GP227 CLINICAL SPECTRUM OF CLASSICAL GALACTOSAEMIA ASSOCIATED WITH FRIEDREICH'S ATAXIA IN A PAEDIATRIC COHORT IN THE REPUBLIC OF IRELAND – AN UPDATE

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Despite early diagnosis through Newborn Bloodspot Screening and strict dietary treatment, there are long-term complications of Classical Galactosaemia, including female infertility, osteopenia, and, in some cases, learning disabilities or neurological symptoms such as tremor or ataxia. Therefore, neurological symptoms may easily be attributed to an underlying diagnosis of Classical Galactosaemia. However, the coexistence of classical Galactosaemia and Friedreich's Ataxia (FRDA) was previously reported amongst the Irish Traveller population. Classical Galactosaemia and FRDA are both autosomal recessive conditions, the gene loci for which are located on either side of the centromere of chromosome 9. FRDA is one of the most common forms of autosomal-recessive ataxia and slowly progressive; it also commonly involves the heart. We here present the clinical spectrum of 10 Irish patients currently being treated in our Metabolic Centre in whom a diagnosis of Classical Galactosaemia together with FRDA was made. All patients were diagnosed with Classical Galactosaemia through Newborn Screening first. All were diagnosed with the common Classical Galactosaemia GALT mutation Q188R/Q188R. Eight of the ten patients later presented with progressive ataxia, between the ages of 7–14 years. One child presented in cardiac failure secondary to dilated cardiomyopathy at 7 years of age. It was noted that he was not ataxic at presentation of FRDA and that he had normal tendon reflexes. Another patient who was diagnosed at 6 years of age still had an essentially normal neurological exam almost 4 years later. The diagnosis of FRDA was confirmed by detecting the common pathogenic GAA repeat expansion mutations in both alleles of the frataxin gene (FXN) in affected individuals.

Taken together, neurological signs may easily be attributed to an established diagnosis of Classical Galactosaemia. However, one should be vigilant for the coexistence of Classical Galactosaemia and FRDA in a high-risk population, particularly when monitoring patients with a complex phenotype, such as a neurological or cardiac presentation.

GP228 NEUROPSYCHOLOGICAL PROFILE ON NEPSY IN CHILDREN AT PERINATAL RISK WITH AND WITHOUT CEREBRAL PALSY – SIMILAR OR DIFFERENT?

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Objective To examine the neuropsychological profile of children at perinatal risk with or without CP, compare them to each other and to the normative group. It is expected that more specific cognitive deficits will be found in both clinical groups in relation to the normative group, as well as more deficits in children with CP compared to children at perinatal risk without CP.

Design/study groups clinical sample of 46 children with milder CP (the CP group) and 55 children at perinatal risk without CP (the group at risk) in the age range between 5 and 12 years with normal verbal intelligence (according to WISC-III) were examined. The groups are equalized in terms of demographic variables (child's age and sex; mother's education) as well as in terms of perinatal variables (gestational age, birth weight, Apgar scores, presence of brain lesion – 78% in each group), and EEG findings at the time of examination.

Main outcome measures Developmental Neuropsychological Assessment (NEPSY) has been applied to measure neuropsychological functions, all the core subtests except Phonological Processing.

Results Both clinical groups had significantly lower results in 12 out of 13 measures applied in relation to the normative group: in Auditory and Visual Attention, Speeded Naming, Comprehension of Instructions, Fingertip Tapping, Imitation Hand Positions, Visuomotor Precision, Design Copy, Arrows, Memory for Faces, Memory for Names and Narrative Memory (z-score = -.29 to -1.67 in the CP group and z-score = -.38 to -1.07 in the group at risk). The CP group had lower results in comparison to the group at risk in 5 measures which include a motor component (oral or manual) in performance. The group at risk had worse results in the Memory for Names than the CP group.

Conclusion The children at perinatal risk achieved significantly lower neuropsychological results in comparison to the normative group, regardless of motor deficit (in the most of measures) or any demographic and perinatal variable or EEG findings. It may be concluded that both clinical groups are at risk for specific cognitive deficits. That has significant implications for neuropsychological examination and treatment, where the model of developmental neuropsychological psychotherapy may be applied.

GP229 THE USE OF THE KETOGENIC DIET IN A METABOLIC PATIENT WITH GLYCOGEN STORAGE DISEASE TYPE IIIA

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Background Glycogen Storage Disease (GSD) Type IIIa is a recessively inherited disorder caused by a deficiency in the debranching enzyme amylo-1,6-glucosidase. This deficiency allows for the accumulation of glycogen in the liver, heart and skeletal muscle. Typically patients present in infancy with recurrent hypoglycaemia and hepatomegaly. Standard treatment is a high carbohydrate, moderate to high protein and low fat diet, with regular feeds to help maintain euglycaemia. Conversely the ketogenic diet (KD) consists of a very high fat, low carbohydrate diet with moderate protein intake and has traditionally been used for treatment of epilepsy. It has well noted that ketone bodies can be used as an alternative energy source when carbohydrate intake is low to maintain euglycaemia.

Patient×is a 3 year old male who had neonatal hypoglycaemia and confirmed homozygosity for the GSD Type IIIa gene. Patient×was commenced on the KD at 8 months of age when progression of his GSD resulted in severe cardiomyopathy. The following outlines the transition onto the KD and clinical findings between 8-22 months

Method Standard dietetic treatment was provided from birth to maintain euglycaemia along with placement of a percutaneous endoscopic gastrostomy. Continuous 24 hour feeding was required due to unsuccessful bolus feeding. A modified KD incorporating MCT fat -which was has been noted to further aid ketosis was commenced at 8 months with a ketogenic ratio of 0.5:1 building to 1:1 within 2 weeks. Ketones and blood sugar levels were closely monitored with a threshold of 2.6 mmol/L of glucose and ketones >1 mmol/L before hypoglycaemia intervention was required.

Results Prior to the KD, there was a high glucose infusion rate (GIR) of 9.75 mg glucose/kg/minute. After initiation of the KD, the GIR reduced initially to 5.8 mg glucose/kg/minute, with a gradual increase of MCT fat from 6% to 28% and the GIR further reduced to 2.73 mg glucose/kg/minute. There were no episodes of hypoglycaemia and ketones ranged from 1– 2.9 mmol/L. Echocardiographs showed a significant improvement in cardiac function with a cardiac output reduction of 137 to 39 mmHg.

Discussion The KD was trialled as an alternative treatment. It resulted in the reduced intake of carbohydrate and the subsequent reduction of glycogen build-up within cardiac muscle. Ketones were used as an alternative fuel source and euglycaemia was maintained

Conclusion The KD should be considered as an alternative treatment for GSD Type IIIa where standard intervention is not effective.

GP230 FETAL ACETYLCHOLINE RECEPTOR INACTIVATION DUE TO MATERNAL MYASTHENIA GRAVIS: AN UNDERRECOGNISED, DEVASTATING BUT POTENTIALLY PREVENTABLE AND TREATABLE DISORDER

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Aim Fetal acetylcholine receptor inactivation syndrome (FARIS) occurs in offspring of mothers affected by myasthenia gravis (MG), from in-utero exposure to acetylcholine receptor (AChR)-antibodies targeting the fetal AChR γ-subunit. FARIS causes damage to the fetal neuromuscular junction which is crucial in muscle development, causing a persistent myopathy. FARIS may initially be mistaken for Transient Neonatal Myasthenia Gravis (TNMG), congenital neuromuscular disorders and one of the many causes of neonatal hypotonia. This study aimed to determine the clinical spectrum of FARIS and assess oral salbutamol as a novel pharmacological therapy.

Methods Detailed review of antenatal and postnatal clinical features in novel FARIS cases seen in international neuromuscular centres. Antibody data analysis was performed at the Oxford neuroimmunology research laboratory. Oral salbutamol was trialled in five cases based on previously reported benefit in one of our patients.

Results We identified 12 novel FARIS cases. At delivery resuscitation was required in all and intubation in nine, all had severe generalised hypotonia. Two infants with arthrogryphosis-multiplex-congenita phenotype died in the neonatal period. Among survivors, there was requirement for mechanical ventilation (n=9), NIPPV (n=2), oxygen (n=1), and supplemental NG/PEG feeding (n=12). The presence of severe generalised hypotonia with dysmorphic features prompted investigations for other neuromuscular, genetic and metabolic disorders which were negative. Common features included facial weakness (n=12) and limb contractures (n=9). Newly described disease features: diaphragmatic paresis (n=5), hearing impairment (n=3), CNS involvement (n=3), pyloric stenosis (n=2), extra-ocular eye restriction (n=2), non-progressive scoliosis (n=2), and jaw opening contracture(n=1). Motor development of patients improved with time. Respiratory complications (tracheostomy;n=2), feeding difficulties (PEG;n=2), facial weakness and speech impairment (from velopharyngeal incompetence) persisted in most. TNMG treatments(immunotherapy/pyridostigmine) were little or no benefit. Novel use of oral salbutamol improved fatiguability, ptosis, oromotor dysfunction, muscle tone, articulation and voice volume in all patients. In 8/12 pregnancies maternal myasthenia gravis hadn't been established antenatally, and many mothers were pauci/asymptomatic. All had AChR-antibodies targeting the fetal γ-subunit confirming diagnosis. Where subsequent pregnancies were treated aggressively(immunotherapy), infants had improved outcomes.

Conclusions This report demonstrates and expands the phenotypic spectrum of FARIS, and emphasises oral salbutamol therapy as a potentially beneficial treatment. FARIS should be considered (mothers or infants tested for fetal specific AChR-Abs) in infants presenting with neonatal hypotonia, myopathic features and/or a suggestive antenatal history, even in the absence of a maternal MG diagnosis. Aggressive treatment with immunotherapy in pregnancy may improve outcomes.

GP231 REVIEW OF INVESTIGATIONS CARRIED OUT DURING THE FIRST PRESENTATION OF ACQUIRED DEMYELINATING SYDNROMES OVER A TEN YEAR PERIOD

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Aims A first episode of suspected demyelination presents a diagnostic challenge often having non-specific signs which overlap with other inflammatory white matter, neurometabolic and genetic disorders. The first episode may be a presentation of acute disseminated encephalomyelitis, multiple