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ABSTRACT BOOK

TIMETABLE

CO01

Neurological involvement and long-term outcome in Multisystem Inflammatory Syndrome in Children

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Objectives:

The authors describe neurological manifestations, EEG, MRI and CSF findings, and long-term outcome, including cognitive, behavioral and affective functions and Quality of Life (QoL), in children with multisystem inflammatory syndrome (MIS-C).

Content:

Patients consecutively admitted to the Pediatric Department of V. Buzzi Children's Hospital between October 1, 2020 and March 31, 2022, with a diagnosis of MIS-C meeting the WHO criteria, were enrolled (62 children, 45 M, age 8 months–17 years, mean age 9 years). Managed by an interdisciplinary MISC team, all were treated and followed-up in accordance with our institutional clinical protocol. Post-discharge neurological follow-ups were scheduled at 6 and 12 months. In the acute phase, neurological involvement was documented in 58/62 (93.5%) patients. Altered mental status was observed in 29 (46.7%), focal neurological signs in 22 (35.4%), and non-specific symptoms in 54 (87%). EEG was performed in 26/62 children: 20 showed EEG slowing, diffuse or predominantly over the posterior regions. Ten patients underwent brain MRI: three showed a cytotoxic lesion of the corpus callosum. CSF analysis, performed in six patients, was normal. Two profiles of neurological involvement were identified: 16/62 (26%) patients presented encephalitis with rapid-onset encephalopathy, focal neurological signs, and EEG slowing; 42/62 (68%) showed mild neurological involvement with mild or non-specific neurological signs. All patients received intravenous immunoglobulin and methylprednisolone (MTP). Children with severe encephalopathy received MTP at 30 mg/kg/day for 3 days, obtaining rapid clinical and EEG improvement. Neurological assessment at discharge was normal in all cases. 60/62 patients were seen at 6 and 43/62 at 12 months. Neurological examination and EEG were normal at 6 and at 12 months. Irritability, regressive behaviors, fatigue, health concerns, and sleep disturbances were reported in 13/60 (21.7%) at 6 and in 8/43 (18.6%) at 12 months. Cognitive level was within normal limits. CBCLs revealed problems concerning affectivity and thought in 9/60 (20.9%) at 6 and in 7/43 (16.3%) at 12 months. 12/60 (20%) patients at 6 and 6/43 (13.9%) at 12 months presented a decline in QoL, mainly involving psychosocial aspects.

Conclusion:

Neurological involvement in MIS-C is frequent but not usually serious: around two thirds of the affected children had mild and short-lasting symptoms. A quarter of them presented acute immune-mediated reversible encephalitis. None presented serious long-term sequelae, but behavioral and affective problems together with a decline in QoL were reported in a fifth of the children at 6 months and persisted in one in six at one year.

CO02

Psychiatric and behavioral disorders in inborn errors of metabolism: A study of 57 Tunisian children

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Objectives:

The aim of the study is to describe psychiatric features in a cohort of Tunisian children with Inborn Errors of Metabolism (IEM).

Content:

Retrospective study over 12 years (2004 – 2022) of children with IEM associated or revealed by psychiatric signs. Epidemiological and clinical features were described. 57 children are included. The sex-ratio was 0.5. The mean age at onset was 6 years. Seventeen patients were managed for Sanfilippo Disease. Behavioral disturbances and motor tics revealed the diagnosis in 3 cases. The other patients developed later behavioral disturbances and irritability. Metachromatic leukodystrophy was diagnosed in 22 patients. They developed irritability concomitant with psychomotor regression. Seventeen patients had Phenylketonuria. Eight among them had Attention deficit hyperactivity disorder. Autistic behavior was observed in 12 other cases. One case of Lesch Nyhan syndrome was noted and revealed by Self-mutilation.

Conclusion:

Psychiatric and behavioral signs in IEM are more frequently a part of a more diffuse clinical picture. However, in some diseases (Sanfilippo Disease), they may be apparently isolated. Early recognition of psychiatric presentations of IEM is important to initiate specific treatment, to prevent the occurrence of irreversible neurological complications and to allow genetic counseling.

CO03

Adaptive Behaviour, Cognitive Functions and Emotional Competence in Ataxia Telangiectasia

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Objectives:

Ataxia Telangiectasia (AT) is a rare autosomal recessive disease characterized by early onset cerebellar ataxia, oculomotor apraxia, extrapyramidal involvement, ocular telangiectasias, immunodeficiency and cancer predisposition. While a number of studies in AT have provided information regarding the evaluation of neurological symptoms, the existing neurological rating scales don't take into account the effect of the progressive neurodegeneration on daily living skills and quality of life. We collected preliminary data on adaptive behaviour, cognitive functions and social-emotional competence in a cohort of patients with AT, in order to measure parameters of disease progression according to the complex multisystemic involvement and to create a framework for a disease-specific functional scale.

Content:

39 patients (14M, 25F; mean age 16y 2mo, range 3y 11mo–29y 8mo) were enrolled and grouped into four different age subgroups (subgroup 1: age 3-5 years; subgroup 2: age 6-11 years; subgroup 3: 12-18 years; subgroup 4: ≥19 years). The evaluation included a history, clinical, developmental and neurological examination. International Cooperative Ataxia Rating Scale (ICARS), Vineland Adaptive Behavioural Scales II (VABS), Wechsler scales (WPPSI, WISC, WAIS according to the age) and Child Behavior Checklist (CBCL) parameters were recorded. Progression of ataxia, measured by ICARS total score, showed a positive correlation with increasing age (Spearman's correlation $r=0.71$, $p<0.001$), but this correlation was lost after the age of 12 (subgroup 3). The VABS overall score was lower with increasing age (Spearman's correlation $r=0.56$, $p<0.001$) with a linear decrease in daily living skills domain, while communication and socialization showed a swift deterioration after the age of 19 (subgroup 4). Patients in subgroup 1 performed at the low of the average range on total IQ, with mild impairment limited to visuoperceptive skills; IQ total score showed linear decreased performance in older patients (Spearman's correlation $r=0.40$, $p < 0.001$) with more widespread cognitive difficulties except for linguistic processing, that remains mildly affected. No participants in any age subgroup scored more than the clinical cutoff in CBCL internalizing and externalizing behaviour scales.

Conclusion:

Existing neurological rating scales do not reflect the complex progressive deterioration that dramatically affect daily functioning in AT. Profiling not only ataxia progression but also the age-related impairment in adaptive behaviour, cognitive functions and emotional competence is a crucial starting point to build the frame for a functional scale specific for AT patients, in order to ameliorate their follow-up and define the type, the timing and the effect of pharmacological and rehabilitative intervention.

CO04

Neonatal arterial ischemic stroke: role of brain monitoring and seizure treatment response

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Objectives:

To investigate the response to anti-seizure medications (ASMs) in neonates with acute provoked seizures due to arterial ischemic stroke (AIS).

Content:

Methods: this retrospective, multicentric, multinational study analyzed the clinical, neuroradiological and electroencephalographic (EEG) characteristics of term newborns with neonatal diagnosis of AIS, with or without hemorrhagic transformation, who presented seizures and were monitored by continuous EEG or aEEG monitoring. Patients were included if they received at least one ASM and adequate (a)EEG documentation regarding response to ASMs was available. The choice and doses of ASM were at the discretion of the treating clinician. Treatment response was defined as EEG-confirmed seizure resolution without recurrence within 30 minutes after initial loading dose of ASM. Results: sixty-five neonates referred to eight European level III neonatal intensive care units (ICUs) and diagnosed with AIS had continuous EEG and/or aEEG recordings available for review. 21/65 were excluded because of fragmented data about diagnosis, ASM administration, or because of duration of monitoring lasting less than 24 hours after the last seizure. Forty-one patients were included for the analysis of treatment response. The most frequently recorded seizure type was focal clonic (73%); a significant percentage presented ictal apnea (18%). Most neonates (41/44, 93%) had confirmatory continuous brain monitoring commenced 7.9 ± 12.9 hours after onset of symptoms. aEEG was the main monitoring tool (54.5%). Mean time to treatment was 8.6 ± 12.8 hours and the most frequently administered first-line ASM was phenobarbital in 82% of neonates. Seizures were completely controlled within 24 hours from onset in 46% of neonates. Interestingly, phenytoin was effective in the vast majority on neonates (16/17, 94%) in whom it was trialed, while phenobarbital was effective only in a minority (10/36,28%) of neonates who received it ($p < 0.001$). Furthermore, patients treated with PB needed more additional doses than those treated with phenytoin, resulting in significantly higher mean doses of PB than PHT ($p < 0.001$).

Conclusion:

Our findings obtained from a homogeneous cohort of neonates with AIS-associated seizures, provide evidence of efficacy of phenytoin compared with other ASMs, in particular phenobarbital. Further studies, particularly randomized-controlled are needed to confirm our data and allow a more accurate and etiology-targeted treatment of seizures in the neonatal period.

CO05

The procedural deficit hypothesis: investigating sequences learning-related brain connectivity processes in children with self-limited focal epilepsy

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Objectives:

The functional brain processes underlying poor procedural memory abilities in epilepsy remain unexplored. This prevents a proper understanding of some cognitive and language difficulties frequently observed in this population. To fill this gap, we investigated changes in resting-state functional brain connectivity (rsFC) processes associated with procedural learning in self-limited focal epilepsy (SLFE).

Content:

Methods. Magnetoencephalography (MEG) was used to investigate changes in rsFC (2*5 minutes) before and after a behavioural procedural learning session in 10 children with SLFE compared to 28 matched typically developing (TD) children. After removing artefacts/epileptiform discharges through independent component analyses, a functional connectome was estimated using band-limited power envelope correlation. Unpaired T-tests were used to compare learning-related changes in rsFC between groups. Results. Compared to TD, children with SLFE showed differences in learning-related changes in rsFC connectivity within brain networks including frontal, parietal, cerebellum and basal ganglia aeras in the theta (4-8Hz), alpha (8-12Hz) and beta-low (12-21Hz) frequency bands.

Conclusion:

Discussion. Our results suggest that atypical procedural learning-related rsFC observed in SLFE within brain regions previously associated with (visuo-)motor and/or sequential learning processes could be related to some language and nonverbal cognitive difficulties in these patients.

CO06

Fluoxetine as adjunctive therapy in pediatric patients with refractory epilepsy: A retrospective analysis

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Objectives:

Approximately 30 % of children with epilepsy develop refractory epilepsy, which has a major impact on neurodevelopmental processes, cognitive functioning, and daily life. Furthermore, children with highly refractory epilepsy are at particular risk of sudden unexpected death. Fluoxetine, a selective serotonin reuptake inhibitor (SSRI), has shown antiseizure action and was associated with a decreased severity of peri-ictal hypoxemia in adult patients with focal epilepsy. However, therapeutic studies on SSRI use in children are scarce. We aimed to report the effect of fluoxetine on epilepsy in a cohort of pediatric patients.

Content:

We retrospectively recruited 14 pediatric patients; inclusion criteria were i) refractory epilepsy ii) frequent generalized or focal seizures (more than 1/week) iii) treated with fluoxetine as adjunctive therapy for one month at least. We analyzed their clinical outcome (efficacy and tolerance). The median age at fluoxetine initiation was 9.5 years (2–19), and fluoxetine was combined with a median number of 4 (2–6) anti-seizure medications. The median dose of fluoxetine at the last follow-up was 0.4 mg/kg/day (0.2− 0.8). Among the 14 patients, we observed 6 (43 %) good responders. Complete freedom from seizures with cyanosis was reached in 3 (21 %) patients, and only one patient with early-onset epilepsy related to an FHF1 mutation was completely seizure-free. None of the recruited patients experienced seizure worsening, and 8 patients showed no effect on seizure frequency.

Conclusion:

Fluoxetine as adjunctive therapy in refractory epilepsy could be a beneficial therapeutic option. Future prospective, randomized and controlled studies are needed to study the efficacy of fluoxetine better.

CO07

Associations between interictal epileptic discharges patterns and cognitive performance in children with self-limited focal epilepsy with centrotemporal spikes (SLFECTS)

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Objectives:

To investigate brain-behaviour associations between interictal epileptic discharges (IED) patterns and cognitive performance in a population of children with an EEG pattern of self-limited focal epilepsy with centrotemporal spikes (SLFECTS).

Content:

This retrospective study included 16 patients with an EEG pattern of SLFECTS (2 patients without seizures, 10 patients with typical SLFECTS and 4 patients with epileptic encephalopathy with continuous spike and wave (SW) during sleep) who underwent an extensive neuropsychological assessment. Two quantitative EEG indices were analysed on anonymised awake and sleep EEG, i.e. the Spike Wave Index (SWI) and the Spike Wave Frequency (SWF), evaluating the intensity of SW activity, and one qualitative EEG index, i.e. the EEG score, evaluating the spreading of focal SW to other parts of the brain. The neuropsychological measurements assessed verbal memory (WISC-V verbal short-term memory and episodic memory - RLS 15) and non-verbal short-term memory (Block Tapping test), attentional abilities (tonic and phasic alert - Test of Attentional Performance - TAP) and executive function (visuospatial planning, and cognitive inhibition - Tower of London and Stroop test). We investigated associations between EEG indices and neuropsychological performance with non-parametrical Spearman tests including correction for multiple comparisons. A $p_{corr} < 0.05$ was considered statistically significant. Results showed a negative correlation between (i) the awake EEG score and the Block Tapping test, a visuospatial short-term memory task, and (ii) the sleep SWI and the Tower of London, a visuospatial planning task ($p_{corr} < 0,05$).

Conclusion:

This retrospective study conducted in a population of children with an EEG pattern of SLFECTS showed an association between SW intensity during sleep and visuospatial planning as well as between the spreading of focal SW to other parts of the brain in wakefulness and visuospatial short-term memory. It suggests that, in children with SLFECTS, the EEG analysis should include an EEG score investigating wake- and sleep-related qualitative parameters and that neuropsychological assessment should include visuospatial skills.

CO08

Diagnostic gap in early onset epilepsies

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Objectives:

Genetic epilepsies often present in the first year of life. Many patients face diagnostic delays of months or years. Particularly challenging is the diagnosis of epilepsy with onset the very first months of life. We aimed to assess the gap between seizure onset and definite diagnosis and its implications for management.

Content:

Methods:We retrospectively included children seen in a single tertiary care center between August 2018 and December 2020, diagnosed with early onset (< 3 months) genetic epilepsy, for whom full video-EEG recordings from onset, medical records, neuroimaging and genetic results were available. Symptom onset was defined as time when ictal events were first reported by the caregiver. Time to seizure diagnosis, to epilepsy diagnosis, and to definite diagnosis was defined as the interval between symptom onset and diagnosis of seizures, symptom onset and diagnosis of epilepsy, and symptom onset and genetic diagnosis, respectively. We considered a delay an interval of > 4 weeks from onset of symptoms to the recognition of the specific epilepsy phenotype. The time interval between onset and appropriate management and/or treatment was also assessed. Results:Among 22 infants with early-onset genetic epilepsies, 4 were excluded because of lack of genetic confirmation, and one because EEG was not available. Seventeen infants (59% male) were included. Nine (52%) had KCNQ2/3-related epilepsies, two SCN2A-SFNIE, two CDKL5-DEE, one BRAT1-encephalopathy, one KCNT1-EIMFS, one FGF12-related epilepsy, and one SMC1A-encephalopathy. The correct diagnosis was reached in a median of 7 months (1 day - 8 years). A diagnostic delay occurred in 14/17 (82%) infants, varying from 1-3 months in 5/14 (36%), 6-12 months in 4/14 (28%), and > 12 months in 5/14 (36%). Time to genetic diagnosis ranged from 1 month to 8 years (median 7 months). The most frequent initial diagnosis was “neonatal seizures” in 6/17 (35%). A correct epilepsy diagnosis resulted in a substantial change of care in 82% of patients, including effective treatment and redirection of care. Mean time to appropriate treatment was 13.2 months (onset – 8 years). We found three main factors associated a diagnostic gap: lack of recognition of the paroxysmal events as seizures by pediatricians in 6/17 (35%), lack of EEG-recorded seizures 5/17 (30%), lack of recognition of the specific epilepsy phenotype by child neurologists 12/17 (70%).

Conclusion:

The most common factor contributing to diagnostic delay in early-onset epilepsies is the lack of recognition of specific phenotype, especially in neonates when the generic term “neonatal seizures” is used.

CO09

Diagnostic work-up of infantile and childhood-onset nystagmus

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Objectives:

The aims of this study are a) to describe a pediatric cohort of patients with nystagmus and b) to develop a diagnostic flowchart to sustain the approach to infantile and childhood-onset nystagmus from a neuropsychiatric perspective.

Content:

We performed a retrospective study based on the review of medical records of children referred to the Developmental Neuro-ophthalmology unit of IRCCS Mondino Foundation based in Pavia, Italy, over a 10-years period. Inclusion criteria were a) the presence of nystagmus at the first consultation, and b) the presence of an adequate amount of information about patient's medical history or examinations. Nystagmus could be either the reason for referral or a neurologic sign found during the first clinical examinations. Collected data regarded the child's family and medical history, associated symptoms, visual function and ophthalmologic evaluations, and diagnostic testing results. To pursue the first aim of the study, we performed descriptive analyses. For the second aim, we implemented decision tree models to obtain a statistically relevant classification method. A total of 358 subjects were identified, 295 of which met the inclusion criteria. Among these, 178 (60,34%) were male, with a mean age at the first evaluation of 9.44 months (median 4.00, SD 19.86, range 0-144 months). 208 children (70.51%) had a normal neurological examination and 153 (51.86%) presented a normal development. Nystagmus was isolated in 270 children (91,52%) and 49 subjects (16.61%) had visual acuity in the normal range. The most frequent final diagnoses were idiopathic nystagmus (20.68%), congenital inherited retinal dystrophy (19.32%), genetic syndromes with developmental involvement (12.22%), posterior fossa abnormalities (10.17%). The diagnosis classification tree had the psychomotor development as a root node and obtained an accuracy of 0.59 (95% CI 0.53-0.65) and AUC of 0.86.

Conclusion:

In the present study, we describe the clinical and diagnostic features of a large cohort of children with nystagmus. Furthermore, we propose a statistically relevant diagnostic flowchart, derived from data analyses and clinical expertise, to help infantile and childhood nystagmus diagnostic workup. Our results point out the importance of early and thorough neuropsychiatric and developmental assessments together with ophthalmologic evaluations to guide the diagnostic approach. We believe this flow chart could be a useful tool for the child neurologist facing nystagmus.

CO10

Type I Alexander disease: validation and future perspectives of a new clinical evolution-based classification

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Objectives:

Refine the current classifications of Alexander Disease in order to guide clinicians into the broad phenotypic spectrum of AxD.

Content:

Alexander disease (AxD) is a rare progressive leukodystrophy caused by autosomal dominant mutations in the Glial Fibrillary Acidic Protein (GFAP) gene. Three main disease classifications are currently in use, the traditional one defined by the age of onset, and two other based on clinical features at onset and brain MRI findings. Recently, we proposed an updated classification, which takes into consideration not only the presenting features, but also data related to the clinical course. We found out that, basing on follow-up data, we might classify patients with Type I AxD into four subgroups: Ia, Ib, Ic, Id. IN the present study we applied this modified classification system to pediatric-onset AxD described in literature from 1949 to date. We included articles which reported patients with a confirmed diagnosis of pediatric-onset AxD and of whom there were available information about age and symptoms at onset, developmental milestones and loss of motor and language skills. Clinical data from 205 patients with pediatric-onset AxD were retrospectively reviewed. Among these, we identified 65 patients, of whom we had enough information about the clinical course and developmental milestones, and we assessed their disease evolutionary trajectories over time.

Conclusion:

The results confirmed that patients with Type I AxD might be classified into four subgroups (Ia, Ib, Ic, Id) basing on follow up data. In fact, despite the great variability of phenotypes in AxD, there are some shared trajectories of the disease evolution over time. Our classification system should be considered for future studies design, patients' recruitment, definition of outcome endpoints. For these reasons, it would be of great importance to identify biochemical, radiological, and genetic markers able to define from early disease phases to which subtype a patient belongs.

CO11

Review of a Combined Paediatric Neurogenetics service in North-West London

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Objectives:

In the UK access to whole genome sequencing (WGS) is now unrestricted for eligible patients from all medical specialities, following earlier national pilot projects evaluating feasibility ("DDD" 2011-2015 & "100K" 2015-2018). WGS significantly increases success rate of accurate diagnoses in children and young people (CYP) with severe neurodisabilities and rare diseases. However, handling genomic data is challenging for clinicians. Innovative ways of collaboration are required to interpret genomic results in the context of phenotypic presentation.

Content:

Method Technology during the Coronavirus lockdown supported the launch of a virtual multidisciplinary neurogenetic forum (MDT) at Imperial Healthcare, London, in 2020. This evolved in 2021 into monthly face-to-face joint paediatric neurogenetic clinics with a paediatric neurologist, a clinical geneticist and a genomic practitioner. Prior to the clinic: i) patient imaging is reviewed in a neuroradiology MDT ii) with discussion of any identified variants in a regional bi-monthly genomics laboratory MDT, attended by geneticists and clinical scientists in North-West London. Results Phase 1 - virtual MDT (Sept 2020-June 2021): 121 patients discussed who underwent genome screening (virtual panels) in the 100K project. Implications of variants of unknown significance were evaluated. Phase 2 – face-to-face clinics: 49 patients, assessed jointly by neurologist and geneticist - 26 families proceeded to Trio (parents & child) WGS, 6 families declined, 2 diagnosed with a chromosome disorder, 6 patients attended for variant interpretation/ family segregation and 3 were referred for management advice following a recent neuro-genetic diagnosis. Mislabelling of 'cerebral palsy' is an emerging theme. Some challenges: i) identification of target group most likely to benefit from Trio WGS (monogenetic versus multifactorial disease) ii) relatively long turn-around times for results (high pressures on national genomics lab. services) iii) currently no access to individual datasets

Conclusion:

By combining clinical expertise, our model offers a one-stop clinic that shortens the patient's diagnostic journey, increases patient satisfaction and facilitates effective working in CYP with rare diseases. It has also enabled earlier identification of misdiagnoses. This setting offers deep-phenotyping with greater understanding of rare diseases.

CO12

Electroencephalogram (EEG) and Alternating hemiplegia of childhood (AHC): A prospective EEG study of a large cohort of 32 patients

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Objectives:

Alternating hemiplegia of childhood is an early encephalopathy, associating paroxysmal hemiplegia/dystonia episodes, and often epilepsy. Currently there is no publication exclusively dedicated to EEG aspects during and/or outside paroxysmal events. We aim to describe EEG aspects in AHC.

Content:

Twenty-four consecutive patients with AHC were included in the study and their EEGs, mostly of long duration (24 hours, n=20) were read by two senior electro-physiologists. A third electro-physiologist (1st author) compiled, compared and analysed the results. Eight patients (33%) had an abnormal background activity. Sixteen of them (~58%) had focal abnormalities. Of the five EEGs with hemiplegic seizures, two had contralateral slow waves. On four EEGs with dystonic seizures an unusual homolateral occipital pattern was seen during the events. In the three patients where paroxysmal eye movements were recorded, no electrical correlate was found. Five patients had epileptic seizures (focal, atonic, tonic, generalized, dysautonomic, and status epilepticus), two of them with unusual patterns of extremely slow discharge progression. Other unusual patterns were prolonged unilateral slow waves (n=3), during sleep, and pseudo-periodic posterior waves (n=3) outside or in the period preceding or following paroxysmal events. Five patients presented dysautonomic, non-epileptic episodes (brady-, tachy-cardia, desaturations).

Conclusion:

At present, there are extremely few EEG studies available on AHC. They highlight a sometimes slow background rhythm, and some episodes of hemiplegia are collected, without uniform/characteristic pattern. Recently, changes in the EEG spectral analysis before the plegic access have been reported. We confirm these observations and describe new and extremely unusual EEG patterns of complex interpretation.

CO13

Early EEG background assessment in infants undergoing therapeutic hypothermia: a useful tool for predicting seizure risk

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Objectives:

Therapeutic hypothermia (TH) is standard of care for infants with moderate-severe hypoxic-ischemic encephalopathy (HIE). Seizures occur in about 30% of cooled infants and must be diagnosed and treated promptly. To date, neither laboratory nor clinical variables have been shown to be a reliable predictor of EEG-confirmed seizures, while the EEG background tends to correlate better with seizure occurrence. We aim to determine the predictive value of early conventional video-EEG (cEEG) for seizures in infants with HIE undergoing TH.

Content:

Methods: Consecutive neonates with HIE who underwent TH at Cliniques universitaires Saint-Luc over a 4-year period (January 2019 - November 2022), were considered for inclusion. C-EEG was initiated as soon as possible after the beginning of TH, and continued until rewarming was completed. The actual full video-EEG recordings were reviewed and the early EEG background (as recorded in the first 12 hours of life) was classified based on the worst pattern persisting for more than 1 hour of recording. Clinical characteristics were extracted from patient's medical record. Results: Forty-seven patients underwent TH, 29 (62%) were included in the study. Eighteen patients were excluded: 12 started EEG after 12 hours of life; 5 were only monitored with aEEG, one had an early redirection of care. EEG was started at a median of 6±3 hours of life and continued for a median of 68±25 hours. Seizures occurred in 6/29 infants (20%), in 4 of whom they were exclusively electrographic. Among the 21 infants with an early normal EEG-background, only one developed seizures, after rewarming, secondary to a cerebral haemorrhage due to thrombocytopenia caused by a congenital CMV infection. On the other end, among the 8 infants with moderately/severely abnormal EEG background, five (62,5%) developed seizures at a mean of 16±4 hours of life: one had isolated seizures, one had recurrent seizures, and three developed status epilepticus. Seizures were subclinical in all but two patients, who presented with clonic seizures and ictal apneas respectively. Overall, 92 electrographic seizures were recorded and most of them were electrographic only (80%).

Conclusion:

In our cohort, a moderately/severely abnormal early background was associated with a high risk of seizures, while neonates with a normal/mildly abnormal early EEG had only a minimal risk. We suggest that, in the context of limited resources, focus should be on neonates with an initial abnormal EEG, who need monitoring for at least 24 hours, as they are at high-risk of developing electrographic-only seizures.

CC01

Recurrent paraneoplastic cerebellar ataxia and encephalitis revealing Hodgkin's lymphoma in a 16 years old patient: a case report.

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Objectives:

Paraneoplastic syndromes, a diagnostic challenge.

Content:

A 16 years old girl presented sudden-onset left upper limb paresis and dysesthesia. The tests revealed first multiple lymph nodes on the cervical MRI, then increase of sedimentation rate at 120 mm/h and decreased amplitude of the sensitive lateral branch of the medial nerve showed by conduction nerve velocities. Two months later, after a spontaneous recovery, she deteriorated with the development of ataxia and bradypsychia. Despite of a normal brain MRI, whole-body FDG-PET showed multiple bone marrow hypermetabolic lesions in the spine and in both humerus with right hypermetabolic lymphadenopathy and hypometabolism in the cerebellum and the temporo-parietal regions bilaterally. Paraneoplastic cerebellar ataxia and encephalitis were suspected and a lymph node biopsy revealed stage IV Hodgkin's lymphoma. Autoimmune evaluation revealed the presence of onconeural antibodies in the serum and in the cerebrospinal fluid with negative specific antibodies. She was treated with chemotherapy and radiotherapy that led to remission of her lymphoma with a normal all body and cerebral FDG-PET and a normal neurological examination fourteen months after the diagnosis. Unfortunately, eight months after the radiotherapy, she presented progressive ataxia with headaches and diplopia rapidly progressing into a flaccid quadriplegia with areflexia, respiratory failure characterized by absence of respiratory drive that required invasive ventilation, coma and refractory focal epilepsy. Whole-body FDG-PET revealed bilateral cerebellar and occipital hypometabolism, compatible with a paraneoplastic syndrome. Nevertheless, no hypermetabolism was demonstrated in the lymph nodes or the bones, excluding Hodgkin lymphoma relapse. She was treated with steroids, intravenous immunoglobulin, plasma exchanges and cyclophosphamide pulses without any improvement. Due to the lack of improving respiratory conditions, she got a tracheostomy. After rituximab, awakening time improved from minutes to hours and muscle strength increased from 0/5 to 2-3/5 without recovery of the respiratory function. Finally, two months later, the patient presented a third neurological deterioration in a context of two episodes of sepsis with focal seizures and depressive affects. Tocilizumab treatment was started.

Conclusion:

In conclusion, this case report illustrates that 1) The clinical presentation can be particularly severe especially with the persistent involvement of the brainstem in our case 2) Whole-body and cerebral FDG-PET is a very useful diagnostic procedure in the context of this severe disease where the absence of specific antibodies makes the diagnosis challenging 3) Recurrence of the paraneoplastic syndrome independently of the primary tumor may appear several months to years after remission 4) Prognosis seems usually very poor.

CC02

Epilepsia partialis continua associated with anti-Hu antibody : a diagnostic and therapeutic challenge

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Objectives:

We discuss here the case of a 3-year-old child who presented with epilepsia partialis continua revealing anti-Hu (type 1 Anti-Neuronal Nuclear Autoantibodies, ANNA-1)-associated paraneoplastic encephalitis with delayed discovery of a ganglioneuroblastoma.

Content:

This is a 3-year-old child who had a normal birth and typical development. She started a focal epilepsy with left orofacial clonus that rapidly evolved into a persistent focal motor status epilepticus or epilepsia partialis continua of the left arm with right central paroxysmal abnormalities on the EEG. This epilepsy was rapidly followed by a global psychomotor regression. The presence of a right insular cortical hyperintensity on a first MRI initially led to the suspicion of focal cortical dysplasia for which a pre-surgical workup was initiated. The stereo-electroencephalography (SEEG) recorded contralateral discharges which made the hypothesis of an underlying unique cortical dysplasia questionable. A biopsy showed aspecific reactive gliosis. Further investigations revealed intrathecal immunoglobulin synthesis in the CSF and the presence of anti-Hu antibodies in the blood and in the CSF, orienting towards a dysimmune etiology. A first malignancy workup including MIBG scan and abdominal ultrasound, urine homovanillic acid, and urine vanillylmandelic acid were unremarkable. A third cervico-thoracic MRI performed 9 months after epilepsy onset finally found a cervical ganglioneuroblastoma, not accessible to surgery. Several lines of anti-epileptic treatments were tried, without effectiveness on the continuous partial epilepsy which persists at 3 years of evolution with frequent hospitalizations for status epilepticus. Currently aged 5 years old, she has a severe developmental disorder with no language, no autonomous walking and severe behavioral problems. Treatments has included 4 courses of chemotherapy associated with monthly pulsed of steroids and cyclophosphamide for 1 year. She did not tolerate plasma exchange and rituximab. The tumor remained stable on follow-up imaging.

Conclusion:

Epilepsia partialis continua can be associated with a lesion in the sensorimotor area or revealing an autoimmune encephalitis like Rasmussen or paraneoplastic encephalitis. This case reminds us of the importance of immune investigations in this situation which should raise the suspicion of paraneoplastic encephalitis in the presence of Anti-Hu antibodies and lead to an exhaustive and repeated search for an occult tumor. Despite the use of various immunomodulatory treatments, the prognosis remains very poor.

Clinical and diagnostic challenges in patient with acute psychotic episode and parkinsonism

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Objectives:

We report a clinical case of a psychotic episode with variable and fluctuating clinical features associated with parkinsonian symptoms resulting in challenging psychiatric care.

Content:

The patient experienced an uneventful pregnancy and perinatal period, with a history of heart birth defects (atrial and ventricular septal defects) and oligodontia with multiple agenesis of permanent teeth. Female karyotype (46, XX). Normal psychomotor development. Positive family history for seizures. This girl, with no previous psychiatric and neurologic history, was first admitted to our Center at 16 years of age presenting an acute onset of psychiatric symptoms followed by a parkinsonian-like movement disorder and dysautonomia; symptoms showed up during a group holiday trip. The clinical course varied in severity over time, with no response to antipsychotic therapy, but improvement chronologically correlated with intravenous immunoglobulin treatment (10 days timeframe). The serological and cerebrospinal fluid (CSF) analysis excluded the infectious and post-infectious associated encephalopathies. The clinical course and the immunoglobulin treatment response were strongly suggestive of autoimmune encephalitis, but the diagnostic criteria were not fulfilled. Serum and CSF analysis with no significant abnormalities and negative anti-neuronal antibodies. Initial normal EEGs became subsequently abnormal with transient intercritical diffuse paroxysmal activity, improved after steroid treatment. The brain Magnetic Resonance Imaging performed at the beginning and the control-one demonstrated normal findings. Whole body PET imaging showed no significant cerebral metabolic change but revealed a diffuse intrahepatic vascular dilatation (arterial Doppler-ultrasound evaluation and abdominal magnetic resonance imaging detected a normal intrahepatic vascular system). Chest X-ray, chest CT and abdominal ultrasound findings were normal with no detectable onconeural antibodies, supporting the non-paraneoplastic encephalitis hypothesis. Systemic inflammation and autoimmune classic disease were excluded by the specific work-up (including autoimmune antibodies and IFNsignature). No useful information from urinary and hair drug testing. Investigations ruled out secondary Parkinsonism hypothesis; isolated hypermanganesemia was found but imaging features did not guide to manganese encephalopathy diagnosis. CT-pulmonary angiogram showed pulmonary arterial hypertension. Array-CGH detected variants of unknown clinical significance. Focused Exome identified a splicing variant in MAPT gene annotated as loss of function, inherited from her mother.

Conclusion:

This complex clinical case highlights challenges in evaluating and managing an acute psychotic episode. The clinical evaluation and investigations do not allow a definite diagnosis. MAPT gene variants can confer susceptibility to early-onset frontotemporal dementia, while her mother is asymptomatic. The clinical significance of the genetic variant is still unclear and will be evaluated during follow-up, including periodical neuropsychological assessment.

CC04

Antibody negative autoimmune encephalitis, are they really negative?: A pediatric patient with GFAP antibodies.

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Objectives:

Encephalitis comprises a group of inflammatory disorders of the brain that result in altered mental status, and focal neurologic deficits. The steady identification of new types of autoimmune encephalitis together with a fairly stable number of infectious etiologies, has led to a reduction of cases of unclear etiology, but there is still a substantial number of patients whose cause of encephalitis is unknown. These cases are often described as “seronegative or antibody negative autoimmune encephalitis” even though in many instances the extent of antibody testing is limited. This may lead to errors of considering seronegative a patient who, in fact, has neuronal antibodies (i.e., seropositive). Here we present a case with GFAP antibodies found through an extensive workup in a research laboratory to exemplify that in rare cases if the suspicion is high the search of antibodies should persist.

Content:

We present a 15-year-old patient who presented with drowsiness, diplopia and gait instability with prodromal fever 3 weeks earlier. As personal background a mature cystic teratoma was removed by surgical intervention 4 months prior to the encephalopathy. Extensive workup showed a CSF with predominantly mononuclear pleocytosis and proteinorrachia (normal CSF opening pressure) with negative PCR for viruses and bacteria. Bilateral papilledema was observed. Brain MRI showed bilateral hyperintense T2-FLAIR lesions in capsula interna. In order to rule out autoimmune etiology CSF and serum samples were sent to a research laboratory in which immunohistochemistry in rat brain tissue showed typical pattern for GFAP. This was confirmed by in-house cell based assay in both serum and CSF. She received pulses of methylprednisolone with good recovery. She is now clinically stable without chronic immunomodulatory therapy.

Conclusion:

Autoimmune GFAP astrocytopathy is an immune mediated inflammation of the central nervous system. Autoimmune GFAP antibodies have been reported more frequently in adults than in children, however it should be suspected when the clinical picture is suggestive. We wanted to present this case to share and review the clinical characteristics of GFAP autoimmune etiology in pediatric population and to highlight the importance of research work-up in this kind of patients. This cooperative work avoids wrong etiological labels (i.e. seronegative) and provides better therapeutic approaches, towards a customized medicine.

P01

A case of anti-NMDA Receptor Encephalitis presenting initially as focal epilepsy

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Objectives:

To describe a patient with anti-NMDA receptor encephalitis (anti-NMDARE) initially presenting with focal epilepsy and neuropsychiatric symptoms

Content:

We present 16-year-old female, previously fit and well with mild self-reported anxiety background. She presented with focal seizures with tonic-clonic movements of the right upper limb, altered awareness, collapse and urinary incontinence, and focal to bilateral tonic-clonic seizures with head and eye deviation to the right. Simultaneously, she developed episodes with involuntary, irregular movements of her limbs of unknown nature and panic attacks and was thought to also have non-epileptic attack disorder (NEAD). She subsequently developed episodes of expressive aphasia, right-sided paraesthesia, coordination difficulties and short-term amnesia. The electroencephalogram (EEG) showed slow waves in the left posterior hemisphere without epileptiform discharge. Brain magnetic resonance imaging (MRI) was normal. Serum and cerebrospinal fluid anti-NMDA receptor antibodies were positive. Imaging of the chest, abdomen and pelvis excluded neoplasms. She received Levetiracetam and, due to seizure relapse, Clobazam add on. Following diagnosis of anti-NMDARE, she received five days of intravenous methylprednisolone 1g daily with tapering oral steroids and five days of intravenous immunoglobulin with good clinical response and seizure freedom. The EEG improved with persistent left-hemispheric slow waves. Six weeks post-treatment, she had a mild relapse with speech and memory difficulties and received a further course of IV methylprednisolone with good response. To reduce the risk of further relapses, she received treatment with Rituximab. Approximately 60% of paediatric anti-NMDARE are reported to have epileptic seizures and 70% psychiatric symptoms. A few case studies have reported NEAD but its incidence is unknown

Conclusion:

We describe a case of anti-NMDAR receptor encephalitis presenting with epilepsy, cognitive and psychiatric symptoms showing good response to antiseizure medication and immunotherapy. The variety of neuropsychiatric symptoms in this condition can be misleading and combination of accurate semiology and investigations are necessary to avoid delayed diagnosis.

P02

Hyperkinetic movement disorder with febrile exacerbations in a 2 years old child

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Objectives:

Background Hyperkinetic movement disorders in children can be of acquired (e.g. infectious, inflammatory, toxic) or genetic origin, and include tics, stereotypies, dystonia, choreoathetosis, tremor, and myoclonus. Tremor can occur at rest (rest tremor), during action (kinetic tremor) or maintenance of posture (postural tremor). Holmes tremor, a low frequency tremor combining rest, postural and kinetic tremors, is caused by lesions in the basal ganglia, midbrain or cerebellum.

Content:

Case presentation We report a two-year-old boy, initially referred for developmental delay, who developed dystonic posturing of both legs and feet and Holmes tremor during a febrile illness. A treatment with dopaminergic agonists partially relieved abnormal movements. Brain MRI showed a slight hypotrophy of the white matter. EEG, spinal MRI and brain and whole-body FDG PET-CT were normal. Spinal cell counts and protein level were normal, and anti-neuronal membrane receptors and paraneoplastic antibodies were absent. Serum and spinal lactate and glucose levels were normal. Metabolic workup revealed ketonuria and a slightly abnormal acylcarnitine profile with an isolated C14 elevation. Trio clinical exome sequencing disclosed compound heterozygous missense variants in WARS2, c.148G>C (p.Gly50Arg) and c.37T>G (p.Trp13Gly), classified as likely pathogenic using ACMG criteria. The p.Trp13Gly variant, already demonstrated to impair the mitochondrial localization of the protein, is a hypomorphic variant, already described as pathogenic in combination with a more deleterious allele, but not in the homozygous state.

Conclusion:

Conclusion Biallelic variants in WARS2, a nuclear gene encoding for mitochondrial tryptophanyl-tRNA synthetase, are associated with developmental delay, intellectual deficiency, complex movement disorder, and inconsistently epilepsy. Severity is highly variable, from severe infantile leukoencephalopathy with lactic acidosis and early death to an infantile or juvenile-onset developmental delay with intellectual deficiency and abnormal movements. Mitochondrial diseases, and more generally metabolic diseases, should always be considered in the differential diagnosis of neurodevelopmental disorders with abnormal movements, even in the presence of a normal metabolic workup.

P03

Sertraline modulation of social anxiety and cognitive outcome in pre-scholars with Fragile X syndrome

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Objectives:

To evaluate the effects of low doses of sertraline in Spanish Fragile X syndrome patients aged 2 to 6 years old, and evaluate if there is an improvement on their cognitive outcome and their adaptive behavior.

Content:

Fragile X syndrome (FXS) is a genetically based cognitive-behavioral disorder that involves mild to moderate cognitive impairment, with physical and behavioral distinctive characteristics. It is caused by amplification (>200 repeats of CGG triplet) of the promoter region of FMR1 (Xq27), which codes for FMRP (repressor of numerous genes), modifies neuronal development and conditions reactions of hyper excitability and anxiety. Sertraline, being an inhibitor of the reuptake of serotonin and dopamine, can correct this alteration and favor neuronal stabilization, especially critical in the pre-school stage of the neurodevelopment. Sertraline was administered at 2.5 mg/day for 4 weeks, and subsequently 5 mg/day, for at least 6 months. Neurological evaluations and neuropsychological (Bayley-III, WPPSI-IV, ABAS-II) were performed at baseline, 6, 12, and 24 months of treatment. Of ten patients who started treatment, two withdrew due to secondary adverse events(24h post dose and 4 weeks after treatment onset) that disappeared when the drug was discontinued; the remaining eight and the one who dropped out after 4 weeks, presented especially improvement in social interaction. The youngest patients also presented improvement in language and cognitive tasks performance, and increased tolerance to social stress.

Conclusion:

Behavior disorders and social anxiety modify quality of life of FXS patients. Low doses of sertraline, in FXS children with pre-school ages, can improve social avoidance and adaptative behavior. This may mean reaching a better quality of life for these patients and their families.

P04

Development of a global offer of support and resources in conjunction with health professionals with a view to dedicated offers (Health, Education and Justice) and proximity for children with ADHD and their parents.

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Objectives:

Development of a global offer of support and resources in conjunction with health professionals with a view to dedicated offers (Health, Education and Justice) and proximity for children with ADHD and their parents.

Content:

Health professionals receive more and more families in need of support, perceived as "educating their child badly", children in distress, teachers helpless when faced with children who may behave inappropriately in class, and justice personnel mobilised for worrying situations. After a first regional colloquium on ADHD at school in 2018, which brought together 376 professionals, a working group was set up in 2019 to bring together local players (university hospital services, health and medical-social establishments, Protection and Education services, private professionals and parents) to discuss a global project for support dedicated to these problems. In addition to support for the coordination of complex pathways for children with ADHD attending schools, which has been offered in the region since 2006, and a regular training programme, the first Barkley-type Parenting Skills training workshops run by two neuropsychologists and a neuro-paediatrician have been rolled out in the region. Based on the concepts of cognitive-behavioural psychotherapies, their objective is to improve parenting skills and family harmony in a support project lasting several months and promoting peer emulation. Based on the success of these workshops, the Regional Health Agency has supported the deployment of a training offer open to all health professionals involved in these courses (psychologists, doctors, psychiatrists, paediatricians, neuro-paediatricians, etc.) wishing to develop this type of project. 90 health professionals have already been able to benefit from it. The clarity given to the initiatives developed (in institutions, by private individuals, in conjunction with parents' associations...) has led to the emergence of new projects encouraging referrals for the families concerned to a local offer in addition to a new training offer aimed at teachers, but also at the staff of the Justice Department, who are very frequently called upon to deal with worrying situations involving children, whether diagnosed or not (any professional who has to intervene with minors in the context of child protection).

Conclusion:

This co-constructed approach has enabled the reinforcement of the territorial network through the development of professionals' skills in accordance with the recommendations, favouring access to better support for a greater number of families, and has enabled all the actors concerned to better understand the issues involved in caring for these children in an ecological and shared approach.

P05

Sleep and circadian rhythm disorders in Alternating Hemiplegia of Childhood (AHC)

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Objectives:

AHC is a rare developmental encephalopathy caused by ATP1A3 mutations that encode for the alpha3 subunit of Na+/K+ ATPase. It is characterized by several paroxysmal events (plegic, dystonic, abnormal eye movements, others). The resolution of the paroxysmal events upon sleep is among the core features of the disease. At the same time, many other features of the disease (specific triggers, medications, epilepsy, neurodevelopmental & neuropsychiatric disorders) are known predisposing factors for sleep and circadian cycle disorders. The aim of this ongoing study is to evaluate the frequency of sleep disorders, the sleep architecture and the circadian rhythm in patients with AHC.

Content:

Methods: We prospectively included 21 patients with AHC after informed consent [mean age 15,41 years (min 1,77 years, max 39,91 years), male 61,9%]. We have analysed sleep-related questionnaires (n=18), actigraphy(n=10), polysomnography (n=14) and urinary melatonine cycle (n=15) along with clinical details from patients' medical records was. SPSS 27.0 was used for statistical analysis.
 Results: According to sleep questionnaires, 52,9% of patients with AHC have a morning circadian phenotype; 28,6% were under regular melatonine treatment. PSG was suggestive for a sleep pathology in 85,7% of patients; however, no severe pathology requiring immediate intervention was detected. The most striking results were a low sleep quality and high sleep fragmentation. Median sleep efficacy was at 79.75% (min: 54.8%, max: 95.8%) and median arousal index at 20.25 micro-arousals/h (min: 4.9/h, max: 52.6/h). Median obstructive apnea-hypopnea index (AHI) was at 0,55 events/h (min: 0/h, max: 5.7/h) and median central AHI was at 0,6 events/h (min: 0/h, max: 3.4/h). Low melatonine urinary secretion was found in 46,7% of patients. Actogram non-parametric circadian rhythm comparisons with healthy population have shown a delay of 2 hours in L5 (onset of the least active 5 h) in children and a high intra-daily variability (IV) (0.80, p= 0.04) in adults.

Conclusion:

There is a low quality of sleep that may be underestimated by caregivers. We found a low urinary melatonin secretion in AHC patients; if further confirmed, this observation could have therapeutic implications. The preliminary results of the actogram analysis indicate a possible alteration of the rest- activity cycle in AHC. Patient recruitement is ongoing in order to confirm these preliminary results in a larger population and investigate potential correlations with patients' phenotype/genotype.

P06

Length perception déficit in preterm birth, a new disorder?

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Objectives:

To investigate the prevalence of elementary visuo-spatial perception (EVSP) deficit in preterm children without cerebral palsy consulting for suspected neurodevelopmental disorder (NDD).

Content:

A screening test designed and validated to measure dorsal EVSP ability without motor response was administered by the clinicians among other neuropsychological tests used to diagnose NDD in 70 preterm children aged between 6- and 15-years. This screening test was not considered for the diagnosis but retrospectively analyzed according to prematurity criteria and NDD diagnosis. This study had approval of the Research Ethic Boards of the University Hospital of Lyon (CPP Sud-Est II, number 2015- 54-2). The prevalence of EVSP deficit (27%) was significant in the total sample of these preterm children coming for out-patient consultation. This included frequent deficient perception of length, angle, midline, and relative position in cluttered environment. The magnitude comparison ability, correlated with gestational age (GA). EVSP performance was best explained when associating GA and growth development. Among children with DCD diagnosis, 28% scored as outliers at the landmark comparison tasks. Children with DCD and comorbidities were severely impaired in EVSP with almost half scoring as outliers. Importantly, even children not diagnosed with any NDD exhibited impaired EVSP performance: 23% scored as outliers at total score, and 31% scored as outlier at the magnitude sub-score. This visuo-spatial profile was specific to this population without clinical care.

Conclusion:

While the visuo-spatial profile of pre-term children with NDD did not differ from those of term-born children, a specific disorder of length perception linked to prematurity criteria emerged for children without any NDD diagnosis but scholar complaints. Early EVSP screening test in pre-term children without visible deficiency could allow these children at-risk for developmental and academic difficulties to benefit from early scholar adaptation and/or clinical follow up, as do pre-term children with CP.

P07

Visual function profiling in children with Joubert Syndrome

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Objectives:

With this study, we aim to describe the visual function profiles of a cohort of children with Joubert syndrome (JS) and to investigate the possible associations between basic visual functions and cognitive aspects.

Content:

This work is based on the retrospective review of medical charts of a cohort of children consecutively referred to the Developmental Neuro-ophthalmology Unit of IRCCS Mondino Foundation based in Pavia, Italy over a 18-years period. All children were diagnosed with JS based on suggestive clinical and MRI features. Patients' clinical data refer to their latest admission. Fifty-nine participants (33 males and 26 females) were included in the study, aged 4 months – 23 years (median age 8 years, mean age 9 years 2 months ± 6.3 years). All enrolled subjects underwent an evaluation protocol including basic visual functions (best corrected visual acuity or BCVA, contrast sensitivity, fixation, smooth pursuit, saccades, extraocular movements), ophthalmological tests (fundus oculi, VEP, ERG), and developmental/cognitive assessment. Next-Generation Sequencing (NGS) was performed either on a targeted panel of ciliary genes or on the Whole Exome (WES). Organic involvement was also investigated with appropriate exams. Concerning analyses, variables are described in terms of row counts and percentages. To evaluate whether clinical features, including visual function parameters, would influence neuropsychological development, we conducted chi squared test for independence per each neuropsychological variable. Ocular motor apraxia (OMA) was the most frequent sign at disease onset. 69.5% of subjects presented with severe developmental delay or intellectual disability. A significant percentage of subjects presented fundus oculi alterations and reduced BCVA. A significant association between retinal dystrophy and intellectual disability was found (p 0.047) and confirmed at post-hoc analyses (p 0.052). Furthermore, reduced BCVA both for near and far distances, absence of stereopsis, refractive errors, and impaired fixation were associated with intellectual disability.

Conclusion:

OMA is a key feature of JS and is frequently associated with perceptual deficits (i.e., reduced BCVA). Visual impairment may originate both from perceptual and oculomotor deficits and negatively affects cognitive development in children with JS. An early and multidisciplinary assessment and follow up of visual functions is mandatory in children with JS, both to help the diagnostic approach and to plan personalized rehabilitation strategies. Further studies are needed to correlate visual functions and diagnostic aspects (i.e., neuroradiological and genetic).

P08

The impact of visual functions in hypomyelinating leukoencephalopathies

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Objectives:

This study aims to describe the visual function profiles in a cohort of children affected with hypomyelinating leukodystrophies.

Content:

We conducted a retrospective analysis of the medical records of a cohort pediatric patients referred over 10 years to the Developmental Neuro-ophthalmology Unit of IRCCS Mondino Foundation, Pavia, Italy, and the Leukodystrophy Center COALA at Paediatric Neurology Unit of Buzzi Children's Hospital, Milan, Italy. The inclusion criterion were a formal neuroradiological diagnosis of hypomyelinating leukodystrophy and at least one neurophtalmological assessment done during follow-up. We revised data concerning medical history, clinical details, and diagnostic exams including brain Magnetic Resonance Imaging (MRI) and genetic testing. Neuro-ophthalmological data included basic visual functions such as best corrected visual acuity (BCVA) and ocular motor abilities (fixation, smooth pursuit, saccades) as well as funduscopic examinations and electrophysiological exams (visual evoked potentials – VEP, electroretinogram, ERG). The Visual Function Score (VFS) was used to categorize these findings. 12 patients were included in the study, 7 males and 5 females. Median age at first neurophthalmological examination was 5.6 years (range 1-12 years), median follow-up was 3.6 (range 2-14 years). 11 out of 12 patients had positive genetic testing (3 POLR3, 1 TUBB4, 4 PLP1, 2 RARS1, 1 GJC2) while in 1 all genetic analyses including WES were inconclusive. All patients showed moderate to severe reduction of BCVA and moderate oculomotor impairment mainly involving saccades (in terms of fluidity and precision). Furthermore, all patients presented nystagmus of a moderate to severe entity with the association of cyclorotatory and pendular components.

Conclusion:

This paper points out how visual function impairment represents a recurrent feature in hypomyelinating leukodystrophies, significantly involving both perceptual and ocular motor aspects. An early and multidisciplinary assessment and follow-up of visual functions would be important to sustain diagnostic work-up when a white matter disease is suspected. Furthermore, re-habilitation in such children, often presenting with a relevant neuromotor involvement, should include the training of visual functions. Indeed, an effective use of residual visual acuity would be helpful to sustain the overall development and everyday life of these children. Further studies are needed to provide insight into the trend over time of visual functions in hypomyelinating disorders and to investigate associations between visual function profiles and other features, such as MRI and genetic findings.

P09

CASE REPORT : Intracranial complications of acute sinusitis in children

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Objectives:

Intracranial complications of sinusitis (ICS) are rare but dangerous and call for early, aggressive treatment. We report the story of a girl that, though banal in the beginning, reminds us of the risk of complications.

Content:

A 14-year-old girl without significant medical history was brought to our ER with headaches and confusion. She'd been diagnosed with acute sinusitis 12 days earlier; symptoms faded after 72h, without antibiotics. Upon examination, our patient was tachycardic and febrile, with GCS of 12 (E3V3M6). She had left peri-orbital edema, exophthalmia, neck stiffness and photophobia. Laboratory tests showed raised CRP (366 mg/L) and leukocytosis (25900/mm3, 92% neutrophils). Two hemocultures isolated Streptococcus intermedius. CT-scans showed maxillary, ethmoidal and sphenoidal sinusitis with osteolysis, bitemporal edema and pachymeningeal enhancement, as well as extensive veinous thrombosis of cavernous and transverse sinuses, left ophthalmic and internal jugular veins. In the absence of intracranial hypertension signs, lumbar puncture was allowed and showed CSF pleocytosis (1034/mm³, 91% neutrophils), slightly elevated proteins and normal glucose levels, with negative PCR panel and CSF culture. Treatment was quickly initiated with IV dexamethasone, heparin and broad-spectrum antibiotics (cefotaxime, vancomycin, metronidazole). Sinuses were surgically drained. 24h later, MRI imaging showed left temporal empyema, pre-suppurative bitemporal encephalitis and intra-orbital abscess. Due to persistence of the collected lesion and intense headaches, ethmoidal trepanation was performed 3 weeks later with antibiotic instillation. After 6 weeks of antibiotics and 3 months of LMWH, patients presents no sequelae except for intermittent headaches. ICS are rare but possible, especially in adolescents. In that case, the most described patterns of growth are Streptococcus species, most commonly S. milleri. Infection can spread directly through bony defects and osteolysis or indirectly via retrograde thrombophlebitis of diploic veins. Patients often lack nasal symptoms or focal neurological signs. Orbital complications are frequent. Medical management requires aggressive, culture-directed IV antibiotics during 2-6 weeks. Neurosurgical interventions and endoscopic sinus surgery are often indicated. Long term neurological deficits such as epilepsy, vision loss and focal paresis can occur in up to 35%.

Conclusion:

Though rare, ICS can cause significant long-term morbidity and mortality. The best chance to improve patient outcome is through early and aggressive treatment.

P10

Dravet syndrome: Genetic, clinical, electrophysiological and therapeutic aspects

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Objectives:

To describe the clinical, electrophysiological, therapeutic and genetic aspects of Dravet syndrome (DS) in a hospital case series.

Content:

We conducted a retrospective descriptive study over 13 years (from 2009 to 2022), including patients hospitalized in the department of Child and Adolescent Neurology of the National Institute of Neurology of Tunis, Tunisia. The diagnosis of DS was retained according to the 2011 Dravet criteria. Genetic analysis by Whole exome sequencing was performed. Eight patients were included. The mean age of onset was 5 months [3-6]. The sex ratio was 1. The history of febrile seizure was noted in 6 patients. The onset symptoms were epilepsy (n=8), psychomotor delay (n=1) and encephalitis-like episode (n=1). Initial psychomotor development was normal in all cases. The neurological exam revealed cognitive impairment (n=8), autistic features (n=4), ataxic gait (n=3) and movement disorders (n=3). The seizures were frequently triggered by fever (n=7) with typically prolonged generalized (n=8) or hemiclonic focal seizures (n=3). Other seizure types were seen like myoclonus (n=6), atypical absences (n=4) and focal seizures (n=5). Status epilepticus was frequent in 5 cases. The initial interictal EEG was normal in 3 cases. Background slowing was detected in 3 cases. Photosensitivity was noted in 2 cases. Brain MRI showed diffuse cerebral atrophy in two cases. All patients were treated with at least 2 major anti-epileptic drugs. They were treated with sodium valproate as first line therapy. Second line therapy included Levetiracetam (n=5), Clobazam (n=4) and Stiripentol (n=3). Improvement was noticed in 4 cases. The Whole exome sequencing revealed mutations in 2 genes: SCN1A (n=6), and PCHD19 (n=1).

Conclusion:

Our study illustrates the variable spectrum of DS and highlights the phenotypic heterogeneity of SCN1A mutation. Advances in genetics made it possible to develop specific therapies, predict prognosis and establish genetic counseling.

P11

SCN2A developmental and epileptic encephalopathy in an infant with bilateral peri-central and peri-sylvian polymicrogyria and a stroke-like lesion

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Objectives:

The objective of this clinical case report is to highlight the impact of gene-specific therapy in early-onset SCN2A-seizures and report new SCN2A-associated brain MRI findings.

Content:

SCN2A mutations have been associated with a wide phenotype spectrum that includes developmental and epileptic encephalopathy. We report the occurrence of a refractory status epilepticus in a 2 month-year-old infant, related to a SCN2A mutation with an expected gain-of-function effect. His clinical response to the sodium-channel blocker phenytoin was dramatic, when other anti-epileptic drugs had been ineffective. Interestingly, he also presented an extensive cortical malformation with bilateral peri-central and peri-sylvian polymicrogyria, which is believed to stem from the same genetic mutation, as well as a stroke-like lesion on the initial brain MRI after prolonged seizures in the neonatal period. In our clinical case, the efficacy of the treatment using sodium-channel blockers suggests that the mutation per se, more than the brain malformation, was responsible for the epilepsy course. He remains seizure-free at 18 months follow-up.

Conclusion:

Our case report supports that sodium-channel blockers should be considered as an effective personalized therapy in SCN2A early-onset developmental encephalopathy and it further suggests that SCNA2 mutations might be considered in the differential cause of brain cortical malformations, such as polymicrogyria. A stroke-like phenomenon is a newly reported feature in this condition.

P12

Development and evaluation of the usefulness of an electronic diary (e-Diary) for the recording of paroxysmal events in Alternating Hemiplegia of Childhood (AHC)

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Objectives:

Costumed-designed tools for AHC patients and caregivers in order to record paroxysmal events (plegic, dystonic, epileptic, abnormal eye mouvements, others) with reliability and ease are lacking. We evaluated the usefulness of a smart phone and web accessible version (e-Diary) of an event calendar developed for AHC.

Content:

Methods: The e-Diary was offered to the participants of 4 European sites (France, Italy, Spain, UK) of the OBSERV-AHC study (IAHCRC consortium). The paper version of this Diary was developed by a panel of caregivers and experts in the field. Mandatory fields for completion included the date, time, duration and type of the recorded spells. The presentation of the e-Diary was (usually) followed by an illustrative training on the identification of the type of the spells. Caregivers' feedback on the e-Diary was evaluated via a telephone survey. IBM SPSS 21 was used for quantitative data analysis and qualitative analysis for caregivers' free text comments. Results: Survey responses from caregivers of thirty-three AHC patients [(mean age: 13.5 years (range: 1.8- 41.3 years, SD: 1.8); 51.6% male] were collected. Half of them (N=17) used the e-Diary with for a mean duration of 10.47 months (range 1- 24 months, SD: 1.96). Log rank tests showed no differences in the time of usage of the e-Diary when patients were grouped according to the frequency of paroxysmal events. The users mostly appreciated: the ease of the reporting (27.6%), the feeling of contribution to better understanding of the disease (20.7%). The main reasons for no/end of usage were lack of practicality (21.2%) and time (21.2%). Eighty-eight percent of the respondents agreed/strongly agreed that the e-Diary was a good initiative. Ninety-six percent of the caregivers (including those that did not use the e-Diary in the context of this study) responded that they could engage to use it in the future (82.1% for more than 2 years) with the condition that some modifications would apply. According to the qualitative analysis, those modifications were mainly with regards to an easier access and availability of their recordings to the user.

Conclusion:

An electronic version of a disease specific AHC calendar could be useful for caregivers. Modifications of the e-Diary according to caregivers' suggestions could contribute to its sustainable usage for research and for better patient clinical care. Acknowledgements: USA CureAHC Foundation, French (AFHA), Icelandic (AHC Samtökin), Dutch (AHC Vereniging Nederland), Spanish (AESHA), UK (AHC UK), German (AHC18+ e.V.), Polish (AHC-PL) and Italian (AISEA) Associations.

P13

Audit of the concordance of teenagers with epilepsies with their antiseizure medication regimes

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Objectives:

Lack of adherence to antiseizure medication (ASM) may impact the seizure control, safety, and quality of life of teenagers with epilepsies. The study aims to measure the concordance of teenagers with epilepsies with their antiseizure medication (ASM) regimes.

Content:

We created a questionnaire for patients attending the teenage epilepsy clinic. Simple descriptive statistics were used. This was a registered clinical audit (21-102C). In total 74 analysable questionnaires corresponding to 53 patients aged 12-18 years (median 16) were included. 37/74 (50%) had generalised epilepsies, 35/74 (47%) had focal epilepsies and 2/74 (3%) unclassified epilepsies. During the previous month, 36/74 (49%) questionnaires reported no missed doses: concordance score (CS) 7/7; 34/74 (46%) reported missing 1-5/60 doses: CS 6/7; 3/74 (4%) between 6-10/60 missed doses: CS 5/7; one patient reported no dose taken: CS 1/7. Among the patients reporting the best CS 7/7: 27/36 (75%) had >90% reduction of their seizures, 8/36 (22%) had 50-90% reduction; and 1/36 (3%) had more than twice as many seizures. Among the patients reporting a poor concordance CS 5/7 and 1/7: None had a seizure reduction >90%, 2/4 (50%) had a seizure reduction between 50-90%, and 2/4 (50%) had less than 50% reduction or no change in seizure frequency. Data collection is ongoing and more data will be analysed by March 2023.

Conclusion:

Among our patients, most reported good concordance with ASM treatment. Best concordance was associated with good seizure control whereas none of the patients with the poorest concordance had a >90% seizure reduction. More data will be collected to confirm these preliminary impressions, and validate the CS method. As no single assessment of concordance is completely reliable, we hope that self-reported concordance, as assessed in the audit, will prove to be a useful aid in management. Eventually an audit action plan will be developed.

P14

Aneurysmal malformations of the vein of Galen: Clinical and paraclinical study of Tunisian pediatric cases

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Objectives:

To describe clinical and paraclinical features of Aneurysmal malformations of the vein of Galen (VGAM) in a Tunisian pediatric serie.

Content:

We conducted a retrospective descriptive study over years (from 2012 to 2022), including patients diagnosed with VGAM and carried out in the department of Child and Adolescent Neurology of the National Institute of Neurology of Tunis, Tunisia. All our cases underwent conventional cerebral angiography to confirm the diagnosis. Four patients (3 girls and 1 boy) were included. The mean age was 5.8 years. The mean age of onset was 3.3 years [1.5-5]. All patients didn't have any notable personal history and their psychomotor development was normal. The onset symptom was epilepsy (n=2), transient neurological deficit (n=1) and macrocrania (n=1). Neurological examination revealed cognitive impairment (n=2), macrocrania (n=1), hemiparesis (n=2) and dystonia (n=1). During follow-up, one patient developed heart failure, and another patient developed cerebral venous thrombosis. We identified common radiological features in magnetic resonance brain imaging with venous angiography showing aneurysmal dilatation of the ampulla of Galen. Conventional cerebral angiography showed the appearance of ellipsoid varix confirming the diagnosis. Two patients were treated with embolization, which was successful.

Conclusion:

VGAM are rare etiology of cerebral venous thrombosis, epilepsy and neurological deficits. The clinical spectrum is heterogeneous, essentially depending on the type and age of discovery. The prognosis can be fatal due to cardiac complications. It's currently transformed thanks to endovascular interventions. Thus, early diagnosis and antenatal screening can reduce surely the mortality.

P15

Post-COVID neuro-lupus in a child with a NOD2 heterozygous truncating variant

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Objectives:

To describe a case of chronic auto-immune disease triggered by a mild COVID-19 infection in a young boy, heterozygous for a non-sense NOD2variant, that might represent a susceptibility factor to dysimmunity.

Content:

We report the case of a previously healthy 3-year-old boy who developed subacute ataxia, lower extremity paresis and acquired oculomotor apraxia 3 weeks following a SARS-CoV2 infection of mild course. Brain MRI found a focal contrast-enhancing, poorly demarcated lesion of the vermis with slight compression of the fourth ventricle. There was mild contrast-enhancement of the cauda equina on spine MRI. ENMG confirmed a pure motor demyelinating polyradiculoneuropathy in the lower extremities. CSF analysis showed mild hypoglycorachia, high IgG index and positive oligoclonal bands. Serum testing revealed positive anti-SSA-Ro antibodies, anti-nuclear antibodies and anti-DNA double-stranded antibodies as well as slightly decreased C4 levels, suggestive of neurolupus. Systemic features were absent. Non-identifiable anti-cerebellar antibodies were also reported in the serum at onset and persisted at 12-month follow-up in CSF and serum. He responded initially to monthly bolus methylprednisolone and intravenous immunoglobulins, worsening upon immune therapy cessation. He did not significantly improve after 5 cycles of plasmapheresis but has shown stabilization and mild improvement on rituximab at 6-month follow-up. Given his chronic course of disease, he had an extensive work-up to exclude other immune, tumoral and genetic disorders. After trio exome sequencing, a heterozygous non sense variant was identified in the NOD2gene, NM_022162.3:c.1689C>A;(p.Tyr563Ter), that could contribute as a predisposing factor to dysimmunity and auto-inflammatory/immune diseases. This variant was inherited from the unaffected father.

Conclusion:

Long term immune consequences of SARS-CoV2 infection are emerging. The case reported here highlights the possibility that some predisposing genetics variants, such as loss of function variants in NOD2, could be implicated in the occurrence of secondary immune diseases triggered by the viral infection, particularly in children.

P16

Striking clinical and imaging similarities between glutaric aciduria type 1 and Aicardi-Goutières syndrome due to homozygous RNASEH2B pathogenic variant: a report of 3 cases

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Objectives:

To point out significant similarities of clinical picture and imagery between two uncommon and substantively different pathologies: Aicardi-Goutières syndrome (AGS) and Glutaric Aciduria type 1 (GA1).

Content:

A 11-month-old boy (case 1), with good initial psychomotor development, was admitted for subacute neurodevelopmental regression following a febrile illness. On examination, he was irritable, unable to babble nor sit, exhibited severe axial hypotonia and dystonic posturing of 4 limbs. Eye contact and movements remained unaffected. Initial MRI revealed global atrophy, abnormal signal intensity in basal ganglia and white matter rarefaction. The clinical picture was surprisingly similar to another child's, who was hospitalised during the same period for respiratory distress. This 4-year-old female (case 2) was a refugee patient from Syria with GA1, confirmed by biochemistry and genetic evaluation in Lebanon. Unfortunately, she could not receive the appropriate diet at that time. After an initial normal development, she showed a regression of her motor skills at 6 months, following a febrile infection, with loss of head control at 14 months. On first evaluation in Switzerland at four, she had axial and proximal peripheral hypotonia, hypertonia of extremities and absence of any voluntary movements, initially thought to be related to advanced stage of the untreated disorder. It was later discovered that she also had a severe bulbomedullary myelopathy and atlantoaxial instability which worsened her clinical picture. Brain imaging was surprisingly similar with abnormal signal and atrophy of basal ganglia, rarefaction of supratentorial white matter and a thin corpus callosum. She ultimately passed away. Her 2-year-old brother, (case 3), had a milder phenotype with dystonic posturing and axial hypotonia, but unaltereded voluntary movements. Because of the striking similarities between case 1 and these two siblings, thorough metabolic and genetic investigations were undertaken and a poor lysine diet with carnitine supplementation was started pending results. Metabolic investigations failed to confirm GA1. Whole exome sequencing revealed a homozygote variant of the RNASEH2B gene, compatible with AGS. Repeated MRI and brain CT-scan revealed striatal calcifications. Interferon signature was positive. Patient was started on Janus kinase 1 blockade and oral steroids and is currently stable. Cases 1 and 3 phenotypes remain strikingly similar.

Conclusion:

These two pathologies are uncommon in our everyday practice. One must be aware of their clinical and radiological similarities. Being a treatable disorder when promptly recognised, GA1 must be considered in infantile onset encephalopathy with dystonia. Predominant basal ganglia manifestations expand the phenotype spectrum of RNASEH2B-related AGS.

P17

Evaluation of the swallowing function in patients with spinal muscular atrophy: validation of an functional questionnaire and an intraoral pressure measurement tool

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Objectives:

Spinal muscular atrophy (SMA) is a recessive genetic neuromuscular disease secondary to the deletion of the survival motor neuron type 1 (SMN1) gene. It causes muscle atrophy and, in the most severely affected patients, respiratory and bulbar damage. Swallowing disorders are a frequent complication, but still poorly assessed to date with little available litterature. Goals 1) Validate the use of 2 tools: a swallowing questionnaire (Qdéglut) and intraoral pressure measurements (Pmax) with the Iowa Oral Performance Instrument (IOPI) for the evaluation of swallowing function in a pediatric control population . 2) Evaluate the potential of both tools as biomarkers of swallowing function in SMA patients and also the evolution of swallowing over time

Content:

Methods Two groups were recruited: the first comprising 53 healthy children and the second comprising 27 SMA children aged 2.5 to 17 years. All SMA patients included benefited from a treatment that modulated the expression of the motor neuron survival protein and one had benefited from gene therapy with Onasemnogène abéparvovec. The children included answered to the swallowing function evaluation questionnaire and took part in one or a second objective measurements of the maximum oral pressures (lingual, labial, masseterine) by the Iowa Oral Performance Instrument (IOPI). Results The average of the Qdeglut scores is higher in the SMA group compared to the control group (control: 2.89±2.18 vs SMA 16.13±16.16). In addition, the different mean pressures at the different locations are lower in SMA patients (lingual: control: 44.3±16.5 vs SMA: 24.41±15.67 – labial: control 29.2±8.94 vs SMA 18.17±12.34 – masseterine: control 85.9±17.8 vs SMA 60.19±29.79). The evolution over time of the pressure measurements in the type 1 SMA group shows an improving trend , although not significant, for the 3 locations. This is also true for the type 2 SMA group. For type 3 SMA, we observe an improvement in the results for 2 locations (lingual and labial) but not for the masseteric pressure where a slight decrease is observed. HMFSE score shows a negative correlation with Qdéglut but correlation does not reach statistical significance when compared to mouth pressures.

Conclusion:

From this pilot project, we could show that IOPI measurement system and Qdéglut can be applied reliably and easily in the context of a simple outpatient consultation. Early results indicate that SMA patients, although benefitting from a disease modifying therapy, demonstrate clear weaker oral pressures. Impairment appears to be more severe along the SMA spectrum (SMA1>SMA2>SMA3).

P18

Clinical added value of interictal automated electrical source imaging in the presurgical evaluation of MRI-negative epileptic patients: a real-life experience in two paediatric cases

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Objectives:

To show the clinical utility of interictal automated electrical source imaging (ESI) in difficult-to-manage epileptic children undergoing pre-surgical evaluation.

Content:

Two girls (16 and 9 years) underwent a pre-surgical evaluation for refractory focal epilepsy in St-Luc University Hospital (Brussels, Belgium), including long-term 25-channel EEG monitoring, 3-Tesla brain MRI, FDG-PET scan and neuropsychological assessment. EEG and seizure semiology were compatible with left frontal epilepsy. No lesion was found on MRI, despite the use of a dedicated epilepsy protocol, a second reading by an expert neuro-radiologist and a voxel-based morphometry analysis. PET-scan revealed lateralizing (on left side for both patients) but no localizing results (hypometabolism found in more than one lobe: fronto-parietal for the first patient and fronto-temporal for the second). The multidisciplinary team formulated its hypotheses about epileptogenic zone (EZ) location and planned stereo-electroencephalography (SEEG), according to the aforementioned results. In a second step, ESI analysis derived from interictal EEG and patient's own MRI (Epilog PreOp, Epilog NV, Ghent, Belgium) was revealed and clinically interpreted. For the first patient, clusters of epileptic abnormalities pointed in the left middle/posterior cingulate cortex; for the second patient, ESI localized the EZ in the left orbito-frontal region. These results changed the management for the two patients, leading to modifications in the SEEG plan to cover the brain regions pointed out by ESI. The changes proved to be crucial: i) the seizure onset zone identified by SEEG coincided with the sublobar location provided by ESI; ii) the resection site included the ESI sublobar location and both patients are seizure-free after 2-year postoperative follow-up (ILAE 1); iii) histopathology revealed focal cortical dysplasia type 1 in one patient and gliotic changes in the other.

Conclusion:

These two cases illustrate the additional value of ESI when integrating in the phase I pre-surgical assessment for refractory epilepsy and interpreted in the context of the multimodal evaluation. The major contribution provided by ESI concerns the SEEG plan which represents a crucial step in the clinical management to optimize adequate coverage of the suspected EZ, using a limited number of depth electrodes to reduce perioperative complications. This is particularly true in MRI-negative cases where a lesion-based SEEG plan is not possible and the risk of implanting non-lesional brain cortex is higher. Finally, EEG and MRI are compulsory elements in the pre-surgical evaluation, thus the input data for ESI are available in all centers, with no need for additional and less accessible investigations.

P19

Epileptic seizures in children with neurofibromatosis type 1

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Objectives:

This study aims to establish an association between neurofibromatosis type 1 and epileptic seizures.

Content:

This is a retrospective study, made in a tertiary clinic of pediatric neurology, over 10 years. 76 patients were diagnosed with neurofibromatosis type 1 accordingly to the revised diagnostic criteria from 2021 and 15 of them had associated epileptic seizures (19%). 4 children had febrile convulsions (26.6 %) and only one patient had complex type. The remaining 11 patients (73,3 %) presented epilepsy with seizures either focal (54,5%), or generalized (45,4 %). 8 children (72,7%) had associated epileptogenic cerebral structural abnormalities (hippocampal sclerosis, hydrocephalus, glioblastoma, pilocytic astrocytoma, hydrocephalus, neurofibromatosis bold objects in thalamus). All 4 patients with febrile seizures had a good evolution, without necessity of continuous prophylactic treatment. From 11 patients with associated epilepsy, only 4 (36,3 %) have an unfavorable evolution (only one of them was not diagnosed with a cerebral lesion).

Conclusion:

Epileptic seizures have a higher incidence of association with neurofibromatosis type 1 comparing to the general population with good prognosis in general, but it should be looked for a structural cause in the drug resistant cases.

P20

Epidemiological, clinical and electroencephalographic aspects with a Centro-temporal spike-wave epilepsy

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Chu Gabriel Toure, Mali

Objectives:

Étudier les aspects épidémiologiques, cliniques et électroencéphalographiques de l'épilepsie avec des pics centro-temporaux chez les enfants âgés de 2 à 15 ans.

Content:

PATIENTS ET METHODES : Il s'agit d'une étude rétrospective, descriptive et analytique d'enfants âgés de 2 à 15 ans suivis pour épilepsie avec des pointes centro-temporales au CHU Gabriel Touré et à la clinique Kaïdara sur une période allant de janvier 2015 à décembre 2019. RÉSULTATS: la fréquence était de 21,9% et le groupe d'âge des 2-4 ans était le plus touché. Le sex-ratio était de 1,26 en faveur des garçons. L'âge moyen au début était de 5,25 ans. Le nombre maximal de cas a été diagnostiqué entre 4 et 8 ans, soit 54,3%. 40/70 enfants, soit 57,1 %, n'étaient pas scolarisés. Parmi les écoliers (30/70), 18 enfants (60%) ont eu de bons résultats scolaires. 56% des patients n'avaient pas d'épilepsie familiale ATCD. La notion de consanguinité a été retrouvée dans 14,3%. Les crises motrices focales étaient les plus fréquentes et observées chez 59/70 patients, soit 84,3%. Des crises généralisées n'ont été observées que chez 11/70 patients, soit 15,7%. Les crises nocturnes ont représenté 43/70 patients, soit 61,43%. 55/70 patients ont eu moins de 3 crises par an, soit 78,3%. L'électroencéphalogramme a été réalisé chez tous nos patients et en sommeil chez 45/70 patients, soit 64,3%. Les anomalies relevées étaient centro-temporelles chez 50/70 patients, soit 71,4%. La tomodensitométrie cérébrale a été réalisée chez 16/70 patients, soit 22,9%, et était normale dans tous les cas. La monothérapie a été instaurée chez 95,7% de nos patients. La rémission a été obtenue chez 67,1% de nos patients sur une période de 2 à 3 ans après le début du traitement.

Conclusion:

CONCLUSION: L'épilepsie centro-temporale reste la forme la plus fréquente d'épilepsie focale chez nos patients et l'électroencéphalogramme joue un rôle important dans son diagnostic et sa prise en charge. Mots-clés : Épilepsie centro-temporale. Électroencéphalogramme. Enfant. Pédiatrie.

P21

NUBPL-related leukodystrophy: further phenotypic expansion

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Objectives:

Mitochondrial Leukodystrophies constitute a group of different conditions presenting with a wide range of clinical presentation but with some shared neuroradiological features. Genetic defects in NUBPL have been recognized as cause of a paediatric onset mitochondrial leukodystrophy characterized by onset at the end of the first year of life with motor delay or regression and cerebellar signs, followed by progressive spasticity. Early MRIs show white matter abnormalities with predominant involvement of fronto-parietal regions and corpus callosum. A striking cerebellar involvement is usually observed. Later MRIs show cerebellar involvement evolving to global atrophy and progressive involvement of brainstem. After the 7 cases initially described, 11 more subject were reported. Some of them were similar to patients from the original series while few other broadened the phenotypic spectrum.

Content:

we recently observed a new patient who further expand the spectrum of NUBPL-related leukodystrophy. He is a 16-month-old boy who presented during the first months of life with failure to thrive and mild neuromotor developmental delay. At the age of 8 months he presented with a rapid neurological deterioration with marked irritability, truncal hypotonia with pyramidal signs, swallowing difficulties. He lost head control and he was no longer able to smile or babble. Brain MRI showed a widespread T2 hyperintensity of the cerebral white matter with bilateral cystic degeneration at the level of corona. A mitochondrial leukodystrophy was suspected, muscle histological examination was normal while spectrophotometric measurement of OXPHOS complexes showed a marked reduction of complex I activity on both muscle and cultured fibroblast. Next Generation Sequencing (NGS) of a panel of genes associated with mitochondrial disorders demonstrated two heterozygous missense variants in NUBPL.

Conclusion:

With our study we confirm that the association of cerebral white matter and cerebellar cortex abnormalities is a feature commonly observed in early stages of the disease but beside the original and so far prevalent presentation, there are also uncommon phenotypes: clinical onset can be earlier and more severe than previously thought and signs of extraneurological involvement can be observed. Brain white matter can be diffusely abnormal without antero-posterior gradient, can progressively worsen and cystic degeneration can be present. Thalami can be involved. Basal ganglia can also become involved during disease evolution.

P22

Sequelae of febrile convulsive status in children from 0 to 15 years old in the pediatric department of the CHU Gabriel Toure and at the Kaïdara clinic.

A. Toure

Chu Gabriel Toure, Mali

Objectives:

OBJECTIF: étudier les séquelles liées à l'état fébrile convulsif de mal épileptique avec coma chez les enfants de 0 à 15 ans dans le service pédiatrique du CHU Gabriel Touré et à la clinique de Kaïdara.

Content:

PATIENTS ET MÉTHODES: Il s'agissait d'une étude rétro-prospective sur 19 mois sur des enfants âgés de 0-15 ans vu en consultation dans le service de pédiatrie et à la Kaïdara clinique avec séquelles liées à l'état de mal épileptique convulsif fébrile. avec coma. RÉSULTATS: L' La fréquence hospitalière était de 2,5 %. L'âge moyen était de 119,3 mois avec un sex-ratio de 1.68. Les troubles du comportement étaient le motif de consultation le plus fréquent (48.18%). Les séquelles les plus fréquentes étaient les troubles du comportement (23,64 %), l'aphasie (21,82 %), l'épilepsie (19,10 %). L'étiologie principale était le paludisme cérébral (57,73%). Tomodensitométrie cérébrale objectivée corticale diffuse et sous-corticale atrophie dans 22,27% des cas. Les soins étaient la rééducation psychomotrice et motrice physiothérapie (80,91 %) et orthophonie (54,55 %).

Conclusion:

CONCLUSION : le la prévention et la prise en charge correcte des pathologies infectieuses réduiraient Les séquelles liées à un état fébrile convulsif de mal épileptique avec coma. Mots-clés : séquelles, convulsions, fièvre, coma, enfant, pédiatrie

P23

Typical absences and good neurodevelopment associated with a Dravet (SCN1A-positive) clinical picture, with good response to Fenfluramine

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Objectives:

Dravet syndrome, is an epileptic encephalopathy, mostly due to mutations of the SCN1A gene, characterized by focal, often hemi-body, febrile, prolonged motor seizures beginning in the first year of life, which are later associated with other types of drug-resistant seizures, and developmental delay that becomes evident in the second year. Typical absences have been rarely described. Since February 2021, fenfluramine FINTEPLA® can be proposed to drug-resistant patients aged 2 years and older. Our aim is to describe two patients associating typical absences among their seizures' type, good neurodevelopment, and a satisfactory response to the introduction of fenfluramine to their drug regimen.

Content:

Clinical cases The first patient is a girl of 4 years and 3 months, that from the age of 7 months, presented febrile statuses (from 10-50 min) and afebrile seizures, then at the age of 20 months, typical electro-clinical absences with generalized spike - waves at 3 Hz. Genetic analysis with an Epilepsy Gene Panel revealed a truncating mutation of the SCN1A gene. It is a de novo duplication leading to a premature stop codon (not yet reported): NM_001165963.2:c.2680dup or p.(Thr894Asnfs*21). After multiple therapies, the addition of FENFLURAMINE to VALPROATE and CLOBAZAM at the age of 3 years allowed to stop the seizures. The second patient is a boy of 3 years and 3 months. From the age of 7 months, he repeatedly had febrile or afebrile long hemi-corporeal or bilateral motor statuses (from 30-50 min), then at the age of 26 months, appearance of typical electro-clinical absences with generalized spike - waves at 3 Hz. Genetics revealed a missense mutation of the SCN1A gene : a de novo yet unreported variant: NM_001165963.2:c.758T>C or p.(Leu253Pro). After multiple therapies (including lamotrigine that was complicated by myoclonic seizures and aggravation) the addition of TOPIRAMATE to VALPROATE allowed a transient improvement, then its replacement by FENFLURAMINE and CLOBAZAM at the age of 3 years stopped the seizures.

Conclusion:

We describe two cases of Dravet syndrome linked to new variants of the SCN1A gene, with unusually typical absences and good neurodevelopment. The use of FENFLURAMINE allowed a cessation of seizures, in association with VALPROATE and CLOBAZAM. At the age of 4 years and 3 months and 3 years and 3 months, respectively, the two children maintain a good neurodevelopment, particularly in the language domain.

P24

Newborn Screening for X-Linked Adrenoleukodystrophy: the first Italian experience

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Objectives:

X-linked adrenoleukodystrophy (X-ALD) is a genetic disorder, caused by variants in the ABCD1 gene, that affects the brain and the adrenal glands. Primary adrenal insufficiency, cerebral ALD (cALD) and adrenomyeloneuropathy are the main phenotypes observed in males affected by X-ALD. cALD consists in a devasting cerebral demyelination associated with rapid clinical decline and, if untreated, death. The standard treatment for cALD is hematopoietic stem cell transplantation, which, only if performed early in the disease, arrests white matter degeneration. Most of X-ALD males also develop Addison disease, which is associated to high morbidity and mortality, and must be treated promptly with a hormone replacement therapy; therefore it is important for X-ALD patients to monitor adrenal hormone levels during their lifetime. For this reason, early diagnosis of X-ALD is essential to enable timely treatment and several countries have already implemented their newborn screening program (NBS) with the assessment of C26:0-lysophosphatidylcoline (C26:0-LPC) values as screening for X-ALD.

Content:

In June 2021, a pilot study for the implementation of X-ALD in the Italian NBS program was launched by an Italian group in Lombardy. X-ALD screening consists of a three-tiered approach that first involves the quantification of C26:0-LPC and other metabolites in dried blood spot with FIA-MS/MS (Firts Tier), and with the more specific ultra-performance liquid chromatography-tandem mass spectrometry (UHPLC-MS/MS) technique (Second Tier); all non negative cases at the First and the Second Tier are then genetically confirmed via focused NGS (Third Tier). Genetically confirmed X-ALD patients are then evaluated periodically, according to a specific disease monitoring protocol, created based on literature data and personal direct experience. In this way, patients can promptly start a specific treatment if, and when, first signs of brain damage or adrenal insufficiency appear.

Conclusion:

The primary aim of this pilot study is to develop a model able to improve the early diagnosis and subsequent follow-up and timely treatment of X-ALD patients in Italy.

P25

GRIA2 developmental and epileptic encephalopathy: a case report of a recent genetic diagnosis in a 18 years old patient with a good response to cannabidiol

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Objectives:

We report a patient with a diagnosis of GRIA2 developmental and epileptic encephalopathy (GRIA2-DEE), with significant improvement under cannabidiol (CBD). This is the first to our knowledge report of the efficacy of CBD in this rare DEE.

Content:

This 18-year old Caucasian female with profound developmental delay, and autism, was born after a term pregnancy complicated with an insulin-dependent diabetes, with unremarkable delivery. Developmental problems became obvious at the age of 2 months, with subsequent important delay (walking at 33 months, absence of language development). She currently walks held by hand, in a dystonic way and clinical examination reveals dysmorphic features and member spasticity. Family also reports episodes of limb tremor, and paroxysmal limb hypotonia or dystonia. She also has severe behavioural issues. She started having epileptic spasms at age 3 months, progressively followed by focal, and focal onset to bilateral, drug-resistant seizures reported or filmed by parents. Unfortunately, ictal – EEGs are not available, because of difficulties obtaining good quality, long EEGs due to behavioural problems. Interictal EEGs showed progressively marked slowing and poor organization. Nevertheless, they show few epileptiform discharges mostly focal bi-frontal spikes, with right predominance. A marked right hemispheric slowing during sleep (post-ictal?) was recorded twice. MRI revealed bilateral hippocampal atrophy and signal abnormality with right predominance. She was included in the national project of whole genome sequencing (WGS) in trio that revealed a likely pathogen de novo variant in the GRIA2 gene on chr4:g.157341331A>G NM_001083619.3:c.1912A>G, p.(Thr638Ala). At the age of 17 years, she continued to have up to 20 seizures per month, and since one year, CBD oil, at a dosage of 20mg/kg/day was added to her ongoing treatment by phenobarbital and clobazam. Since then, her seizures and other paroxysmal events have been reduced by 50-75% and she has better eye contact and general comfort. This results from the seizure calendar reviewed in monthly medical visits.

Conclusion:

We report a case of GRIA2-DEE diagnosed via WGS and sharing similar phenotype to the other already reported 28 patients. We observed significant improvement on CBD. GRIA2 gene encodes the GluA2 subunit of the AMPA receptor. There is experimental evidence of the potential effect of CBD on the modulation of AMPA receptor kinetics through its interaction with the N-terminal domain of GluA1/GluA2. Early diagnosis of GRIA2- DEE, further observations and functional studies are needed to elucidate whether CBD could be a personalized treatment option for affected patients.

P26

Motor neuron disease and Allgrove syndrome: a report of three pediatric cases

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Objectives:

To describe the clinical and paraclinical features of three unrelated children followed for Allgrove syndrome with neurological involvement.

Content:

Two boys and one girl were followed at the pediatric neurology department of the National Institute of Neurology of Tunis for Allgrove syndrome with neurological manifestations. Patient 1 had delayed walking with acquisition of an abnormal gait at the age of 2,8 years. Diagnosis was made at the age of three in presence of signs of adrenal insufficiency. Examination at the age of five showed signs of upper and lower motor neuron involvement, failure to thrive and slight dysmorphic features. Brain magnetic resonance imaging (MRI) showed cortico-subcortical atrophy with T2 hyperintensities of the posterior biparietal white matter and corpus callosum hypotrophy. Electroneuromyography (ENMG) objectified signs of asymmetric axonal motor neuropathy in four limbs. Patient 2 presented with gait disturbances at the age of ten. Diagnosis was made two months later following the onset of dysphagia and asthenia. Physical examination found spastic paraparesis and cutaneous hyperpigmentation. Brain and spine MRI and ENMG were normal. Patient 3 was followed for Allgrove syndrome since the age of three years. He developed walking difficulties at the age of nine. Examination found signs of upper and lower motor neuron involvement. Brain and spine MRI was normal. ENMG showed decreased motor potential amplitudes in the ulnar nerves.

Conclusion:

Neurological involvement in Allgrove syndrome encompasses a wide range of manifestations affecting the central, peripheral and autonomic nervous system. Usually, these appear in the second decade following the extra neurological symptoms, as in Patient 3. However, neurological signs preceded the diagnosis of Allgrove syndrome in the other cases, with an early onset in Patient 1. Indeed, walking delay has not been reported previously. Also, isolated spastic paraparesis has not been described. Regarding the ENMG, asymmetrical peripheral neuropathy was reported in the literature. Selective involvement of the ulnar nerve is a characteristic feature. Radiologically, the abnormalities found in the brain MRI of the first patient were not previously described. Thereby, our findings expand the clinical spectrum of Allgrove syndrome. This diagnosis should be evoked regards of any case with upper or lower motor neuron involvement. Hyperpigmentation, alacrimia and dysphagia should be searched to guide the diagnosis.

P27

Early pediatric multiple sclerosis

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Objectives:

Pediatric-onset multiple sclerosis have their own specificity. With a case report of an early onset multiple sclerosis we would like to highlight their frequent infratentorial presentation and the difficulty to adapt adult's treatment to children.

Content:

We present a seven year-old boy who developed over one week right hemiparesis, ataxia, impaired language and right dysmetry. There were no history of recent infection or immunization. Brain MRI showed multiple lesions of the supra- and infra-tentorial white matter including an injury in the right cerebellar hemisphere, a right frontal lesion and a left precentral sulcus lesion. All lesions showed central mild enhancement. Medullar MRI was normal. Lumbar puncture revealed normal blood cell count and protein level. Further analysis showed the presence of CSF specific oligoclonal bands. Anti-MOG and anti-AQP4 blood antibodies were negative. Patient received a course of intravenous high dose corticotherapy. The clinical course was marked by the persistence of difficulties in fine motor skills of the right upper limb. Six months later brain MRI control revealed reactivation of the previous right frontal lesion with a clear increase in size and enhancement, without any clinical concordance. Treatment with subcutaneous beta interferon was initially proposed but could not be achieved due to the patient's lack of subcutaneous fat. We therefore proposed an oral treatment with Teriflunomide. The brain MRI performed at one year of the first episode did not reveal any new lesions.

Conclusion:

Pediatric-onset multiple sclerosis can present with infratentorial presentation which is unusual in adults. Treatment can be very challenging as no disease-modifying therapy has been approved under 10 years-old. Small weights and lack of subcutaneous fat have to be considered in those patients.

P28

Uridine monophosphate synthase deficiency as a potential treatable cause of epilepsy of infancy with migrating focal seizures (EIFMS): a case report.

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Objectives:

We aim to demonstrate that uridine monophosphate deficiency may be a new treatable cause of epilepsy of infancy with migrating focal seizures (EIMFS).

Content:

We report the case of a 4-month-old girl, third child of a consanguineous couple who consulted for developmental delay and abnormal movements. Neurological examination revealed microcephaly, absence of eye contact, axial hypotonia and disorganized spontaneous movements. EEG showed a hypsarrhythmic pattern and vigabatrin was started with a modest effect on seizures. Cerebral MRI, an extensive metabolic work-up, visual and auditory evoked potentials and an ocular fundus were performed and non-contributive. A long-term EEG could record several stereotyped sequential seizures starting with tonic seizures followed by clusters of spasms. Despite pyridoxine, pyridoxal phosphate, carbamazepine, topiramate, levetiracetam, clobazam, diphantoin, phenobarbital and ketogenic diet, epileptic seizures gradually worsened to status epilepticus with hundreds of focal seizures and several migrating focal seizures per day. In trio exome analysis revealed a homozygous intronic c.3217-9C>G variant of unknown significance in the CAD gene, encoding the carbamoyl phosphate synthetase, aspartate transcarbamylase and dihydroorotase that catalyzes the first three steps of the de novo uridine 5'-monophosphate biosynthesis. Uridine monophosphate, 100 mg/kg/day, was given and seizures stopped for 5 days. Focal seizures recurred thereafter, but at a lower frequency. Uridine monophosphate 400 mg/kg/d associated with ketogenic diet and lacosamide permitted to reduce child's seizure severity and frequency allowing a discharge from the intensive care unit. Currently, the child epilepsy is stable with 1 to 3 short focal seizures per day with, still uridine monophosphate 400 mg/kg/d and continuous decrease of all her anti-seizure medications.

Conclusion:

Although mRNA sequencing, and functional analysis of CAD activity on fibroblast, are ongoing to evaluate the deleterious effect of the variant, we hypothesize that the administration of high doses of uridine contributed to reduce the severity of seizures. Our case suggests that CAD deficiency may cause EIFMS. Moreover, it suggests that a trial of high dose of uridine could be given in every patient with EIFMS, a severe refractory epileptic encephalopathy.

P29

Extensive cerebral venous sinus thrombosis (CVST) in a toddler after presumed SARS-CoV-2 infection

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Objectives:

After over two years of pandemic, a high number of reports, research groups and guidelines concerning SARS-CoV-2 thromboembolic complications (immunothrombosis) has been published worldwide concerning adult patients. Data in children are limited and the majority of them are MIS-C related thrombotic events. Several molecular pathways and coagulation dysregulations have been proposed which differ among adult and paediatric patients. We report of a case of a child with extensive cerebral venous thrombosis (CVST) after recent SARS-CoV-2 infection.

Content:

A previously healthy 4-year old boy, with no family medical history was admitted with extensive cerebral venous thrombosis during the pandemic. Twelve days prior to his admission, he presented a non identified febrile upper respiratory tract infection. On admission he complained of a new-onset frontal headache associated with emesis. He was alert, oriented with normal vital signs and physical examination and no focal neurological deficits. Due to the severity of the headache, a work up was performed on emergency basis. Fundoscopy revealed bilateral papilledema while visual acuity was normal. Opening CSF pressure was elevated (30cmH2O). MRI venography revealed extensive thrombosis of the left sigmoid sinus, the transverse sinus, the upper part of the left jugular vein, the superior and inferior parts of sagittal sinus and the straight sinus. Regarding admission labs, D-dimer and fibrinogen were elevated (5,53 mg/L and 4,54 g/L respectively) with otherwise normal coagulation parameters and negative inflammatory markers. A complete work up of thrombophilia was performed and homozygous state of MTHFR (C677T) mutation was identified. SARS-CoV-2 PCR on admission was negative but SARS-CoV-2 S protein IgG value was high (2943,9 AU/ml), indicative of recent infection. He received acetazolamide for 3 months and tinzaparine for 7 months, with complete resolution of his symptoms and no further complications. Control brain MRI showed partial venous recanalization and patient remains asymptomatic at the one-year follow up.

Conclusion:

Except in the MIS-C, unlike adults, thrombotic complications seem very uncommon in children with SARS-CoV-2. Adolescent patients and previous thrombotic risk factors may be considered when thinking of initiating thromboprophylaxis in children with COVID-19. Further studies are needed to clarify risk factors among children with COVID-19 in order to develop specific recommendations.

P30

Juvenile myasthenia gravis: epidemiological, clinical, therapeutic and evolutive aspects

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Objectives:

Juvenile myasthenia gravis (JMG) is an antibody-mediated autoimmune disorder of the neuromuscular junction, occuring in children under the age of 18. The aim of this study was to assess the epidemiological particularities, clinical presentations, treatments and outcomes in a Tunisian pediatric cohort.

Content:

We conducted a retrospective study in the department of child neurology of the national institute Mongi Ben Hmida of Tunis over a period of 11 years (2011-2022). All children diagnosed with JMG were included. Epidemiological, clinical, para-clinical, therapeutic and evolutive features were collected and analyzed. Eight patients were included (Two males and six females). The mean age of onset was 12,7 [8-17 years]. The inaugural signs were ocular muscles weakness in one patient, bulbar muscles involvement in one patient and generelized muscles involevement in the other patients. The electromyogram showed a significant decrement in low frequency repetitive nerve stimulation in all patients. Six were acetylcholine receptor antibody (AchR-Ab) positive, one was thyrosine-kinase receptor antibody (Musk-Ab) positive, and one was negative for the two antibodies. The thoracic CT scan performed in all patients was normal in 5 cases and showed thymic hyperplasia in 2 cases. All patientsreceived pyridostigmine. Immunosuppressive treatments combined with corticosteroids were used in five patients. Two patients need polyvalent immunoglobulins and one of them was hospitalized in the intensive care unit and needs mechanical ventilation. Thymectomy was performed in four patients. Three of them did not develop relapses after thymectomy and one patient presented a small worsening at the degression of corticosteroids with a good subsequent evolution.

Conclusion:

JMG is a rare form of the disease representing 10% to 15% of all cases of myasthenia gravis. The generalized form of the disease with positive AchR-Ab is the most frequent as found in our cohort. The form with Musk-Ab give an exclusive or predominant bulbar muscles involvement. JMG has a better prognosis than adult forms and Myasthenic crisis with respiratory muscles involvement are rare but the evolution is always unpredictable, hence the interest of an early diagnosis and management.

P31

When an early morning consultation can delay a diagnosis !

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Objectives:

Congenital myasthenic syndromes are rare genetic diseases affecting the neuromuscular junction and responsible for ocular, bulbar, as well as limb weakness with diurnal fluctuations of symptoms. Due to these fluctuations and variable course, diagnosis can be challenging and delayed.

Content:

Here we present the case of a 5-year-old girl with presumed benign infantile hypotonia. Generalized hypotonia and head-lag were noted at birth. Metabolic workup was normal and Prader-Willy syndrome was excluded. Following spontaneous and rapid improvement, the baby was discharged at day 8 without further investigations and a planned follow-up in neurology. At 12 and 24 month visits conducted early morning, neurological examination was only remarkable for mild gross motor delay and persisting low tone in the extremities with preserved muscle strength and reflexes. The child was readdressed at age 5 with the complaints of intermittent bilateral ocular ptosis, evening fatigue and significant head drop during intercurrent illnesses. On examination, this time in late afternoon, bilateral ptosis with a positive Simpson test was evident. Given the clinical suspicion of congenital myasthenia syndrome, we carried out a work-up that included genetic testing. A homozygous pathogenic variant in the RAPSN gene was identified, responsible for a post synaptic form of congenital myasthenia. Symptomatic treatment by pyridostimine was started. Auto-immune forms of myasthenia were also excluded. The treatment brought significant improvement, however with reported excessive nighttime snoring. Overnight home polygraphies (PG) were conducted to search for obstructive apnea enhanced by oro-pharyngeal muscle weakness. First PG demonstrated a pathological apnea/ hyponea index. After receiving an evening dose of pyridostigmine before sleep, drastic improvement was obtained. Considering this clinical response, treatment plan was modified including a bedtime dose. RAPSN gene codes for a complex of proteins within the post-synaptc membrane of the neuro-muscular junction that fixes the receptor of acetylcholine. Children with this disorder exhibit striking hypotonia and feeding difficulty at birth, respiratory distress and even arthrogryposes. The clinical evolution is generally spontaneously favorable, except during infections when typical head-drop can be noticed.

Conclusion:

In conclusion, here we report the case of a child affected by a mild form of congenital myasthenia, with fluctuating head drop and palpebral ptosis that showed significant diurnal fluctuations leading to delayed diagnosis. Benign infantile hypotonia should remain a diagnosis of exclusion. Atypical features should lead to reconsider potential causes, including congenital myasthenia syndrome. Overnight polygraphy should be included in the work-up of these patients.

P32

Janus kinase Inhibitors treatment in Aicardi-Goutières Syndrome

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Objectives:

Aicardi-Goutières syndrome (AGS) is a rare genetic encephalopathy due to mutations in genes encoding for proteins involved in nucleotide metabolism and/or sensing and resulting in the induction of a type I IFN response. Janus kinase (JAK) inhibitors may be effective in blocking IFN activation. Few case reports and a clinical trial seem to support the hypothesis that JAK-inhibitors can reduce the interferon score and ameliorate the neurologic status and brain MRI in subjects with AGS. We report the clinical response to JAK-inhibitors therapy in two children with AGS.

Content:

CASE REPORT Patient 1: a 5-year-old girl affected by AGS type 6 (ADAR1 mutation). The disease onset was at 3 years of age with asthenia, irritability, disturbed sleep-wake patterns and extrapyramidal signs and by bilateral striatal necrosis at brain MRI. At 38 months of age, ruxolitinib was started. After 20 months of follow-up, we observed an improvement of communicative and cognitive abilities (Griffiths-ER: communication from 34th to 43th percentile, performance from 3rd to 41rd percentile and practical reasoning from 8th to 58th percentile), a mild recovery of the gross motor function and a persistence of the fine motor deficit (GMFM-88 total score: from 68 to 81%; Griffiths-ER: locomotor <1st, eye and hand coordination from 5th to 2nd percentile). Patient 2: a 4-years-old girl affected by AGS type 2 (RNASEH2B mutation). The disease onset was at 15 months of age with gait disturbances followed by irritability and loss of neuropsychomotor skills evolving to spastic tetraplegia and absence of words production. At brain MRI, leukodystrophy was detected. At 3 years of age, baricitinib was started. After 12 months of follow-up, we observed an improvement of communicative, cognitive and personal-social abilities (Griffiths-III: foundations of learning from 5th to 54th percentile, communication from 2nd to 36th percentile, personal-social domain from 2nd to 26th percentile), while the motor deficits persisted (GMFM-88 total score: from 21 to 20%; Griffiths-III: eye and hand coordination from <1st to 1st percentile and gross motor <1st percentile). The treatment with JAK Inhibitors was well tolerated in both the children.

Conclusion:

Our data support the hypothesis that children with AGS may respond favorably to JAK-Inhibitors, especially for the communicative and cognitive domains, while the fine and gross motor functions seem to be less sensible to the positive effects of therapy. It is important to underline that literature data reported a slight improvement of the disease also in the absence of any drug therapy.

P33

Expression of phenotype in girls with mosaic mutations in epilepsy genes

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Objectives:

CDKL5 and SMC1A developmental and epileptic encephalopathies are X-linked disorders, characterized by early-onset refractory seizures and severe to profound intellectual disability. However, there is clinical variability, which may depend on the type of mutation, its location on the protein, as well as somatic mosaicism. We describe the electro-clinical phenotype of four patients with somatic mosaicism in CDKL5 and SMC1A genes.

Content:

We analyzed the clinical and LTM ictal and interictal EEG findings of two girls with pathogenic mosaic variants in CDKL5 gene, and two girls with mosaic variants in SMC1A gene and compared them with the girls with germline variants. The two girls with mosaic mutations in CDKL5 gene presented with tonic asymmetric seizures rapidly followed by hypermotor-tonic-spasms sequence at 5 and 7 weeks of life respectively. Both girls have mild to moderate psychomotor developmental delay. They can walk independently and have achieved verbal communication skills at the ages of 3 and 5 years, respectively. Genetic analysis revealed a frameshift variant c.982C>T, p.(Gln328*) at a rate of mutant allele of 9%, and a deletion variant c.745-3007_825+774del at a rate of mutant allele of 21.6%. The two girls with mosaic mutations in SMC1A gene had seizure onset at 19 and 23 months respectively. One of them presented with focal impaired awareness seizures and myoclonic seizures. The second presented with generalized tonic and tonic-clonic seizures occurring in clusters. They walked independently at 14 months and 3 years, respectively. One female has mild intellectual disability at the age of 29 years, with normal motor development and normally acquired speech skills. The second girl has a mild psychomotor developmental delay, with an acquired independent walk, and the ability to pronounce words but no sentences at 3 years of age. The genetic analysis confirmed the presence of a frameshift variant c.2266C>T, p(Gln756*) at a rate of mutant allele of 25%, and a deletion variant including the exons 20-25 of SMC1A gene at a rate of mutant allele of 20%.

Conclusion:

Our data show that, in girls with mosaic variants in CDKL5 and SMC1A, the ictal pattern is the same as in girls with somatic variants, while the intellectual and motor disability is definitely milder. Detection of mosaic variant may be difficult. Recognizing the clinical phenotype may guide genetic testing. Videos will be presented.

P34

Psychosomatic presentations of dysimmune neurological disorders: report of 2 cases

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Objectives:

To present two cases of inflammatory neurological disease who were first diagnosed as psychosomatic troubles.

Content:

The first case is a 9-year-old girl without significant past history who started complaining of daily nausea with occasional vomiting. She lost weight and was the victim of school harassment. She was first treated with antidepressant drug. Then she developed gait difficulties. A cerebro-medullar MRI was performed and identified extensive cervico-dorsal myelopathy, with T2 hyperintensity including area postrema. Neurological exam was normal except for dysuria. Lumbar punction analysis displayed normal cell count and mild hyperporteinorrachia (0,48g/L). Search for oligoclonal bands, anti-MOG and anti-AQP4 antibodies in blood and CSF was negative. Searches for inborn error of metabolism and acquired metabolic disorders, infectious agents and paraneoplastic syndrome were negative. A diagnosis of myelitis was considered and she was first treated with intravenous steroid pulses. The second case is a 6-year-old boy who had a history of speech delay, but normal motor development. He consulted for secondary enuresis and pelvic pain. Cerebro-medullar MRI and lumbar punction were normal (1 element/mm3 and proteinorrachia 0,13g/l). A diagnosis of psychosomatic trouble was considered and he was treated with laxatives for a fecaloma. Mictions improved partially but bladder intermittent catheterizations were needed. Vesical ultrasound suggested a neurogenic bladder. He was referred to a neuropediatrics unit. Neurological examination showed discrete pyramidal signs in the lower limbs. Anti-MOG and anti-AQP4 auto-antibodies were negative in blood and CSF. Mycoplasma pneumoniae serology was positive and he was treated as a mycoplasma pneumoniae-related myelitis with high dose intravenous methylprednisolone and macrolides. Gait and motor examination normalized and vesical dysfunction improved. Five months later, bladder symptoms reappeared with progressive dysphagia and lost independent walking. Exam showed irreducible scoliosis, pyramidal signs and myoclonus. A diagnosis of PERM syndrome (progressive encephalomyelitis with rigidity and myoclonus) was considered. Cerebral and medullar MRI was controlled as normal. Auto-antibodies, especially anti-GAD and glycine receptor antibodies were negative. He was treated with high dose intravenous steroids pulses and bromazepam. He relapsed 6 months later with need of steroids pulses, plasma exchange and Rituximab.

Conclusion:

These 2 cases show the difficulty to make an early diagnosis of some inflammatory neurological diseases because of non-specific subtle symptoms overlapping with psychosomatic disorders. We will discuss and try to identify red flags that must lead to neurological explorations.

P35

Highly significant ≥75% and ≥80% responder rates with stiripentol in Dravet syndrome patients: Data from the STICLO pivotal trials

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Objectives:

the effectiveness of stiripentol (STP) for treating seizures associated with Dravet syndrome was demonstrated in two phase 3 double-blind placebo-controlled trials (STICLO-France and STICLO-Italy). This work takes the benefit of the data collected during these two clinical trials and analyses the efficacy results of the pooled studies.

Content:

Efficacy results were analysed in Intent to Treat (ITT) and Per Protocol (PP) populations, in terms of percentage change from baseline in seizure frequency and responders (≥50% reduction in seizure frequency). Seizure reductions ≥75%, ≥80% and 100% (seizure free) were also calculated. Following the 2-month treatment period, STP administration led to an 84.4% median decrease in generalized tonic-clonic seizures (GTCS), compared to -5.8% in the placebo group ($p<0.0001$) in ITT analysis. In PP, STP group experienced an 87.5% median decrease in GTCS compared to -6.5% in the placebo group ($p<0.0001$). In ITT and PP, 69.7% and 74.2% of the STP-treated patients were responders respectively, while they were only 6.5% and 8% in the placebo group ($p<0.0001$). Also, 54.6% and 51.6% of the STP-treated patients had a ≥75 % and a ≥80 % decrease in frequency of GTCS respectively, compared to 3.2% in the placebo-treated patients ($p<0.0001$ in both cases) in ITT. In PP, 58.1% and 54.8% of the STP patients had a ≥75 % and a ≥80 % decrease in frequency of GTCS respectively, compared to 4.0% and 4.0% in the placebo group ($p<0.0001$ in both cases). Finally, 36.4% and 38.7% of STP-treated participants remained free of GTCS during the second month in the ITT and PP respectively, versus none in the placebo group ($p=0.0002$ and $p=0.0005$).

Conclusion:

Results of the pooled studies demonstrate the strong reduction in seizures on STP and confirms the highly significant difference with the placebo-treated patients. Reducing frequency of GTCS may alleviate burden of the disease.

P36

Development of a global offer of support and resources in conjunction with health professionals with a view to dedicated offers (Health, Education and Justice) and proximity for children with ADHD and their parents.

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Objectives:

Development of a global offer of support and resources in conjunction with health professionals with a view to dedicated offers (Health, Education and Justice) and proximity for children with ADHD and their parents.

Content:

Health professionals receive more and more families in need of support, perceived as "educating their child badly", children in distress, teachers helpless when faced with children who may behave inappropriately in class, and justice personnel mobilised for worrying situations. After a first regional colloquium on ADHD at school, which brought together 376 professionnals, a working group was set up in 2019 to bring together local players (university hospital services, health and medical-social establishments, Protection and Education services, private professionals and parents) to discuss a global project for support dedicated to these problems. In addition to support for the coordination of complex pathways for children with ADHD attending schools, which has been offered in the region since 2006, and a regular training programme, the first Barkley-type Parenting Skills training workshops run by two neuropsychologists and a neuro-paediatrician have been rolled out in the region. Based on the concepts of cognitive-behavioural psychotherapies, their objective is to improve parenting skills and family harmony in a support project lasting several months and promoting peer emulation. Based on the success of these workshops, the Regional Health Agency has supported the deployment of a training offer open to all health professionals involved in these courses (psychologists, doctors, psychiatrists, paediatricians, neuro-paediatricians, etc.) wishing to develop this type of project. 90 health professionals have already been able to benefit from it. The clarity given to the initiatives developed (in institutions, by private individuals, in conjunction with parents' associations, etc.) has led to the emergence of new projects encouraging referrals for the families concerned to a local offer in addition to a new training offer aimed at teachers, but also at the staff of the Justice Department, who are very frequently called upon to deal with worrying situations involving children, whether diagnosed or not (any professional who has to intervene with minors in the context of child protection).

Conclusion:

This co-constructed approach has enabled the reinforcement of the territorial network through the development of professionals' skills in accordance with the recommendations, favouring access to better support for a greater number of families, and has enabled all the actors concerned to better understand the issues involved in caring for these children in an ecological and shared approach.

P37

Development of a global offer of support and resources in conjunction with health professionals with a view to dedicated offers (Health, Education and Justice) and proximity for children with ADHD and their parents.

J. Laguillier (1), M. Erard (2), M.J. Penniello-Valette (3)

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Conclusion:

This co-constructed approach has enabled the reinforcement of the territorial network through the development of professionals' skills in accordance with the recommendations, favouring access to better support for a greater number of families, and has enabled all the actors concerned to better understand the issues involved in caring for these children in an ecological and shared approach.

P38

A missed diagnosis

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Objectives:

Evaluate the possibility of phenylketonuria in children coming from countries where newborn screening is not available and the possible use of spectroscopy in addressing the diagnostic suspicion of phenylketonuria.

Content:

Clinical case of a 6 years and 3 months old girl, born in Morocco from non-consanguineous parents. Pregnancy referred as normal, eutocic post-term delivery. Perinatal course without complications. Regular motor development; first words reported at 12 months old and later speech delay, sphincter control never acquired. The clinical picture of the patient was characterized by intellectual disability, behavioral problems, and autism spectrum disorder (stereotypies, repetitive behaviors, selective feeding, serious difficulties in interacting with peers, and absence of symbolic play). General and neurological examination was normal (only hypertelorism was reported), no skin anomalies were present. Among the numerous diagnostic investigations performed, brain MRI demonstrated the involvement of the periventricular white matter and posterior regions. Spectroscopy showed a modest peak of N-acetylaspartic acid (NAA). The dosage of plasma amino acids showed a picture of hyperphenylalaminemia, with a Phe/Tyr ratio = 30.5 (cut-off < 0.9), biochemically compatible with phenylketonuria1.

Conclusion:

The clinical picture of the patient and the neuroimaging data were found to be compatible with a picture of leukodystrophy with demyelinating aspects2. The finding of hyperphenylalaninemia allowed the diagnosis of phenylketonuria and the consequent initiation of specific dietary therapy. The absence of a neonatal metabolic screening has led to a diagnostic and therapeutic delay, with probably poor future therapy efficacy. This case remarked the importance of evaluating the possibility of phenylketonuria in children coming from countries where newborn screening is not available. Furthermore, the alteration to spectroscopy found, never reported in the literature in PKU, in our experience could be useful in addressing the diagnostic suspicion of PKU. Bibliography: 1. Van Spronsen FJ, Blau N, Harding C, Burlina A, Longo N, Bosch AM. Phenylketonuria. Nat Rev Dis Primers. 2021 May 20;7(1):36. doi: 10.1038/s41572-021-00267-0. PMID: 34017006; PMC ID: PMC8591558. 2. Scarabino T, et al. Phenylketonuria: white-matter changes assessed by 3.0-T magnetic resonance (MR) imaging, MR spectroscopy and MR diffusion. Radiol Med. 2009 Apr;114(3):461-74. English, Italian. doi: 10.1007/s11547-009-0365-y. Epub 2009 Mar 10. PMID: 19277839.

P39

MELAS syndrome: clinical, paraclinical and evolutionary aspects of a pediatric series

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Objectives:

To describe the demographic, clinical, paraclinical and evolutionary aspects of a pediatric cohort followed for "Mitochondrial Encephalomyopathy, Lactic Acidosis and Stroke-like episodes" (MELAS) syndrome.

Content:

It's a retrospective study including patients followed in the pediatric neurology department at the National Institute of Neurology of Tunis between 2004 and 2022 for MELAS syndrome. The diagnosis was made according to the criteria of Hirano et al, 1992. Three boys and one girl were included. Mean age at onset was 8 years [3-15 years]. Inaugural manifestations were a stroke-like episode (SLE) in two cases, epileptic seizures and deafness in one case and failure to thrive in one case. During the disease course, three patients presented SLE and epileptic seizures. These were focal in three cases and generalized in two cases, with status epilepticus occurrence in one case. Exertion fatigability was noted in three cases, headaches in two cases and gastrointestinal disturbances in one case. Clinical examination found intellectual disability in all cases, deafness in two cases, failure to thrive in two cases, dysmorphic features in two cases, neurogenic syndrome in one case and delayed puberty in one case. Brain imaging showed poorly systematized cortico-subcortical lesions in all cases, which were multiple and bilateral in three cases. The location of the lesions was temporal or temporo-insular in three cases, occipital in three cases, parietal in two cases and frontal in one case. All patients had high lactate level in blood or cerebrospinal fluid, with metabolic acidosis in one case. The electroneuromyogram, performed in one patient, showed signs of sensory-motor axonal neuropathy in the lower limbs. Sanger sequencing of the MT-TL1 gene, performed in three patients, found the m.3243A>G variant in the heteroplasmic state in all cases. All patients were put on Coenzyme Q10 and L-carnitine, with recurrence of SLE in one case. An improvement of fatigue, anorexia and gastrointestinal disorders was noted in one case. None of the patients had sequelae after SLE.

Conclusion:

MELAS syndrome should be considered in any child with SLE with multisystem involvement. The clinical picture can be misleading especially at the beginning of the disease. The presence of headaches, fatigue on exertion, failure to thrive, delayed puberty or deafness should suggest the diagnosis. Treatment with vitamins, cofactors and antioxidants can be beneficial and management must be multidisciplinary.

P40

Clinical and genetic study of leukodystrophies in Tunisian cohort

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Objectives:

to determine the clinical and mutational profile of Tunisian patients with Leukodystrophy (LD) without apparent biochemical markers and to implement a targeted diagnostic strategy for the most frequent forms.

Content:

It was a descriptive, longitudinal and prospective study over 5 years (2014-2019) which included all the patients followed for "leukodystrophy"" defined as bilateral, symetrical and confluent involvement of the WM. We expertized the patient files with a clinical and radiological correlation and we carried out molecular investigations by targeted sequencing of genes either by the classic Sanger technique or by new-generation sequencing techniques. 45 patients belonging to 39 families were genetically confirmed and analyzed in our study. Among the 8 forms of LD, four were hypomyelinating LD (Pelizaeus Merzbacher disease by mutation of the PLP1 gene (2 cases); Pelizaeus Merzbacher-like disease by mutation of the GJC2 gene (12 cases); leukodystrophies linked to polymerase III by mutations of the POLR3A (5 cases), POLR1C (1 case) and POLR1D (1 case) genes and hypomyelination with congenital cataract by mutations of the FAM126A gene (5 cases) and four demyelinating LDs (Aicardi Goutières syndrome by mutation RNASEH2B (6 cases), TREX1 (4 cases) and ADAR (2 cases); Megalencephalic Leucoencephalopathy with subcortical cysts by mutation of the MLC1 gene (5 cases); CACH/VWM syndrome by mutation of the EIF2B5 gene (1 case) and Alexander's disease by mutation of the GFAP gene (1case)).

Conclusion:

Our study contributed to a better knowledge of leukodystrophies in Tunisia and focused on the strong clinical, genetic and mutational heterogeneity of these conditions.

P41

Gamma-sarcoglycanopathy (LGMDR5): clinical and genetic study of a pediatric Tunisian cohort

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Objectives:

To determine the clinical and genetic characteristics of a Tunisian series of LGMDR5.

Content:

Retrospective study from 2012 to 2021 collecting demographic, clinical, biological and genetic data of patients with genetically confirmed LGMDR5. 11 boys and 13 girls from 18 families with a mean age of 7.1 years were included. Consanguinity was noted in 17 families. Familial history of similar case was noted in 8 families. Motor milestones were normal (100%). The mean age of onset was 3.7 years. The most frequent inaugural symptoms were difficulties to run and to climb stairs. Clinical examination revealed proximal weakness that was more apparent in pelvic girdle muscles (100%) and calf hypertrophy (83%). Cognitive impairment was observed in 12.5% of patients. Serum creatine kinase levels ranged from 2280 to 18461 U/L. High levels of transaminase were observed (100%). Electromyography showed myogenic pattern (100%). The homozygous c.525delT mutation in the SGCG gene was found in 100% of patients. Steroids were prescribed at the dose of 0.75mg/kg/d in 83% of patients. Six patients (25%) were wheelchair-bound at a mean age of 11.7 years. Respiratory involvement was reported in 12.5% of patients.

Conclusion:

Our study highlights the recurrent founder mutation in the Tunisian population. Targeted mutational research in the LGMDR5 will enable early diagnosis and facilitate genetic counseling.

P42

Systemic lupus erythematosus (SLE) and Aicardi-Goutières syndrome (AGS)

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Objectives:

While the presence of clinical and biological dysimmunity is well described within the AGS spectrum, there is no report in the literature of SLE leading to the diagnosis of AGS, especially in non TREX1 mutation.

Content:

We report the case of a 15 year old girl who arrived in France from Algeria and was taken into emergency care for an altered general state and multivisceral failure, after a deteriorating condition over the course of the year. Positive FAN at 1/1280 in Algeria suggested a SLE. Investigations revealed pulmonary lesions, vascular purpura, chilblain lesions, oral ulcerations, polyarthritis, pericarditis, proteinuria, macrophage activation syndrome, positive Farr's test, increased erythrocyte sedimentation rate. Neurologically, she presented a confused state, episodes of agitation, stereotypies, staring, and other symptoms suggestive of agitated catatonia; on examination, we observed tetraparesis predominating on the left side, with dystonia spasticity and (surprisingly) retractions. Exhaustive lumbar puncture was unremarkable; Brain MRI showed flair and T2 hyperintensities of the left periventricular deep white matter, of the right frontal cortico-subcortical location , without contrast enhancement nor diffusion restriction. A first line of treatment in Algeria with corticosteroid infusions and cyclophoaphamid had not been effective. On arrival, she was given infusions of methylprednisolone followed by oral corticosteroids, in combination with mycophénolate. Facing the lack of improvement in her neuropsychiatric state, a protocol of immunoadsorptions was decided, allowing finally a return to her baseline state. Repeating anamnestic data, it appeared that before her lupus decompensation, she could walk and speak although a stable moderate tetraparesis was reported as sequelae of an unexplained neurological deterioration occurred at the age of 9 months. A brain scan performed at this time showed deep calcifications and a mild atrophy. This initial history , suggestive of an Aicardi-Goutières syndrome, led us to the identification of the recurrent homozygous pAla177Thr mutation in RNASH2B.

Conclusion:

This case reinforces the already discussed hypothesis of a possible biphasic evolution of the disease, characterized by an early phase of cerebral inflammation, limited in time, followed after several years by a systemic inflammation, and justifies monitoring of dysimmunity during the follow-up of AGS patients, in order to optimize their management.

P43

Childhood aphasia: A case study

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Objectives:

In this study, we.wish to mâle an echaustive description of language and cognitive desorders in children with acquired aphasia using a neuropsychological battery we developed for Algerian children.

Content:

Despite the rarity of the cases, acquired childhood aphasia generated a considerable interest from acquired syndromes in the child. Observations on the incidence, duration, prognosis, and anatomical correlations of such early aphasia have formed the basis for theories on the origin and development of hemispheric specialization. Acquired childhood aphasia is not a simple task. It is commonly known that aphasia is an acquired communication disorder following a brain injury that is manifest in an impairment of the ability to transmit or exchange information and feedings especially in speaking. It may also affect writing, comprehension of spoken language, and reading (Sarno, 2017). However, this définition raises a number of questions about the age of the onset of this syndrome. Indeed, defining it raises a crucial debate that we will ecpose it. Forthemore, using a neuropsychological battery we developed for children aged between 4 to 13 years old, we will describe oral omprehension and verbal expression disorders, and cognitive deficits.

Conclusion:

Despite the small group studied here, the battery we developed allowed us to describe a number of language disorders and some cognitive deficits.

P44

Infant masturbation presented as infantile spasm

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Objectives:

The objective of this communication is to show the importance of video recording when an infant presents movements disorders in order not to confuse it with infantile spasm. But also not to give unnecessary treatment to the infant.

Content:

INTRODUCTION Gratification disorder is a form of masturbatory behavior that has often been mistaken for epilepsy, abdominal pain, and paroxysmal dystonia or dyskinesia. Little research has been published regarding this early childhood condition. However, most pediatricians agree that masturbation is normal and common behavior among preteens and should be recognized as such. Failure to recognize this behavior can lead to unnecessary and invasive testing. Although the behavior could be mistaken for an epileptic seizure, the cessation, following distraction, and intact consciousness during an episode suggest that it is not an epileptic seizure. OBSERVATION This is a 3 month and two week old infant. this boy had been referred to us from another hospital with a diagnosis of infantile spasms. The mother of the child will tell us that the abnormal movements for which she came to consult dated back to the age of three months. He was treated with phenobarbital for three weeks. The neurological examination was normal. the video recordings allowed us to recognize the typical characteristics of these events presented by the child, that are compatible with masturbatory behavior. The child had a toned posture associated with the crossing of the thighs, stroking his external genitalia, without loss of consciousness and his eye movements were normal. This was associated with grunting, hyperventilation and sweating. Hematology and electroencephalogram were normal.

Conclusion:

Infant masturbation should also be considered in infants who are seen for seizures, and apart from EEG monitoring, a detailed history and careful observation, as well as video recordings are very important factors in the differential diagnosis of these two different conditions. This would avoid unwarranted support.

P45

Cognitive, Motor and Social Development of Toddlers Aged 12 To 36 Months Old during the Covid-19 Pandemic in the National Capital Region, Philippines: A Single Tertiary Hospital Study

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Objectives:

During the first three years of life, rapid growth ensues to facilitate development. With lockdown restrictions, toddlers during the COVID-19 pandemic had significantly reduced environmental stimulation, leading to missed opportunities for learning and play. Studies revealed declining scores in children's developmental assessments since the pandemic started. This was the first study in the Philippines to describe the cognitive, motor and social development of children aged 12 to 36 months during the COVID-19 pandemic, using the Early Childhood Care and Development (ECCD) Checklist. This study also identified factors correlated with increased risk of developmental delay.

Content:

Methods. A descriptive cross sectional study was done among children aged 12 to 36 months. The ECCD Checklist was administered to determine the children's risk of developmental delay. Statistical Analysis. Descriptive statistics determined the demographics. Factors correlated with developmental delay determined using Chi-square test, Multiple Logistic Regression and Odds Ratios, (CI=95%, α=0.05). Results. 145 children aged 12 to 36 months were included (μ=25.28±7.078 months). Compared to pre pandemic data, more children (25.5%, n=145) were identified at risk for delays in one or more developmental domains. The odds of toddlers being at risk of developmental delay increased by two-fold among those with daily screen time of an hour or longer (p=0.033, OR=3.055). 73.1% (n=145) of toddlers had daily screen time of an hour or longer, contrary to AAP recommendations. Though 61.4% (n=145) had less than an hour of daily informal study sessions, 93.1% (n=145) had daily physical activity of an hour or longer despite lockdowns.

Conclusion:

During the COVID-19 pandemic, more toddlers were at risk for developmental delay, with odds increased with longer screen time. These findings may guide educational sectors in formulating interventions to prevent delays as we continue online classes in the Philippines. All this to help children adapt better as the country moves through the new normal.

P46

Medulloblastoma in a patient Mucopolysaccharidosis type 2

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Objectives:

We report the case of an MPS II patient in whom a tumoral intracranial process was discovered following the appearance of HIC.

Content:

After his follow-up, he has episodes of vomiting and headache. An objective FO papillary oedema. A cerebral CT scan shows an intra axial cerebral process of left hemi cerebellar FCP suggestive of medulloblastoma. Objective brain MRI an intraaxial tumor process of the left vermo-cerebellar FCP oedematogen compresses the V4 with upstream ventricular tri-dilation and discrete sign of transependymal resorption responsible for engagement through the magnum foramen. The evolution under peritoneal ventriculo bypass and enzymotherapy, is marked by the regression of symptoms. Cerebral control MRI shows an extensive intra cranial process under left cerebellar vermi tentorial, solid kysto compressing V4 without current hydrocephaly. Diffuse hypersignal of periventricular white matter with cavitation lesions accompanied by global atrophy of the corpus callosum with micro cavitation.

Conclusion:

medulloblastoma is a benign tumor not described in the MPS, the evolution under drainage of hydrocephalus is favorable with a stationary state currently under enzymotherapy

PF01

Onset, evolution of clinical manifestations and treatment outcome in children with anti-NMDAR encephalitis

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Objectives:

We analyzed the onset and evolution of clinical manifestations and treatment outcome in children with anti-NMDAR encephalitis.

Content:

Children (ages 1 – 18 years) with autoimmune encephalitis who were hospitalized in the department of Pediatric Neurology, Al. Obregia Hospital from January 2018 to December 2022 were retrospectively analyzed. Demographics, clinical data, treatment outcomes, and follow-up records were reviewed. Eleven patients (8 females and 3 males) with anti-NMDAR encephalitis were enrolled with a median age of 8 years. As onset symptoms, five (45%) patients had neurological symptoms, three patients (27%) presented with seizures, 2 (18%) had symptoms of dyskinesia but the majority of patients, 8 (73%), presented with psychiatric symptoms. During hospitalization all (100%) patients developed psychiatric symptoms, 4 (36%) presented with hallucination, 6 (55%) presented with personal behavioral change, 5 (45%) presented with sleep disorders and 3 more (27%) developed neurologic symptoms of dyskinesia or seizure and one with aphasia and autonomic instability. Out of the 11 patients 10 (91%) fully recovered, 3 (27%) patients having recovered after a 1st line treatment, 7 (64%) recovered after a 1st and 2nd line treatment, 1 (9%) is still having moderate psychiatric symptoms and is still on the 2nd line treatment with an expected positive outcome. On follow-up records same 10 patients had no relapse, only 1 having a relapse after 10 years.

Conclusion:

All patients with anti-NMDAR encephalitis had an onset of psychiatric symptoms or developed them consequently during hospitalization. Out of the 8 patients with initial psychiatric symptoms, 3 were directly admitted in the department of Psychiatry and were treated for their symptoms, which delayed immunotherapy. All patients eventually received an individualized treatment but most commonly steroids, intravenous immunoglobulin and plasma exchange. Eight of them required rituximab or cyclophosphamide. Recovery is slow (up to a few years) and patients are left with minor lasting defects which impact their quality of life (academic achievements, personal relationships).

PF02

Highlighting the Dystonic Phenotype Related to GNAO1

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Objectives:

Most GNAO1 mutations have been associated with a severe phenotype: a developmental epileptic encephalopathy or a neurodevelopmental disorder with predominant chorea which could exacerbate, with or without seizures. The aim was to characterize the clinical and genetic features of patients with mild GNAO1-related phenotype with prominent movement disorders (MD).

Content:

We included patients diagnosed with GNAO1-related movement disorders of delayed onset (>2 years). Patients experiencing either severe or profound intellectual disability or early-onset epileptic encephalopathy were excluded. Twenty-four patients and 1 asymptomatic subject were included. Mean age at disease onset was 6.6 years (range: 0.25–47). Initial manifestations included developmental delay (13), with hypotonia in 4 patients, dystonia (10), myoclonus or seizure (1). All patients showed dystonia as prominent MD. Mean age of dystonia onset was 10.1 years (range: 2–47). Dystonia was segmental (brachio-cervical) in 11, generalized in 13; oromandibular dystonia with dysarthria was reported in 19 patients. Dystonia was combined with parkinsonism in 7 subjects, with myoclonus in 3, with chorea in 2; dystonia was associated with mild to moderate ID in 12 patients. Dystonia was non-progressive in 11. Only 3 patients presented an acute exacerbation of dystonia and 3 others presented epileptic seizures between the age of 4 and 19 years. Movement disorders response to medication, including anticholinergic drugs, levodopa, tetrabenazine, amantadine, clonazepam, or methylphenidate, was poor. Six patients received pallidal deep brain stimulation (DBS), with improvement for 5 of them. Most of the variants identified were novel; two variants recurred in multiple families (11/20), suggesting that mild phenotypes could be related to specific mutations.

Conclusion:

We highlighted a mild GNAO1-related phenotype, including adolescent-onset dystonia, broadening the clinical spectrum of this condition. GNAO1 mutations should be considered as a cause of adolescent or adult-onset nonprogressive dystonia, particularly in the presence of a speech involvement, even in the absence of acute exacerbation, seizures or ID.

PF03

Autoimmune encephalitis: a valid diagnostic option in teenage patients with an acute onset of psychiatric symptoms

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Objectives:

At symptoms onset, to differenciate autoimmune encephalitis from a primary psychiatric disease can be challenging . Our aim is to underline how in adolescents, acute/subacute onset of psychiatric symptoms, associated with a decay of superior cognitive functions and the presence of slow waves at the EEG should raise the suspicion of autoimmune encephalitis, even before the appearance of neurological signs.

Content:

Patient 1: Female, 16 yo, unremarkable clinical history. She presented a subacute onset (two months) of irritability, psychomotor agitation, hallucinations, rapidly followed by speech and memory impairment and insomnia. An EEG was performed, showing the presence of slow waves (right>left). MRI showed no significant findings. She then developed a movement disorder with stereotyped/dystonic movements, bradykinesia and tremors, quickly followed by autonomic disfunction. The CSF and serum examination showed anti-NMDAR antibodies positivity.
 Patient 2: female, 13 yo, unremarkable medical history. She presented an acute onset (one month) of mood deflection, separation anxiety, hyperarousal; she then developed confusion, insomnia, global aphasia, altered comprehension, cognitive-motor slowdown and gait instability. The EEG showed temporal-posterior slow waves (left>right); CSF examination only showed increased FLC Lambda Index; MRI was normal; PET scan showed diffuse hypometabolism of the forebrain, cerebellum and brainstem, suggestive of autoimmune encephalitis . No infectious, autoimmune, paraneoplastic, metabolic or toxic cause was found. Both patients were treated with first line immunotherapy: Methylprednisolone(IV)+ IVIG. Patient 2 showed an immediate clinical improvement so the therapy was repeated for the following 6 months with an almost complete remission of symptoms. On the contrary, Patient 1 showed an insufficient response, requiring second line immunotherapy (Rituximab). After 4 months, she presented an early relapse, treated with another cycle of IVIG. Most of her symptoms improved, although the behavioural and cognitive disorders are still not completely solved.

Conclusion:

The cases we present underline how an acute onset of psychiatric symptoms in adolescents together with suggestive EEG findings (localized or generalized slow waves) should lead to a prompt start of immunotherapy even before the confirmation either instrumental (PET scan in patient 2) or with serum/CSF tests (Anti-NMDAR antibodies positivity in patient 1) of a diagnosis of autoimmune encephalitis. In both our patients the response to first/second line immunotherapy was also, and should be in general, highly suggestive of autoimmune encephalitis. Although the similarities in onset presentation of the disease, our cases display many differences, showing the heterogeneity of the clinical, laboratory and instrumental findings and therapy response, of autoimmune encephalitis.

PF04

Characteristic electroclinical phenotype in PRRT2-related infantile epilepsy

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Objectives:

Pathogenic variants in PRRT2 have been identified as a cause of self-limiting familial infantile epilepsy. Seizures often occur in short clusters, often difficult to capture on video-EEG. We monitored the electroclinical ictal findings in two infants with PRRT2-related epilepsy.

Content:

Prolonged video-EEG recording of two infants who presented with clusters of episodes at 8 and 5 months respectively were analyzed. Family history was positive for severe migraines in the first patient, and infantile epilepsy and paroxysmal choreoathetosis in adulthood in the second patient. MRI was normal in both patients. Seizure were short, in cluster, during wakefulness, and characterized clinically by psychomotor arrest and staring, at times followed by tonic eye and head deviation, with and without upper limbs hypertonia and perioral cyanosis, and associated to temporal or occipital discharges. The 8-month old infant was initially treated with valproate with seizure recurrence, while the 5-month old patient was initially treated with phenytoin IV with rapid resolution of the cluster. Both patients responded to carbamazepine with long-lasting seizure freedom. Carbamazepine was well tolerated and no side effects were observed. An epilepsy panel revealed a pathogenic variant in the PRRT2 gene in both patients. The study of the family segregation showed that the variant was inherited from the father in the second case.

Conclusion:

These findings contribute to the characterization of the ictal electroclinical phenotype with pathognomonic clusters of focal hypomotor seizures in infants with PRRT2-related epilepsy. Early recognition of this condition could lead to early treatment with sodium channel blockers which have been shown to be safe and effective. (Videos will be presented)

PF05

Febrile infection-related epilepsy syndrome (FIRES) with a positive neurocognitive outcome: is there a possible role of treatment

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Objectives:

to describe a patient affected by febrile infection-related epilepsy syndrome (FIRES) with favorable neurocognitive outcome, probably associated to well-timed pharmacological treatment.

Content:

FIRES is a subtype of new-onset refractory status epilepticus (SE) of unknown etiology, with a history of a febrile infection occurring between 24 hours and two weeks before seizure onset. The clinical outcome is usually poor, with up to 10% of cases ending to death and 50% of survivors having intellectual disability. Despite the etiopathogenesis is unknown, it seems to be determinant the role of some interleukins and related receptor antagonists. We report the case of a previously healthy girl, with seizures onset occurring at the age of 10 years and 2 months, four days after a simple febrile infection. The focal onset seizures became highly recurrent and evolved rapidly into super-refractory epilepticus status (SRSE). During SRSE, EEG showed diffuse slow activity with delta-brushes-like activity and multifocal ictal discharges. On the first day, brain MRI was performed and a reversible lesion of the splenium of the corpus callosum was observed; on days 8, 22 and 46, hyperintensity (T2-FLAIR) of the hippocampus and claustrum was detected. Antiseizure medicaments (levetiracetam, phenobarbital, cannabidiol, lacosamide, phenytoin) and anaesthetic drugs (propofol, ketamine, dexmedetomidine, fentanyl) were administered without efficacy. High levels of IL-1, IL-2 and IL-6 were detected by CSF cytokine assay. On the twelfth day, ketogenic diet and anakinra (dose of 10mg/kg) were administered with a significant electroclinical improvement and a resolution of SRSE, lasting 18 days. To date, six months after seizure onset, neurological examination was normal, focal onset seizures persist with weekly frequency. EEG showed background alpha rhythm and multifocal paroxysmal abnormalities. On the third month, a cognitive assessment (WISC IV) was administered, and it showed a normal cognitive profile, with a strength in processing speed.

Conclusion:

FIRES is usually associated with a severe prognosis, drug-resistant epilepsy, and cognitive impairment. This case showed a good neurocognitive outcome probably related to well-timed start of high-dose immunomodulatory therapy and a ketogenic diet. As already reported in the literature, our report suggests the possible determinant role of some interleukins and related receptor antagonists in the pathogenesis of FIRES.