence of cognitive impairment and strabismus ($p<0.01$), unstable fixation ($p=0.03$), smooth pursuit and saccadic abnormalities ($p=0.01$), reduced visual acuity and contrast sensitivity deficit ($p<0.01$); and a relationship between adaptive difficulties and strabismus ($p=0.03$), reduced visual acuity and contrast sensitivity deficits ($p<0.05$).

Finally, the Vineland total score and communication domain ($p<0.01$), the AGS severity scale ($p<0.001$), and cognitive deficit ($p<0.001$) strongly correlated with the visual total score.

Conclusion

Several visual disorders seemed to correlate with clinical severity, suggesting that the visual system may be particularly vulnerable to the overproduction of interferon. Early detection of these impaired visual functions could serve as a promising tool for monitoring disease progression and tailoring interventions in affected individuals.

CO08

Disease associated with antibodies against myelin oligodendrocytic glycoprotein (MOGAD) in pediatric age: a single-center study

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Objectives

The disease associated with antibodies against myelin oligodendrocytic glycoprotein (MOGAD) is a rare entity in the pediatric population, with several clinical, diagnostic, therapeutic and prognostic specificities. This study intended to analyze the characteristics of the pediatric population with MOGAD followed at the reference hospital in central Portugal.

Content

Material and methods. An observational and retrospective study was carried out in the pediatric population diagnosed with MOGAD, established between January 2015 and December 2024, according to the criteria proposed by the International Panel, followed at the Hospital Pediátrico de Coimbra. Sociodemographic, clinical, laboratory, imaging and therapeutic variables were studied. A descriptive and inferential analysis was carried out (Chi-Square and Kruskal-Wallis tests), considering the existence of statistical significance when $p < 0.05$. Results. Twenty (n=20) children were included, 12 males (M:F 1.5:1), with a median age at diagnosis of 5 years. The most prevalent clinical phenotype was Acute Disseminated Encephalomyelitis (ADEM). In 65% of cases there was a previous infection. The initial median EDSS score was 2.0. The laboratory technique used in the diagnosis was always cell-based assay, with no titer recorded in 3 cases. Oligoclonal bands were identified in the CSF in 20% of children, and pleocytosis in 45%. For all cases, the first therapeutic option was corticosteroid therapy, with a median of 5 days of treatment. Only 4 underwent maintenance therapy. In 90% of cases, complete functional recovery was confirmed. The majority presented a monophasic course (14/20) and 10 seroconverted during follow-up. No statistically significant relationships were found between the quantitative variables studied.

Conclusion

Conclusion. Sociodemographic, clinical and evolutionary characteristics of MOGAD identified in the pediatric population of our region (central Portugal) correspond, in their vast majority, to those described in the literature. The clinical approach to this situation followed current international recommendations.

CO09

Pediatric posterior circulation arterial ischaemic stroke : a diagnostic challenge

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Objectives

The aim of this study is to describe specificities of posterior arterial ischaemic strokes, with vertebral occlusions diagnosed in majority on few symptoms. The second purpose is emphasize the high initial risk of recurrence, even if well administred treatment

Content

Pediatric arterial ischaemic stroke are rare with an annual estimated incidence as 2-8/100 000 children, the posterior circulation is involved in one-fifth to one-third of cases. Previous studies reported male predominance in posterior cerebral arterial ischemic strokes. Children are older than in anterior ischemic strokes. Diverse aetiologies are described. Vertebral artery dissections incidence is estimated to 1-1.5/100 000 in pediatric population which is less common than carotid dissection. It has been described that minor traumatisms, occurred some hours or days before. Another mechanism of posterior circulation infarct is focal vertebral arteriopathy, which can extend to basilar artery, with progressive occlusion, leading to stenosis. Symptoms are usually non-specific, related to posterior infarcts, which results in diagnostic difficulties. The gold standard for diagnosis of posterior infarcts in children is MRI, finding multiple bilateral and aged different infarct involving posterior fossa, thalamus, brainstem, occipital cortex. Anticoagulation is the recommended treatment for extracranial vertebral artery dissection (VAD) or in posterior arteriopathy according to expert recommendations. The risk of recurrence seems to be important in early time, due to embolic nature of VAD-related stroke or basilar artery occlusion. We report seven pediatric cases of posterior circulation stroke complicating vertebral artery occlusion to describe clinical presentation, brain and artery imaging, ischemic stroke recurrence and treatment management. We describe six boys and one girl between five and fifteen years old presented with acute neurological signs, two of them with a history of minor traumatism. MRI revealed different infarcts in posterior circulation. All have vertebral occlusion, two with basilar occlusion, five others with vertebral artery dissection/arteriopathy. All underwent initial anticoagulation treatment, three of them have early recurrence under treatment. Antiplatelets and corticoids were then added.

Conclusion

Presence of multiple posterior circulation infarcts at presentation have to lead to consider diagnosis of vertebral occlusions, by repeating imaging if necessary. It insists on the

evolution of arterial abnormalities over time despite adapted treatment. High stroke reccurence rate is an argument for treating quickly, raising question of initial aggressive treatment. Good clinical outcome was observed despite their imaging. Long-term outcome, specifically on neuropsychological aspects, have to be explored in posterior circulation infarcts.

CO10

Neonatal subpial hemorrhage: Padua experience and systematic review

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Objectives

Subpial hemorrhage (SPH) is a rare subtype of intracranial hemorrhage, predominantly affecting term neonates and often associated with cortical-subcortical infarction. We described the epidemiology of SPH by analyzing cases referred to our hospital and concurrently conducting a systematic review of the cases reported in the literature. We also illustrated factors associated with severe outcome. A retrospective study was conducted on neonates with SPH referred to our hospital from 2013 to 2023 (cohort 1). Additionally, a systematic literature review on neonatal SPH was performed using PubMed, Scopus, Cochrane, and Web of Science up to April 2024 (cohort 2). Cohorts 1 and 2 were pooled for combined analysis.

Content

A total of 173 cases were analyzed, 10 original cases (cohort 1) and 163 literature cases (cohort 2). Ninety-two percent were term/near-term neonates (59% male). Clinical presentations included seizures (36%), apnea (36%), and encephalopathy (18%). Ninety-four percent were diagnosed with brain magnetic resonance imaging and/or cranial ultrasound. Lesions were located in the temporal lobe in 62%, with infarctions adjacent to SPH in 89%. Sixteen percent died, 52% had neurological deficits, and 8% were diagnosed with epilepsy. In a subcohort of 67 patients with available individual data (10/10 from cohort 1, 57/163 from cohort 2), low birth weight, seizures, neonatal infections, and parenchymal hemorrhage were significantly associated with severe outcome.

Conclusion

To our knowledge, this is the first systematic literature review on SPH. Although neonatal SPH is rare, understanding and characterization of the condition are expanding. SPH is predominantly located in the temporal lobe, and we identified a distinctive clinical presentation, including apnea (potentially of ictal origin) and seizures. Neurologic sequelae are common, with parenchymal hemorrhage showing a strong correlation with neurological impairment in our study.

CO12

Epileptological natural history and electrographic evolution of metachromatic leukodystrophy patients: ad interim results from a longitudinal study

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Objectives

To characterize EEG patterns and epilepsy features in MLD patients.

Content

Background: Metachromatic leukodystrophy (MLD) is a progressive lysosomal storage disorder caused by mutations in the ARSA gene, causing progressive demyelination and neurodegeneration. Few data are available on its epileptological natural history. Methods: This is a single-center, retrospective, and prospective observational study on MLD patients enrolled in a natural history protocol from January 2000 to December 2023. Clinical data including history of seizures and seizure frequency, drugs and dosage, EEG tracings were collected. Results: Fifty patients, 25 late infantile (LI), 12 early juvenile (EJ), 7 late juvenile (LJ), 6 adult-onset (AD), were included. Median follow-up was 4 years (IQR: 2-8; range: 1-20), with 360 EEG tracings. Epilepsy was documented in 78 % (39/50) of patients, specificially in 80% (20/25) of LI, 100% (12/12) of EJ, 43% of LJ (3/7) and 67% of AD (4/6). Epilepsy occurred on median time of 27 (IQR: 12-40) months after disease onset in LI, 19 (IQR: 7-42 months) in EJ, 93 (IQR: 76-169) months in LJ and 111 (IQR: 64-156) months in AD. The main seizure types reported were focal and focal-to-bilateral tonic-clonic seizures. Generalized ictal manifestations persisted in 8/39 despite therapy. Status epilepticus was reported in 30% (13/39) of patients, coinciding with epilepsy onset in 4/39 patients. Disease subtypes presented distinct EEG patterns: LI group presented rapid background deterioration, frequent seizures, and bursts of low-voltage rapid activity. Among Juvenile-onset patients, divergent patterns were observed, with EJ having more similarities with the LI group and LJ displaying a slower progression. AD presented mildly disorganized backgrounds with sporadic focal anomalies.

Conclusion

In contrast to what previously reported, epilepsy represent a significant comorbidity in MLD patients, especially LI and EJ groups, often presenting with drug-resistant seizures. Moreover, distinct MLD subtypes present with different EEG features, hence this could

represent a tool to further characterize MLD variants, disease progression and treatment response.

CO13

Harnessing Quantitative EEG to Distinguish Infants with Non-accidental head trauma from Controls and Predict Outcomes at 2 Years

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Objectives

Background: Non-accidental head trauma (NAHT), whiplash baby syndrome or abusive head trauma (AHT) differs from traumatic brain injury, due to differences in its physiopathology and brain lesions. The high incidence and the death rate of this pathology are rendering it a public health concern. The prognosis link to SBS is poor but Biomarkers or risk factors of bad prognosis are debated, do not help in everyday routine analysis and show no EEG implication or findings Objective: Our study evaluates quantitative EEG's prognostic value for AHT, aiming to determine its role as a diagnosis and a prognosis biomarker, we wanted to determine whether qEEG could serve as a predictive tool for identifying poor neurological outcome or mortality in cases of SBS.

Content

Participants and Setting: This retrospective monocentric case-control study, included children under two with confirmed AHT and controls undergoing EEG for non-traumatic conditions. Methods: We collected demographic, clinical, and EEG data from AHT and control groups. Quantitative EEG features were analyzed to predict trauma occurrence and long-term neurological prognosis using machine learning. Results: We analyzed 84 EEGs from 75 participants, including 46 EEGs from 40 infants with AHT and 38 EEGs from 35 controls. Early EEGs in AHT showed decreased complexity and increased monotony, particularly in those with severe outcomes (POPC4-6). Quantitative features (e.g., delta power, entropy, and Hurst exponent) were significantly reduced in AHT versus controls ($p<10^{-4}$). Differences in EEG features also distinguished mild (POPC1-3) and severe (POPC4-6). outcomes. A machine learning model perfectly classified AHT versus controls, while another achieved 72.5% accuracy in predicting long-term outcomes using EEG-derived features. Combined models identified control, POPC1-3 and POPC4-6 groups with 80% accuracy.

Conclusion

Conclusions: EEG is crucial in diagnosing and predicting outcomes in AHT, offering real-time brain function insights. Integrating AI enhances EEG analysis, enabling precise assessments, continuous monitoring, and improved clinical decision-making in pediatric neurocritical care. We have showed that qEEG could be a powerful to discriminate bad and good prognosis and could be useful in the future in early or mid-time EEG. Power spectra analysis seems to really highlight acute and early brain injury that could come from anoxic ischemia and cerebral hypertension. This phenomenon could disrupt

electrophysiological brain activity with neuronal death in the acute phase and secondarily be erased by cellular gliosis, multicystic degeneration, cerebral atrophy in late EEG. qEEG could an efficient and reproductive tool evaluation of the prognosis of individuals at early stages of SBS.

CO14

Broadening the phenotype associated with pathogenic variants in the FGF12 gene: from developmental and epileptic encephalopathy (DEE) to drug-responsive epilepsy with favorable cognitive outcome

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Objectives

The FGF12 gene encodes a protein interacting with voltage-gated sodium channels. Two mains variants, p.(Arg52His) and p.(Gly50Ser), have been repeatedly associated with developmental and epileptic encephalopathy-47 (DEE47, MIM #617166) with poor outcome. NM_004113.6:c.155G>A;NP:004104.3:p.(Arg52His), NM_004113.6:c.148G>A;NP:004104.3:p.(Gly50Ser) We aim to refine the electroclinical phenotype and outcomes of ten unpublished patients (2- 38 years) with these recurrent pathogenic variants in the FGF12 gene without DEE (Arg52His: n=4; Gly50Ser: n=6).

Content

This national retrospective multicentric study examined patients with FGF12 variants and early-onset epilepsy without a DEE phenotype. We report eight unrelated patients, along with two related patients, with early-onset epilepsy without DEE and pathogenic FGF12 single nucleotide variants. At the last follow-up, the median age was 7.6 years (range 2 to 38 years), and 70% were female. Epilepsy Seizure onset ranged from 3 days to 4 months, with earlier onset in Patients A-D (p.(Arg52His), 3–48 days) and a later onset for Patients

E-J (p.(Gly50Ser), 3–4 months). EEG findings Four of ten patients had normal interictal EEGs. Seizures were recorded in five patients, with ictal EEG showing focal involvement in four. Temporal lobe seizures were recorded for three. Antiseizure medication (ASM) Seizure clusters or status epilepticus were successfully treated with phenytoïn (or fosphenytoin) for four patients. The ASM chronology is shown in Figure. The sodium channel blocker (SCB) carbamazepine was the most used ASM (6/10 patients), and oxcarbazepine for one patient. ASM withdrawal trials was systematically failed. One patient with normal neurodevelopment did not receive early SCB treatment, while others with early SCB administration developed mild intellectual disability (ID). This aligns with previously reported cases of FGF12-related epilepsy. However, our findings highlight a key distinction: the three patients with mild ID had ongoing epilepsy despite ASM, whereas all seven patients with normal neurodevelopment were seizure-free. Brain MRI Two patients presented with abnormal brain MRIs without cerebellar abnormalities. Neurodevelopmental assessment and outcome Neurodevelopmental trajectories were normal in seven patients (2.1–38 years, median 6.8), including two with Arg52His and five with Gly50Ser. Seizure remission before age one was achieved in all with normal outcomes. Intellectual disability was associated with uncontrolled epilepsy without prolonged remission. Genotype-phenotype correlations

Conclusion

Our series of ten cases broadens the phenotypic spectrum associated with FGF12 pathogenic variants, highlighting cases of sporadic good neurodevelopmental outcome epilepsy. This study aims to enhance the awareness about the significant clinical variability of FGF12 variants. Early therapeutic interventions with sodium channel blockers such as carbamazepine, may influence this variability.

CO15

Diagnostic rate, mutation landscape and perspective of personalized therapy in 155 children with Developmental and Epileptic Encephalopathy.

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Objectives

We studied a retrospective cohort of children with developmental and epileptic encephalopathy (DEE), a group of neurological conditions characterized by early onset epilepsy and severe developmental delay.

Content

Cases were recruited from three university hospitals based on clinical criteria. After a blinded cross-validation process, 155 subjects were included. Most were subject to both array-CGH and exome-based gene panel analyses. A genetic diagnosis was identified in 105 (68%). A majority of patients (71%) had onset of symptoms before the age of one year. In this age group a disease-causing variant was identified in 73% of children, the highest proportion of cases reported so far. Genetic heterogeneity was high, involving 40 different genes. The most prevalent was SCN1A. Eight genes were identified in multiple patients and accounted for 50% of all diagnoses. The remaining genes represented ultra-rare disorders. We evaluated the disease-causing variants in an intention-to-treat approach and found that almost half would theoretically be amenable to personalized therapy using antisense oligonucleotides (ASOs).

Conclusion

In conclusion our work confirms that molecular diagnosis is part of first line screening in cases of severe epilepsy with altered neurodevelopment, especially in patients with onset of epilepsy in the first year of life, regardless the type of epilepsy. A molecular diagnosis is essential as it may allow for treatment adaptation, either with existing therapies or, increasingly, by inclusion into dedicated clinical trials.

P01

Early visual intervention through a digital personalized platform in infants at risk for Cerebral Visual Impairment: the VIPPSTAR-G1 project

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Objectives

Infants with early visual deficits arising from early brain damage are recognized as being a highly vulnerable clinical population, given the fact that visual impairment (VI) is likely to have an impact on all areas of development, namely motor, behavioural, cognitive, social-communicative and emotional abilities. With particular regard to Cerebral Visual Impairment (CVI), specific strategies of early intervention are crucial, especially during the first three years of life when neuroplasticity is highest. Despite digital health technologies offer a promising avenue for personalized care, sufficient clinical validation in pediatric populations are lacking. We aim to test the effectiveness of an early visual intervention protocol based on digital health services (e-learning platform) to promote visual functions in infants diagnosed/at risk for CVI .

Content

The VIPPSTAR project, funded by the European Commission (HORIZON-HLTH-2024-STAYHLTH-01-02-two-stage-101156763), addresses this gap by conducting a multicenter, multinational, single-blind randomized controlled trial. This trial aims to evaluate the effectiveness of early visual training in infants (0–35 months) diagnosed/at risk for CVI. The intervention is delivered through a digital health platform designed to improve visual and neurodevelopmental functions. Primary outcomes will concern visual functions (visual acuity, contrast sensitivity, visual fixation, smooth pursuit, and reactive saccades) and neurodevelopment (cognition, language, motion and behavior). Secondary outcomes will focus on adaptive functions, communicative and language development. Assessment will be conducted before, immediately after, and six months post-intervention. The study will enroll 48 subjects: per treatment group (TG) and 48 in the control group (CG) across three countries: Italy, Belgium, and Moldova. Families in the TG will access a dedicated eLearning MOOC with individualized, parent-mediated activities,

while the CG will receive standard care. Parental counseling will support self-efficacy and engagement.

Conclusion

This study expects to validate the effectiveness of digital early visual training in improving children's abilities and enhancing family quality of life

P02

Deep Brain Stimulation for Progressive Generalized Dystonia in a Pediatric Patient: A Case Report

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Objectives

Generalized dystonia in pediatric patients presents a complex diagnostic and therapeutic challenge, particularly when associated with progressive motor
 impairment and negative etiological investigation. Deep Brain Stimulation (DBS) of the internal segment of the globus pallidus (GPi) is a safe and effective treatment for
 generalized dystonia in patients who remained impaired, despite optimal medical therapy.

Content

A 12-year-old male was referred to Pediatric Neurology after experiencing his first generalized tonic-clonic seizure. His medical history revealed global developmental delay, toe-walking gait with frequent falls, language impairment,and learning difficulties. From age 7, he developed an akinetic-rigid syndrome with left foot dystonia. There was no family history of neurological disorders. His medication regimen included Clonazepam 0.5mg twice daily and botulinum toxin injections. Neurological examination showed frequent blepharospasm, oromandibular dyskinesia, dysarthria, axial dystonia with leftward inclination, and peripheral dystonia. Upper limbs exhibited mirror movements and positive reinforcement maneuvers, while the lower limbs showed leg extension and foot inversion, without tremor. Motor impersistence and a bizarre gait with choreiform movements were noted. MRI revealed enlarged lateral ventricles and moderate diffuse atrophy of the bilateral striatum, likely sequelae. EEG demonstrated slight diffuse slowing(7Hz) and brief photoparoxysmal responses(18 and 25Hz). Comprehensive laboratory investigations, including peripheral blood smear, lumbar puncture, and metabolic, neurodegenerative, autoimmune and infectious disease studies were unremarkable. Genetic testing excluded Huntington's disease and Huntington-like syndromes and exome sequencing detected no pathogenic variants. Pharmacological management with risperidone showed a poor response in choreiform movements. A

therapeutic trial with levodopa and trihexyphenidyl resulted in no clinical improvement of dystonia, which became generalized with severe gait impairment. Patient underwent bilateral GPi-DBS at 13 years and 6 months, followed by physiotherapy and speech therapy. Buspirone was initiated to control depressive symptoms. Eight months post-GPi-DBS,there is significant clinical improvement, notably reduction of left foot dystonia allowing brief assisted ambulation, improved oromandibular dystonia and decreased blepharospasm. Albeit functional improvement supported by caregivers and therapists, speech production became more difficult and hesitant, in what appears to be an hesitance of speeach/stutter.

Conclusion

This case highlights the potential of GPi-DBS as a promising therapeutic option for managing severe, progressive dystonia in pediatric patients with inconclusive etiological diagnoses and refractoriness to conventional treatments. The clinical improvement observed, particularly in motor function, emphasizes the positive impact of this intervention in enhancing quality of life. We pretend to discuss both the ethiology of the dystonia and the mechanisms of stutter, a “side effect” of GPi-DBS which is compromising communication.

P03

From symptoms to diagnosis: exploring the spectrum of neuroinflammatory acute ataxia

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Objectives

Acute ataxia is a common clinical presentation in pediatric emergency care, encompassing a variety of clinical presentations and etiologies. We describe a cohort of children with neuroinflammatory diseases presenting with acute ataxia, focusing on their clinical and paraclinical findings and long-term outcomes.

Content

Our cohort consisted of 45 patients (26 males) with a median age of 4 years (range: 1–14 years), hospitalized at Buzzi Children's Hospital between 2014 and 2024. At onset, altered mental status was documented in 70%, cerebellar signs—dysmetria and tremor—in 33%, speech alterations in 24%, seizures in 17%, and cranial nerve involvement in 15%. Cerebral MRI was performed in 83%, revealing abnormalities in 47% of cases. EEG, conducted in 54%, showed focal or diffuse slow-wave activity in 60%. Cerebrospinal fluid analysis, available for 67%, demonstrated neuroinflammation in 39%. Based on clinical, paraclinical findings, and long-term outcomes, we identified three clusters of patients. The first group included 17 children (38%) with normal MRI and complete recovery. Fourteen were diagnosed with post-infectious cerebellitis (VZV, Rotavirus, CMV, and others), while three had no specific etiology identified. The second group comprised eight children (18%) with demyelinating disorders, including three with multiple sclerosis, two with MOG Antibody Disease (MOGAD), two with Guillain-Barré syndrome, and one with a combined central and peripheral neuroinflammatory condition. The third group consisted of 20 patients (44%) with varied clinical and MRI findings. Six children (30%) presented with encephalopathy and focal neurological signs and were diagnosed with infectious encephalitis (VZV, Rotavirus, CMV, and others). Brain MRI showed multiple hyperintensities in cortical-subcortical regions, cerebral lobes, basal ganglia, and the limbic system. Three of these children developed epilepsy, with one case associated with speech delay. Eleven children (55%) were diagnosed with autoimmune seronegative encephalitis based on clinical presentation, MRI findings (inflammatory parenchymal alterations in five children), CSF, and EEG results. Eight fully recovered, while two developed epilepsy and one had behavioral alterations. Three children had cerebellar alterations on MRI. Two were diagnosed with infectious cerebellitis, and in one, a specific

etiology was not identified. Two fully recovered, while one presented with cognitive impairment at follow-up.

Conclusion

In our cohort of children with acute ataxia, the majority exhibited a typical clinical presentation with a positive response to standard therapies. However, a significant group presented with a more complex clinical syndrome and abnormal findings, requiring specialized expertise for case management.

P04

Neuropsychological profile associated to atypical PKAN

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Objectives

We present data collected through the administration of standardized scales to describe the cognitive phenotype of individuals with atypical PKAN. Six patients (3 males and 3 females), diagnosed with atypical PKAN by molecular testing, participated in the study. Their ages ranged from 10 to 20 years, with symptom onset between ages 7 and 15. The time between symptom onset and assessment ranged from 1 to 11 years. The severity of motor impairment varied, and half of the patients had undergone surgical treatment with deep brain stimulation (DBS).

Content

Pantothenate kinase-associated neurodegeneration (PKAN) is a rare disorder with a prevalence of 1-3 cases per 1,000,000 people and is the most common condition in the group of neurodegenerations with brain iron accumulation (NBIA). It is caused by homozygous pathogenic variants in the PANK2 gene located on chromosome 20p13, which encodes the enzyme pantothenate kinase 2. Patients with PKAN show iron accumulation in the brain, primarily in the basal ganglia, with a characteristic T2 magnetic resonance imaging (MRI) pattern. The classic phenotype is characterized by stiffness, dystonia, dysarthria, choreoathetosis, and pigmentary retinal degeneration, with symptom onset typically occurring before age 6. The atypical PKAN phenotype is distinguished by later onset, speech abnormalities, psychological disorders, and slower disease progression. Additionally, PKAN is associated with intellectual impairment and progressive loss of cognitive abilities, particularly difficulties in executive functioning, attention, spatial and verbal learning, memory, judgment, and persistence. However, the intellectual, behavioral, and functional aspects of this condition are not extensively documented. We assessed dystonia severity using the Burke-Fahn-Marsden Dystonia Rating Scale (BFMDRS). To evaluate cognitive skills, we used the Wechsler Adult Intelligence Scale – Fourth Edition (WAIS-IV) for subjects over 16 years and the Wechsler Intelligence Scale for Children – Fourth Edition (WISC-IV) for those under 16. The Behavior Rating Inventory of Executive Function – Second Edition (BRIEF-II) and Raven's Progressive Matrices were used to assess executive functions. For adaptive behavior, we used the Adaptive Behavior Assessment System – Second Edition (ABAS-II), Child Behavior Checklist (CBCL), and the Children’s Yale-Brown Obsessive Compulsive Scale (CY-BOCS). Finally, the Pediatric Quality of Life Inventory (PedsQL) was used to provide a general overview of the patients' health-related quality of life.

Conclusion

In conclusion, this study aims to describe the intellectual and cognitive profile of children affected by atypical PKAN, considering different ages and varying time intervals since the onset of symptoms.

P05

Ceroide lipofuscinose type II, encéphallopathie myoclonique progressive léthale

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Objectives

Savoir évoquer une Céroide lipufiscinose devant une encéphalopathie myoclonique progressive.Dépistage des cas asymptomatiques et leur traitement par thérapie génique

Content

Cas 1:DM ,fille de 5ans, aux développement psychomoteur normal , 2eme d'une fratrie de 2enfants bien portant, mariage non consanguin, orienté pour une régression psychomotrice, depuis un 1an,L'histoire de la maladie depuis un an, marqué par mauvais appui du pied gauche, puis une hypotonie s'est installé au bout de 1mois, le malade ne pouvait plus se tenir debout, jusqu'à une perte totale de la marche ,ou le malade a été orienté chez le neuropédiatre, puis le neurogénéticienne ,et le diagnostic de maladie métabolique type céroide lipofuscinose a été évoqué devant :la consanguinité , les ATCD familiaux chargé ,d'épilepsie dans la famille, de décés dans la fratrie,l'age de début de la maladie, 4ans, le type d'épilepsie : épilepsie myoclonique progressive , avec une régression psychomotrice , EEG décharge de pointes généralisés et leur activation par la SLI lente. L'IRM cérébrale montrait une atrophie cérébélleuse. Le diagnostic de céroide lipofuscinose a été confirmé par l'étude génétique par la présence de tripeptyl peptidase L'évolution était vers un multihandicape malgré un traitement symomatique, l'étude gnétique du frére agé de 9mois est positive, en attende d'un traitement au stade asymptomatique . Cas 2: Ishak Nassim de mariage consanguin, Né le 09/02/2017 ,6ans aux ATCD néonataux, dévéloppement psychomoteur normal, issu d'un mariage consanguin, avec ATCD de plusieurs cas d'épilepsie dans la famille, orienté pour une perte des acquisitions psychomotrices ,et une régréssion psychomotrice ,un nette déclin cognitif, puis des crises motrices à types de myoclonies, depuis l'âge de 4ans.L'examen clinique retrouve un enfant hypotrophique à 19K, PC à 51,5cm, quadriparésie spastique, nystagmus, strabisme, ROT vifs, babinski présent bilatéral ,cécité totale, aucune acquisition, retard neurocognitif sévère, intellectuel de langage, et déficit attentionnels.EEG sur un tracé de fond théta ,delta, désorganisé ,dénué d'éléments physiologique de sommeil ,on remarque une décharge de pointes et de polypointes ondes généralisés ,synchrones, et de pointes ondes à 3cycles secondes correspondant à une encéphalopathie épileptique mycoclinique avec absences,l'avolution vers une encéphalopathie myoclonique sévére et multihandicape .

Conclusion

La CLN2 est une maladie neurodégénerative, rare ,et mortelle en absence de traitement. Ces 2 cas illustrent le phénotype sévère de cette maladie , la reconnaissance précoce

et son investigation permet un traitement précoce par la celipase et améliore le pronostic.

P06

Pediatric Guillain-Barré Syndrome: the experience of a tertiary center in central Portugal

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Objectives

BACKGROUND: Guillain-Barré Syndrome is characterized by rapidly progressive, ascending flaccid paralysis, with reduced or abolished osteotendinous reflexes. It´s the most frequent cause of acute flaccid paralysis worldwide since poliomyelitis' eradication. We aimed to characterize the population of patients diagnosed with Guillain-Barré Syndrome (GBS) at a tertiary hospital in central Portugal - Coimbra´s Paediatric Hospital (HPC). METHODS: We conducted a retrospective and descriptive analysis, with collection of demographic, clinical and complementary investigation, between January 2011 and January 2025.

Content

RESULTS: 31 patients were included, 51,6 % female, with an age average of 6.65 years (minimum 5 months, maximum 17 years). An infectious trigger was observed in 80,6 % of patients (n=25), more than half of whom (60 %) had upper respiratory tract infections with no identified agent. Previous gastrointestinal infection by Campylobacter jejuni was observed in 3 patients and respiratory infection by Mycoplasma pneumoniae in 2 patients. The average time between symptoms onset and hospital admission was 6.38 days. Dysesthetic complaints were the first symptom in 54,8% of patients (n=18), all involving the lower limbs. Hyporeflexia was the most frequently observed symptom, in 87,1 % of patients (n=27), followed by muscle weakness mostly of the lower limbs. Cranial nerve paralysis was observed in 11 patients (35,5%), 8 had involvement of the pairs responsible for oculomotricity, 6 (54,5 %) had bulbar dysfunction and 6 had facial paralysis. Gait ataxia was observed in 10 patients (32,2%) and in fewer cases (n=3) dysautonomia was present (arterial hypertension). Lumbar puncture (LP) was performed in all patients, with average protein concentration in cerebrospinal fluid of 125,8 mg/dL. In the first LP albumin-cytological dissociation was seen in 70.9 % of cases (n=22). A spine and brain MRI was performed in 58,1% of patients (n=18), with root enhancement in 50 % of them. 27 patients underwent an electromyography (87.1%), 22 (77.8%) with a demyelinating pattern, 2 (7.4%) with an axonal pattern and 4 (14.8%) with no changes. All patients were treated with intravenous immunoglobulin and one underwent plasmapheresis (modified zipper method). 5 patients were admitted to the pediatric intensive care unit, 3 requiring mechanical ventilation. Full recovery was observed in 25

cases, one with treatment related flutuation needing two more hospital admissions until recovery.

Conclusion

CONCLUSIONS In our cohort we highlight that some patients kept osteotendinous reflexes during the initial assessment and the course of the disease. Dysesthesia seems to be a frequent and early symptom in this population

P07

Children with Cerebral Palsy due to Stroke in the Portuguese Surveillance of Cerebral Palsy Program

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Objectives

Neuroimaging improved the identification of lesions explaining the clinical features of cerebral palsy (CP). We describe children with cerebral palsy (CP) and stroke registered in the Portuguese Surveillance of Cerebral Palsy (PVNPC).

Content

PVNPC registers 5-to-8-year-old children with CP, born since 2001. We retrieved clinic, MRI findings (SCPE MRI classification system), and function data from children born in Portugal in 2007-2015, with positive diagnosis of stroke. Common SCPE definitions, classifications and tools were used. Portuguese scales for CP Complexity (CPCS) and integration in schooling were used. From 2733 registered children, 255 stroke cases were identified (9.3%; 95%CI 8.30-10.48). Stroke was mostly an event of near-term (8.3%; 95%CI 5.71-11.86) or term-born children (22.7%; 95%CI 19.97-25.61), infrequent in children born <32 weeks (2.0%; 95%CI 1.15-3.63). Apgar >5 at 5' was most frequent in children with stroke (96%vs.83%;p<0.001); admission into the NICU was less frequent (39%vs.67%;p<0.001); early neonatal seizures were similarly registered (22%vs.25%;p>0,05). The timing of the event was registered as either pre-perinatal (67%), postneonatal (20%) or unknown (13.3%). Stroke was the cause of 27% (95%CI 21.5-34.2) of the cases of post-neonatal CP, attributed to isolated stroke (59%), stroke associated to surgery or other medical intervention (22%) or to infection (16%). The predominant lesion on MRI was classified as C-grey matter in 81.5% (C3-median cerebral artery 91%, C2-parasagital 6% and C1-basal ganglia 3%), followed by B-white matter in 8%. CP was predominantly spastic in 98.4% of the cases, 85.5% unilateral, without significant lateral predominance. CP was predominantly dystonic or ataxic in 2 cases each. Children with stroke classified on levels I-II of GMFCS in 84%, BFMF 76%, MACS 79%, drooling control 88% and Viking Speech Intelligibility 82%; IQ<50 in 15%; severe vision deficit was reported in 5% and hearing loss in 2%; all these, lower (p<0.001) than among the remaining children in the Register. Active epilepsy was reported in 38% (vs.47% in the remaining Register; p<0.01). In 59% of children with stroke, no parameter of the CPCS was registered (vs. 28% in the remaining;p<0.001). Integrated kindergarten and elementary school were more frequent among children with stroke (86%vs.72% and 88%vs.49% respectively;p<0.001).

Conclusion

Stroke caused circa 10% of CP in Portugal, mostly in term born children and in a larger proportion of postnatal CP. Despite most of the cases having high functional unilateral spastic CP, an important proportion is severely affected. Prevention and treatment of paediatric stroke contribute to the prevention of CP.

P08

Mineralizing angiopathy as a rare etiology of pediatric stroke: report of three cases

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Objectives

Arterial ischemic stroke (AIS) is the leading cause of stroke in children. Pediatric AIS main risk factors include non-atherosclerotic arteriopathies, cardiac disorders, and prothrombotic states. Recently, mineralizing angiopathy has emerged as an age-specific stroke syndrome, characterized by basal ganglia infarction and lenticulostriate calcification after minor head trauma, typically in previously healthy children aged 6–24 months Stroke recurrence can follow subsequent minor trauma. Neurodevelopmental outcomes are generally favorable unless recurrent strokes occur. The aim of our study was to describe the clinical and neuroradiological features and clinical outcome in three infants with stroke and mineralizing angiopathy.

Content

Case 1: A previously healthy 2-year-11-month-old girl presented to the pediatric Emergency Department (ED) with right facial and upper limb paresis identified in the morning upon awakening. Patient history reported a frontal minor head trauma the evening before and no previous similar events; family history was negative for early-onset cardiac and cerebrovascular disorders. MRI revealed an acute ischemic lesion in the left basal ganglia. CT confirmed lenticulostriate calcifications. No abnormalities were found in cardiac or laboratory tests. Treated with aspirin, she achieved full recovery within three weeks. Follow-up MRI showed no new findings, and developmental outcomes were positive. Case 2: A previously healthy 14-month-old boy presented with reduced mobility in the right limbs following a minor fall. Medical history included preterm birth. Imaging showed a left cerebral ischemic lesion and thalamic calcifications. Viral serology and CSF analysis confirmed intrathecal VZV IgG synthesis. He was treated with intravenous Acyclovir and oral aspirin. While functional recovery was achieved by four months, a language delay was noted at 12 months. At 30 months developmental assessment revealed a general developmental score (PGS) of 72 (3rd percentile). Case 3: A previously healthy 3-year-2-month-old boy presented with reduced right upper limb activity and speech difficulties after a frontal head trauma without loss of consciousness due to a minor fall. MRI revealed ischemic lesions and basal ganglia calcifications. Laboratory and cardiological investigations were unremarkable. Treated with aspirin, he fully recovered within four months. By age 7, he exhibited no recurrence or deficits.

Conclusion

Mineralizing angiopathy, though rare, should be considered in idiopathic ischemic stroke in children under 2 years. CT scans aid diagnosis despite age limitations. Risk factors include minor head trauma, male sex, infections, and genetic predisposition. Aspirin prophylaxis is recommended to mitigate recurrence risk.

P09

Impact of Psychiatric Disorders on Adolescent Epilepsy: Disease Control and School Performance

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Objectives

Epilepsy during adolescence is often associated with psychiatric disorders, which may influence quality of life and disease control. This study aims to analyze this relationship and its impact on disease management and school performance in adolescents.

Content

METHODS: Retrospective analysis of the relationship between epilepsy and psychiatric disorders in disease control and school performance among adolescents attending Pediatric Neurology consultation from 2022 to 2024 in a level II hospital in Lisbon, Portugal. Data were compared between adolescents with and without psychiatric disorders, using Chi-square tests for statistical analysis (Microsoft Excel, Office 365®). RESULTS: In a total of 94 adolescents with epilepsy (49 males, median age 15 years – minimum 12, maximum 18 years) followed in consultations, 23 (22,96%) presented with psychiatric disorders: behavioral and socialization disorders (8), ADHD (7), anxiety disorders (6), adjustment disorders (2), Autism Spectrum Disorder (2), and schizophrenia (1), with nine (39,1%) of them diagnoses predating epilepsy. Adolescents with psychiatric disorders had less epilepsy control, 56.5% compared to 78.9% of those without psychiatric comorbidities (p-value=0.035). Compliance to medication was lower in adolescents with psychiatric disorders (78,2%) when compared to 91.4% in the other group (p-value = >0,05). Attending to school performance, 65.2% of those with psychiatric comorbidities required special education support and showed poorer performance, versus 36.7% without (p-value=0.016). Retention rates were 65.2% and 23.9%, respectively (p-value = 0.0003).

Conclusion

It is crucial to consider psychiatric comorbidities and their management in adolescents with epilepsy. While psychiatric disorders do not appear to significantly impair medication compliance, they may contribute to greater difficulty in achieving epilepsy control. In terms of school performance, the coexistence of epilepsy and psychiatric disorders seems to have a negative impact, with increased need for educational support and higher retention rates. This underscores the necessity of multidisciplinary follow-up, ensuring timely and adequate support to address the greater needs of these adolescents.

P10

Dystrophinopathies: 25 Years of Experience in a Portuguese Tertiary Center

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Objectives

Background and Objectives: Dystrophinopaties are a spectrum of neuromuscular disorders due to dysfunction of dystrophin protein, encoded by DMD gene, located on chromosome X. It is characterized by progressive muscular weakness, typically with poor long-term prognosis. Management is ideally multidisciplinary and promising new disease-modyfing therapies may change the clinical picture in a near future. We aim to characterize our cohort of patients in the last 25 years.
 Methods: Data was obtained from retrospective review of electronic clinical records. We included patients with the clinical diagnosis of dystrophinopathy, who were followed in our center since 2000. Patients were excluded when available clinical data was insufficient. We consider data on family history, clinical manifestations, genetic diagnosis, presenting CK, muscle biopsy and pharmacological therapy.

Content

Results: From a total of 57, we included 51 patients. Median age at presentation was 4 years old (range 31 days–21 years). Eight patients (16%) had a positive family history. The most common presenting symptom was abnormal gait (39%, n=20), followed by elevated CK (18%, n=9), delayed ambulation (14%, n=7) and hypotonia (6%, n=3). Muscle biopsy data was available in 7 patients (14%). Genetic diagnosis was mostly made by single gene sequencing (51%, n=26). A deletion was identified in 28 patients (55%), while a point mutation was found in 12 (24%) and a duplication in 9 patients (18%). In term of clinical phenotype, patients presented mostly as Duchenne muscular dystrophy (80%, n=41). Seve patients (14%) were classified as Becker muscular dystrophy, whereas 1 patient (2%) presented as isolated cardiomyopathy and another (2%) as an intermediate type. Cardiomyopathy was described in 17 patients (33%). Neurodevelopmental disorders were documented in 12 patients (24%). Twenty-eight (55%) were non-ambulatory at last follow-up, with a median age of 12 years for ambulation loss (range 2–37). Twenty-one (41%) needed non-invasive ventilation. In 20 patients (39%), bone disease was reported. Thirty-five (69%) received pharmacological therapy: corticosteroids in 30 (59%) and ataluren in 8 patients (16%). Ten patients (20%) have died and 38 (75%) maintain active follow-up, with a median age of 18 years (range 2–39).

Conclusion

Conclusion: Our findings are in line with previously published data, underscoring the wide spectrum of disease manifestations and management complexity. On the other hand, our longitudinal data supports the need for an optimized multidisciplinary approach and for new disease-modifying therapy to improve quality of life and life expectancy in patients with dystrophinopathies.

P11

Genetic diseases presenting with ataxia in children: experience from a Portuguese Tertiary Center

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Objectives

Background and Objectives: Genetic diseases presenting with ataxia include a diverse group of disorders with several diagnostic challenges. For determining the etiology of these diseases, a step-by-step approach is advisable, with exclusion of acquired ataxias. We aim to characterize our cohort of affected children, focusing on the diagnostic workflow.
 Methods: We conducted a retrospective case series, with data obtained from electronic clinical records (from 2010-2023). We included children (18 years-old at onset) in which ataxia was a predominant clinical finding, with a diagnosis confirmed by genetic testing. We excluded patients with insufficient data available (>50% missing values).

Content

Results: A total of 36 patients were included, with 16 females and 20 males. Fifteen patients (42%) presented before 12 months of age. Nine patients (25%) presented during school-age, with the maximum age of 9 years. Family history was positive in 5 patients (14%). Autosomal recessive inheritance was reported in 19 patients (53%). The most common presenting finding was ataxic gait (56%, n=20), developmental delay or regression (45%, n=16) and followed by hypotonia (25%, n=9). Seizure occurred in 17 patients (47%). Signs of polyneuropathy were found in 3 patients (8%). In 14 patients (39%), systemic findings were identified. All patients had brain MRI, with reported alterations in 18 (50%). Gene panel sequencing confirmed the diagnosis in 10 patients (28%), whole exome sequencing in 9 (25%) and single gene sequencing was performed in 9 (25%). Seven (20%) patients have died.

Conclusion

Conclusion: Our case series differs from several previously published studies, probably due to methodological differences and distinct ethnic backgrounds. Our results highlight the need for a complete neurological and physical examination, as well as the correct selection of complementary studies, being genetic tests essential. We hope this work serves as a starting point for future protocols, regarding ataxia diagnosis.

P12

Comprehensive Neurodevelopmental Profile of Children with Leber's Congenital Amaurosis

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Objectives

Leber's Congenital Amaurosis (LCA) is a rare genetic retinal disorder characterized by severe vision loss from birth or early infancy. It is the most severe form of inherited retinal dystrophy, associated with mutations in approximately 27 genes. While early visual impairment is known to lead to neurodevelopmental delays, the neuropsychological and neurodevelopmental impact of LCA in children remains broadly underexplored, with limited literature available. This study aims to provide a comprehensive clinical profile of children with LCA, assessing neurovisual, cognitive, adaptive, behavioral, and neurological domains.

Content

Methods
 Twenty children (11 females, 9 males; mean age 9.4 ± 1.75 years; range 11 months–16 years) with genetically confirmed LCA underwent thorough evaluations. Assessments included clinical history, neurological examination (NE), neurovisual assessments, developmental profiling (Griffiths' and Reynell-Zinkin Scales), cognitive testing (age-appropriate Wechsler Intelligence Scales), adaptive functioning (Vineland-II), emotional/behavioral evaluation (CBCL, YSR 11-18), autism spectrum disorder (ASD) risk assessments (CARS, CASD, ADOS), and parental stress (PSI). Results
 NE revealed age-appropriate findings aside from severe visual deficits, ranging from low vision to total blindness. Cognitive testing indicated typical development in 9 children (45%), borderline levels in 4 (20%), and cognitive deficits in 7 (35%). Adaptive functioning was impaired in 8 subjects (40%), including 2 severely (10%) and 6 moderately (30%) impaired. Intellectual disability was identified in 4 of cases (20%). ASD risk assessments showed that 8 children (40%) exhibited autism-like traits and 3 at high ASD risk (15%), with, at the end of evaluations, 2 confirmed ASD diagnoses (10%). Behavioral/emotional assessments identified significant challenges in academic, social, and extracurricular activities in 16 subjects (80%), with 5 cases (25%) at risk for internalizing problems (e.g., anxiety, depression). Parental stress levels remained within normal ranges for all caregivers.

Conclusion

Conclusions
 Children with LCA face profound visual impairment and a broad spectrum of cognitive, adaptive, and emotional/behavioral challenges, potentially arising from both direct effects of LCA genes on the central nervous system and secondary consequences of early visual deficits. This study highlights the need for multidisciplinary interventions, including an early neuropsychiatric evaluation to support not only the vision-related performance, but also the neurodevelopment and neuropsychological well-being.

P13

Acute onset of Hemiplegic Migraine in children and adolescents: a retrospective analysis

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Objectives

To describe the clinical, neuroradiological and neurophysiological findings in children and adolescents with acute onset of Hemiplegic Migraine presenting to Emergency Department, aiming to achieve an accurate diagnosis and appropriate treatment.

Content

Hemiplegic Migraine (HM) is a rare form of migraine with aura, characterized by motor deficits associated with other non-motor manifestations of aura (visual, sensory, speech/language or brainstem symptoms). Headache is present in most patients and can be associated with nausea, vomiting, photophobia and phonophobia. Given the importance of timely treatment for stroke, it is essential to perform acute imaging to ensure an accurate diagnosis and differentiate it from stroke mimics, which are particularly common in the pediatric population. A review of recent literature highlights that MRI includes various features that differentiate stroke from stroke mimics, such as the involvement of specific vascular territories in stroke. Here we present a retrospective analisys of 15 patients (< 16 years old) admitted to the Emergency Department of our hospital, who fulfilled the diagnostic ICHD-III criteria for HM. We analyzed and compared the acute clinical presentation of HM, including motor and non-motor aura, associated symptoms, headache characteristics and duration, as well as the neuroradiological findings of these patients. We also reported the results of genetic testing conducted during the hospitalization or follow-up. In almost 50% of cases the headache onset occurred concurrently with motor aura, which arose as hemiparesis in 10/15 patients. Eight patients presented with sensory aura, four patients had visual alterations, and five patients presented with confusion. Moreover 12 out of 15 patients had speech abnormalities. Three patients out of 15 had a prolonged attack, lasting at least 72 hours. MRI at onset revealed signal variations in the affected brain hemisphere in 6 out of 8 cases, including reduced diffusion, cortical venous congestion, and cortical T2- FLAIR hyperintensity. EEG showed asymmetrical slow-wave activity in the affected brain hemisphere in 9/15 cases.

Conclusion

Clinical and neuroradiological findings have a crucial role in the distinction of cerebrovascular event from typical migraine with aura. We recommend referring pediatric

patients with acute focal neurological symptoms to centers that can provide MRI (including DWI, SWI, and FLAIR sequences) and MRA protocols promptly, to differentiate hemiplegic migraine from stroke, to reduce radiation exposure and to prevent inappropriate treatments.

P14

Off-label zonisamide treatment in a patient with a de novo CACNA1G gain-of-function pathogenetic variant: a case-control study

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Objectives

CACNA1G is a gene that encodes the Cav3.1 subunit of T-type calcium channels highly expressed in Purkinje neurons and deep cerebellar nuclei1. De novo CACNA1G gain-of-function pathogenic variants are related to early-onset severe spinocerebellar ataxia 42 with neurodevelopmental deficits (SCA42ND), that is an ultrarare autosomal dominant syndrome characterized by cerebellar atrophy and/or hypoplasia on magnetic resonance imaging (MRI). Patients with SCA42ND share common features such as global developmental delay and axial hypotonia, manifesting within the first year of life, dysmorphic facial features and digital anomalies2. In addition, a progressive visual impairment and epilepsy are reported. The description of the gain-of-function effect caused by the recurrent pathogenic variants in the T-type Cav3.1 channel raised the hypothesis that T-type channel blockers, such as zonisamide, might have a therapeutic potential, as documented in the last years2,3. The aim of our work was to compare the clinical features of two patients with SCA42ND, one in treatment with zonisamide and the other one without pharmacological treatment.

Content

We present 2 male patients, from two different families, with a de novo CACNA1G gain-of-function pathogenetic variant (p.Met1531Val). They came to our attention for a severe visual impairment when they were respectively 15 months (patient 1) and 8 months old (patient 2). Pregnancy and delivery were uneventful and presented with dysmorphic facial features, digital anomalies and an early-onset epileptic encephalopathy. Within the first year of life they also showed a global developmental delay. Patient 1 started the off-label treatment with zonisamide when he was 5 years old; after 54 weeks of treatment he showed a mild improvement in GMFM (from 7,60 % to 8,60%) specifically in the sitting item (from 3,3% to 8%), in Griffith's scale and in visual function assessment. The dystonic hyperextension movements of the axis disappeared. Patient 2 refused the zonisamide treatment and, over time, he exhibited stability in the motor and visual functions and the persistence of dystonic hyperextension movements of the axis.

Conclusion

So, although limited to a single case-control study, treatment with zonisamide, in association with rehabilitation treatment, may be useful to improve the clinical outcome

of patients with SCA42ND, even if slightly. The presented data are in accordance with the existing literature and demonstrate the possible therapeutic effects of zonisamide. Longitudinal studies with a larger population may be useful to better understand the real efficacy of zonisamide.

P15

Pediatric nystagmus: diagnostic challenges

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Objectives

Nystagmus is defined as an involuntary rhythmic abnormal oscillation of the eyes and its prevalence in the pediatric population is unknown. It can be classified as infantile (congenital) or acquired. Infantile nystagmus can be classified as sensory nystagmus (associated with ocular conditions such as retinal disease), neurological nystagmus (associated with neurological/neuroanatomical abnormalities), fusion maldevelopment nystagmus syndrome (FMNS), spasmus nutans syndrome, and idiopathic nystagmus. On the other hand, acquired nystagmus can be associated with both neurological and vestibular disorders. Differentiating between different forms of nystagmus can be achieved by considering not only the time of onset, but also its characteristics and comorbidity. This study aims to estimate the prevalence of infantile nystagmus in the pediatric population, and to describe the clinical profiles of the nystagmus and the associated characteristics in different neurological diseases/conditions. Further aim is to create a diagnostic flowchart that can guide the diagnostic and therapeutic process in daily clinical practice, since new genetic research and therapeutic modalities are emerging.

Content

We conducted a descriptive and longitudinal analysis on a cohort of 306 pediatric patients referred to the Developmental Neuro-ophthalmology Unit of ASST Spedali Civili of Brescia from January 2014 to November 2024 and followed for "nystagmus". We classified the patients in 6 main cohorts based on the causes of the nystagmus: 98 patients with sensory nystagmus (affected with retinal dystrophy or ocular/oculo-cutaneous albinism, retinopathy of prematurity, congenital cataract, coloboma), 129 patients with neurological nystagmus (periventricular leukomalacia, brain malformation, neuro-developmental syndromes, encephalopathies, and more), 3 with fusion maldevelopment nystagmus syndrome, 1 with spasmus nutans syndrome, 72 patients with idiopathic infantile nystagmus, 3 with acquired neurological disorders. We retrospectively collected the data from clinical examinations (including assessment of ophthalmological features and visual functions), genetic investigations, neuroradiological findings, and comorbidity assessment.

Conclusion

Our preliminary data reveal a specific clinical and neurovisual profile according to etiologies. In particular, we observed that: sensory nystagmus correlates with a severe reduction of visual acuity, specific fundus oculi alterations and normal neurological examination, neurological nystagmus with a near normal visual acuity, isolated optic disc cupping or optic disc pallor at fundus oculi and alteration in neurological examination, and idiopathic nystagmus with a normal neurological picture, visual acuity and fundus oculi. The findings may be of significance in drawing up a shareable flowchart to better organize and orient the health care planning of this population.

P16

Dyskinetic Cerebral Palsy: Distinct Epidemiological, Clinical, and Radiological Patterns Compared to Other Subtypes of Cerebral Palsy

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Objectives

To compare the epidemiological, clinical, and radiological characteristics of dyskinetic cerebral palsy (DCP) with those of non-dyskinetic cerebral palsy (CP).

Content

Methods: This retrospective descriptive study was conducted over 18 years (2005–2023) and included patients diagnosed with CP. The diagnosis of DCP was based on the 2000 Surveillance of Cerebral Palsy in Europe (SCPE) classification. Patients were categorized into two groups: those with DCP and those with non-DCP (NDCP), encompassing spastic and ataxic forms of CP. Clinical severity was evaluated using the Gross Motor Function Classification System (GMFCS). All patients underwent cerebral magnetic resonance imaging (MRI), with imaging data classified according to the MRI Classification System (MRICS). Epidemiological, clinical, radiological, and therapeutic data were collected and analyzed. Results: A total of 240 patients were included (63.3% NDCP; 36.7% DCP). Neonatal factors significantly associated with DCP included hospitalization (59% vs. 29%, $p < 0.001$), anemia (72% vs. 33%, $p = 0.001$), and seizures at birth (61% vs. 31%, $p < 0.001$). In contrast, NDCP was significantly associated with vaginal delivery (43% vs. 30%, $p = 0.046$), emergency cesarean section (28% vs. 41%, $p = 0.037$), and low birth weight (22% vs. 45%, $p = 0.011$). Clinically, DCP was characterized by a higher prevalence of severe motor impairments (63% vs. 21%, $p < 0.001$), swallowing difficulties (78% vs. 26%, $p < 0.001$), bladder and sphincter dysfunction (58% vs. 28%, $p < 0.001$), language disorders (60% vs. 28%, $p < 0.001$), hip dislocations (67% vs. 33%, $p = 0.001$), retractions (52% vs. 48%, $p < 0.001$), and recurrent infections (64% vs. 36%, $p = 0.001$). Radiologically, basal ganglia involvement (81% vs. 19%, $p < 0.001$), thalamic lesions (60% vs. 40%, $p < 0.001$), and MRICS Group C lesions (51% vs. 49%, $p < 0.001$) were significantly more frequent in DCP.

Conclusion

DCP is a rare but notably severe subtype of CP, characterized by profound motor impairments, involuntary movements, and basal ganglia involvement. Compared to other forms of CP, DCP presents with more severe complications, such as swallowing difficulties, bladder and sphincter dysfunction, and recurrent infections, underscoring the critical need for targeted and specialized management strategies. Further research is

essential to refine therapeutic approaches and explore genetic factors underlying its pathophysiology, with the aim of improving patient outcomes.

P17

Efficacy of the Ketogenic Diet as Targeted Therapy in a Cohort of Patients with GLUT1-DS

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Objectives

Glucose transporter type 1 deficiency syndrome (GLUT1-DS) is a rare neurometabolic disorder caused by pathogenic variants in the SLC2A1 gene, leading to impaired glucose transport across the blood-brain barrier. This impairment can result in pharmacoresistant epilepsy, psychomotor delay, acquired microcephaly, and movement disorders.
 The ketogenic diet (KD) is recognized as the gold-standard treatment for GLUT1-DS. This study presents a detailed analysis of a cohort of GLUT1-DS patients treated with KD.

Content

Methods The study included GLUT1-DS patients followed at the Buzzi Children's Hospital in Milan who were treated with KD. All patients underwent pre-treatment dietary counseling, and the KD protocol was customized based on patient age and targeted therapeutic ketonemia levels.
 Data were collected retrospectively through a comprehensive protocol including demographic, electro-clinical, and genetic information. Results Of 46 GLUT1-DS patients in the initial cohort, 27 met the inclusion criteria (median age: 12 years, range: 4–42 years; 10 males, 17 females).
 The median age at symptom onset was five months, and the median age at diagnosis was five years. The most frequently reported initial symptoms were seizures (58%), psychomotor delay (50%), abnormal ocular movements (30.8%), and paroxysmal movement disorders (3.8%).
 The ketogenic diet was initiated at a mean age of five years, with an average follow-up duration of four years. Epilepsy was documented in 23 patients (88.5%). Among them, 11 patients (47.8%) achieved seizure freedom after starting KD, while eight (36.4%) maintained seizure freedom already attained prior to KD initiation.
 Paroxysmal movement disorders were observed in 14 patients (53.8%), with resolution reported in 12 cases (85.7%) following KD treatment.
 Cognitive performance varied widely across the cohort. Notably, six patients (23%) showed improvements in cognitive abilities post-treatment, while nine patients (33.3%) reported enhanced behavioral and attentional capacities.
 Importantly, no adverse effects related to KD were observed during the study period.

Conclusion

This study provides a detailed characterization of a cohort of GLUT1-DS patients, reaffirming the safety and efficacy of the ketogenic diet in managing this condition. KD not only improved seizure control but also had a positive impact on movement disorders, cognitive performance, and behavioral outcomes, highlighting its multifaceted therapeutic potential in GLUT1-DS management.

P18

Sporadic Geniospasm: Clinical and neurophysiological characterization in a 2-years-old toddler

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Objectives

Geniospasm is a rare movement disorder characterized by trembling movements of the chin, caused by involuntary contraction of mentalis muscles. This condition can be sporadic or, chiefly, be genetically inherited with autosomal dominant pattern. Usually the prognosis is good, improving with age despite remission in adulthood is rare. Given the rarity of the disturb our knowledge about history, management and treatment are limited to few case series of affected families around the world. The lack of literature is even more evident in the neurophysiological field, making diagnosis extremely difficult.

Content

A two-years-old toddler presented with inconstant, high frequency and low amplitude involuntary movements of the chin started since the first days of life. Family history, neurological examination and video – EEG with superficial EMG was performed at the Pediatric Neuroscience Department of Istituto Neurologico Besta in Milan. The patient has negative family history, normal motor development and static clinical course with no significant impairment of daily functioning. We performed surface polimiography with video EEG for a better characterization of the movement disorder from a neurophysiological point of view. The polimiography showed a continuous EMG activity characterized by the occurrence of burst 20-30 ms, synchronous on the muscle explored, with a variable frequency between 6-10 Hz compatible with geniospasm.

Conclusion

In this case report we report a toddler with sporadic onset of geniospasm. Improving clinical and neurophysiological understanding on this condition is crucial to recognize it correctly and avoid misdiagnosis.

P19

Pediatric Status Dystonicus : Clinical Course and Management Strategies in a Tunisian Cohort

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Objectives

We present 16 cases of pediatric status dystonicus (SD), and describe their epidemiological characteristics, clinical progression, and treatment approaches.

Content

- Methods: This retrospective descriptive study included 16 patients, followed up in the pediatric neurology department at the National Institute Mongi Ben Hmida of Neurology of Tunis between 2009 and 2024 hospitalized for SD. SD was defined by continuous episodes of generalized dystonic spasms. The Assessment of dystonia severity was made using the Dystonia Severity Scale (DSS), published by Lumsden et al in 2013. - Results: Sixteen patients were included, ten females and six males. Average age of onset of dystonia was 2.4 years old [0;12]. Average age for first SD was 8.1 years old [2;15]. Epilepsy was associated in eight cases. Etiologies of generalized dystonia were anoxo ischemic encephalopathies (n=8), nuclear icterus (n=5), Pantothenate Kinase-Associated Neurodegeneration (n=1), ataxia telangectasia (n=1). Triggers for SD included infection (n=11), medication widhrawal (n=2), or none (n=3). The average number of SD per patient was 2.3 [1;9]. The DSS scores ranged from 2 to 5, with an average of 3. Magnetic Resonance Imaging (MRI) of the brain showed hyperintensities in the deep grey matter internal nuclei in five cases. All patients received intravenous treatment with benzodiazepines: Clonazepam (n=14) , Diazepam (n=2). Other treatments were used as a maintenance treatment : Trihexyphenidyle, antispasmodics, oral benzodiazepines and tetrabenazine. The average hospital stay was 9 days, with clinical improvement observed after a mean duration of 5 days. Three patients required intensive care unit (ICU) admission.

Conclusion

SD is a rare, severe neurological emergency with potentially life-threatening consequences. It predominantly affects children with a history of generalized dystonia, often triggered by infections despite ongoing treatment. Managing SD necessitates a multimodal therapeutic approach, with benzodiazepines emerging as the most effective intervention in this cohort. Prompt and targeted therapies are associated with rapid clinical improvement and shorter hospital stays, although severe cases may require ICU care. Early diagnosis, individualized management, and multidisciplinary collaboration

are essential for improving outcomes. Future research should focus on identifying severity predictors, refining treatment protocols, and developing preventive strategies.

P20

Neurological manifestations associated with ATP8A2 variants : Report of a Tunisian family

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Objectives

To contribute to the genetic and clinical spectrum of ATP8A2-related neurological disorders, we present a case-report of two Tunisian siblings with a pathogenic ATP8A2 variant.

Content

We report the cases of two siblings from a consanguineous marriage presenting with early-onset psychomotor delay and multifocal neurological manifestations. The elder sister exhibited delayed developmental milestones, including poor head control and failure to achieve independent sitting with a severe speech delay. At the age of three years, her clinical evaluation revealed intellectual disability, axial and segmental hypotonia, a frog-leg position, diminished deep tendon reflexes, bilateral convergent strabismus, and a unilateral ptosis. Auditory evoked potentials showed profound hearing loss. Brain MRI revealed cortical and subcortical atrophy with ventricular enlargement. Electromyography was consistent with a myogenic pattern. At the age of nine, she developed generalized dystonia and ophthalmoplegia. Her younger brother also presented with psychomotor delay, along with poor eye tracking, bilateral optic disc pallor, and mixed movement disorders (dystonia and chorea) on his first examination at the age of 18 months. He also exhibited dental misalignement. His brain MRI was normal. Over time, he developed bilateral ptosis. Genetic analysis using WES identified a pathogenic variant in the ATP8A2 gene. Both patients yielded modest improvment of their movement disorders on trihexyphenidyl.

Conclusion

Our case expands the genetic and phenotypic spectrum of ATP8A2-associated disease. In terms of the clinical picture, our findings were consistent with the literature. However, to our knowlegde, the myogenic pattern found in our patients has not been reported in previous cases. ATP8A2 variants are asscoiated with various neurological manifestations involving the central and peripheral nervous system. Early genetic diagnosis and counseling along with symptomatic treatment remains the gold standard in managing these patients.

P21

Ataxia-Telangiectasia: a descriptive study of a Tunisian Pediatric Series

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Objectives

Background Ataxia-telangiectasia (AT) is a the second most common cause of recessive cerebellar ataxia in children. Few studies have sought to describe the features of this disease in the North African population. Our aim was to describe the specificities of AT phenotype in a Tunisian cohort. Methods A retrospective study conducted in the Pediatric Neurology department of National Institute Mongi Ben Hmida of Neurology in Tunisia, included all patients diagnosed with AT. Genetic confirmation was performed using whole exome sequencing (WES). Their demographic, clinical, radiological, biological features and prognosis of the disease were assessed

Content

Results Fourty patients were included. Mean age at onset was 23.7 ± 12.7 months. Sex-ratio (M/F) was 1.2. Consanguinity was noted in 37 cases (92.5%). Seventeen cases of familial recurrence were observed. Inaugural symptoms were recurring infections and gait impairment respectively in 21 and 14 cases respectively (52.5%, 35%). On examination : cerebellar syndrome was noted in all patients, telangiectasia were noted in 37 patients (92.5%), dystonia was noted in 18 patients (45%), chorea in 10 patients (25%) and myoclonus in 4 cases (10%) , Intellectual deficiency was noted in 13 cases (32.5%).. Cerebellar atrophy was absent in 8 cases (20%) and white matter hyperintensities were observed in 3 cases (7.5%). Serum levels of foetoprotein were high in 33 cases (82.5%) and immunoglobulin A was low in 24 cases (60%). The genetic study confirmed the ATM gene mutation in 21 cases (52.5%). Walking assistance was necessary in 19 cases (47.5%). Familial recurrence was correlated to a more severe motor handicap (p=0.037). One patient died from immunological deficiency.

Conclusion

Extrapyramidal features are frequent in our cohort in contrast to previously published reports. Immunological manifestations in AT are an important part of the phenotype of AT given their impact on disease prognosis (immunodeficiency). Their frequency in our cohort is similar to littérature. Correlation between familial recurrence cases and pejorative prognosis has not been reported to date. The broad clinical and immunological spectrum of AT can lead to diagnostic delay. This should be avoided as these patients require immunological and malignancy surveillance which can be life-threatening.

P22

Spectre clinique et évolutif du Déficit en pyruvate déshydrogénase A propos 4cas pédiatriques

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Objectives

Faire évoquer cliniquement ,précocement cette maladie grave héréditaire du métabolisme , évite des explorations inutiles , permet une prise en charge adapté, et un conseil génétique.

Content

Quatre cas pédiatriques dont une fille et 3 Garçon,respectivement âgés de 14mois,9mois, 8mois et 5ans tous de parents consanguins, sont suivi au niveau de la consultation de neuropédiatrie de pédiatrie B. Les 1er symptômes ont débutés la 1er année de vie : sous forme de syndrome de Leigh : retard staturopondéral de plus de moins de DS, retard des acquisitions psychomotrices , une microcéphalie moins 3DS chez 4patients, une ataxie cérébélleuse avec signes de soifs d'air, une dystonie chez deux patients sur 4.Un cas sous forme de retard global du neurodéveloppement , une neuropathie périphérique avec aréflexie . L'épilepsie a été retrouve chez les patients de 8mois et 14mois sous forme de crise. Le diagnostic de PDH a été posé sur la clinique, L'IRM cérébral : leucodystrophie, et une atteinte des noyaux gris centraux, une hypoplasie calleuse , l'élévation des lactates ≥ 250microgramme /L, et la diminution du rapport lactate /Pyruvate moins de 15.La confirmation génétique mutation du gène PDH1, dans un cas. Les deux autres cas l'étude génétique est en cours . L'évolution à déploré une mauvaise évolution chez deux patients avec phénotype sévère : un décès en cours d'une décompensation bronchiolite virale chez le patient qui a présenté une encéphalite herpétique et un handicape neurocognitif et comportemental chez la fille de 2ans, et un trouble autistique et retard mental profond chez l'enfant de 5ans. Un développement normal à 2ans chez le frère de l'enfant décédé sous Vitamine B8.

Conclusion

Le déficit en PDH est une erreur inné du métabolisme inclue dans les le groupe déficit énergétique. Son expression clinique est variable d'un retard du neurodéveloppement type trouble du spectre autistique à un tableau d'encéphalopathie sévère : retard staturopondéral

P23

Prognostic factors for long-term neurological outcomes of therapeutic hypothermia – retrospective cohort study from a single tertiary NICU in Portugal

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Objectives

Therapeutic hypothermia (TH) is the standard of care for managing brain injury following perinatal hypoxic-ischemic encephalopathy (HIE) in term infants. Evidence suggests that the benefits of TH extend into middle childhood. This study aims to characterize the long-term neurological outcomes and identify predictors of adverse outcomes in patients who underwent TH in a tertiary hospital since the program's inception.

Content

Methods:
 Retrospective cohort study based on the review of clinical records of all neonates treated with TH in a single tertiary NICU in Lisbon, Portugal, from the program's initiation in November 2009 to June 2022. Results:
 A total of 152 newborns underwent TH. The mortality rate was 22%, with most deaths occurring in the neonatal period (three patients died during follow-up). Brain MRI showed moderate or severe lesions in 54% of patients, and 68% had significantly abnormal amplitude-integrated EEG (aEEG) at some point. Among those with abnormal aEEG, 65% exhibited normalization after 72 hours of monitoring. Of the 121 patients discharged from the hospital, 96 had adequate follow-up data. Cerebral palsy (CP) was diagnosed in 31% of patients: 40% with GMFCS Levels I-II and 60% with GMFCS Levels III-V. Epilepsy developed in 20% of patients. Significant associations were found between abnormal aEEG ($p<0.001$), lack of aEEG normalization after 72 hours ($p<0.001$), and moderate or severe MRI lesions ($p<0.001$) with the development of CP. Furthermore, non-normalization of aEEG after 72 hours was significantly associated with more severe GMFCS levels ($p<0.001$). Severe MRI lesions ($p<0.001$), abnormal aEEG ($p<0.001$), and non-normalization of aEEG after 72 hours ($p<0.001$) were also linked to worse Pediatric Cerebral Performance Category (PCPC) scores.

Conclusion

The mortality rate, CP types, and GMFCS levels observed are consistent with those reported by other centers. However, the incidence of CP in this cohort is relatively high compared to other studies. Abnormal findings on MRI and aEEG appear to be valuable predictors for CP development and worse PCPC outcomes. Notably, non-normalization of aEEG after 72 hours emerges as a predictor not only for worse PCPC scores and CP but also for its severity.

P24

Post-infectious cerebral vasculitis in children: diagnostic challenges, MRI Insights, and long-term outcomes

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Objectives

Childhood cerebral vasculitis encompasses a heterogeneous group of vascular disorders with a multifactorial etiology, affecting large, medium and small vessels. Infectious and post-infectious causes are not uncommon, with Varicella Zoster Virus (VZV), Cytomegalovirus, and HIV being the most frequently reported pathogens.

Content

We collected a series of five children diagnosed with post-infectious cerebral vasculitis according to Lanthier's 2005 diagnostic criteria, all hospitalized at Buzzi Children's Hospital (mean age: 4 years; range: 0.4 months to 9 years). At presentation, acute or subacute encephalopathy was observed in four children. All exhibited focal neurological signs, including dysarthria and aphasia in three, gait ataxia in two, and cranial motor nerve involvement in one. Two children experienced seizures, with one presenting in status epilepticus. Electroencephalography (EEG) revealed focal or diffuse slow-wave activity in all children, along with epileptic abnormalities in those with seizures. In two children, brain MRI showed stenosis and irregularities in the M1 segment of the middle cerebral artery. Laboratory findings confirmed intrathecal synthesis of VZV-specific IgM and/or IgG, with VZV PCR positivity in one case, establishing the diagnosis of post-VZV vasculitis. At the one-year follow-up, these children achieved complete clinical recovery and normalization of brain MRI findings. In the remaining three children, MRI revealed less specific parenchymal involvement, characterized by hyperintensities in cortical-subcortical regions, cerebral lobes, the lentiform nucleus, and/or the thalamus, occasionally accompanied by edema. Laboratory results indicated intrathecal synthesis of VZV-specific IgM and/or IgG in two children and HSV-1-specific IgM in the third. At follow-up, these three children exhibited outcomes ranging from mild to severe developmental delay. One developed epilepsy and hemiparesis, and all showed evidence of cerebral atrophy on brain MRI.

Conclusion

The clinical presentation of acute cerebral vasculitis in children is often non-specific, making MRI scans essential for establishing an accurate diagnostic framework. While large-vessel cerebral vasculitis is a well-described and easily identifiable phenotype,

cerebral vasculitis associated with parenchymal lesions, likely due to small-vessel pathology, poses a greater diagnostic challenge. In these cases, specific MRI patterns are not typically documented, necessitating consideration of differential diagnoses such as infectious or autoimmune encephalitis. The detection of intrathecal synthesis of specific IgM and/or IgG for viruses provides strong diagnostic support. Definitive confirmation of small or medium vessel involvement would require a biopsy; however, this procedure is rarely performed in current clinical practice.

P25

The use of alglucosidase alfa as a treatment in two patients with Lafora Disease

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Objectives

Lafora Disease is an ultra-rare progressive myoclonic epilepsy that affects previously healthy adolescents and leads to death in early adulthood. The pathogenic mechanism of the disease is associated with the accumulation of polyglucosans within neuronal cells (Lafora bodies). Currently, no approved treatments are available for this condition. Preliminary clinical experiences suggest the potential efficacy of treatment with recombinant human alglucosidase alfa, a therapy currently approved for Pompe disease. The objectives of our study are aimed at monitoring the clinical evolution of two patients with Lafora Disease treated with this therapy.

Content

We administered alglucosidase alfa in two patients (aged 19 and 20 years old) with a dosage of 20 mg/kg every other week. The follow-up protocol included assessments before treatment initiation and scheduled at 3, 6, and 12 months. Specifically, data collection will include clinical evaluations, laboratory tests, video-EEG, the Clinical Scale for the Assessment of Ataxia, the Clinical Scale for the Assessment of Myoclonus, the Lafora Epilepsy Severity Scale (LESS), the Barthel Index, and the Clinical Global Impression-Improvement (CGI-I) scale completed by both the clinician and the caregiver.

Conclusion

Nowadays the time of the follow-up is actually brief. Despite that, the clinical evaluations, as well as reports from the family during this short follow-up period, indicate an improvement in overall clinical conditions. This includes a greater degree of independence in activities of daily living and cognitive improvement. Clinical data and assessments scheduled according to the protocol will be reported. This study provides potential insights into the feasibility of using alglucosidase alfa in patients with Lafora disease. The possible positive effects of such treatment could fill a gap in the aetiological therapeutic management of these patients, for whom there is currently no therapeutic possibility.

P26

A new golgiopathy affecting the GRASP65 protein associates hearing loss, muscle cramps, vitreoretinopathy, learning difficulties, and white matter abnormalities.

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Objectives

GRASP65 is a Golgi-associated peripheral protein encoded by the GORASP1 gene. It is involved with GRASP55 in Golgi cisternae stacking. We report here the first human pathogenic variant in GORASP1 in a young man currently aged 19 years and 6 months.

Content

He is the third child of first-cousin parents with no family or neonatal history. Developmental milestones for the first two years of life were normal, with independent walking acquired at 14 months. Due to a lack of language, a moderate sensorineural hearing loss was identified at age 4. At the age of 5, MRI scans performed in the context of the deafness showed a normal aspect of the inner ear, but an abnormal signal in the supratentorial white matter. Learning difficulties became evident in elementary school, despite the effectiveness of hearing aids. Cognitive assessments revealed poor verbal performance with severe dyslexia, and attention deficit hyperactivity disorder improved by methylphenidate. Simultaneously, myalgia episodes accompanied by cramping muscles that were favoured by exercise occurred without rhabdomyolysis and were alleviated by L-carnitine. The development of severe myopia (>-6diopters) was observed at age 12, rapidly associated with vitreoretinopathy requiring laser treatment. Facial and skeletal dysmorphic features were noted. Trio genome-wide sequencing revealed a homozygous variant in GORASP1 (c.1170_1171del;p.Asp390Glufs*18). Functional analysis revealed that the variant results in a complete absence of GRASP65 but does not affect the structure of the Golgi apparatus, although glycosylation and mitosis abnormalities were detected.

Conclusion

These results indicate that loss of GRASP65 in humans causes a novel golgipathy associated with defects in glycosylation and mitotic progression.

P27

Hereditary Spastic Paraparesis Type 46 due to GBA2 Mutation: Description of familial Tunisian cases

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Objectives

This study aims to describe the clinical features of two siblings diagnosed with SPG46 through genetic testing and comprehensive neurological evaluation.This study aims to describe the clinical features of two siblings diagnosed with SPG46 through genetic testing and comprehensive neurological evaluation.

Content

Background and Aims: Hereditary spastic paraplegia (HSP) encompasses a group of neurodegenerative disorders that mainly involve the spinal portion of upper motor neurons and exhibit significant clinical and genetic heterogeneity. GBA2-related Hereditary Spastic Paraparesis Type 46 (SPG46) is a rare, early-onset, autosomal recessive form of HSP, associated with biallelic mutations in the GBA2 gene. To date, approximately thirty families have been reported worldwide, with only fifteen cases documented in Tunisia. Methods:
 A case report of two siblings diagnosed with SPG46. Results:
 Our patients are, a 17-years-old male (P1) and a 11-years-old female (P2). They were born to non-consanguineous, healthy parents with a family history of gait disorders. Both siblings began to experience gait disorder with difficulty running and frequent falls at the age of 5 and 6 years-old respectively. These motor difficulties were accompanied by poor academic performance. Neurological examination revealed mild intellectual disability, cerebellar dysarthria, ataxic-spastic gait, spastic tetraplegia predominantly affecting the lower limbs, pes cavus and equinus. Sensory examination revealed impaired positional sense in the lower limbs in P1. Ophthalmological evaluations were unremarkable. Routine blood tests including thyroid hormones, vitamin E, and alpha-fetoprotein (AFP) did not yield any significant findings. Electroneuromyography showed demyelinating sensory-motor polyneuropathy. Brain and spinal MRIs revealed nonspecific white matter abnormalities in one patient and cerebellar atrophy in both. Whole-exome sequencing (WES) identified a homozygous frameshift mutation in the GBA2 gene (locus 9p13.3): c.1018C>T (p.Arg340Ter).

Conclusion

SPG46 is a rare, complex form of spastic paraplegia that can present with additional features, including cerebellar dysfunction, peripheral neuropathy, cognitive impairment, and scoliosis. In our cases, cerebellar ataxia was the first symptom, which initially suggested an autosomal recessive cerebellar ataxia. However, as spasticity became

more pronounced, HSP was suspected and ultimately confirmed by genetic testing. This case highlights the essential role of genetic sequencing in diagnosing and managing rare forms of HSP, emphasizing the need for early identification and intervention.

P28

Epilepsy with myoclonic-atonic seizures in the world of synaptopathies

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Objectives

We present 3 patients, among a case series of 44 patients with epilepsy with myoclonic-atonic seizures (EMAtS) admitted at Epilepsy Regional Center of Brescia between 1991 and 2022, whose genetic investigation yielded positive results for synaptic genes.

Content

EMAtS is a syndrome among the Developmental and Epileptic Encephalopathies (DEEs), characterized by onset of multiple generalized seizure types, including myoclonic-atonic seizures, in early childhood. Developmental stagnation/ regression is typically observed during active phase [1]. EMAtS has complex inheritance with a polygenic pattern, which includes genes such as STX1B, SLC6A1, SYNGAP1, GABRG2, responsible also for synaptopathy [2]. This term identifies a class of disorders due to mutations in genes encoding synaptic proteins, considered as the leading causes of genetically determined DEEs. In the sample of 44 patients fulfilling the criteria for diagnosis of EMAtS, 18 underwent genetic investigation as well as clinical, electroencephalographic and neuroradiological follow-up. The genetic analyses used to identify pathogenic variants were molecular analyses for specific genes, exome and NGS epilepsy. Patient 1 - STX1B variant gene (pre-synaptic synaptopathy): epilepsy onset at 12 months of age (disease duration: 12 months), current cessation of seizures. Pharmacological therapy (VPA, ETS, CNZ) was discontinued at the age of 6 years. Cognitive profile is below-normal, associated with language disorder. Patient 2 - SLC6A1 gene variant (post-synaptic synaptopathy): epilepsy onset at 38 months of age (disease duration of 70 months), current cessation of seizures. Pharmacological therapy (VPA, ETS, BDZ) is ongoing. Cognitive profile is below-normal. Patient 3 - GABRG2 gene variant (post-synaptic synaptopathy): epilepsy onset at 16 months of age (disease duration of 44 months), current cessation of seizures. Pharmacological therapy (VPA, ETS) is ongoing. Cognitive profile is normal. Patient 4 and 5 - variants of uncertain significance were found in the CACNA1E (pre-synaptic synaptopathy) and GABRA1 (post-synaptic synaptopathy) genes, which are currently being examined for reclassification.

Conclusion

Considering the overall clinical and epileptological course of the three individuals carrying mutations in STX1B, GABRG2, and SLC6A1 genes, there appears to be good therapeutic efficacy in controlling seizures. Since synaptopathies are not considered distinct nosographic entities yet, no clinical studies are currently available that address

individuals diagnosed with myoclonic-astatic epilepsy also carrying variants in synaptic genes. The hypothesis that these genetic mutations may play a protective role in the disease's course thus stems solely from the analysis of data within this personal case series. This hypothesis would need to be validated in future clinical studies involving larger cohorts of individuals. References [1] doi: 10.1111/epi.17241. [2]. doi:10.1152/physrev.00063.2021

P29

Clinical and epileptological profiles of synaptopathies: presentation of 69 paediatric cases.

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Objectives

We present an observational retrospective study based on the longitudinal analysis of 69 patients with synaptopathy who were admitted at Epilepsy Regional Center of Brescia between 2002 and 2023.We present an observational retrospective study based on the longitudinal analysis of 69 patients with synaptopathy who were admitted at Epilepsy Regional Center of Brescia between 2002 and 2023.

Content

Introduction The term "synaptopathies" is used to identify a class of disorders caused by mutations in genes encoding synaptic proteins that are essential for the nervous system development [1]. They are considered as the leading causes of genetically determined epileptic and developmental encephalopathies [2]. We present an observational retrospective study based on the longitudinal analysis of 69 patients with synaptopathy who were admitted at Epilepsy Regional Center of Brescia between 2002 and 2023. Methods The sample consists of 45 patients with pre-synaptic synaptopathy (gene CLTC, CNTNAP2, NRXN1, NRXN3, PRRT2, SLC6A1, STXBP1, STX1B, SYN1, VAMP2), 23 with post-synaptic synaptopathy (gene CLCN4, DLG4, GABRA1, GABRG2, GRIN2A, GRIN2B, GRIN2D, SHANK1, SHANK3, SLC12A5, SYNGAP1) and 1 patient with extra-synaptic synaptopathy (gene LGI1). Results The diagnosis of epilepsy is made in 68% of cases (15% drug-resistant). 4% of cases presents with isolated seizures. A neurodevelopmental disorder is associated in 63% of total sample (62.3% language disorder, 40.6% intellectual disability, 34.8% movement disorder, 10% ADHD, and 4% autism spectrum disorder). Pre-synaptic synaptopathies start with seizures more frequently (57,8% versus 47,8%), and earlier (18 months versus 4 years) than post-synaptic ones.

Conclusion

Conclusion Epileptic seizures are the main clinical symptom at onset and during follow-up in synaptopathies, with neurodevelopmental disorder in comorbidity. This analysis represents the first known attempt to phenotypically characterize synaptopathies as nosographic entities. Therefore, it can be hypothesized that patients with epilepsy and neurodevelopmental disorder are affected by synaptopathy. References
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P30

MRI Manifestations of MELAS in Pediatric Patients: A 14-Year Retrospective Study

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Objectives

This study aims to describe the MRI findings in pediatric patients diagnosed with MELAS, providing insights into early neuroimaging manifestations of the disease.

Content

Mitochondrial Encephalopathy, Lactic Acidosis, and Stroke-like episodes (MELAS) is a rare mitochondrial disorder that predominantly affects the nervous system and muscles. MRI plays a crucial role in diagnosing MELAS, particularly in pediatric populations, where clinical manifestations can be non-specific, ranging from developmental delays to seizures (1). We conducted a retrospective study over a 14-year period (2008–2022), including five pediatric patients, aged between 6 and 18 years, with a mean age of 12.4 years. All patients were diagnosed with MELAS based on clinical, biochemical, and genetic criteria. Brain MRI, including T1-weighted, T2-weighted, FLAIR, and diffusion-weighted imaging (DWI), was performed on all patients. Radiological findings were reviewed, focusing on characteristic patterns of MELAS, such as stroke-like lesions, cortical atrophy, and basal ganglia involvement. MRI findings across the five patients revealed stroke-like lesions in non-vascular distributions in all cases. These lesions primarily affected the temporal, parietal, and occipital lobes, with hyperintensities visible on T2-weighted and FLAIR sequences. Two out of five patients exhibited cortical atrophy, while two demonstrated significant basal ganglia involvement. DWI revealed restricted diffusion in acute stroke-like lesions. MR spectroscopy indicated elevated lactic acid in one patient, consistent with the metabolic abnormalities characteristic of MELAS. The MRI manifestations observed in this study align with previously reported neuroimaging patterns of MELAS. Stroke-like episodes in non-vascular distributions, cortical atrophy, and basal ganglia involvement are key features that can assist in early diagnosis. Identifying these imaging abnormalities is crucial for timely intervention, as the clinical presentation in pediatric patients can be subtle or non-specific. Early recognition of these neuroimaging features may improve management and enhance long-term neurological outcomes.

Conclusion

MRI is pivotal in the early diagnosis of MELAS in pediatric patients. The detection of characteristic findings, such as stroke-like lesions in non-vascular territories and cortical atrophy, is critical for accurate diagnosis and management. Early identification of these MRI patterns allows for more timely therapeutic intervention in this complex mitochondrial disorder.

P31

Fenfluramine as antiseizure medication in Rett syndrome: preliminary data from a multicenter italian study

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Objectives

Rett syndrome (RTT) is a severe , progressive, neurodevelopmental disorder which affects predominantly females. In most cases it's associated with pathogenic variants in MECP2 gene. RTT is characterized by developmental regression of spoken language and hand use; affected individuals may present multiple other neurological impairments and comorbidities such as seizures. Epilepsy in RTT is often severe and pharmacoresistant. Fenfluramine (FFA) is an amphetamine derivative with serotonergic and sigma-1 receptor activity . Initially introduced as an appetite suppressant FFA also showed antiseizure properties.Fenfluramine is approved in the US for treating seizures associated with Dravet syndrome (DS) and Lennox-Gastaut syndrome (LGS) in patients ≥2 years old and as add-on therapy for seizures associated with DS and LGS in the EU, UK, and Japan in similarly aged patients

Content

Fenfluramine was used as adjunctive ASM in an italian cohort of Rett patients with pharmacoresistant epilepsy, some of them with a diagnosis of Lennox-gastaut type. We analized the use of FFA in the context of ASM polytherapy and drug-drug interactions (DDIs), behavioral issues, EEG modifications, dose titration, and adverse events.

Conclusion

We certainly need a longer follow-up of our patients and a more significant number of cases but our preliminary data suggest that fenfluramine should be considered as a therapeutic option in severe epilepsy affecting patients with diagnosis of Rett syndrome . No significant side effects were reported in our cohort and especially no cases of valvular heart disease or pulmonary arterial hypertension were observed.

P32

Progressive Cerebellar Autosomal Recessive Ataxias: Epidemiological, Clinical, and Paraclinical Aspects

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Objectives

To describe the epidemiological, clinical, radiological, neurophysiological, and genetic aspects of progressive autosomal recessive cerebellar ataxias in a pediatric cohort.

Content

Methods: A retrospective descriptive study conducted over a 19-year period (2005-2024), including patients with progressive autosomal recessive cerebellar ataxia. All patients underwent a brain magnetic resonance imaging (MRI) and biological investigations, including measurements of vitamin E, alpha-foetoprotein, immunoglobulin A and cholesterol levels. Each patient had a follow-up period of at least 12 months. Genetic confirmation was performed using whole-exome sequencing or targeted molecular testing. Epidemiological, clinical and paraclinical data were collected and analyzed. Results: We included 116 patients from 92 unrelated families with a mean age of 13 years [1,17] and a gender-ratio of 1.3. Consanguinity was observed in 78% of cases, and familial recurrence in 16%. Inaugural symptoms were gait disorders (75%), psychomotor retardation (7%), writing difficulties (4%), movement disorders (4%) and dysarthria (3%). Neurological examination revealed predominant cerebellar signs in all cases, neurogenic signs (53%), posterior cord syndrome (15%) and pyramidal signs (35%). Movements disorders were observed in 71 % of patients including dystonia (38%), chorea (17%), myoclonus (11%) and tremor (5%). Ophthalmological findings included nystagmus (53%), oculomotor apraxia (36%), strabismus (23%), optic atrophy (6%) and retinitis pigmentosa (0,8%). Intellectual disability was present in 35% of patients. Recurrent pulmonary infections related to immune deficiency were noted in 19%. Brain imaging revealed diffuse cerebellar atrophy (55%), isolated vermian atrophy (3%) and cortical and subcortical cerebral atrophy (4%). Electroneuromyography identified sensory axonal neuropathy (12%), sensory-motor axonal neuropathy (11%) and demyelinating neuropathy (4%). Elevated alpha-foetoprotein were found in 13% of cases and low vitamin E levels in 5%. Genetic testing confirmed the etiology in 44% of cases including ataxia-telangiectasia (AT,25%) ataxia with vitamin E deficiency (AVED,7%), Friedreich's ataxia (2%), autosomal recessive spastic ataxia of Charlevoix-Saguenay (ARSACS,1%), AT-like disorder (3%), and mutation in the GBA2 (2%) and LMNB2 (1%) genes.

Conclusion

Progressive cerebellar ataxias in children are a heterogeneous group of disorders with significant diagnostic challenges, particularly when genetic testing is unavailable. Our study highlights the value of a meticulous clinical and paraclinical approach, including neurological, ophthalmological, and neuroimaging assessments, combined with targeted biochemical investigations. Such strategies help narrow the diagnostic spectrum and identify treatable conditions like AVED, underlining the importance of early intervention to improve outcomes. Improving access to genetic testing remains essential to confirm diagnoses, refine management strategies, and provide genetic counseling for affected families.

P33

Development of a SESSAD Epilepsy (Special Education and Home Care Service): creation of this new device that combines health and ordinary schooling

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Objectives

The establishment Toul Ar C'Hoat, which has been specialising in supporting children and adolescents with epilepsy for more than 60 years, has been developing support from where they live for 4 years. This project is unique in France, supported by the ARS (Regional Health Agency) Bretagne. A third of our patients started their epileptic disease before the age of 3. Our intervention is usually based on one or more criteria of severity that significantly hinder schooling. For the past 1 year, we have been looking to develop the early management of patients aged 0-6 years. The objective of this early specialized support is to try to reduce the level of disability and the severity of the associated disorders.

Content

The multidisciplinary team is composed of a neurologist, two pediatric neurologists, a psychologist, neuropsychologist, speech therapist, psychomotor therapist, specialized educators, social service assistant, nurses and a department manager. This team travels to allow the child and teenager to remain in his or her environment: home, school, nursery, leisure centre, extra-curricular activities (within a radius of about 45 km around the ITEP). To develop the implementation of this service, permanences are organized in the department of Finistère. We participate in the monitoring of schooling, school arrangements, and the integration of the patient into the various structures where he or she can be admitted. We provide training in epilepsy, seizure management and carry out specialized medical follow-up (adaptation of treatment, EEG sleep-wake). Each child has an annual PPA (personalized support project). Results: We are currently following 22 children: 5 children [0-6 years old], 6 children [7-12 years old], 7 children [13-16 years old] and 4 children > 17 years old. Our youngest patient is 3 years olds (Dravet syndrome). 55% have self-limited focal epilepsies (58% of which are of lesional origin), 18% have developmental and/or epileptic encephalopathies and 27% have generalized epilepsies Among the 0-6 age group: 60% have developmental and/or epileptic encephalopathies (Dravet syndrome, Doose syndrome).

Conclusion

Our challenge for the next few years is to mobilize all the surrounding skills to support children with epilepsy whatever their age. The objective is to improve the quality of life of its children and their families, to reduce the risk of long-term comorbidities and to promote social integration.

P34

Neuroimaging Findings in Pediatric Wilson's Disease

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Objectives

Our aim was to describe the neuroradiological findings in children with Wilson's disease (WD).

Content

Methods: We conducted a retrospective descriptive study over a period of ten years (2014-2024), including children with genetically confirmed WD. Clinical, biological and brain magnetic resonance imaging (MRI) data were analyzed. Results: We included six patients (four boys and two girls) from five unrelated families. The mean age at the time of diagnosis was 10 years [6-13]. The main clinical onset signs were: behavioral changes (4/6), gait disorders (3/6), dysarthria (3/6), handwriting difficulties (2/6) and epilepsy (2/6). Neurological examination showed parkinsonian syndrome (4/6), focal dystonia (4/6), and pseudobulbar syndrome (1/6). Brain MRI findings were classified into two patterns: lesions of the basal ganglia and brainstem (6/6) and subcortical white matter abnormalities (3/6). MRI showed bilateral and symmetric high T2 signal intensities in the putamina (6/6), pons (4/6), midbrain (4/6), thalamus (3/6) and globus pallidus (2/6). "Face of giant Panda" sign was noted in two patients, one of whom had a "Face of the miniature Panda". Bilateral and symmetrical subcortical T2 hyperintensities were observed in three patients. They involved the temporal lobes in two cases and were parieto-temporal in one case. One patient had splenial T2/FLAIR hyperintensities with restricted diffusion related to a post-ictal cytotoxic lesion of corpus callosum (CLOCCS). Cerebral atrophy was noted in two patients. All patients underwent copper chelation therapy. Control MRI performed in three patients showed marked decreases in the high signal subcortical in two cases and of pallidal intensities in one case.

Conclusion

WD is a rare genetic disorder characterized by the abnormal accumulation of copper in various organs, including the brain. The basal ganglia and thalamus are the most commonly affected structures in WD, often leading to severe neurological and psychiatric symptoms. As it is a treatable condition, recognizing these specific patterns in children is essential for early intervention. Our findings highlight the role of neuroimaging in clinical practice for diagnostic guidance. Further studies are needed to prove the role of neuroimaging in long-term treatment follow-up.

P35

Personalized follow up and genetic diagnosis update of FMR1 related conditions: a change in diagnosis, prognosis and expectations

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Objectives

Fragile X syndrome (FXS) is the main cause of intellectual disability and autism of inherited genetic origin, due to the expansion of the promotor region of Fragile Methyl Ribosome 1 (FMR1). In recent years, the accuracy of genetic testing has greatly improved, including our ability to detect the number of CGG triplet repeats in the diagnosis of FMR1 related disorders. This increased diagnostic accuracy is helping to outline new diagnoses and improve counseling and treatment in families with a history of FXS, especially when clinical signs differ from the expected. The goal of or team is to improve clinical management of FXS and FMR1-related deseases, providing an appropiate molecular diagnosis and genetic counselling to our patients and their families.

Content

We present a group of families who were followed up in our rare disease unit due to a diagnosis of FXS in at least one family member, performed during the 1990s either in our center or in a different one, mainly with Southern Blot Technique. Some of the affected members of these families, although classified as FXS, had a different evolution than expected compared to other families, such as milder symptoms in full mutation (FM) male carriers, or absence of anxiety in FM female carriers, so the genetic study was repeated by our lab with updated techniques (RT-PCR). This way, we have proved that several patients with FXS full mutation (FM) diagnosis where actually mosaics for FM and premutation (PM), others were PM carriers instead of FM carriers, and a 3rd group were FM carriers (a woman with childbearing desire, an unmethylated FM man) instead of PM carriers.

Conclusion

Reviewing and updating old genetic diagnoses guided by clinical unexpected (milder) evolution and offering genetic counseling to families improves personalized follow-ups, customized treatments and setting realistic expectations for offspring.

P36

Episode de rhabdomyolyse sévère d'évolution favorable révélant une polymyosite post-infectieuse à Entérovirus

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Objectives

Devant une rhabdomyolyse sévère, la crainte principale est celle d'une maladie métabolique avec une morbi-mortalité élevée. Nous rapportons le cas d'une rhabdomyolyse sévère d'évolution rapidement favorable.

Content

Il s'agit d'un enfant de 6 ans et ½ ayant comme seul antécédent un TDAH sous Methylphenidate. Il n'avait jamais présenté d'épisode de douleurs musculaires ou de coloration rouge des urines. Tableau initial de fièvre, céphalées, douleurs abdominales et vomissements. 48 heures plus tard, sont apparues des douleurs importantes des 2 membres inférieurs avec marche sur la pointe des pieds. Un premier bilan sanguin ne retrouvait pas de rhabdomyolyse (CPK à 116U/L). A J4, apparition d'un œdème de l'ensemble des membres inférieurs prenant le godet et persistance des difficultés à la marche avec douleurs aux mollets et aux cuisses. Le testing moteur était limité du fait de la douleur, les ROT bien présents. La biologie retrouvait rhabdomyolyse avec CPK à 27 622U/l, ionogramme et CRP normal. Une antalgie par morphiniques a été mise en place ainsi qu'une hyperhydratation avec alcalinisation et Furosémide en raison d'une oligurie. Transfert ensuite en Réanimation pédiatrique devant une majoration des CPK à 70 000U/l à J5 avec maintien d'une fonction rénale normale. Il présentait une induration et une contracture importante des loges musculaires des 2 membres inférieurs. Une majoration du taux de CK jusqu'à 98370U/L a été observée à J6, puis une baisse progressive. Les différentes causes de rhabdomyolyse sévère ont été recherchées. L'IRM musculaire a mis en évidence une polymyosite étendue aux différentes loges musculaires des deux membres inférieurs, et à minima des loges antérieures des deux avant-bras sans signe de chronicité notamment pas d'involution graisseuse, pas d'atrophie Le bilan infectieux a mis en évidence une PCR entérovirus positive dans les selles, le bilan métabolique est revenu normal. A J12, le taux de CPK était alors à 2850U/l. Il gardait initialement des difficultés à la marche et une légère faiblesse musculaire, n'était pas capable de nager. L'évolution clinique a été par la suite favorable avec récupération d'une marche et d'une force musculaire normale. Actuellement, il n'y a plus aucune limitation fonctionnelle, aucune douleur. Le taux de CPK s'est normalisé à J20 d'évolution.

Conclusion

Devant une rhabdomyolyse sévère, la crainte principale est celle d'une maladie métabolique avec une morbi-mortalité élevée. Cependant, les causes post-infectieurses

existent avec possibilité d’évolution rapidement favorable avec récupération clinique complète en moins de 1 mois.

P37

Real-World use of Stiripentol in the USA

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Objectives

The STIRUS study was designed to collect data in patients who have been prescribed stiripentol since the US marketing authorization in August 2018. This was a retrospective, non-interventional, multicenter, chart review study conducted in US patients with Dravet syndrome who received stiripentol for a minimum of 3 months. All patients diagnosed with Dravet syndrome and treated with stiripentol for a minimum of 3 months in routine practice were eligible. Index date was the date of stiripentol initiation, and patients were followed up from the index date to their last intake of stiripentol.

Content

99 patients were included in 10 participating US sites. Patients' median age at first seizure was 5 months, and at diagnosis of Dravet syndrome was 15 months. Median age at stiripentol initiation was 6.9 years. At stiripentol initiation, patients were receiving a median of 3 antiseizure medications, mainly benzodiazepines (clobazam n=81; clonazepam n=11), cannabidiol (n=45), valproate (n=42), fenfluramine (n=24) and levetiracetam (n=23). Mean initial daily dosage of stiripentol was 14 mg/kg/d, then increased to a target dose of 31 mg/kg/d. Mean daily dose at last follow-up visit was 31.8 mg/kg/d. Following stiripentol initiation, a reduction in seizures frequency was observed, that was maintained over the long-term follow-up, with a marked or a mild reduction in seizure frequency in 38.1% of the patients during the last 3 months.33.7% of patients experienced at least one episode of status epilepticus (convulsive seizures lasting >5 minutes) at baseline, that decreased to 16.3% during the first 3 months of treatment, and to 14.9% in the final 3 months. Both a significant decrease in rescue medication use and less emergency room visits and/or hospitalizations were reported, that resulted in an improved patients' and family/caregivers' quality of life. From a safety perspective, 99 adverse effects were reported in 50 patients, with no unexpected or significant adverse reactions observed.

Conclusion

STIRUS provided real world evidence of Dravet syndrome management in the US. Median age at diagnosis of Dravet syndrome was 1.25 years while it was 5.4 years in 2012, indicating better knowledge of the disease resulting in early diagnosis. The study confirmed stiripentol efficacy in decreasing the frequency of generalized tonic-clonic seizures and the number of status epilepticus, resulting in less hospitalizations. This was observed regardless of concomitant clobazam use. No unexpected adverse effects were

identified. Somnolence, lethargy and decreased appetite were the most frequent, and may regress when the dose of concomitant antiseizure medications is reduced.

P38 Névrite optique inflammatoire révélateur de mogopathie pédiatrique ›

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Objectives

Attirer attention, que la névrite optique inflammatoire à anticorps antiMOG+ ,peut inaugurer une pathologie à anticorps antioliguodendrocytes, même s'il s'agit un 1er épisode . Discuter le traitement de 2éme ligne ,car les corticoïdes sont insuffisants ,pour sauver le pronostic visuel, mise en jeu .

Content

Cas 1 : Chaima âgée de 11 ans,dmise pour une Panuvéite + Névrite optique bilatérale. Le Début remonté au mois de Mai 2024 marqué par l'installation des troubles visuels, BAV de l'œil droit et douleur oculaire, motif pour lequel ils ont consulté au niveau du service d'ophtalmologie et sa hospitalisation avec 03 bolus de corticoïdes a été faite. Puis un relais per os a été prescrit. Après arrêt de Cortancyl, il y a 03 semaines de cela, une récidive de la symptomatologie a été constatée pour les deux yeux, d'où son orientation à notre hôpital et son admission. L'IRM cérébrale (24/06/2024) : Prise de contraste de la portion intra-orbitaire du nerf optique droit, Angiographie rétinienne : OD = Papillite. ODG = Papillite, périphlébite, Examen ophtalmologique fait le 09 / 10 / 2024 :- AV : 4/15 eme, -LAF : ODG : tundal (+) , tyndal vitrine, - FO : oedeme papillaire stade 1. IRM cérébrale sans anomalies.
 Le diagnostic a été posé devant la névrite optique inflammatoire, avec deux épisodes récidivante, le siège antérieur intraorbitaire, l'association autoimmune papullite, tundal. Devant l'échec aux corticoides, l'amélioration est notable sous Gammaglobullines avec diminution de l'épaisseur des fibres nerveuses, de l'œdème papillaire, réhausse de l'acuité visuelle à 7/10.

 Cas 2 : Adem Amine âgé actuellement de 13 ans, aux antécédents pathologiques de déficit en G6PD depuis l'âge de trois ans, Admis le 19- 01-2024 à notre niveau pour la prise en charge d'une BAV de l'œil droit d'installation brutale. Chez qui l'examen clinique objective : - Notion de céphalée ; BAV de l'œil droit, strabisme divergeant, anomalie du champ visuel (scotome central). - Radiologique : IRM orbito- cérébrale : NORB de OD et deux lésions démyélinisantes de la substance blanche cérébrale. La ponction lombaire : 7éléments lymphocytaires, CRP à 2mg/L. L'évolution était partielle avec une acuité visuelle normale à gauche, il compte des doigts à 50cm.

Conclusion

La névrite optique inflammatoire unilatérale, peut-être la seule expression d'une Mogopathie, avec des anticorps antiMOG+.Son évolution trainante, et récidivante, impose un protocole thérapeutique adapté ,pour sauver le pronostic visuelle.

P39

Méningite à pneumocoque compliqué de Myélite aigue chez un nourrisson

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Objectives

Décrire une complication rare et léthale de myélite avec extension bulbaire compliquant une méningite bactérienne à pneumocoque suite à une angine et des douleurs abdominales .Signaler son issu fatale lié à l'atteinte bulbaire malgré un traitement adapt

Content

Haithem 11ans, consulte pour une fièvre ,altération de l'état général, un syndrome méningé ,une léthargie, et une paraplégie flasque des membres inférieurs ,avec abolition des réflexes ostéotendineux , troubles sphinctériens ,abolition des réflexes cutanées-abdominaux, un niveau lésionnel et un Babinski bilatéral. L'analyse cyto-bactériologie du liquide céphalorachidien confirme une méningite bactérienne :polynucléose à 2000, hypoglucorachie à 0,3G/L, Hyper-protéinorachie à 1,5G/L. L'agent responsable pneumocoque a été évoqué devant une angine dans les 48heurs avant, les douleurs abdominales simulant, un abdomen chirurgicale. La myélite aigue compliquant une méningite à pneumocoque associé à la polyraduculite à l' atteinte bulbaire par extension aux voies longues , évoqué devant la méningite, les signes dysautonomiques avec paralysie des paires crâniennes, somnolence et syndrome rachidien sus cité ,motivant un transfert en réanimation .Le décès est survenue le 8eme jour de son séjour en réanimation dans un tableau d'hypoxie et d'instabilité hémodynamique bulbaire. Il s'agit d'une méningite bactérienne à pneumocoque compliqué de myélite, de polyradiculonévrite avec atteinte bulbaire avec décès malgré l'antibiothérapie, corticothérapie et ventilation artificielle. Notre cas illustre rejoint les cas de myélites exceptionnelles compliquant une méningite bactérienne avec issu fatale.

Conclusion

La myélite ou la méningo-radiculo-myélite sont des complications très rares des méningites bactérienne à pneumocoque, avec un issu fatale malgré un traitement adapté .La prévention par la vaccination anti-pneumocoque reste la seule alternative en absence de traitement radicale de ces complications.

P40

La panencephalite subaigue sclerosante de vonbogaerd pees Encéphalite autoimmune post rougeole

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Objectives

But de Faire connaitre Le profil clinique électrique; biologique de la PESS ;souligner sa gravité et son issu fatal ;attirer attention sur les mesures préventives et la vaccination

Content

l'âge moyen de survenue de la maladie est de 23mois allant de 2ans a 4ans ; une prédominance masculine de 3G/1 3filles ;avec une répartition géographique de tous est Algérien. Biskra en premier lieu. Les antécédents notés chez ces enfants étaient : infection par la rougeole entre 6-12mois ;absence d'allaitement maternelle ,non vaccinés pour la rougeole.Le début était progressif de 15 j a 2 mois ; déclenché par une infection virale le plus souvent Covid 19 .Le motif de consultation était des chutes ;une épilepsie myoclonoastatique simulant un syndrome de Doose ; une régression psychomotrice.L'examen clinique retrouvait des signes moteurs :syndrome pyramidal ;syndrome cérébelleux statique et cinétique ; et un syndrome extrapyramidal avec des mouvements dystoniques ;une épilepsie associant plusieurs types de crises myoclonies ; des absences ;des crises tonicocloniques généralisées ; et des crises partielles et même des spasmes ;et une régression neurocognitive.EEG a été dans 100% des cas contributif ; avec des complexes très lents périodiques ;l'IRM cérébral était normale ou début. La confirmation diagnostic de PEES a été posé par la présence de pic oliguoclonal dans le LCR et la positivité des autoanticorps IgG rougeole dans le sang et dans le LCR .L'évolution a été stable dans 20% des cas (3/15). Les autres cas ;ils ont évolués soit vers le décès dans 20% des cas par altération progressive de état de conscience ;signes dysautonomiques ;déshydratation et malnutrition sévère par anorexie lié aux troubles de la déglutition;soit vers une encéphalopathie épileptique sévère avec épilepsie pharmacoresistant avec retard cognitif et troubles psychiatriques mutisme akinetique

Conclusion

La PESS est une complication rare mais grave de l'infection Cérébral par la rougeole évoluant vers le décès ou le hanticape neurocognitif majeure. Sa prévention passe par la promotion de l'allaitement maternel ; la vaccination antirougeole avec une couverture vaccinale efficace et connaissance du status serologique de la mère et la vaccination des femmes seronegatives pour les AC de la rougeole .

P41

Is unavoided cerebral palsy in asphyxic neonates surviving induced hypothermia more severe at 5-years of age?

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Objectives

Induced hypothermia (IH) reduces the occurrence of death or cerebral palsy (CP) among term neonates with moderate-to-severe hypoxic-ischemic encephalopathy (HIE). Is the severity of CP among survivors of HIE after IH similar to their counterparts not submitted to IH?

Content

The Portuguese Surveillance of Cerebral Palsy registers 5 to 8-year-old children with CP, born since 2001. A partner of Surveillance of Cerebral Palsy in Europe (SCPE), both share methodology. We retrieved clinic, MRI findings (SCPE MRI classification system), and function scores data from children born in Portugal between 2007 and 2016, at ≥36 weeks gestation, admitted to neonatal care. We excluded: TORCH infection, brain malformation, syndrome causing neurologic compromise, postneonatal CP and children with MRI classified as C3-MCA infarction, C4-Normal or C5-Miscellanea. We compared 5-year-old survivors of HIE whereas submitted or not to IH, using Chi-square or fisher-exact tests and Odds Ratio. From 135 eligible children, 112 (83%) had data on application of IH: 37 children (33%) had been on IH. Children submitted to IH more likely had 5' Apgar Score <6 (OR 13.3; 95%CI 4.50-48.30) and early neonatal seizures (OR 3.6; 95%CI 1.06-16.62). Dyskinetic:spastic CP ratio was 54%:46% if submitted to IH vs. 38%:61% if not (p>0.05). Children submitted to IH had more often predominant grey matter lesion (95%vs.75%; p=0.03), with a similar proportion of basal ganglia lesions (64%vs.60%; p>0.05). Those submitted to IH had worse function scores as GMFCS IV-V 73%vs.51% (OR 2.5; 95%CI 1.08-6.23; p<0.05), BFMF IV-V 68%vs.47% (OR 2.4; 95%CI 1.04-5.92; p<0.05) or IQ<50 75%vs.54%, (OR 2.8; 95%CI 1.07-7.52; p<0.05), tended to worse speech intelligibility (Viking IV) 69% vs.56% (OR 1.8; 95%CI 0,77-4.34; p=0.08) and had higher odds for more CP complexity (>1 indicator of complexity) 74% vs.51% (OR 2.7; 95%CI 1.07-7.52; p<0.05). These indicators reveal an improvement from previous analysis of the 2007-2013 cohorts.

Conclusion

Children with CP, born ≥36 weeks gestation, with HIE, if having been on IH, seem to have higher odds for predominantly grey matter brain lesion, their function scores being lower

and more likely to have high complexity CP. These surveillance data provides useful information on the effectiveness IH to prevent death or CP after HIE and may be used to update inform on prognosis and for anticipating intervention needs.

P42

Deciding in the Limbo: Deep Cerebral Venous Thrombectomy in pediatric age

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Objectives

To report the case of a teenager with deep cerebral venous thrombosis (CVT) refractory to anticoagulant treatment that was submitted to endovascular therapy.

Content

Sixteen-year-old girl with a medical history of ulcerative colitis and juvenile idiopathic arthritis, treated with Mesalazine and Methotrexate. She presented to the emergency department complaining of headache in the previous weeks that worsened in the last 24 hours, associated with vomiting, fatigue and right-sided paresthesia.This headache was characterized by nocturnal awakenings and was refractory to analgesic medication. Neurologic examination showed lethargy, slight mental confusion, hypophonia, right central facial palsy and arm paresis along with ipsilateral hypoesthesia, as well as gait imbalance. The computed tomography (CT) scan and CT-venography revealed complete thrombosis of the deep venous system and a left thalamic hypodensity suggesting venous congestion and anticoagulation therapy was started. She was admitted to the Intensive Care Unit. Neurological deterioration occurred in the following hours with aphasia, left conjugate eye deviation and lower limb paralysis. Follow-up CT scan now showed hypodensity and swelling of both thalami. The patient underwent endovascular treatment, which included a combination of venous mechanical thrombectomy—using a stent retriever and aspiration catheter—and intra-sinus thrombolysis with alteplase, resulting in partial recanalization and improvement of venous congestion in the internal cerebral veins. After the procedure, she recovered from the aphasia, the motor and sensory deficits and the gait imbalance. Follow-up CT scans showed improvement of the thalamic swelling. Magnetic resonance imaging (MRI) nonetheless revealed bilateral thalamic venous infarction with hemorrhagic transformation, predominantly affecting the left thalamus, alongside microhemorrhages in the caudate nucleus head and temporal and parietal regions. There were still residual clots in the deep venous system. Laboratory workup for autoimmune and hypercoagulable disorders, including antiphospholipid antibodies, protein C and S deficiencies, activated protein C resistance and homocysteine levels didn't reveal any abnormalities. The genetic thrombophilia study is pending. The patient was discharged with right superior quadrantanopia.The remainder of the neurological examination was unremarkable.

Conclusion

This case highlights the insidious presentation of deep CVT in a teenager with thrombotic risk factors that was in the limbo of life and death. Deep CVT is associated with a particularly high mortality. The patient presented with altered consciousness, a poor prognostic factor in CVT, and likely would have faced a fatal outcome without endovascular therapy. We underscore the potential role of venous thrombectomy, a treatment still being refined, in patients with neurological and/or imaging deterioration despite anticoagulation.

P43

Using a novel Complexity Score to classify children with cerebral palsy reported to a National Registry

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Objectives

A condition with diverse etiologies, cerebral palsy (CP) has very heterogeneous clinical and functional presentations. Several tools are used to classify patients based on specific functions and associated clinical conditions. For epidemiological purposes, a tool that globally classifies the complexity of CP is very useful. The effectiveness of applicating such a toll on children with CP registered to the Portuguese National Registry is reported.

Content

The Portuguese Surveillance of Cerebral Palsy (PVNPC) registers 5 to 8-year-old children with CP, born since 2001. A partner of Surveillance of Cerebral Palsy in Europe, both share methodology. Based on common classification tools, PVNPC developed a secondary Complexity of Cerebral Palsy Scale (CCPS), that scores 0/1 to each of these four variables: GMFCS III-V, QI < 50, active epilepsy and severe vision/hearing deficit. The final classification scores 0-4, defining 5 levels. The feasibility of its application and its discriminative ability were explored on the sample of children born from 2001 to 2015. Proportions are presented with 95% confidence intervals, as adequate, and compared using Chi-square or fisher-exact test. It was possible to apply the CCPS to 1720/2701 registered children (63.7%, annual variation 50.8%-72.7%), distributed as follows: 0 variables 570 (33.1%); 1 variable 399 (23.2%); 2 variables 254 (14.8%); 3 variables 305 (17.7%); 5 variables 192 (11.2%). CCPS associated with the predominant clinical pattern ($p<0.001$): 0 variables in 36.5% if spastic CP, 24.1% if ataxic CP and 14.6% if dyskinetic CP. CCPS associated with MRI findings ($p<0,001$): CCPS was lower among children with predominant lesions of white matter (B), grey matter (C) or normal MRI (E); higher among those with encephalic malformations (A) and miscellanea (D). CCPS was lower among children born at <32 weeks gestation ($p<0.001$), adequate for gestational age ($p<0.05$), from twin gestation ($p<0.001$), were given 5' APGAR score ≥6 ($p<0.001$) or had not seizures through their first 3 postnatal days ($p<0.001$). CCPS was lower among children with higher weight percentile ($p<0.001$) and among those included in regular kindergarten ($p<0.001$) and elementary school ($p<0.001$); the discriminative power of CCPS 0-1 was better for integrated schooling (sensitivity 0.88 [95%CI 0.834-0.906], positive predictive power 0.88 [95%CI 0.840-0.911]) than for integrated kindergarten (sensitivity 0.40 [95%CI 0.367-0.430], positive predictive power 0.53 [95%CI 0.490-0.564]).

Conclusion

CCPS is feasible to apply in a national, populational register of children with CP, allowing to discriminate between children with different clinical CP types, encephalic lesions, risk factors and integration.

P44

The Diagnostic Dilemma of Hypotonia and Elevated CK

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Objectives

Introduction: Prader-Willi syndrome (PWS) is a rare genetic disorder due to abnormal DNA methylation within the critical region of chromossome 15 (15q11.2-q13), leading to hypothalamic dysfunction and neurodevelopmental, endocrine, and metabolic manifestations. Prenatal findings like abnormal fetal growth, decreased fetal movements and polyhydramnios are highly suggestive. Neonatal hypotonia, feeding difficulties, and poor weight gain are hallmark features, often requiring intensive nutritional support. Early recognition is essential for appropriate intervention and multidisciplinary management.

Content

Case Report: A full-term male was delivered by caesarean section due to pelvic presentation, with Apgar scores of 6/7/8 and weight of 2900g. The pregnancy was uneventful. Immediately after birth, the newborn (NB) exhibited bradypnea and hypotonia, requiring positive pressure ventilation with recovery at 20 minutes. On D1 of life, due to hypoglycemia was admitted to the NICU. He presented facial dysmorphism (retrognathia, high palate, high forehead), generalized and severe hypotonia, hyporeactivity, with the Moro reflex nearly absent (worse at the right side) and bilateral cryptorchidism. Blood analysis revealed elevated CK (18541 U/L), LDH (1961 U/L), AST (477 U/L), and ALT (103 U/L). Metabolic parameters and thyroid function were normal. Clavicular X-ray was normal. Ultrasound identified testicles located in the iliac fossae. Brain MRI and echocardiography were normal. Array CGH revealed uniparental disomy of chromosome 15, and genetic testing for Prader-Willi syndrome confirmed the diagnosis. Physiotherapy was started on D5. CK levels showed a downward trend, with subsequent normalization. Oxygen support via nasal cannula was required until D15. Despite persistent hypotonia, NB showed progressive improvement in feeding skills, achieving full oral autonomy. The NB was discharged on D29, with follow-up in neuropediatrics, rehabilitation, endocrinology, neonatology, and genetics. At three months, he continues physiotherapy and speech therapy.

Conclusion

Conclusion: PWS typically presents with severe neonatal hypotonia, feeding difficulties, and poor weight gain. This case is unusual due to absent typical prenatal features, significantly elevated CK levels and good weight progression, with full oral feeding autonomy by discharge. While CK elevation is rare in PWS, its progressive decline suggests a transient perinatal influence rather than an underlying neuromuscular disorder. This case highlights the phenotypic variability of early-onset PWS and

emphasizes the importance of genetic testing in NB with unexplained hypotonia, even in the presence of atypical biochemical and clinical findings.

P45

Small Beginnings, Big Challenges: The Complexities of a Perinatal Stroke

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Objectives

Introduction: Perinatal stroke occurs between 20 weeks of fetal life and 28 days postnatally, caused by disrupted cerebral blood flow that causes ischemia or hemorrhage. Risk factors include cardiac lesions, coagulation disorders, infection, trauma and asphyxia. Diagnosis is challenging due to nonspecific findings and subtle symptoms and it is often underdiagnosed, thus, a high index of suspicion is essential. Diagnosis is made by neuroimaging.

Content

Case report: A 38-week gestation male newborn was delivered by emergent C-section due to prolonged fetal heart rate decelerations. His first minute Apgar score was 4, requiring resuscitation maneuvers. He was admitted to the Neonatal Intensive Care Unit (NICU) due to tachypnea and hypoxia. The pregnancy was uneventful. At 36 hours of life, he experienced two episodes of apnea requiring vigorous stimulation. Amplitude electroencephalogram (aEEG) revealed randomizations compatible with seizures at that day and electroencephalogram (EEG) performed on 5th day of life was suggestive of severe encephalopathy but with no clinical seizures. The brain magnetic resonance imaging (MRI) revealed extensive bilateral ischemic stroke involving multiple vascular territories, including left carotid artery, right middle cerebral artery, and bilateral posterior cerebral arteries. Persistent blood pressure differential with lower values at the right arm was also detected. At day 7, an arm and cervical vessels Doppler ultrasound followed by brain and cervical computed tomography angiography showed extensive bilateral ischemic lesions in the frontoparietal cortico-subcortical regions and vascular occlusions (left internal carotid artery at C2-C3, right proximal M1 segment, and right subclavian artery). Echocardiogram ruled out intracardiac thrombi and placenta pathology was unavailable. There was a family history of stroke at an early age on paternal side. Laboratory evaluations revealed a slight protein S deficiency in the mother, while thrombophilia studies of both the patient and father showed no abnormalities. He started phenobarbital and because he still had paroxisms in EEG, added levetiracetam. He took enoxaparin for about 4 weeks and started daily physiotherapy. Nowadays he is followed multidisciplinary and is awaiting results from genetic panel for vasculopathies.

Conclusion

Discussion: This case highlights the complexity of managing neonatal strokes, especially with regard to treatment. In all cases is very important a multidisciplinary approach. Prognosis depends on the extent of cerebral damage and the effectiveness of therapeutic interventions. Ongoing genetic and thrombophilia studies may clarify underlying etiologies, aiding in prevention for future cases. Continuous attention to neurodevelopment will be crucial in mitigating potential long-term sequelae.

P46

"Chronicle of a Foretold Intersection"

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Objectives

Brown-Séquard syndrome (BSS) is a rare spinal cord injury that results in hemisection of the spinal cord. Although the exact incidence is unknown due to its rarity, it occurs more frequently in adults and is usually associated with trauma caused by stab wounds, gunshot injuries or motor vehicle accidents. It is characterized by ipsilateral loss of motor function, vibration, and proprioception, along with contralateral loss of pain and temperature sensation.

Content

A previously healthy 9-year-old child presented with a productive cough and rhinorrhea (Day 1). Two days later (Day 3), complaints of cervical pain radiating to the right upper limb were reported, accompanied by a sensation of loss of strength in the right upper and lower limbs the following day (Day 4). There was paresthesia and loss of sensation in the left limbs, with the onset of urinary incontinence. At the emergency department, a CT scan and brain MRI were performed, revealing no abnormalities. She was transferred to a tertiary center with neurological examination raising suspicion of right-sided pyramidal syndrome (upper and lower limbs), with impairment of proprioceptive sensation at the high cervical level on the right, pain hypesthesia at the high cervical level on the left, and early sphincter involvement. Due to suspected high cervical BSS, a vertebro-medullary MRI was performed, suggesting myelitis. A lumbar puncture and analytical study were conducted, showing no relevant alterations. Treatment was started with methylprednisolone pulses, ceftriaxone and ciprofloxacin. Respiratory multiplex testing identified Mycoplasma pneumoniae, with serology confirming recent infection. Ceftriaxone was suspended and after 12 days of corticosterois, 14 days of ciprofloxacin and a week of physiotherapy, the patient showed significant improvement, with noticeable recovery in overall strength and gait, and no sphincter complaints, leading to discharge. The corticosteroids were gradually tapered, and the patient was scheduled for follow-up in rehabilitation and demyelinating disease clinics.

Conclusion

In addition to the classic respiratory manifestations, Mycoplasma pneumoniae can cause neurological involvement, which occurs more frequently in children and includes a broad

range of clinical presentations, one of which is myelitis, being the exact pathophysiology undefined. In this case, the particularity lies in the fact that the myelitic lesion has a topography that allowed the manifestation of a BSS. Its early treatment, after the respective cause has been identified, leads to significant symptom improvement in most patients.

P47

Atidarsagene autotemcel (autologous hematopoietic stem cell gene therapy) preserves cognition, language, and speech and slows brain demyelination and atrophy in early-onset metachromatic leukodystrophy

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Objectives

The aim is to present outcomes of arsa-cel on cognitive function, language, speech, and brain MRI severity scores in pre-symptomatic LI (PSLI), pre-symptomatic EJ (PSEJ) and early symptomatic EJ (ESEJ, able to walk independently and without cognitive decline before treatment) MLD patients, compared to a natural history (NHx) cohort of 43 untreated early-onset MLD patients (26 LI, 17 EJ).

Content

Background: Metachromatic leukodystrophy (MLD), a demyelinating lysosomal storage disorder caused by arylsulfatase A (ARSA) enzyme deficiency, results in progressive neurological impairment and early death. In advanced MLD, patients lose all motor and cognitive skills and communication, severely impacting their quality of life (QoL).
 Method: Atidarsagene autotemcel (arsa-cel) consists of autologous CD34+ cells transduced ex vivo with a lentiviral vector encoding the human ARSA cDNA with constitutive expression driven by a human PGK promoter, infused intravenously after busulfan conditioning. We previously presented primary efficacy outcomes from 37 patients with early-onset MLD (18 late infantile [LI, onset ≤30 months], 19 early juvenile [EJ, onset between 30 months and <7 years]) treated with arsa-cel across two prospective clinical trials and an expanded access program.
 Results: Median follow-up was 6.76 years (range 0.64-12.19). Most arsa-cel treated patients (81%, 30/37) maintained performance and language standard scores representing normal (≥85) or mildly impaired (≥70 and <85) cognitive and language skills at the last available neuropsychological assessment. In contrast, all NHx patients develop severe cognitive and language impairment early in their disease course. Accordingly, the risk of experiencing confirmed severe cognitive impairment or death was markedly reduced for the arsa-cel PSLI ($p<0.001$), PSEJ ($p=0.044$), and ESEJ ($p=0.003$) treated subgroups versus MLD subtype-matched NHx patients. Furthermore, arsa-cel reduced the risk of experiencing complete loss of speech in PSLI ($p<0.001$), PSEJ ($p=0.042$), and ESEJ ($p=0.032$) treated subgroups versus NHx patients, most of whom lost all speech. Brain MRI total adapted Loes scores

in arsa-cel treated patients were markedly lower at 5 years post-treatment compared to age-matched NHx patients [PSLI (n=8), $p<0.001$; PSEJ (n=3), $p<0.001$; ESEJ (n=3), $p=0.025$] and were stable over time, indicating prevention or slowing of brain demyelination and/or atrophy in treated patients. Additionally, several patients (1 PSLI, 2 PSEJ, 1 ESEJ) showed slight decreases in brain MRI scores after treatment that can be attributed to improved brain myelination.

Conclusion

With up to 12 years follow-up, arsa-cel shows benefits to treated patients' QoL by preserving cognition, language abilities, and speech, supported by evidence from brain MRI.

PF01

From symptoms to diagnosis: exploring the spectrum of neuroinflammatory acute ataxia

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Objectives

Acute ataxia is a common clinical presentation in pediatric emergency care, encompassing a variety of clinical presentations and etiologies. We describe a cohort of children with neuroinflammatory diseases presenting with acute ataxia, focusing on their clinical and paraclinical findings and long-term outcomes.

Content

Our cohort consisted of 45 patients (26 males) with a median age of 4 years (range: 1–14 years), hospitalized at Buzzi Children's Hospital between 2014 and 2024. At onset, altered mental status was documented in 70%, cerebellar signs—dysmetria and tremor—in 33%, speech alterations in 24%, seizures in 17%, and cranial nerve involvement in 15%. Cerebral MRI was performed in 83%, revealing abnormalities in 47% of cases. EEG, conducted in 54%, showed focal or diffuse slow-wave activity in 60%. Cerebrospinal fluid analysis, available for 67%, demonstrated neuroinflammation in 39%. Based on clinical, paraclinical findings, and long-term outcomes, we identified three clusters of patients. The first group included 17 children (38%) with normal MRI and complete recovery. Fourteen were diagnosed with post-infectious cerebellitis (VZV, Rotavirus, CMV, and others), while three had no specific etiology identified. The second group comprised eight children (18%) with demyelinating disorders, including three with multiple sclerosis, two with MOG Antibody Disease (MOGAD), two with Guillain-Barré syndrome, and one with a combined central and peripheral neuroinflammatory condition. The third group consisted of 20 patients (44%) with varied clinical and MRI findings. Six children (30%) presented with encephalopathy and focal neurological signs and were diagnosed with infectious encephalitis (VZV, Rotavirus, CMV, and others). Brain MRI showed multiple hyperintensities in cortical-subcortical regions, cerebral lobes, basal ganglia, and the limbic system. Three of these children developed epilepsy, with one case associated with speech delay. Eleven children (55%) were diagnosed with autoimmune seronegative encephalitis based on clinical presentation, MRI findings (inflammatory parenchymal alterations in five children), CSF, and EEG results. Eight fully recovered, while two developed epilepsy and one had behavioral alterations. Three children had cerebellar alterations on MRI. Two were diagnosed with infectious cerebellitis, and in one, a specific

etiology was not identified. Two fully recovered, while one presented with cognitive impairment at follow-up.

Conclusion

In our cohort of children with acute ataxia, the majority exhibited a typical clinical presentation with a positive response to standard therapies. However, a significant group presented with a more complex clinical syndrome and abnormal findings, requiring specialized expertise for case management.

PF02

Deep Brain Stimulation in Pediatric Patients- Experience From a Tertiary Hospital

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Objectives

Deep Brain Stimulation (DBS) surgery is a therapeutic option for reversible and programmable neuromodulation, employing precise electrical stimulation targeting specific brain areas. The use of DBS in pediatric patients has gained increasing importance, particularly in the treatment of dystonia when medical therapy is ineffective or poorly tolerated. The goal of these work is to characterize the series of cases involving all pediatric patients who underwent DBS surgery in a tertiary hospital.

Content

Methods:
 A retrospective study based on the review of clinical records of pediatric patients who underwent DBS surgery since 2012, combined with telephone interviews to qualitatively assess the impact of the surgery on quality of life up to 2025. Results:
 A total of 14 patients underwent surgery, 12 of whom were male, with a median age of 10 years (range 6–17). The surgery was performed to treat dystonia (n=11), self-injurious behaviors (n=2), and parkinsonism (n=1). All cases presented symptoms refractory to medical therapy. Diagnoses were associated with prematurity (n=2), neonatal asphyxia (n=3), Pantothenate Kinase-Associated Neurodegeneration (n=2), idiopathic dystonia (n=1), DYT1 (n=1), post-drowning anoxic encephalopathy (n=1), GNAO1 genetic mutation (n=1), Lesch-Nyhan syndrome (n=1), Tourette syndrome (n=1), and Parkinson’s disease (n=1). In one case, the stimulation system was temporarily removed due to surgical site infection but was successfully re-implanted. Ten patients experienced significant improvements in quality of life, particularly in autonomy for daily activities and the ability to participate in specific tasks.

Conclusion

The series of 14 cases demonstrated positive outcomes in terms of improved quality of life and a low incidence of surgical complications and adverse effects. DBS appears to be an effective therapeutic option for selected cases. However, there is a need for more robust and formal recommendations regarding its use in pediatric populations, particularly for cases of cerebral palsy.

PF03

Retrospective Observational Study of Pediatric-Onset Multiple Sclerosis Patients in a Portuguese Island Region (2011–2024)

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Objectives

Characterize a cohort of pediatric-onset multiple sclerosis (POMS) followed at the Pediatric Neurology Unit in a portuguese insular region.

Content

This study is a retrospective observational analysis. Clinical records of all patients diagnosed with pediatric-onset multiple sclerosis (POMS) between 2011 and 2024 were reviewed. A total of six patients were included, with a female-to-male ratio of 100:0. The age of the first clinical event ranged from 13 to 17 years, with a mean-age at diagnosis of 16.1 years-old. The initial clinical manifestations observed in this cohort included transverse myelitis in four patients, optic neuritis in three, brainstem syndrome in two, cerebellar syndrome in two, and other nonspecific symptoms such as headache, fatigue in one patient. Oligoclonal IgG bands in the cerebrospinal fluid were detected in five patients. Criteria for dissemination in time and space, as defined by 2017 McDonald criteria, were met at presentation in four of the six patients. The remaining two patients, who initially presented with clinically isolated syndrome (CIS), fulfilled the criteria after two months and after one year following the first clinical event, respectively. Supratentorial and infratentorial involvement in typical multiple sclerosis regions were identified on the first brain magnetic resonance imaging (MRI) of five patients. Among these, two exhibited optic nerve abnormalities. All patients demonstrated a relapsing-remitting multiple sclerosis course. Acute MS attacks were treated with intravenous methylprednisolone pulse. Five patients began treatment with β-interferon as first-line therapy, while one started natalizumab due to extensive lesion burden at presentation. Until the age of 18, only one patient required a switch to second-line treatment (natalizumab) due to refractory disease. The Annualized Relapse Rate during pediatric age was calculated as 0,92. In adulthood, it is noteworthy that five of the six patients are currently on second-line therapies. Regarding follow-up, persistent neurological deficits were documented in a group of patients: two continued to exhibit gait imbalance, one reported chronic sensory disorder, one with motor dysfunction, and one persisted with ataxic gait. Of particular note, two patients included in this study are dizygotic twins, diagnosed at the ages of 13 and 16 years-old, respectively. Despite their genetic relationship, they exhibited distinct clinical presentations and therapeutic responses.

Conclusion

The symptomatology of POMS is often paucisymptomatic, requiring a high clinical suspicion for accurate diagnosis. MRI has proven to be an essential tool in establishing the diagnosis, as well as in guiding and optimizing therapeutic strategies.

PF04

Deep Sequencing and Phenotyping in “No Mutations Identified” Tuberous Sclerosis Complex Patients

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Objectives

Tuberous sclerosis complex (TSC) is a genetic disorder with multisystemic impact. Despite meeting clinical criteria, 10-25% of patients remain without genetic confirmation following conventional testing of TSC1 and TSC2 genes. Advances in next generation sequencing (NGS) technologies, particularly deep sequencing approaches with very high horizontal and vertical coverage, enable the detection of previously reported non-coding variants, and low allele fraction variants in cases of mosaicism. The purpose of this study was to apply a deep sequencing approach to TSC patients without molecular confirmation, followed at a tertiary center.

Content

From a cohort of TSC patients, deep sequencing was performed on those who had negative results after TSC1/TCS2 Sanger sequencing and MLPA. Clinical and paraclinical data were collected for phenotypic characterization. 7 out of 62 TSC patients (11%) previously tested negative for TSC1 and TSC2 variants using conventional techniques. 6 males, aged 2 to 30 years (median 14 years), with a median age at diagnosis of 2.25 years (IQR 0.56–5.25 years). Deep sequencing identified pathogenic intronic variants in the TSC2 gene in 3 of the 7 patients (diagnostic yield of 43%). One further patient presented a variant of uncertain significance (VUS) also in TSC2. All three patients with TSC2 intronic variants exhibit intellectual disability, one of which has autism spectrum disorder. These patients, along with the one with the VUS (4/7) have epilepsy and hypopigmented macules. All 7 patients demonstrate brain MRI abnormalities, including subependymal nodules or cortical tubers. Four patients had cardiac rhabdomyomas, two have renal cysts (both with TSC2 intronic variants), and two have retinal hamartomas (both with TSC2 intronic variants). None had subependymal giant cell astrocytoma (SEGA). Three patients are undergoing treatment with everolimus. The patients without genetic confirmation exhibited milder phenotypes with no epilepsy or intellectual disability, and lower prevalence of cardiac rhabdomyomas.

Conclusion

Deep sequencing enhanced the detection of intronic variants in our cohort. While genetic tests were performed in DNA extracted blood samples in this study, analyzing other tissue

samples could further enhance the diagnostic yield, particularly in cases of mosaicism. Although TSC remains mainly a clinical diagnosis, identifying a pathogenic variant offers significant benefits. This approach highlights the importance of a new algorithm for genetic diagnosis of TSC patients, aiming to improve not only genetic and reproductive counseling but also access to potential targeted therapies.

PF05

Utility of Exome Sequencing in a Pediatric Neurology Patients Cohort

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Objectives

Whole-exome sequencing (WES) is a powerful diagnostic tool for identifying genetic etiologies of complex and rare disorders. Its use in Pediatric Neurology has increased the diagnostic precision in the past years. This study aimed to evaluate the diagnostic efficacy of WES in a group of children with suspected genetic neurological conditions.

Content

Methods: We conducted a monocentric, retrospective study including patients followed in a Neuropediatrics' Unity of a tertiary pediatric hospital during one year. Patients who underwent WES (with copy number variation and mithocondrial DNA analysis) requested by Pediatric Neurologists in the same accredited laboratory were selected. Data regarding demographics, clinical indication and diagnostic yield was obtained through chart review. Results: A total of 62 patients were selected. Mean age of testing was 7.1 years, ranging from birth to 17 years old and there was a male predominance (37/62). The main concerns for WES request were: epilepsy (19%), epilepsy plus (37%), developmental disorder/ intellectual disability (18%), neuromuscular (13%), motor (6%) or movement (5%) complaints and hemiplegic migraine (2%). WES was positive in 23% (14/62) of cases and 25% (16/62) demonstrated variants of uncertain significance (VUS). After segregation analysis, VUS were reclassified as disease related in four patients, and in two patients results remained inconclusive. The remaining 10 await re-classification of VUS with segregation analysis. From the 31/62 patients classified by the laboratory as negative, thirteen showed potentially relevant secondary findings, one of which with a possible diagnosis of Ehlers-Danlos Syndrome (which explains his motor phenotype). In total, to date, etiologic diagnosis was possible in 30% (19/62) of patients with higher rates anticipated as additional studies of VUS are complete.

Conclusion

These findings support the integration of WES in the diagnosis of complex neurological conditions, providing better understanding of the etiology, guiding patient management and genetic counseling.