ABSTRACTS

RÉSUMÉS

O1

A SUCCESSFUL CASE OF TOTAL CALLOSOTOMY FOR INTRACTABLE SEIZURES IN CONGENITAL BILATERAL PERISYLVIAN SYNDROME

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Introduction: It is well known that children with cortical dysplasia often accompany intractable seizures. But the mechanism to make the seizures intractable is sometimes not clear. We present here a case which suggests one of these mechanisms.

Materials and Methods: The subject was a girl of 18 years old diagnosed by congenital bilateral perisylvian syndrome (CBPS) from MRI findings. From the age of 8 years, she began to show seizures with elevation of arms and head nodding, or sudden drop attacks on the ground. Her seizures rapidly became worsen and she was risked to be injured every day. At the age of 14 years, she received total callosotomy. Before the operation, we evaluate her state by EEG, 18FDG-PET, interictal and ictal 93mTC-SECT.

Results: The interictal PET and SPECT showed bilateral hot regions corresponding to dysplastic regions. EEG showed diffuse polispikes and/or spike and waves. SICOM subtraction Ictal SPECT Co-registered to MRI images showed active regions in the right perisylvian cortex and cerebellar vermis. After the operation, even if her dysplastic regions were conserved bilaterally, not only her seizures but paroxysmal discharges in EEG completely disappeared.

Discussions:
1) Total callosotomy is a good indication for intractable seizures in CBPS.
2) This result suggests that the seizures in CBPS are produced and enhanced to the intractable level by alternative stimulation of paroxysmal discharges from one hemisphere to another through the interhemispheric connection fibers.
3) SICOM images suggest that the cerebellar vermis has a role to mediate drop attacks.

O2

CASK RELATED-DISORDERS: CLINICAL, ELECTROENCEPHALOGRAPHIC AND NEURORADIOLOGICAL DESCRIPTION OF 4 GENETICALLY CONFIRMED CASES

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Introduction: CASK mutations (Xp11.4) were first identified in female patients with cognitive impairment and microcephaly with pontine and cerebellar hypoplasia (MICPCH). CASK encodes a Calcium/calmodulin-dependent Serine protein Kinase, involved in synaptic interaction, protein trafficking and regulation of gene expression during neural development. Alterations in this gene are therefore associated with many different disorders: X-Linked Mental retardation (XLMR), Optic Atrophy and Brainstem and Cerebellar Hypoplasia, X-linked Intellectual Disability with/without nystagmus, FG syndrome, epileptic encephalopathy and, very recently, with Autism Spectrum Disorders. Loss of function CASK mutations cause severe phenotype, while missense mutation seems to produce milder phenotypes. Deletions and intragenic mutations are associated with MICPCH syndrome more commonly than duplications.
Few studies describe the characteristics of epilepsy in patients with CASK mutations. In this report we present 4 genetically confirmed patients with diverse genetic and clinical phenotypes.

Methods: CASK gene screening using Array-CGH and sequencing of the coding region showed a de-novo mutation in 4 patients (4 F, age range 17-2,8 years) presenting different clinical and electroclinical phenotypes. Clinical and neuroradiological data have been collected and EEG documentation has been reviewed.

Results: all 4 patients presented different de-novo CASK mutations (two deletions, two puntiform mutations). Neuroradiological pattern was typical for CASK mutations spectrum, but two patients had mild phenotypes with/without epilepsy associated with structured EEG, while the others had a drug- resistant epileptic encephalopathy.

Conclusions: CASK-related disorders compose a complex phenotypical spectrum. Epilepsy and epileptic encephalopathies may be the most important clinical presentations, also with atypical features. Future studies are necessary for a genotype-phenotype correlation.

O3

DIAGNOSTIC EXOME SEQUENCING IN PATIENTS WITH EPILEPSY

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Diagnostic exome sequencing is becoming a useful tool in the diagnosis in patients with epilepsy. Large series of patients have shown diagnosis rates up to 30% in selected patients.
We describe the results of exome sequencing performed in a hundred patients with epilepsy meeting at least one of the following criteria:
(1) benign epileptic (familiar) syndromes in newborns and infants;
(2) epileptic encephalopathies in newborns and infants;
(3) seizures related to fever;
(4) absence epilepsy with early onset or with autosomal dominant inheritance pattern or associated to non-epileptic paroxysmal disorders;
(5) epilepsy with myoclonic-atonic seizures;
(6) epilepsy with continuous spike-waves during sleep;
(7) epilepsy related to malformations of cortical development;
(8) not well classified epilepsies associated to intellectual disability.
We present the diagnostic yield of exome sequencing in our series of patients and discuss the contribution to the management of these patients.

In conclusion, exome sequencing performed in selected patients is a useful tool in clinic practice influencing diagnostic and therapeutic decisions.

O4

EARLY EPILEPSY SURGERY IN A PATIENT WITH INFANTILE SPASMS AND FOCAL SEIZURES, DUE TO FOCAL CORTICAL DYSPLASIA, AND TSC2 GENE MUTATION: CONSIDERATIONS ABOUT THE IMPACT OF GENE MUTATION ON THE CORRECT SURGICAL TIMING IN THE PRESURGICAL EVALUTATION

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Introduction: A goal of epilepsy surgery in children is the early approach to avoid the negative impact of the epilepsy on the brain development. More complex and still under study is the management of the surgery for gene-correlate epilepsy.

Methods: We describe a case of Infantile Spasms (IS) and focal seizures (FS), associated with focal cortical dysplasia (FCD), and TSC2 gene mutation. Our aim is to discuss 1) the correct surgical timing, 2) the impact of the genetic analysis on the surgical management of patients with focal epilepsy.

Results: Many per day IS and FS began at age 22 days, after normal pregnancy/delivery. EEG showed a epileptogenic zone over the right fronto-temporal region. MRI revealed a FCD over the right frontal-operculo-insular region. Rapidly a drug-resistant epilepsy and a developmental delay emerged. Genetic analysis showed a TSC2 gene mutation. At 11 months a surgical tailored resection was done, with seizures freedom. The pathological study confirmed a FCD type IIa. The patient is now a healthy 2 years old child.

Conclusions: In patients with IS and FS showing electro-clinical and MRI concordance, the surgical resection should be performed as soon as is possible, especially before the age of 1 year, avoiding the negative impact on the dynamic development of the brain networks. The surgical decision should not be influenced by the genetic result when a clear anatomo-electro-clinical concordance exists, also if it concerns the potentially «dynamic» STC2 mutation.

O5

EARLY SEIZURE ONSET IN TSC: PROBING FOR PROGNOSTIC MARKERS

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INTRODUCTION: Tuberous Sclerosis Complex (TSC) may be considered a genetic developmental and epileptic encephalopathy (Scheffer er al. 2017), according to the fundamental contribution of both genetic factors and epileptic activity. The aim of our study is to verify whether strict monitoring of EEG activity and clinical observation before seizure onset may give prognostic clues to developmental outcome in TSC children.

METHODS: Since the perinatal suspicion of TSC due to ultrasound detection of cardiac rhabdomyomas, 6 babies (4 M and 2 F), were followed with EEG monitorings and neurological evaluations every 2-4 months, up to 2 years. Patients underwent a complete clinical, neuroimaging, genetic and developmental assessment as recommended for TSC.

RESULTS: Four of the babies developed epilepsy: epileptic spasms were the first seizures in 3, one started with focal seizures. Cognitive development was normal in the children with no epilepsy, but also in two children in which spasms were controlled by vigabatrin and no other seizure types occurred. The two children with drug-resistant, multiple type seizures developed intellectual disability and autistic features. All children except one (who did not develop epilepsy) carried a TSC2 mutation. At brain MRI multiple cortical and subcortical tubers, and subependymal nodules were evident in all the patients.

DISCUSSION: In TSC, seizure onset in the first year of life is recognized to negatively contribute in worsening the final outcome. In our limited sample of children, the major contribution to neurodevelopment seems not only linked to seizure onset but rather to the opportunity of their prompt control.

O6

GRIN1-RELATED EARLY ONSET ENCEPHALOPATHY, A DISTINCT NMDA RECEPTOR DYSFUNCTION

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Introduction: pathogenic variants in GRIN1, which encodes the GluN1 subunit of the NMDA receptor, have been identified in patients with non syndromic intellectual disability but also in early onset epileptic encepahalopathy. We describe the phenotypic spectrum of 3 patients with de novo mutations in GRIN1, all diagnosed by NGS analysis (clinical exome) highlighting some clinical features to suspect the disorder.

Case reports:

Case 1. Baby girl who presented with episodes of four limbs hypertonia and abnormal ocular movements since 30 hours of life together with hypokinesia, and dystonic postures. At 3 months, onset of infantile spasms and tonic seizures refractory to antiepileptic drugs. At 9 months, no eye tracking nor visual attention, axial hypotonia without head control, limbs spasticity, and superior eye gaze deviation resembling oculogyric crisis. She deceased at 10 month in the context of respiratory insufficiency.

Case 2. 23 months baby girl with severe development delay, axial hypotonia, no visual contact/attention, hyperkinetic movements and epilepsy onset at 5 months with good seizure control with VPA. Episodes of superior eye gaze deviation resembling oculogyric crisis that improved with age.

Case 3. 19 years old girl with severe intellectual disability, axial hipotonia and 4 limbs spasticity, refractory epilepsy since 12 months of age, stereotyped movements, and ASD with severe behavior problems.
Video-EEG: multifocal paroxysmal activity with slow background activity. Brain MRI: asymmetrical ventriculomegaly (case 1) and cortical atrophy. Metabolic screening including NT in CSF: normal. A three different De Novo missense variants in GRIN1 were found in a highly conserved domain of the protein and the bioinformatics predictive effect of the variants were deleterious. Functional analysis is in process.

Conclusions: although a comprehensive phenotypic spectrum of GRIN1 pathogenic variants remains to be determined, key features of the disorder seem to be infantile-onset seizures with hyperkinetic and stereotyped movements, no visual contact and occasional abnormal eye movements resembling oculogyric crisis.

O7

LONG TERM FOLLOW-UP IN TWO FAMILIES WITH ADENYLOSUCCINATE LYASE (ADSL) DEFICIENCY AND GENOTYPE-PHENOTYPE CORRELATIONS THROUGH A REVISION OF LITERATURE

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Study objectives Adenylosuccinate Lyase (ADSL) Deficiency is a rare autosomal recessive disorder of purine metabolism resulting in a wide spectrum of disease, from a mild form with intellectual disability and autistic features to fatal form with neonatal onset.

Methods We describe the cases of two brothers and two siblings, who developed an early onset encephalopathy with epilepsy, with different severity of the disease and outcome in the two families. We performed genetic analysis and we reviewed the literature in order to find genotype-phenotype associations.

Results Both the two brothers and two siblings displayed psychomotor regression followed by epilepsy. The two brothers displayed a drug resistant epilepsy with several electrical and electroclinical status epilepticus together with a progressive pyramidal and extrapyramidal syndrome, autistic features, visual and severe cognitive impairment. In the other two siblings a self-limiting epilepsy with a less severe encephalopathy were identified. In all of them MRI showed progressive cerebral atrophy and white matter abnormalities. In the two brothers neurophysiological evaluations (Electroencephalograms, visual evoked potentials, electroretinograms) showed progressive deterioration of signals, while in the two siblings EEG showed only epileptiform discharges.
Genetic analysis revealed different omozygotic mutations on ADSL gene: c.1277G>A, p.R426H in the first family and c.1288G>A, p.D430Asn in the siblings. Reviewing the literature, we have found genotype-phenotype associations in ours and others mutations.

Conclusion We will discuss different clinical, EEG and neuroradiological presentation of the disease and their evolution during time, through a long-term follow-up up. We will define previously unreported genotype-phenotype correlations and therapeutic options specific for ADSL deficiency.

O8

THERAPEUTIC CANNABINOIDS IN PAEDIATRIC NEUROLOGICAL DISEASES: EXPERIENCE FROM A TERTIARY REFERRAL CENTER

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Aim of the study: to verify safety and efficacy of cannabinoids used in add-on to treat seizures, spasticity and dystonia in children and young adults.

Subjects, methods: 20 patients (11 females, 9 males; age range 2.5 - 23.2 years) with epileptic encephalopathy or symptomatic epilepsy were studied. Spasticity and dystonia were present in 60% of patients. Eleven out of 20 subjects received cannabinoids with different products and dosages and were studied retrospectively. From April 2017 eleven patients started a prospective open trial with FM2 (inflorescence from italian cannabis with CBD 7,5-12% and THC 5-8%). Patients were treated with a mean value of CBD of 1.16 ± 0.46 SD mg/kg/day and THC 0.75 ± 0.31 SD, mean follow-up was of 2.6 months.

Results: among our 20 patients, 6/20 stopped the treatment for adverse events or difficulties of administration. Adverse events were detected in 14/20. Tolerability was after all good since all these events were mild or transitory. We compared seizures frequency, EEG, spasticity and dystonia before and after cannabinoids administration. In the whole group, we find that higher doses of CBD correlated to improvement of dystonia, while higher doses of THC brought to a lower antiepileptic efficacy. Analysing prospective data, we found a reduction >50% in seizure frequency and an improvement in spasticity at MAS Scale in 60% of patients. A reduction in dystonic BFM level was detected in 40%.

Conclusions: these preliminary results showed good safety and possible efficacy of cannabinoids in children with epileptic encephalopathy, dystonia and spasticity.

O9

ASSESSMENT OF ADHD IN A COHORT OF CHILDREN AND ADOLESCENTS WITH EPILEPSY

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BACKGROUND: Attention deficit hyperactivity disorder (ADHD) is a common neuropsychiatric comorbidity associated with epilepsy. Aim of the study is to assess the prevalence of ADHD in our clinical cohort of children and adolescent with epilepsy and to identify possible clinical or demographic risk factors.

METHOD: We included 55 patients (58% M and 42 % F), aged 6-17 (mean age 11.4 +/- 3.4 years), with diagnosis of epilepsy and no intellectual disability (QIT&gt,70). We retrospectively chart-reviewed the clinical information about epilepsy and EEGs and screened ADHD symptoms with questionnaires (CBCL, CPRS-R e CTRS-R, SNAP-IV). The patients at risk for ADHD received a formal clinical and neuropsychological assessment.

RESULTS: The prevalence of ADHD in our cohort is 25.5% (14/55), 57.1% males and 42.9% females. The subtypes of ADHD are 71.4% ADHD-Combined (C) and 28.6% ADHD-Inattentive (I). Mean age at ADHD diagnosis is 9.21 +/- 2.15 years. The most common epilepsy type is idiopathic generalized epilepsy (IGE) (52.7%), followed by self-limited focal epilepsy (SLFE) (21.8%). The majority of the patients are on antiepileptic treatment: 56.4% monotherapy (mostly valproate) and 9.1% combination therapy.

CONCLUSION: The prevalence of ADHD in our cohort of children and adolescents with epilepsy is high (25.5%) and distributes almost equally in males and females, differently from children without epilepsy in which there is a male predominance. SLFE is associated to ADHD-C subtype, instead ADHD-I subtype is more commonly seen in IGE. The results of our study indicate that screening for ADHD is highly recommended in children with epilepsy.

O10

AUTOMATIC IMITATION IN YOUNG PATIENTS WITH GILLES DE LA TOURETTE SYNDROME: A CASE CONTROL STUDY

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Introduction
Echopraxia, a complex tic involving the imitation of other people's actions, is a repetitive behaviour commonly reported in patients with Gilles de la Tourette syndrome (GTS). Little is known about the neurodevelopmental trajectory leading to the development of echopraxia in patients with GTS. The present study assessed the development of automatic imitation inhibition skills in patients with GTS from childhood to adolescence.

Methods
We explored automatic imitation in a group of 17 young patients with GTS and a control group of 15 typically developing children, aged between 6 and 16 years. According to the study protocol, following a standardised clinical interview participants were asked to respond by imitation, both in a congruent and incongruent way, to a biological visual stimulus (i.e., finger movement).
Proportion of correct responses and average reaction times for the correct responses were assessed independently as task performance measures.

Results
Patients with GTS exhibited faster reaction times and a significantly greater number of errors than typically developing children, indicating automatic imitation tendencies.

Conclusions
Our findings raise the possibility of an overactive orless suppressedmirror neuron system in GTS than healthy controls, and prompt further studies to confirm this hypothesis.

O11

CEREBRAL VISUAL IMPAIRMENTS AND AUTISM SPECTRUM DISORDER

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Cerebral visual impairment (CVI) relates to injury, congenital anomaly or malfunction of the visual pathways or visual centres in the brain. As for many neurodevelopmental disorders, CVI is not a single diagnosis, it is an umbrella term for all types of visual impairment due to brain injury, anomaly or dysfunction. Although still largely unrecognised by the clinical and research communities, cerebral visual impairment (CVI) has become the primary cause of visual impairment and blindness in children in industrialized countries.Vision is used from birth to acquire new skills in an array of fields, to understand the surrounding world and to enable appropriate action. For this reason, CVI is a significant risk factor in cognitive, motor, and social development disorders. The detrimental effects of CVI are more severe when the deficit occurs early in life. Correspondingly, patients with autistic spectrum disorders (ASD) also present visual deficits with a greater occurrence than typical subjects. In order to investigate the potential link between visual dysfuntion in ASD subjects and in patients with CVI, we submitted control participants (n=12), Children with CVI (n=10) and children with ASD (n=9) to a battery of visual tests, autistic quotient and a computerized task of emotions categorization. Four emotions were presented in different spatial frequencies (local vs global processing) during 100ms. ASD and CVI subjects show very similar performance in the neurovisual examination as well as in the emotions categorization task. In addition, we found a significant correlation between visual dysfunction and the emotion processing impairment.

O12

CORPUS CALLOSUM AGENESISAND INTERHEMISPHERICCYSTS: EPILEPTIC EVALUATION AND LONG-TERM OUTCOME IN 30 CHILDREN

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Objective: to describe a cohort of patients with CCAg and Interhemispheric Cysts (IC).

Design/Methods: we selected 30 patients with CCAg (partial or complete) and IC from our imaging databases at Gaslini Children Hospital (Genova) and Child Health and Human Development Research Institute (Montreal) from January 2005 to December 2017. Inclusion criteria were presence of all clinical, radiological and EEG data. Patients with diagnosis ofAicardi Syndrome were excluded. Presence of polymicrogyria (PMG) or nodular heterotopia (NH) was recorded. Data on perinatal history, other associated malformations, neurological examination, IQ, genetic tests, EEG, age of onset of seizure (if present) with drug responsivity (DR) were collected.

Results: Mean age at follow-up was 10,4 years +/-7,2 sds. CCAg was complete in 15/30 cases and partial in the remaining 15 cases. PMG was present in 16/30 and NH in 11/30. Epilepsy was detected in 9/30 patients, with DR in all cases. In these 30 patients, male sex was more represented (21/30) and no major neurological defects were found. IQ was borderline in 3/30 cases and mild intellectual disability was found in 2. CGH-Array was performed in 23/30, revealing variants of unknown significance in 3 cases.

Conclusions: CCAg associated with IC other than Aicardi Syndrome may be associated with a good outcome: occurrence of epilepsy is rare and usually with DR. Further investigations on larger populations are awaited to clarify the etiology, eventual genetic background and long-term outcome of this interesting milder clinical phenotype.

O13

A NEW NEURODEGENERATIVE DISEASE OF CHILDHOOD

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Background: A new neurodegenerative disease of early childhood was recently identified in seven patients with motor and cognitive regression carrying a e novo heterozygous c.628G>A (p.Glu210Lys) UBTF variant This mutation modifies the initial steps of ribosomal DNA transcription necessary for ribosomal biogenesis1. We found the same mutation by WES in a boy with a similar phenotype in whom all previous etiologic searches were negative.

Case report: This boy had normal developmental milestones until 2 yo. Then, mild speech and language difficulties and unsteady gait were described. At 5 yo he had moderate global developmental delay and ataxia. He subsequently presented a slowly progressive behavioural, cognitive and motor regression with episodes of subacute deterioration, possibly triggered by febrile illnesses. Concurrently he developed intermittent non-progressive myoclonus without EEG correlate. At 11 yo he is non-verbal, severely intellectual disabled and unable to walk alone. Physical examination reveals ataxia and mild dystonic movements. He is normocephalic and no sensory or peripheral nerve impairment were documented.

Brain MRIs showed progressive cortico-subcortical atrophy and diffuse T2 whitematter hyperintensities but preserved cerebellum. EEGs revealed generalized spikewaves with normal background activity; pseudo-periodic delta waves were observed intermittently between 7 and 9 yo. Extensive workup for metabolic, infectious and inflammatory disorders, CGH array and genetic panel were negative.

Conclusion: This case is, to our knowledge, the first reported since Edvardson et al's publication in August 2017. It supports the phenotype-genotype correlation and brings new insights into the clinical features of this disease that unveils new mechanisms of neurodegeneration.

O14

ANALYSE DE LA BIOPSIE DE PEAU DANS LES LIPOFUSCINOSES CÉROÏDES

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Introduction : nous avons procédé à une étude retrospective de la correlation entre les données morphologiques et génétiques des biopsies de peaux analysées positives pour le diagnostic de CLF dans notre laboratoire durant les 15 dernières années.

Résultats : nous avons retrouvé 95 biopsies porteuses soit de CVB, soit de FP, soit de GRODs, ces lésions étant isolées ou en association.

Les lésions les plus fréquemment retrouvées sont les CVB isolées ou en association avec des FPs (plus de 50%) et elles sont associées à des mutations respectivement des gènes CLN2 et CLN7. Les gènes les plus frequemment impliqués dans notre cohorte sont à égalité les CLN2, 6 et 7.

Enfin, ce sont les lésions de type CVB+FP pour lesquelles la probabilité de mettre en évidence une mutation CLN est la plus élevée : a contrario, la mise en évidence de FPs et de GRODs est pour l'instant peu suivie de diagnostic génétique de CLN.

Conclusion : notre étude montre l'indispensable complémentarité entre l'abord génétique et l'abord morphologique du diagnostic des CLN en termes de résultats mais également d'orientation des analyses génétiques.

SKIN BIOPSY IN CEROIDELIPOFUSHINOSIS

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Introduction: we present a retrospective study of the skin biopsies analyzed in our laboratory during the past15 years. We compared ultrastructural and genetic data for the biopsies displaying positive CLN features.

Results: we found 95 positive skin biopsies i.e. displaying either curvilinear bodies (CBV), fingerprints (FP) or GRODS.
CVB represented the prominent population (> 50%), isolated or in association with FP and occurred respectively in CLN2 and CLN7 mutations.
Conversely, CLN2, CLN6 and CLN7 mutations represented the most frequent mutations in our population.
The CBV+FP lesions are the ones with the higher probability of having a CLN genetic definition, while Fps and GRODs remained poorly genetically defined.

Conclusion: our study highlights the essential complementarity between the morphological and the genetic approach for the CLN diagnosis elaboration, in terms of results but also the orientation of genetic analyses.

O15

NEUROTRANSMITTER DEPLETION IN EARLY EPILEPTIC ENCEPHALOPATHIES AND POSSIBLE THERAPEUTIC OPTIONS

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The role of monoamines in epilepsy is not clearly reported in the literature. Seizures are associated with release of catecholamines when the CSF is analyzed in a less than 2 hour period after the epileptic event. However no detailed studies regarding intercritical alterations have been described. Clinical data and levels of neurotransmitters (NT, biogenic amines) in cerebrospinal fluid (CSF) of 90 patients with early epileptic encephalopathies (EE) followed in HSJD, Barcelona, were recruited. Data about the epileptic syndrome type and other neurological features, EEG, genetic studies, brain MRI and extensive metabolic screening were collected The series was composed by 51 females and 39 males with a median age of 1.37 years at the moment of lumbar puncture and 0.52 years at the epilepsy onset. 31 patients had abnormal levels of biogenic amines (34,4 %). 16 had isolated alteration of 5-HIAA (serotonin metabolite) and 10 abnormal isolated HVA levels (dopamine metabolite), 5 patients had a combined HVA+5-HIAA decrease. 25 patients had a positive genetic diagnosis. Onset age was the only factor related to higher probability of NT depletion. So far only 4 patients with low CSF NT levels have been treated (one with 5-hidroxytriptophan and 3 with combined L-dopa+carbidopa and 5-hydroxytriptophan). All of them showed a sustained reduction of seizures (very striking in two patients and moderate in the other two) and improvement in other neurodevelopmental skills. Although this is an ongoing study and requires further analysis, biogenic amines seem to be importantly affected in EE, in particular in very young children. Studies about therapeutic replacement in long series of patients are badly needed to establish formal treatment recommendations, but these preliminary results are promising.

O16

GLUT1-DS IN A GIRL WITH TRANSITORY ABNORMAL EYE MOVEMENTS AND SEIZURES RESPONDING TO CARBAMAZEPINE

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Introduction: diagnosing GLUT1 deficiency syndrome (GLUT1-DS) is sometimes challenging because of its broad clinical spectrum. The diagnosis may be delayed when the first manifestations are considered as less typical for the disease. It is usually assumed, for instance, that seizures will be resistant to conventional antiepileptic drugs. Other clinical manifestations, such as early-onset abnormal eye movements, are probably underrecognized as a suggestive feature.

Case report/Methods: we report the findings of a baby who presented at 2 months with paroxysmal abnormal eye movements, that progressively disappeared and were thought to be related to immaturity of the optic pathways. These were followed a few months later by the appearance of myoclonic, tonic-clonic, and tonic seizures as well as absences. Seizures rapidly and fully responded to low doses of carbamazepine. GLUT1-DS was diagnosed genetically at two years, after global developmental delay, ataxia, as well as short dystonic left hand movements had emerged. Molecular analysis identified a de novo heterozygous deletion -c.1033_1042del, p.(Ala345Profs*4)- on SLC2A1. Hypoglycorrhachia 1.5mmol/l was present. A ketogenic diet was started.

Discussion: a high level of suspicion is needed to diagnose GLUT1-DS. Early abnormal eye movements should be recognized as suggestive for the disease, even in the case of progressive remission. Our case also illustrates the fact that in GLUT-1 DS patients, seizures may respond favorably to classic AEDs. This should by no means be considered as exclusive for the diagnosis.

O17

NEUROLPATHOLOGICAL EFFECTS OF ENZYME REPLACEMENT THERAPY IN GAUCHER TYPE 3 PATIENTS : REPORT OF TWO CASES

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Introduction: gaucher Disease (GD) is the commonest lysosomal storage disorder leading to systemic and neurological symptoms due to glycosylceramide accumulation in viscera and central nervous system. GD is also one of the rare lysosomal diseases for which enzyme replacement therapy is available. Three distinct phenotypes exist : the non-neuronopathic type 1, and two neurononopathic, acute type 2 and chronic type 3. Enzyme replacement therapy had change life expectancy in the type 1 GD . Treatment is ineffective on type 2. In type 3, well-being and partial neurological improvement have been reported. Pathological reports of treated patients are sparse ; none concern type 3 GD. Here we report the first neuropathological data of two GD type 3 treated patients.

Results : Both patients were boys for which GD Type 3 was diagnosed respectively at 2 years and 9 months . For both, enzyme infusions started one year later till they both died suddenly (at 7 and 19 years).
Visceral autopsy was done only for patient 2 and concluded to a pulmonary cause of death related to massive lung infiltration by Gaucher cells (GC) .
Neuropathological study was done for both patients and revealed similar features : discrete neuronal loss, perivascular cuffing and intraneuronal storage. Intraneuronal storage was not associated with cytoplasmic distension; as in GC, it was PAS-positive and at the ultrastructural level corresponded to tubulo-helicoidal structures.

Discussion: comparing our neuropathological data with those of untreated type 3 GDs , therapy seems partially effective on the CG perivascular accumulation and intracortical neuronal depletion. By constrast, in our cases, intratraneuronal storage was significantly accentuated. From a physiopathological point of view, these features could be related to an indirect extracerebral effect of the enzyme therapy (attenuation of the perivascular GC cuffing).

Conclusion: here we provide data that argue for a partial efficiency of enzyme infusions on neuropathological symptoms in a type III Gaucher disease.

O18

HYDROCEPHALUS IN CHILDREN: ABOUT 75 CASES

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Introduction: hydrocephalus is a common problem, heterogeneous in nature and complex in pathogenesis. It can be the result of an extrinsic event acting upon a structurally normal brain or can also occur in the setting of an identifiable clinical or molecular syndrome, or can be purely idiopathic.

Objectives: to study the epidemiological, clinical, etiological and therapeutic profile of the child's hydrocephalic diseases in Tunisian pediatric department . Methods: we retrospectively review the data of children hospitalized, in Sahloul pediatric Unit (Sousse, Tunisia), with the diagnosis of hydrocephalus during the period from 2007-2017.

Results: during the last ten years, 75 cases were reviewed, 38 boys and 37 girls, aged between 1 day and 13 years old. The prenatal diagnosis was performed into 12 children (16%). Acute fetal distress was reported in 25 cases (33%). The first clinical signs observed are macrocranium (37%) and seizures (14,6%). The average diagnosis time was one month. The clinical features varies according to age and etiology, dominated by hypotonia (46,6%), macrocrania (37%), bulging anterior fontanel (29,3%), seizures (25,3%), psychomotor retardation and look at sunset (each 22,6%). The diagnosis was confirmed by brain CT or MRI, showing a triventricular hydrocephalus in 43 cases (57%) and quadriventricular in 32 cases (43%). The predominant etiology is Dandy Walker syndrome (24%), followed by meningitis (22,6%), congenital aqueduct stenosis (14,6%), neural tube defects and posterior fossa tumor (10,6% each), and agenesis of corpus callosum (9%). A ventriculoperitoneal shunt was performed in 51 children and ventriculocisternostomy in 3 others, with an average delay of 2.2 months. The evolution was favorable in 29 cases (38,6%) with a clear improvement of the symptomatology. The main complications encountered are meningitis (22,6%), valve obstruction (14,6%), valve migration (8%), and over drainage (5%). Forty patients died. 37 children became epileptic (49%).

Conclusion: hydrocephalus is a polymorphic disease, as much in its clinical presentation, etiological as its evolution. Although diversions have saved countless children, they have also created recurrent complications that plague their lives. In many infants with hydrocephalus, physical and radiological findings guide the genetic workup.

O19

L'ATAXIE CONGÉNITALE PEUT RÉVÉLER UNE MALADIE DE LA DÉGLYCOSYLATION LIÉE À NGLY1

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Parmi les patients présentant une ataxie congénitale adressés pour exploration moléculaire, nous avons identifié des mutations homozygotes du gène NGLY1 chez 2 patientes. Cette nouvelle entité, CDDG ou syndrome d'alacrimie-choréoathétose-hépatopathie, est une pathologie de la déglycosylation caractérisée par un début précoce, une hypotonie, un retard de développement, des mouvements anormaux et une hypo ou alacrimie, souvent associés à une microcéphalie, des crises épileptiques, des mouvements oculaires anormaux, une dystrophie rétinienne, une dysfonction hépatique et une hypocholestérolémie. L'IRM cérébrale retrouve parfois une dilatation ventriculaire.

C'est vers l'âge de 1 an que les parents de ces 2 patientes se sont inquiétés devant un retard des acquisitions motrices avec hypotonie et ataxie du chef et du tronc. Elles ont acquis la marche à 2,5 et 3 ans. Une déficience mentale modérée/ sévère est devenue évidente, associée à un tremblement, une dysarthrie, des dyskinésies, un trouble oculomoteur et une neuropathie périphérique. Une hypotrophie staturopondérale s'est installée. Malgré une hyperhémie conjonctivale chronique le diagnostic d'alacrymie a été tardif. Chez la patiente la plus âgée des troubles psychiatriques sont survenus à 17 ans. Aucune de ces patientes n'a convulsé. Les IRM ont retrouvé une dilatation ventriculaire. L'ERG était altéré chez l'une. Une hypocholestérolémie était présente chez les deux patientes, mais leur bilan hépatique était normal.

Ces 2 patientes ont présenté initialement une ataxie congénitale, au cours de l'évolution leur symptomatologie s'est enrichie avec l'apparition de troubles psychiatriques chez la plus âgée.

Ces observations élargissent le spectre phénotypique de cette maladie de la déglycosylation.

O20

SEPN1-RELATED MYOPATHY: DESCRIPTION OF TWO NEW PATIENTS

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SEPN1-related myopathy (SEPN1-RM) is characterized by predominant axial muscle weakness, early scoliosis, rigid spine and severe respiratory insufficiency. Mutations of SEPN1 are associated with autosomal recessive rigid spine muscular dystrophy 1 (RSMD1) [MIM# 602771], the classical form of multiminicore disease (MmD), desmin-related myopathy with Mallory body-like inclusions and congenital fiber-type disproportion. SEPN1 located on chromosome 1p36, code for the selenoprotein N1, an endoplasmatic reticulum glycoprotein and is expressed in numerous tissues, including skeletal muscle.

We reported the clinical, histopathological, radiological (MRI), and genetic screening of French (Mayotte) brothers from non-consanguineous parents, affected with RSMD1. Sanger sequencing revealed one novel homozygous mutation c.1405C&gt,T (p.469Trp) of SEPN1 which is inherited from the parents.

The first brother was born at 40 weeks of amenorrhea by caesarian section because of premature rupture of membranes. He walked at 13 months. He has a progressive restrictive lung defect. He has slight weakness in his limb girdle muscles. The muscular RMI revelated a global amyotrophy. The muscular biopsy showned the presence of multiple &quot,minicores,&quot, also describe in RYR1 mutations.

The second brother was born at term without any complication. He walked at 10 months. He presents the same phenotype as his brother but the scolosis is more severe.

This report underlines the clinical diagnostic clues of early but slow progression of respiratory involvement to suspect a SEPN1-RM and the usefulness of muscle MRI in conjunction with clinical features to achieve the diagnosis. We also expand the mutational spectrum of the SEPN1 associated RSMD1.

O21

SINE CAUSA TETRAPARESIS: A PILOT STUDY ON ITS POSSIBLE RELATIONSHIP WITH INTERFERON SIGNATURE ANALYSIS AND AICARDI GOUTIERES SYNDROME RELATED GENES ANALYSIS

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Introduction: spastic Dystonic Tetraparesis (SD-T) is cause of chronic childhood disability due to different aetiologies. Aicardi Goutieres Syndrome (AGS) is a genetic encephalopathy whose clinical manifestations may include SD-T. Interferon signature is a reliable biomarker for AGS and could be performed in sine-causa SD-T. Aims of the study are to examine a sample of sine-causa SD-T throughout interferon signature and AGS-related genes analysis to find the positive ones and to unveil which aspects of history, clinical picture and brain imaging better characterize SD-T due to interferonopathy.

Methods: out of 47 SD-T patients we selected 10 subjects with unremarkable pre-peri-postnatal history. Exclusion criteria were a clinical and neuroradiological diagnosis of cerebral palsy or metabolic disease. Our sample underwent accurate anamnestic data collection, clinical examination, brain imaging review, interferon signature and AGS-related genes analysis, if interferon signature was elevated.

Results: at clinical onset 8 patients showed developmental delay, 2 of them had psychomotor regression. 6 presented feeding failure, one had sleep disorders and another one irritability. Brain-MRI was normal in 5, with non-specific alterations in 3 and with cerebral calcifications in 2. At follow-up 3 patients presented new white-matter injuries (associated with brain calcifications in one). Interferon signature was elevated in one case, subsequent AGS-related genes analysis showed IFIH1 mutation.

Conclusions: AGS should be considered in sine-causa SD-T: 10% of our sample showed mutation in AGS-related genes. Core features of interferonopathy-related SD-T might be onset during first year of life, early psychomotor regression, brain white-matter lesions with late calcifications and elevated interferon score.

DDC1

SEEG EN… FAMILLE

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Nous présentons une famille avec 4 membres présentant une épilepsie focale : Deux membres avec épilepsie frontale, un avec épilepsie fronto-temporale et le 4ème avec des crises à début focal à début non précisé.

Il s'agit de deux enfants: une sœur (cas index) âgée de 12 ans avec début de son épilepsie à l'âge de 6 ans et présentant une épilepsie focale frontale gauche (crises diurnes et nocturnes) et son frère âgé de 16 ans avec début de son épilepsie à l'âge de 12 ans qui présente une épilepsie focale frontale droite (crises également diurnes et nocturnes). Leurs IRM (même 3T) sont normales et les deux enfants ont un développement psychomoteur normal, mais avec des difficultés scolaires, en lien à une exposition au Valproate in utéro pour la fille et une prématurité pour le garçon.

La mère des enfants âgée de 44 ans a débuté son épilepsie à l'âge de 3 ans et présente depuis une épilepsie très pharmacorésistante. Elle a eu deux opérations après exploration stéréoncéphalographique à l'âge de 36 et 40 ans et l'examen anatomopathologique a démontré une dysplasie corticale focale de type I.

Le frère de la mère (oncle des enfants) âgé de 47 ans a présenté le début de son épilepsie à 14 ans et présente des crises focales secondairement généralisées.

Nous allons présenter cette histoire familiale par ordre chronologique (au début l'histoire familiale n'était pas évidente) avec les différents diagnostics différentiels avant la mise au point du diagnostic définitif. Nous présenterons les points d'intérêt concernant ce diagnostic, les perspectives qui s'ouvrent et les implications sur la conduite à tenir et la prise en charge future de ces patients.

We present a family with 4 members with focal epilepsy: two members with frontal epilepsy, one with frontotemporal epilepsy and the fourth with focal onset seizures of unknown localization.
There are two children: a 12-year-old sister (index case) with onset of epilepsy at age 6 with left frontal focal epilepsy (daytime and night attacks) and her 16-year-old brother with onset of epilepsy at age 12 with right frontal focal epilepsy (also diurnal and nocturnal seizures). Their MRIs (even 3T ones) were normal and both children have a normal psychomotor development, but with mild academic difficulties, that may be in part due to exposure to Valproate in utero for the girl and a premature birth for the boy.
The 44-year-old mother of the children began her seizures at the age of 3 and has had a very drug-resistant epilepsy since then. She had two operations after stereo-encephalographic exploration (SEEG) at the age of 36 and 40 years and histopathological examination demonstrated a type I focal cortical dysplasia.

The 47-year-old mother's brother (uncle of the children) presented the onset of his epilepsy at age 14 and presented secondarily generalized focal onset seizures.
Genetic analysis allowed us to identify the presence of a 5-10 exons deletion of the NPRL3 gene, which belongs together with the DEPDC5 and NPRL2 genes to the GATOR1 complex, a negative regulator of the mTORC1 pathway.

DDC2

BULBAR PALSY WITH SENSORIAL IMPAIRMENT: AN AMAZING OUTCOME!!

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Childhood onset motor neuron diseases or neuronopathies are a clinically and genetically heterogeneous group of disorders, with usually limited therapeutic perspective.
We report the case of a female patient who presented at 8 years of age a progressive sensori-neural hearing loss. From the age of 12, she exhibited unsteadiness; at 14, she underwent scoliosis surgery. From 16, the patient reported progressive visual impairment. The patient was finally referred at 17 years of age. Examination disclosed global motor weakness mainly involving the upper limbs and the bulbar region related to axonal neuropathy; ophthalmological investigation confirmed optic neuropathy; cognitive skills were normal. During the following months, the motor and sensorial function rapidly deteriorated, leading the patient to be wheelchair bound with severe visual loss; ventilation and swallowing skills gradually weakened, requiring tracheotomy, mechanical ventilation and enteral nutrition via a gastrostomy.
The various diagnosis hypothesis suggested by this case, and the therapeutic strategy will be discussed. The unexpected outcome of the patient, with four years of follow-up, will be described.

P1

ABNORMAL PSYCHOMOTOR DEVELOPMENT REVEALING A HIV INFECTION IN A YOUNG BOY

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Due to preventions measures, HIV infections in infants became very much uncommon over the past decade in our countries. This is rewarding as such transmission can be responsible for several dramatic infectious disorders as well as cerebral and development disturbances. We report here the case of a 14 month-old boy sent to the pediatric neurology clinic for a developmental delay and EEG analysis. The mother reported that the boy couldn't hold a sitting position and even less a standing position. The neurological examination was pathological showing significative axial hypotonia and abnormal head lag during the pull-to-sit test and lack of movements. General physical observation revealed a very pale and grumpy boy. The abdominal palpation detected a splenomegaly around 5 centimeters under the costal edge.

Retrospective anamnesis and medical record analysis revealed that the boy was born through a vaginal birth from an HIV positive and Hepatitis C positive mother who wasn't regular taking her medication for a year. On the day of the delivery she had an undetectable viral load (HIV-PCR < 40 copies) as well as her boy was negative for HIV-PCR. No other blood samples was ever done since then.

The abdominal ultrasonography confirmed a splenomegaly measured at 8,4 cm, and showed multiples hypertrophic peri-aortic, peri-splenic and mesenteric lymph nodes. The initial blood sample showed an iron deficiency anaemia (haemoglobin (Hb) 5.6 g/dl, ferritin (Fe) 8.3 µg/L, total ironbinding capacity (TIBC) 5%), EBV VCA-IgM and IgG were positives, a positive detection of p24 Ag and anti-HIV antibodies, positive IgG Coombs's test, an increased CD3 cell count (3.819.000/ µL, a low CD4 cell count (4,2%), and a low CD4/CD8 ratio (0.09). The Serum Protein Electrophoresis (SPEP) showed a polyclonal increase of the gamma fraction.The second blood sample showed a persisting iron deficiency anaemia (haemoglobin (Hb) 5.5 g/dl, ferritin (Fe) 7.9 µg/L) but the PCR for the HIV viral load identified 1 million copies/ml. The requested EEG showed no irritative signs but diffuse slow activity. Cerebral MRI revealed diffuse cerebral atrophy. At this point, the boy and her family have been refered to the CHR-CHU HIV reference center to initiate an ARV therapy.

This case is a typical case of post-partum HIV contamination which could have happened due to a non-recommended and unsupervised breast-feeding. It also shows the importance of a regular follow-up with blood tests for children born from HIV positive mothers. For those children, the HIVPCR should be tested at birth, at fifteen days, at 1 month and at 3 months of life. Early diagnosis of HIV children promotes their immediate access to treatment with ARV therapy in order to prevent general and neurolgical complications.

P2

BACTERIAL MENINGITIS IN INFANTS AND CHILDREN: 11-YEAR REPORT IN A TUNISIAN PEDIATRIC TERTIARY UNIT

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Introduction: bacterial meningitis in children remains a serious public health problem because of its incidence and mortality.

Objectives: we conducted this study to describe the epidemiological, the bacteriological profile and the evolution of a hospital series of bacterial meningitis.

Methods: this is a retrospective and descriptive study of all cases of bacterial meningitis treated in the pediatric unit of the University Sahloul Hospital (Sousse-Tunisia) from 2006 to 2016.

Results: we identified 61 cases. The mean age of the patients was 20 months with a male predominance (sex ratio = 1.8). The main isolated organisms were Haemophilus influenzae and Neisseria meningitidis in 26.8% and 24.4% of cases respectively. The mortality rate was 8.2% with an average death delay of 6.8 days. One Sequela or more were found in 21.3% of cases.

Conclusion: bacterial meningitis is associated with a heavy burden of morbidity and mortality, hence it is necessary to strengthen the existing prevention programs.

P3

BRAIN ABSCESS IN CHILDREN: ABOUT 9 CASES

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Introduction: brain abscess (BA) is an uncommon intracranial suppurative infectious disease, especially in children. Its treatment involves surgery and prolonged antibiotics courses.

Objective: our study aimed to describe the clinical characteristics of children with BA treated in Sahloul pediatric Unit (Sousse, Tunisia) Materials and methods: This is a retrospective study conducted over a period of 5 years (2012-2017).

Results: nine cases were identified with BA. A male predominance was noted (77.7%), with an average age of 25.8 months (range 24 days and 12 years). The abscess was brutally revealed in 7 cases with headaches (7 cases), seizures and fever (6 cases), nuchal rigidity (5 cases) and altered level of consciousness (4 cases). The diagnosis was confirmed by brain MRI in all our patients. The preferred seat was temporoparietal in 5 cases. A biological inflammatory syndrome was present in 8 cases. A germ was found in 5 patients. All our patients received medical treatment associated with surgical treatment in 7 cases. The main etiology was meningitis in 6 patients, otitis in 1 patient and unknown in 2 cases. The evolution was favorable in 6 cases (66.6%) and 3 patients had epilepsy as sequelae (33.3%).

Conclusion: intracranial infections in children are serious conditions that need aggressive treatment. Successful management requires a multidimensional approach including, diagnostic imaging, antibiotic administration and surgical drainage. Advancement in surgical techniques and newer antibiotics will be needed to continue the trend of decreasing mortality and improving outcomes.

P4

CDKL5 ENCEPHALOPATHY IN MALES: FOLLOW UP IN THREE PATIENTS, NEW INSIGHT IN PHENOTYPICAL SPECTRUM AND OVERVIEW OF LITERATURE

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Aim of study: mutations in Cycline Kinase-like 5 (CDKL5) gene have been reported as related to X-linked early onset infantile epileptic encephalopathy (EIEE) in less than 30 male patients up to now in literature.

Methods: we present three follow up cases of male patients with pathogenic de novo mutations in CDKL5. Clinical and electroencephalographic data, including age at seizure onset, seizure type, interictal and ictal Video-EEG recordings, treatment schedule and effects, brain MRI and genetic characterization have been evaluated on the basis of literature data review.

Results: we will focus on core phenotypical characteristics, represented by early onset seizures, with polymorphic seizures often with a complex semiology including multiple seizure types in the same epoch (focal seizures and infantile spasms in particular, but also myoclonic seizures, tonic seizures and generalized tonic-clonic seizures), severe hypotonia, intellectual disability with extremely limited development and autistic features. But we will also focus on extra-neurological signs which are not defined as typical but have been found in our sample.

Conclusion: CDKL5 related EIEE should be suspected in any case of early onset seizures, with polymorphic characteristics and tendency to be refractory to pharmacotherapy, associated to severe delay or absence of psychomotor development, poor or absent eye contact and hand stereotypies. Severe congenital laryngeal stridor and severe GERD should be carefully investigated because they could be peculiar characteristics of such syndrome as our case reports suggest.

P5

CEREBRAL VENOUS THROMBOSIS: ABOUT 11 CASES

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Introduction: cerebral venous thrombosis (CVT) is rare in children, characterized by a wide variability of clinical presentations and modes of appearance, which often leads to delayed diagnosis. Objectives: To determine the clinical, radiological, etiological and prognosis profile of this affection in children

Materials and Methods: this is a retrospective study of 11 children with CVT over a 10-year period (2007-2017).

Results: the average age of the patients was 4.5 years [range: 45 days to 12 years]. The sex ratio was equal to 0,8. The clinical presentation was variable: seizures (5 cases), altered levels of consciousness (4 cases), headache and fever (3 cases), and intracranial hypertension and hemiplegia (2 cases). The diagnosis was suspected on CT scan in all patients, confirmed by MRI in 8 cases. An echocardiogram showed a VDDI with pulmonary valve stenosis in 1 case. The topography of the TVC was variable, interesting the superior sagittal sinus (4 cases), the lateral sinus (3 cases), sigmoid sinus (2 cases), straight and transverse sinuses (one case) and multiple thrombosis involving both the sinuses and the cerebral veins (1 case). Etiologies are multiple, dominated by infectious causes in 6 cases. The treatment was based on anticoagulants (9 cases), antibiotics (5 cases) and corticosteroids (1 case). The evolution was favorable in 6 patients with complete recovery. The sequelae were epilepsy in 2 cases and sequential hemiparesis in one patient.

Conclusion: TVC is rare in children. Infectious causes remain frequent, and occupy the first place. The etiological survey should be complete and systematic in all cases.

P6

CHARACTERISTICS OF THE CHILDREN WITH EPILEPSY FOLLOWED IN A TUNISIAN UNIVERSITY HOSPITAL

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Introduction: epilepsy is one of the most frequent neurological diseases in the pediatric population. Many epidemiological studies have been published, but with rather discordant results, because of methodological differences. In our context, epilepsy constitutes a public health problem.

Objectives: we aimed to describe the characteristics of children with epilepsy, analyze the risk factors and to assess the impact of the disease on schooling.
Methods: this was a retrospective study concerning 90 children attending the Sahloul University Hospital Center pediatric unit in Sousse, from January 2006 to December 2016. Epileptic syndromes were classified according to the criteria of International League against Epilepsy of 1989.

Results: ninety children (47 boys, 43 girls) were included. Average age was 9 years 8 months. Age of seizure onset ranged from 2 months to 14 years. Male gender predominated. Parental consanguinity and family history of epilepsy were found in 23.3 and 10% of cases, respectively. Perinatal history of hypoxic ischemic encephalopathy was reported in 41%of cases. Generalized seizures were most common (80%). Association with cerebral palsy was identified in 38.9% of cases, with mental retardation in 24.4%. The epilepsy was idiopathic for 57.5% of the children. Generalized epileptic syndromes were the most frequent (18.9%). The most common partial epileptic idiopathic syndrome was benign childhood epilepsy with centrotemporal spikes (8.9%). Schooling was perturbed in 64.4% of the school-age children. Single-drug therapy was the rule for first intention treatment (98.9%). Sodium valproate was the antiepileptic drug most widely used (82.1%). Treatment led to resolution of the seizures in 85.4% of the children.

Conclusion: preventive measures should be reinforced in our context with a considerable proportion of children presenting neonatal risk factors. Efforts should be made to improve schooling for children with epilepsy.

P7

DELAYED ONSET OF POST-RABIES VACCINATION ENCEPHALITIS: A CASE REPORT

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Introduction: acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating disease that typically occurs following a viral infection or vaccination. The incidence of ADEM following rabies vaccination has become very low since introduction of non-neural rabies vaccine and only few cases had been reported. Here we report a rare case of delayed post vaccinal ADEM.

Case Report: A 3 years old child was scratched by a healthy and vaccinated dog two weeks before his hospitalization. A week later he received three doses of rabies vaccine. Five days after the vaccine, he was hospitalized for convulsive seizure with consciousness disorder. On examination, he was febrile at 39.5, he was awake but not communicative. There was a complete right hemiplegia, hyperreflexia, and positive Babinski's sign. The cerebellar functions were normal and there was no other system involvement.
Patient's haemogram, liver enzymes, renal function tests and cerebrospinal fluid were normal.
MRI head showed spread demyelination. There was no enhancement on gadolinium. During her hospital stay he was managed with pulse methylprednisolone for 5 days and was followed by prednisolone daily for two weeks without any improvement.

Conclusion: The exceptional nature of ADEM post-rabies vaccine must not in any way call into question the obligation of vaccination in children at risk, given the gravity of rabies in our country.

P8

DEVELOPMENTAL DELAY, TREMORS AND EEG ABNORMALITIES: A CASE OF KCTD7 GENE MUTATION

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BACKGROUND: progressive myoclonic epilepsy type 3 is an epileptic encephalopathy associated with homozygous KCTD7 gene mutations. The disease starts in infancy. Patients typically show a severe epileptic disorder, associated with cognitive regression and ataxia and movement disorder. The severity of the disease is variable from one patient to another, even within the same family. Homozygous KCTD7 gene mutations have been linked also with a rare, infantile-onset of NLC subtype designated as CLN14.

CASE REPORT: we report the case of a 15 months old girl from Pakistan, daughter of consanguineous parents admitted to our ward for severe developmental delay, tremors, slow waves activity at EEG and feeding difficulties. The patient presented at Neurologic examination poor spontaneous motricity, global hypotonia and multifocal myoclonus aggravated by action and posture, tilting head. EEG showed abundant ictal and interictal epileptiform discharges. During hospitalization, the patient presented myoclonic seizures precipitated by fever.

MATHERIALS AND METODS: neuroimaging, neupshysiological exams (Electroretinogram, visual evoked potential, BAEPs, electroneurography, electromyography), genetic (Array-CGH, karyotype, FISH for 4p- deletion, Next Generation Sequencing for RETT syndrome and deletion/duplications of MECP2/MLPA genes), metabolic analysis and skin biopsy were performed.

CONCLUSION: the collection of detailed medical history of the patient, a careful physical examination, aforesaid investigations and rapid worsening of general clinical condition at follow-up evaluations drove us to differential diagnosis between a genetic form of epileptic encephalopathy and ceroidolipofuscinosis. Array-CGH showed a homozygous deletion 7q11, 21, partially involving KCTD7gene. Skin biopsy (currently undergoing) will be essential for specific diagnosis.

P9

ENCEPHALOPATHIE AIGUE NECROSANTE: À PROPOS D'UN CAS

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Introduction: l'encéphalopathie aigue nécrosante (EAN) est une maladie neurologique rare déclenchée à la suite d'une fièvre le plus souvent d'origine virale, affectant des nourrissons jusque là en bonne santé. L'EAN a été associée dans de récentes études à l'existence d'une mutation autosomique dominante du gène de la protéine RAN-binding protein 2.

Observation: NRS de sexe masculin, âgé de 4 mois, issu d'un mariage non consanguin, né par césarienne à 34SA+5j pour chorioamniotite. Apgar correct. Admis pour des crises convulsives toniques partielles droites dans un contexte fébrile.
A l'examen il était fébrile, comateux avec une rigidité périphérique.
La CAT initiale était de le mettre sous oxygène, phénobarbital et zovirax.
A la biologie: pas de SIB, calcémie et iono corrects, PL normale. PCR herpès négative.
Bilan métabolique sans anomalie.
Echo abdominale et TDM cérébrale sans anomalies.
IRM cérébrale a montré une atteinte bilatérale et symétrique des deux thalami qui sont augmentés de taille en hypersignal T2/FLAIR et hyposignal T1.

Conclusion: l'EAN est une atteinte neurologique rare mais pourvoyeuse d'une grande morbi-mortalité. Même si le tableau clinique n'est pas spécifique, les images de nécrose thalamique visibles en IRM sont très caractéristiques.

P10

EPILEPSY AND OTHER CLINICAL FEATURES IN A CHILD WITH PARTIAL DELETION OF CHROMOSOME 15 Q

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A 2-year-old child. He was delivered at term after twin pregnancy by ICSI with intrauterine growth retardation (IURG). Birth weight was 1710 g., length 43 cm and head circumference 31.5. APGAR score was 6I, 8V, 9X. No family history of malformations, epilepsy, or intellectual disability was reported. The twin is healthy. Neonatal brain ultrasound was normal.

Psychomotor delay was reported: he could sit unsupported at around 12 months of age and at 24 months he is unable to walk alone. First phonemes appeared at 24 months. The neurological examination showed severe generalized hypotonia with joint hyperlaxity, brisk symmetrical reflexes, severe psychomotor delay. Severe dorsolumbar scoliosis was evident. Dysmorphological evaluation revealed a triangular face, low-set ears, microcephalia, micrognathia. A craniospinal MRI performed at 2 years of age showed hypoplasia of the adenohypophysis associated with a minor dysmorphism of the brainstem characterized by a shorter midbrain, thinning of the periventricular white matter with enlargement of the lateral ventricles and frontal subarachnoid spaces. Molecular karyotyping (array-CGH) was performed showing partial deletion of 15 q 25.3 q 26.1 that includes 10 genes OMIN. The most important are CHD2, ACAN, PLIN1. At the age of 18 months he presented monthly tonic-clonic generalized seizures and daily absences. An electroencephalogram showed high amplitude centrotemporal spikes or sharp-and-slow wave complexes bilaterally with severe increase during the sleep. He was started on Valproic Acid and then Topiramate with partial seizures control.

P11

EPILEPSY WITH MYOCLONIC ABSENCE IN A PATIENT WITH COL4A1-RELATED DISORDER: A CASE REPORT

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Summary: the clinical spectrum of COL4A1-related disorders includes small-vessel brain disease of varying severity associated with eye defects and systemic findings. Neurological deficits may be severe, including cerebral palsy, developmental delay, intellectual disability and focal epilepsy.

Myoclonic absence is a rare generalized seizure type, usually of unknown cause. Some cases with chromosomic abnormalities have been described. We report the case of a 5-year-old girl with mutation of the gene Col4A1 who presents with refractory epilepsy since age of 18 months, a developmental delay, a microcephaly and a bilateral congenital cataract. She has two different seizure types: rare focal seizures secondarily generalized and multiple daily myoclonic absences. EEG shows

(1) interictal right occipital spikes and
(2) epileptic absences during 3-4 seconds, associated with 3 Hz generalized spike-waves and bilateral upper limbs myoclonia on deltoid EMG. Brain imagery shows signs of leucopathy with periventricular Flair T2 hypersignal.

Conclusion: until now myoclonic absences were not reported with COL4A1 mutation. Our case demonstrates the utility of genetic screening for COL4A1 mutations in young patients who have sign of leucopathy on brain imaging and epilepsy with myoclonic absences.

P12

EPILEPTIC ENCEPHALOPATHY WITH RECURRENT FOCAL STATUS EPILEPTICUS AND EPILEPSIA PARTIALIS CONTINUA IN PATIENT WITH DE NOVO DNM1L MUTATION: ELECTRO-CLINICAL FEATURES

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Child with a history of failure to thrive, sucking and swallowing disorder, speech delay. From 3 years onwards, he presented relapsing episodes of refractory motor focal status epilepticus (SE), involving the left side or the right side of the body, followed by transient epilepsia partialis continua and motor impairment.

The patient gradually developed tetraparesis. Currently (8 years) he has global development delay, aphasia, cortical visual impairment, kinesigenic dyskinesia and segmental erratic myoclonus. Other clinical features include hypothyroidism, adrenocortical insufficiency, hypogammaglobulinemia, dysautonomia.

MR images in SE demonstrated changes on diffusion-weighted imaging in the affected hemisphere. Follow up MR imaging reveals cortical and subcortical atrophy, especially of the left hemisphere.

Ictal EEG showed rhythmic high amplitude delta with superimposed spikes and polyspikes, correlated with MRI changes as well as ictal symptoms. Interictal EEG shows widespread background slowing with paroxysmal multifocal discharges. Polygraphic recordings show segmental myoclonic jerks, epileptic and non- epileptic.

Diagnostic work-up for metabolic encephalopathy included plasma and liquor lactate levels and muscle biopsy- resulted normal- and genetic testing (NGS panel tailored to mithocondrial diseases), which reveled heterozygous missense mutations in DNM1L [c.1207C&gt,T (p.R403C)].

SE was refractory to multiple therapies, requiring several epileptic drugs, steroids, intravenous immune globulin, ketogenic diet and pharmacologic coma with propofol. Movement disorder did not recover, despite high doses of benzodiazepine, baclofen, nootropil and trihexyphenidyl.

The aim of this report is to describe the electroencephalografic features to give a better contribute to the definition of the phenotype in a patient with DNM1L-related encephalopathy.

P13

GUILLAIN-BARRE SYNDROME IN CHILDREN: ABOUT 20 CASES

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Introduction: barred Guillain Syndrome (GBS) is an acute polyradiculoneuropathy that is benign but may be life-threatening or have long-term sequelae.

Materials and Methods: this is a retrospective study over a 10-year period (2007-2017). Objectives: To study the epidemiological, clinical and evolutionary profile of children with GB.

Results: the average age of diagnosis was 6 ½ years (range 13 months to 14 years), and 65% were boys. Antecedent infectious diseases were reported in 7 cases (35%). The facility is 80% acute and sub-acute in 20% of cases. All our patients had a motor deficit on admission, represented by paraplegia (46%), paraparesis (23%), tetraplegia (19.5%) and tetraparesis (11.5%). Most patients had ROT abolished (95% of cases). Sensory symptoms, mainly numbness or parasthesias were present in 35% of cases, myalgia (20%), respiratory impairment (20% of which 2 patients required mechanical ventilator support), swallowing disorders (15%) and sphincter disorders (10%). Cytoalbuminologic dissociation was present in 90% of cases. A CMV infection was found in 4 cases. EMG has been performed in all our patients and confirmed the diagnosis. Hospital stay was 18 days on average (9 to 32 days). Immunoglobulins were administered in 60% of patients at a dose of 1g/kg/day for 2 days. The evolution was marked by complete recovery in 65% of cases, and 35% of patients had sequelae, residual motor deficit (71%), attenuated ROT (57%) and attitude tremor (28%).

Conclusion: recognition of the particularities of pediatric forms of GBS makes it possible to establish an early diagnosis of this medical emergency and to optimize care.

P14

INCONTINENTIA PIGMENTI IN A NEWBORN MALE WITH KLINEFELTER SYNDROME: CLINICAL, ELECTROENCEPHALOGRAFIC AND NEUROIMAGING FINDINGS

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Incontinentia Pigmenti (IP, MIM 308300) is a rare X-linked genodermatosis that included well-defined dermatological features but also central nervous system abnormalities. Although IP is usually lethal in males, occurrences of the disease in boys have been reported, but phenotype has not been well characterized. We report on neurological, electroencephalographic (EEG) and neuroimaging findings in a male infant with IP and a 47, XXY karyotype.

The baby presented at birth with generalized vesiculo-pustular eruption and the diagnosis of IP was confirmed by skin biopsy and by IKBKG gene mutation. Chromosome analysis was consistent with the diagnosis of Klinefelter syndrome.

At 2 months of age he experienced a convulsive status epilepticus managed with endovenous phenitoin and phenobarbital (PB). MRI revealed multiple acute phase spotty high-intensity lesions on diffusion-weighted images (DWI) involving both cerebral hemispheres, compatible with multiple cerebral infarctions.

Oral PB gave seizure control for 2 months, when he developed daily clusters of seizures characterized by eye twitching and extensor spasms of one arm lasted few seconds. EEG showed background disorganization and multifocal abnormalities with focal clinical and electrographic seizures. Carbamazepine was started but seemed ineffective, and the frequency of seizures was reduced after Vigabatrin was added. In follow-up evaluation clinical picture was characterized by severe developmental delay with poor spontaneous motility, generalized hypertonia, severe visual deficit due to bilateral retinal detachment and poor feeding with difficulty swallowing. Due to the clinical variability of this rare condition, awareness of the association between IP and epilepsy will help to plan treatment for both conditions.

P15

ITPA ENCEPHALOPATHY, A UNIQUE NEURORADIOLOGY PATTERN AS A HALLMARK OF THE DISEASE

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Background: ITPA encephalopathy, described recently by Kevelam et al., is characterized by early onset encephalopathy, progressive microcephaly, seizures, variable cardiac defects and early death. It is related to recessive pathogenic variants in ITPA gene which encodes an ITPase involved in purine metabolism. We present a case of ITPAencephalopathy and highlight the importance of the MRI pattern recognition.

Case presentation: a 3 months-old male who presented, immediately after birth, with jitteriness and irritability. Third son of healthy and non-consanguineous parents. Pregnancy and delivery were uneventful. Metabolic and infectious screening were normal except for hyperproteinorrachia. At 3 months-old, severe axial hypotonia, progressive microcephaly and lack of visual contact were evidenced. Seizures onset was at 6 months, being refractory to antiepileptic drugs. Brain MRI showed a distinct pattern characterized by bilateral and symmetric high T2 signal and decreased diffusion in DWI in the posterior limb of the internal capsule, cerebellar superior peduncles and cerebral peduncles. The neuroimaging pattern lead us to suspect ITPA encephalopathy and two pathogenic variants in ITPA were found as well as severely decreased enzyme activity in fibroblasts. Parents were carriers of one of the mutations respectively. The patient died at 10 months because an epileptic decompensation in the context of a respiratory infection.

Conclusions: ITPA encephalopathy is a devastating disorder of purine metabolism without a specific metabolic biomarker. The brain MRI pattern is the hallmark of the disease. Despite not having treatment available, genetic confirmation is useful to avoid unnecessary tests, genetic counselling and advice about patient clinical outcome.

P16

LAFORA DISEASE AND DIABETES - ENLARGING CLINICAL PHENOTYPE

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Introduction: Lafora disease (LD) is rare, fatal, autosomal recessive progressive myoclonic epilepsy which results from carbohydrate accumulations in many tissues. We report a case of LD in a 14-year old adolescent associating aggravating neurological manifestations and non auto-immune diabetes.

Case report: A 14-year-old boy was transferred to our department for evaluation and management of seizures. His personal and family medical history is unremarkable, particularly for neurologic or metabolic disorders. His physical exam was normal, but the EEG recording showed many subclinical, paroxystic and photosensitive generalized spikes waves. A multidrug therapy was initiated, with progressive clinical and electrical impairment, and the diagnostic of progressive myoclonic epilepsy was suspected. 6 months later the diagnosis of non-autoimmune diabetes was made, requiring a very low dose of long-acting insulin. Testing for maturity onset diabetes of the young (MODY) found no mutations.
A retinal dystrophy was noted on electroretinogram and the skin biopsy found glycogen inclusions in the excretory ducts of eccrine sweat glands. Two years after the first signs of epilepsy, LD was confirmed with evidence of a c.386C&gt, A p (Pro 129 His) mutation in the malin EMP2B gene. A new evaluation of pancreatic endocrine secretion showed a certain insulin resistance, with no pancreatic antibodies. Diabetes therapy was temporary switched to metformine, with satisfactory metabolic profile, but some side effects.

Conclusion: abnormal glycogen metabolism and autophagy account for multiorgan accumulation of Lafora bodies with neurodegeneration and functional consequences (insulin resistance).

P17

NEUROBORRELIOSIS PRESENTING AS GUILLAIN-BARRE SYNDROME : A CASE REPORT

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INTRODUCTION: neuroborreliosis is a tick-born disease caused mainly by the spirochetes Borrelia burgdorferi. The most common presentation in children is headache, aseptic meningitis, and unilateral facial palsy. Other neurologic manifestations include radiculitis, neuropathies, plexopathies, and transverse myelitis. In rare instances the clinical symptoms and signs present like Guillain-barrÃ© syndrome (GBS), a demyelinating radiculoneuropathy attributed to autoimmune involvement of nerve roots and peripheral nerves. A clear distinction between neuroborreliosis and GBS is sometimes difficult.

CASE REPORT: we presented the case of a 9-year-old boy with acute lower limbs pains, weakness and areflexia. He also complained of blurred vision. Neurological examination did not show meningeal signs nor cranial nerve palsies.

RESULTS: cerebro-spinal fluid analysis showed abnormally elevated protein without pleiocytosis, and electroneuromyographic findings was consistent with the diagnosis GBS. At the same time, investigations showed positive Lyme serology and evidence for intrathecal Borrelia antibody production. The diagnosis of GBS associated with neuroborreliosis was established, and a treatment with intravenous immunoglobulins 1g/kg/days and Cefriaxone 100mg/kg/days was started. Three days after the patient began to recover. A complete resolution of his neurological deficits was observed three weeks after.

CONCLUSION: only a few similar cases have been described in the literature. Some are in favor of the hypothesis that Borrelia Burgdorferi may provoke an autoimmune response causing a GBS. Other observations consider that neuroborreliosis can be atypical and mimic GBS syndrome. In our case, the mechanism is uncertain since the patient recovers after receiving the two treatments, immunoglobulins and ceftriaxone.

P18

PELIZAEUS MERZBACHER-LIKE DISEASE (PMLD): REPORT OF A PATIENT WITH A MUTATION IN THE GJA12/GJC2 GENE

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Introduction: Pelizaeus-Merzbacher disease (PMD) and Pelizaeus-Merzbacher-like disease (PMLD) form an important diagnosic category within the group of infantile hypomyelinating leukoencephalopathies. While X-related PMD is caused by a mutation in the PLP1 gene, PMLD is genetically heterogeneous, with about 8% of patients carrying mutations in the GJA12/GJC2 gene.

Case report: we report a three years-old girl whose previous medical history was unremarkable. Physical growth was normal. Neurologic development had been marked by mild global development delay. The patient was presented with bilateral nystagmus and spastic quadriparesis. On clinical examination, the child showed a permanent horizontal nystagmus, a truncal hypotonia, brisk tendinous reflexes, Spasticity and ataxia of limbs. She had dysarthric speech but she was able to control her head and sit independently. She had normal blood thyroid function and baseline metabolic screening. Brain MRI showed a severe delay of the white matter myelination process, brainstem auditory evoked potentials (BAEP) showed wave I preservation but absent III and V waves, highly suggesting the diagnosis of PMLD. A PLP1 gene analysis was normal. Neither respiratory insufficiency nor seizure was noted during her growing up. Her mental development was retarded.

Conclusion: clinical presentations of PMD/PMLD are generally undistinguishable. GJA12/GJC2 gene mutations have to be looked for in the absence of PLP-1 mutation and most importantly in case of autosomal recessive inheritance.

P19

SCHIMKE IMMUNO-OSSEOUS DYSPLASIA: A PECULIAR EEG PATTERN

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Schimke immune-osseous dysplasia (SIOD) is an autosomal recessive multisystem disorder caused by mutations in the SMARCAL1 gene. SIOD is characterized by spondyloepiphyseal dysplasia resulting in short stature, nephropathy, associated with T-cell deficiency. Neurologic manifestations include atherosclerosis and cerebrovascular disease, which manifest as migraine-like headaches, cerebral ischemia, cardiac dysfunction and cognitive deficiency. Additional features may include hypothyroidism, enteropathy, and normocytic or microcytic anemia. We describe two female patients of 18 years-old (A) and 10 years-old (B) with SIOD. Both patients showed cerebrovascular disease respectively at the age of twelve and ten years-old. Patient A presented also focal seizures treated with Clobazam. Patient B showed, since the age of 6 years-old, migraine-like headaches. Then, one year later, paroxysmal episodes appeared and treated with high dosage of levetiracetam. In addition, sleep disturbance also occured. The two patients showed a pattern EEG peculiar and equal to one another. On a background activity poorly structured we noticed brief (2-3 seconds) and periodic sequence of rhythmic monomorphic cuspidal elements with frequency of 2-3Hz, bilaterally, prevailing on centro-posterior regions. This pattern was evident above all during sleep. In literature we didn't find any description of epilepsy and pattern EEG in SIOD. The two patients showed similar features and we supposed that this pattern could be pathognomonic. But further descriptions are necessary to better define the neurological and epileptological course of this rare disease.

P20

STROKE IN CHILDREN: ABOUT 10 CASES

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Introduction: stroke in children is extremely rare. It is a significant cause of mortality and long-term morbidity. The etiologies are multiple in pediatric population. We aimed to describe clinical presentations, etiologies, and outcomes of stroke in children.

Patients and methods: We retrospectively reviewed the records of children who were diagnosed with stroke in Sahloul pediatric unit (Sousse, Tunisia).

Results: eight children, 6 boys and 4 girls, were identified with stroke from 2010 to 2017 with an average age of 6 years [range: 15 months -12 years]. The most common initial clinical presentation was headache (9 cases). The other presentations were seizures (4 cases), hemiparesis (3 cases), impaired consciousness and hemiplegia (3 cases). The diagnosis was confirmed on MRI in eight cases and on CT in two cases. Stroke was ischemic in 8 cases. Stroke was idiopathic in 7 cases, due to cardiac disorders in 2 cases and high blood pressure in one case. Six patients received antithrombotic treatment. Residual epilepsy was present in 3 patients, while residual motor weakness was present in 2. Four patients died.

Conclusion: despite various etiologies, the etiological assessment remains negative in more than half of the cases. However, the prognosis is related to this etiology with a risk of recurrence according to each context.

P21

TARGETED THERAPY IN CHANNELOPATHIES

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Next-generation sequencing (NGS) techniques in diagnostic setting may lead to an early genetic diagnosis in diseases characterized by high phenotypic and genetic heterogeneity. An early genetic diagnosis is important because it prevents unnecessary investigations, allows appropriate counseling of relatives, and, in rare cases, it is fundamental since it paves the way for specific treatments. We report on 3 patients referred for the diagnostic work-up of an early onset encephalopathy. Patient 1 is a ten months old male who presented at 28 weeks of gestation with macrocephaly, cerebral ventricular dilatation and paroxysmal tachycardia. At birth the clinical picture was characterized by macrocephaly, severe hypotonic-hypokinetic-apostural syndrome, hyponatremia, refractory focal seizures with burst suppression. Exome sequencing revealed a de novo missense mutation in SCN2A. The second patient is a 4 years old female child presenting a neonatal onset encephalopathy initially characterized by developmental delay and generalized jerky dyskinesias, progressively associated to cerebellar signs and, from 2 years of age, prolonged focal seizures triggered by minor head trauma. A customized gene panel for epileptic disorders disclosed a novel missense mutation in CACNA1A. The last patient presented soon after birth with focal refractory seizures that evolved to epileptic spasm at 4 months and finally to a malignant migrating partial seizures of infancy from age 9 months. A gene panel showed a de novo missense mutation in KCNT1 In all patients the precise genetic diagnosis allowed us to start specific treatments, ameliorating the neurological picture.

P22

THE MOYA-MOYA SYNDROME: A REPORT OF TWO CASES

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Introduction: Moya Moya syndrome (MMS) is a rare unique progressive cerebrovascular disease characterized by bilateral stenosis or occlusion of the large intracranial arteries with prominent arterial collateral circulation. We report herein two cases of children with Moya Moya syndrome and we describe.

Case Reports: the first case was a 7 months-old boy, without medical history. He was admitted for partial seizures without fever. The EEG was normal. Brain CT showed right fronto-parieto-temporal cortical atrophy. The evolution was marked by the appearance of a right hemiplegia at the age of 14 months. The neuro-radiological assessment showed extensive ischemic territory of the left fronto-temporo-parietal area. Cerebral angio-MRI showed bilateral stenosis of the internal carotid artery and middle and anterior cerebral arteries, associated with a neovascular network of the base of the skull. The patient received a thrombotic treatment. The evolution was marked by the persistence of a sequential hemiparesis. The second case was a 12 year-old girl, without medical history. He was admitted for a coma and intracranial hypertension. The brain scan showed a right parietal intracerebral hematoma. MRI revealed a distal occlusion of the right internal carotid extending to the anterior carotid artery and the right sylvian with development of collateral circulation. The evolution was favorable and no neurological sequel. No recurrence of ischemic stroke was noted.

Conclusion: MMS is a rare phenomenon in our setting. Ischemic hemispheric strokes and seizures are the commonest presenting features. The therapeutic difficulties are major in the child

P23

VARIABLE PHENOTYPE EXPRESSION OF A MATERNALLY INHERITED 16P13.11 DELETION IN TWIN BROTHERS WITH EPILEPSY

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Deletions at 16p13.11 are implicated in several neuropsychiatric disorders, such as schizofrenia, autism, mental retardation, ADHD and epilepsy. We present the case of an Italian family with deletion in 16p13.11 of 1.2 Mb affecting the mother and the two twin brothers.

The clinical features are different between the three family members: the mother presented epilepsy during infancy and adulthood, now under pharmacological control, without presenting seizures since 15 years. The two siblings now are 8 years old and they presented variable phenotype: the first twin is affected by intellectual disability and language delay and he suffered by epilepsy from the age of seven.

Clinically epilepsy started with complex partial seizures sporadically evolving in second generalization. One years after the onset, he has developed epilepsy with polymorphic episodes (complex partial seizures, secondarily generalized tonic-clonic seizures, myoclonic seizures) and occasional convulsive and non-convulsive status epilepticus. Now he presents seizures several times a week, needing numerous antiepileptic drugs and ketogenic diet. MRI didn't show lesion or malformation.

The second twin is affected by autism spectrum disorder. At the age of two he presented febrile convulsions and from the age of 7-years-old he developed focal epilepsy with secondarily generalization, since now he has shown totally 3 convulsive episodes, and he is under pharmacological control. MRI was performed, showing the presence of a diffuse midline glioma in the talamic region.

In summary our case confirms the variable expressivity of this deletion and its complex clinical variability.

P24

WERNICKE'S ENCEPHALOPATHY AFTER TOTAL PARENTERAL NUTRITION IN PATIENT WITH CROHN'S DISEASE

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Introduction: Wernicke's encephalopathy (WE) is a severe form of thiamine deficiency that can cause serious neurologic complications. Although WE is known to occur frequently in alcoholics, a number of non-alcoholic causes have also been reported
Here, we report a case of non-alcoholic WE that developed in a severely malnourished Crohn's disease (CD) patient who was supported by prolonged total parenteral nutrition without thiamine supplementation.

Case Report: a 14-year-old female patient hospitalized for abdominal pain and vomiting evolving for 2 years. On examination she had general state deterioration and sub-occlusive syndrome, hypoprotidemia without hydro-electrolytic disorders.
A fibroscopy with biopsy was done showing an aspect in favor of Crohn's disease.
She was treated by fasting, high dose steroids, antibiotics and prolonged parenteral nutrition without thiamine supplementation.
After 15 days of fasting, she complained of sudden-onset dizziness and gait ataxia. The next day, her symptoms worsened and new symptoms including mental confusion, and blurred vision developed.
MRI revealed a high signal-intensity lesion at the both right and left sides of the mammillary body and tectum, and the periaqueductal space on a T2-weighted image which was compatible with WE.

Conclusion: encephalopathy Gayet-Wernicke is a rare disease. In front of a risk situation, the triad of ophthalmoplegia, mental confusion and ataxia is evocative. The MRI is the reference examination and the Vitamin dosage will be done if necessary and possible. The treatment early allows to have a favorable evolution and avoid complications.

P25

WEST NILE VIRUS INFECTION IN CHILDREN (5 CASES REPORTED)

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INTRODUCTION: west Nile Virus (WNV) is an emerging flavivirus responsible for a variety of symptoms. In children, WN infection is an uncommon disease, characterized by milder symptoms and better outcome than eldery patients. We aimed to study the characteristics of WNV infections in Tunisian children and their outcomes.

METHODS: We retrospective review the WNV infections collected in the Sahloul pediatric department (Tunisia) over a period of 2 years (2015-2017).

RESULTS: Five patients were identified with WNV infection, 3 boys and 2 girls. The average age was 7.6 years. The encephalitis symptoms were observed in two patients, an acute flaccid paralysis in two patients. The last one presented with cerebellitis. Cerebrospinal fluid (CSF) analysis showed pleiocytosis in all cases with CSF cell count of the cases between 12-30 mm3. Cerebral MRI was normal in 2 cases, showed polyradiculoneuropathy in 2 cases, and cortico-subcortical involvement in the last one. The EEG showed generalized neurologic slowing in two cases. The diagnosis was based on detection of WNV-specific antibodies in serum in all cases. The treatment was symptomatic, only one patient received intravenous plasmin-modified immunoglobulins. The evolution was favorable in all cases.

CONCLUSION: disease symptoms caused by WNV range from fever to neurological complications, such as encephalitis or meningitis. It is currently known that WNV has the potential to cause disease with high morbidity and mortality in older and immunocompromised individuals. However, it can be a life threatening condition in children. WNV must be taken into consideration in suspicious cases with different symptoms.

P26

CEROIDOLIPOFUSCINOSIS TYPE 2 (CLN-2): WHAT ARE THE EARLY NEUROPHYSIOLOGICAL SIGNS?

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We describe a case of CLN-2 for which the EEG low frequency photostimulation guided the diagnosis. A 7 year old male, with normal familiar and medical history except for language delay, at age of 3 years showed the first unprovoked seizure, characterized by head and eyes right deviation, followed by jerks of the limbs, lasting 2 minutes. After 24 hours, he showed the second seizure, characterized by generalized stiffness and cyanosis lasting about 60 seconds. Laboratory tests were normal. Interictal EEG at the onset showed bilateral temporo-parietal abnormalities, intermittent photic stimulation (IPS) was not performed. Brain MRI was normal. Seizure frequency was many per week. Valproic acid and clonazepam therapy was started resulting in seizure freedom. At 4 years, after a febrile episode, a progressive gait instability appeared. New brain MRI showed widespread cortical and subcortical atrophy. Laboratory tests were normal yet. Interictal EEG showed bilateral occipital abnormalities with abnormal photoparoxismal response during low frequencies and flash-per-flash to IPS. Skin biopsy showed vacuolar inclusions of lipids complex. The CLN-2 gene molecular analysis revealed c.509-1G&gt,C compound heterozygosis and c.972_976 delCTATGGAG on CLN2 gene. In conclusion, this case report seems to confirm that the association between severe languange delay and unprovoked seizures onset between 2 and 4 years of age with an abnormal photoparoxismal response during low frequencies and flash-per-flash test could be really suggestive of an early diagnosis of CLN2. That also may led us to start a treatment as soon as possible, considering the currently available therapies.

P27

CERREBELLAR GLIOMA AND ACUTE PSEUDOTUMOR CEREBELLITIS: CONTROVERSIAL DIFFERENTIAL DIAGNOSIS

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Acute ataxia in children is always an alarm sign. When combined with migraine and nausea, posterior fosa tumor is quickly evoked. However, other processes, such as acute pseudotumor postinfectious cerebellitis must be kept in mind, for treatment is completly different.

We present a 6 year old boy who suffered from a 5 day-long migraine, with worsening progression and vomits in the last 48h. At the Emergency room, ataxia, left dysmetria and pathologic Romberg where observed, with lateralization to the right. Suspecting a posterior fosa tumor, a CT scan was performed, revealing a right cerebellar mass, and corticosteroids where iniciated. MRI was consistent with a cerebellar high grade glioma, affecting mostly the right hemisphere, but also the left one. Neurosurgery performed a partial resection of the affected area, but intraoperatory pathology study revealed an inflammatory infiltrate and absence of tumoral cells. The diagnosis of acute pseutotumoral cerebellitis was stablished.

Our patient, although recovered from ataxia, dysmetria and migraines, presents slow (though correct) processing and slow speech, consistent with the cerebellar resection.

This is a rare entity, usually benign, but sometimes menacing the patient's life, if cranial hypertension is present: in that case, neurosurgical decompression may be necessary. However, it is important to make an accurate differential diagnosis before performing neurosurgery, for resection of cerebellar areas have negative consequences in the patient's cognitive performance and his daily life.

P28

DÉFICIT EN PYRIDOXAMINE-PHOSPHATE OXYDASE (PNPO) : CONTRÔLE DE L'ÉPILEPSIE AVEC ÉTATS DE MAL SUBINTRANTS PAR LA MODIFICATION DES MODALITÉS D'ADMINISTRATION DU PHOSPHATE DE PYRIDOXAL

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Les nourrissons présentant un déficit en pyridoxamine-phosphate oxydase (PNPO) répondent habituellement au phosphate de pyridoxal (PLP) à la posologie de 30mg/kg/j en 3 prises. Nous rapportons l'histoire d'un nourrisson qui a présenté dès 3 semaines de vie une épilepsie sévère par déficit en PNPO, n'ayant répondu qu'à la dose de 60mg/kg/j en 4 prises de PLP.
L'épilepsie a été traitée initialement par pyridoxine, puis du PLP. A 3 mois, les crises persistaient, associées à des spasmes atypiques, pharmaco résistantes. La vitaminothérapie arrêtée a été reprise à l'âge de 6 mois, après identification d'un variant faux sens du gène PNPO à l'état homozygote (panel des encéphalopathies épileptiques). A 6 mois 1/2, des états de mal épileptiques sont survenus ne cédant après l'avance de la prise matinale de PLP. L'arrêt des crises n'a été obtenu qu'après l'augmentation et le fractionnement de la posologie du PLP à 60mg/kg en 4 prises. Depuis l'enfant a présenté 3 crises fébriles et 4 crises brèves en contexte de retard de prise de PLP. A l'âge de deux ans, l'enfant a fait des progrès, mais garde un léger retard de développement (marche 20 mois, retard langage)
Chez un nouveau-né ou nourrisson suspect d'épilepsie vitamino-dépendante, l'absence de réponse à la dose standard de PLP n'écarte pas le diagnostic de déficit en PNPO et doit conduire à en augmenter la posologie et le nombre de prises. Cette observation montre aussi l'intérêt du résultat moléculaire qui a permis de reconsidérer le diagnostic de déficit en PNPO.

C1

WHY YOU NEED TO CONSIDER GENETIC TESTING OF CHILDREN WITH EPILEPSY

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Genetic testing and counseling for epilepsy is now being incorporated into everyday practice in many parts of the industrialized world. This advance has mainly been driven by rapid discoveries in the etiology of monogenic epilepsies, paired with technological developments in next generation sequencing, allowing the parallel and economical testing of multiple target genes.

Several studies on targeted gene panel testing or whole exome sequencing have been reported in the past years, showing that the current diagnostic rate can be as high as 25-35%. Furthermore, these studies have shown a clear tendency towards higher positive rates in patients with early onset epilepsies as well as in cases with severe phenotypes.

NGS-based genetic testing has been shown to have a high clinical utility in children with early onset epilepsy, in drug-resistant cases, or familial cases. The impacts are numerous and range from providing the families with a definite diagnosis, to risk counseling and treatment change. In addition, an increasing number of targeted clinical trials has been made possible as new experimental therapies become available.

C2

PERSONALIZED TREATMENT FOR GENETIC EPILEPSIES OF CHILDHOOD

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Over the last few years, advances in genetics have led to the discovery of many novel disease genes involved in childhood epilepsies. Great progress has especially been made in the field of epileptic encephalopathies, and a genetic cause is now identified in 30-50% of patients. The high rate of drug resistant seizures and the lack of therapies targeting the developmental problems, feed the hope that genetic advances will lead to improved treatments for these patients. Precision medicine embraces the idea that treatment can be tailored to the individual patient, taking into account genetic understanding of their disease. The ketogenic diet is an established form of personalized treatment in patients with GLUT1 deficiency, and case series have shown a beneficial effect of the use of sodium channel blockers in patients with KCNQ2, (some) SCN2A and SCN8A mutations. Nevertheless, the mixed results of quinidine use in KCNT1 related epilepsies, despite dramatic effects in the first case studies, illustrate the need for well-designed and controlled multicenter trials that bring together a critical number of patients with rare childhood epilepsies.

C3

THE CONTRIBUTION OF GENETIC COUNSELING TO THE MANAGEMENT OF CHILDHOOD EPILEPSIES

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The recent advances have shown that a large number of epilepsies are related to a monogenic cause, that is to say that a deleterious variant affecting a single gene is strongly associated with the occurrence of the disease. This is especially true when seizures begin early in life, before the age of 1 years or even 3 months and is associated with other neurological (intellectual disability, autism) or extraneurological features. For example, more than a hundred genes are involved in the so-called developmental epileptic encephalopathy. The growing role of genetic testing, particularly since the transfer of high-throughput sequencing to diagnostics, has brought an etiological diagnosis in an increasing number of patients. Genetic confirmation may, in certain cases, provide prognostic or clues for therapeutic adaptation. It also provides genetic counseling to patients and their families. The risk of transmission within the family or of recurrence for a couple is dependent on the mode of transmission. In the field of childhood epilepsies, we all modes of Mendelian transmission may be observed (X-linked, autosomal dominant or recessive) but also other modes of transmissions (chromosomal translocations, heredity of the mitochondrial genome). In the case of epileptic encephalopathies, many mutations occur de novo (they are not found in blood DNA from the parents). In these cases, the risk of transmission in the family is limited for relatives but it cannot be considered as null for a future child of the couple (for each parent, even if they are separated) because germinal mosaic cannot be excluded. Accurate genetic counseling allows the couples at risk to benefit from prenatal or pre-implantation diagnosis. Some phenomena may, however, complicate genetic counseling, such as incomplete penetrance or variability of expressivity, which can be observed in some forms of epilepsy with autosomal dominant inheritance, such as the GEFS+ (genetic epilepsies with febrile seizures plus).

Les avancées de ces dernières années ont montré qu'un grand nombre d'épilepsies sont d'origine génétique et plus exactement monogénique, c'est à dire qu'un variant délétère affectant un gène est fortement associé à la survenue de la maladie. Cela est d'autant plus vrai que l'épilepsie débute précocement, avant l'âge de 1 ans ou même de 3 mois et qu'elle est associée à d'autres troubles neurologiques (déficience intellectuelle, autisme) ou extraneurologiques. Par exemple, plus d'une centaine de gènes sont impliqués dans les encéphalopathie épileptiques développementales. La place croissante des tests génétiques, en particulier depuis le transfert du séquençage à haut débit en diagnostique, a permis d'établir un diagnostic étiologique chez un nombre croissant de patients. Cette confirmation peut apporter, dans certains cas des éléments pronostiques ou d'adaptation thérapeutique. Elle permet également d'apporter un conseil génétique aux patients et à leurs familles. Le risque de transmission dans la famille ou de récurrence pour un couple est dépendant du mode de transmission. Dans le domaine des épilepsies de l'enfant, on peut observer tous les modes de transmission Mendéliens (lié à l'X, autosomique dominant ou autosomique récessif) mais également d'autres modes des transmissions (translocations, hérédité du génome mitochondrial, transmission très particulière des mutations du gène PCDH19. Dans le cas des encéphalopathies épileptiques, de nombreuses mutations surviennent de novo, lors de la gamétogénèse. Dans ce cas, le risque de transmission dans la famille est limité pour les apparentés mais il ne peut pas être considéré comme nul pour un futur enfant du couple (pour chacun des parents, même s'ils sont séparés) car on ne peut pas exclure une mosaïque germinale. Etablir un conseil génétique permet aux couples à risque de disposer d'un diagnostic anténatal ou pré-implantatoire. Certains phénomènes peuvent toutefois compliquer le conseil génétique, comme la pénétrance incomplète ou la variabilité d'expressivité que l'on peut observer dans certaines formes d'épilepsie de transmission autosomique dominante, comme les GEFS+.

C4

METABOLIC DISEASES WITH EPILEPSY VITAMIN RESPONSIVE CONDITIONS

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Vitamin-responsive metabolic epilepsies are a group of inherited disorders characterized by a specific enzyme deficiency, and not a vitamin deficiency state. Epilepsy is usually present at disease onset, and most patients do not respond to antiepileptic drugs. However, personalized treatment with specific vitamin therapy markedly improves both seizures and encephalopathy.

Early diagnosis (molecular genetic testing and biochemical determination of specific biomarkers in blood, urine and CSF) and specific treatment are mandatory when these disorders are suspected as clearly impact in the clinical outcome.

We will describe the pathophysiology and clinical phenotype of vitamin-dependent disorders such as Pyridoxine-dependent epilepsy (Antiquitine deficiency, PROSC mutations), Pyridoxal 5'-phosphate-dependent epilepsy (PNPO- pyridoxamine 5'-phosphate oxidase deficiency), and biotinidase deficiency, and transportopathies such as cerebral folate deficiency and thiamine transporter-2 deficiency. We also describe the response to specific vitamin therapy of these disorders and their outcome.

C5

GLUT 1 DS: VERY RARE DISEASE OR UNDERDIAGNOSED SYNDROME?

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Glucose transporter type 1 deficiency syndrome is a genetically determined, treatable, neurologic disorder that is caused by insufficient transport of glucose into the brain. It is caused by a mutation in the SCL2A1 gene, which is so far the only known to be associated with this condition.
GLUT1 deficiency syndrome is a rare disease, in literature, no more than 350 cases have been described. However the continuous new reports of so-called atypical cases and the demonstration in population of “idiopathic” epilepsies of a percentage greater than 1% of validated mutation in SLC2A1, suggest that GLUT1 deficiency syndrome incidence may be higher but it is still an underdiagnosed disease.
Glucose transporter type 1 deficiency syndrome consists of a wide clinical spectrum that usually presents with cognitive impairment, epilepsy, paroxysmal exercise-induced dyskinesia, acquired microcephaly, hemolytic anemia, gait disturbance, and dyspraxia in different combinations. However, there are other clinical manifestations that we consider equally peculiar but that have so far been poorly described in literature.
In this presentation, supported by a video contribution, we will accurately describe the clinical manifestations of Glut 1 disease in the various periods of life from the first months to adolescence. Particular attention will be paid to the efficacy of the ketogenic diet both on the seizures and on the movement disorder but also on neuropsychological evolution. The possible new therapeutic perspectives will also be discussed.

C6

LAFORA AND NCL: CURES AT LAST?

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Progressive myoclonus epilepsies (PME) are the severest and nearly always fatal among all the epilepsies. On the positive side, almost all are due to single gene defects, and by definition, all are characterized by an initial period of normal brain development. As such, replacing the missing gene should prevent the disease. Adeno-Associated Virus 9 (AAV9) is an innocuous guest of the human host, including the brain, and freely passes across the blood-brain barrier. Intensive work in many laboratories is hastening the further evolution of the virus to infect as many neural cells as possible and thus be used as a vector to replace the missing gene in the PME and other neurogenetic diseases. Currently, the best serotypes infect as many as 70% of neurons in mouse models. Given the otherwise hopeless nature of most PME, work is underway in our and other centers to advance these diseases to AAV-mediated gene therapy trials. Do young brains possess enough plasticity, and will these children benefit with current viral vectors? We shall soon learn.

Meanwhile, in certain PME, alternate gene based therapies are possible. In Lafora disease, murine experiments show that a mere 50% reduction of brain glycogen synthesis near-completely prevents Lafora body formation, and the disease, in mouse models. We show that antisense oligonucleotides against the brain-expressed isoform of glycogen synthase prevent the disease, and in older mice, reverse and near-completely eliminate Lafora bodies. An antisense nucleotide against human glycogen synthase is presently in development and a clinical trial using this drug is in preparation.

The prototypical monogenic disease of the spinal cord, spinal muscular atrophy, has all but been cured with both antisense oligonucleotides and AAV9-mediated gene replacement. Are we ready to rise to the brain?