G470 A RARE CASE OF LESCH-NYHAN SYNDROME

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4 year, male child born out of 2nd degree consanguinous/marriage, came with complaints of vomiting with H/O delayed development of milestones with H/O self destructive biting of fingers and presence of involuntary movement. Antenatal, natal and postnatal course of child was normal, with family H/O similar complaints and death of 1st born male child and abortion of 2nd child. On clinical examination, self mutilated fingers and involuntary movements were noted, with these findings of global developmental delay, dystonia and self mutilation we proceeded our investigation. Serum uric acid level was 45.8 mg/dl (elevated) and urinary uric acid level was 78 mg/dl (elevated). MRI brain showed diffuse cerebral atrophy. Child is suspected to be affected with Lesch-Nyhan Syndrome and has been evaluated for pathogenic variations in the HPRT1 gene. Mutational study for HGPRT assay showed a hemizygous 5’ splice site proximal variation in intron 8 of the HPRT1 gene that affects the position 3 nucleotides downstream of donor splice site of exon 8 (Classified as a variant of uncertain significance). For sequencing the variants in the parents, sample was sent for analysis and results were awaited, which will be intimated after arrival of result. Incidence of Lesch-Nyhan Syndrome was 1 in 3,80,000. It is an X linked disorder of purine metabolism, results from HPRT deficiency, which leads to failure to consume PRPP in salvage reaction result in increase of hypoxantine level which further leads to increase in uric acid levels. Common clinical manifestation includes self injurious behaviour, intellectual disability and dystonic movements. Analysis of HPRT enzyme was used for the confirmation of diagnosis. Treatment includes use of allopurinol, restraints, antianxiety and mood stabilisers, deep brain stimulation and 5-adenosylmethionine. Average life time was found to be 30 to 40 years.

G471 CLINICAL CHARACTERISTICS, LABORATORY FINDINGS AND MANAGEMENT DATA IN A SINGLE-CENTER COHORT OF PATIENTS WITH HETEROZYGOUS FAMILIAL HYPERCHOLESTEROLEMIA

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Background Familial hypercholesterolemia (FH) is an autosomal dominant lipid metabolism disorder characterized by high blood cholesterol levels and early cardiovascular disease. Patients suffer from either a homozygous or heterozygous form. Heterozygous FH is a common genetic disorder with an incidence of 1:500 people. Patients are normally treated with dietary intervention, statins, bile acid sequestrants, or other lipid-lowering agents.

Aim The aim of this study was to record data to characterize the cohort of heterozygous FH patients in our center.

Methods/Case Report We have retrospectively recorded the epidemiological, clinical, biochemical and genetic data of patients with heterozygous FH aged between 10 and 17 years old treated in our hospital over the last 20 years. In addition, we have recorded data in regards to treatment modalities and biochemical parameters related to response in treatment.

Results We are describing 91 patients with a mean age of 14 years (10–17 years). Fifty-one patients were males and 40 were females. The mean age at diagnosis was 8.9 years (range 1 and 16 years). Most of the patients were asymptomatic at diagnosis, while presentations included associated obesity (8 patients), diabetes mellitus (3 patients), xanthomas and xanthelasmata (1 patient each). Mean levels of total and LDL cholesterol at diagnosis were 6.8 mmol/L (4.2 & 10.1 mmol/L) and 4.7 mmol/L (1.92 & 8.3 mmol/L) respectively. Seventy-seven patients had a positive family history of hypercholesteremia. Forty-two patients had their diagnosis genetically confirmed (mutations in LDLR in 36 patients, and apolipoproteins in 6 patients respectively). Management included dietary manipulation in 70 patients and pharmacological therapy in 45 patients. Out of various medications, Atorvastatin was the most frequently used in 35 patients. Six months following treatment the vast majority of patients had a favorable outcome with mean levels of total cholesterol and LDL cholesterol being 5.3 mmol/L (3.4–7.9 mmol/L) and 4.37 mmol/L (1.86–6.5 mmol/L) respectively.

Conclusion Our data suggest that familial hypercholesterolemia is a common metabolic disorder and most of the patients are asymptomatic at diagnosis during childhood. A high index of suspicion is required in subjects with a family history of cardiac or cerebrovascular symptoms. Treatment with Statins is effective and early initiation should be considered to avoid long term complications.

G472 DELAYED DIAGNOSIS OF A GLUCONEGENIC DISORDER IN CHILDREN WITH HYPOGLYCAEMIA AND/OR LACTIC ACIDOSIS: LESSONS LEARNT

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Aim To describe the clinical course of children in whom the diagnosis of an underlying metabolic disorder was delayed due to a failure of obtaining urine for organic acid analysis at the time of initial presentation with hypoglycaemia and/or lactic acidosis.

Method Retrospective review of case notes of children who had a delay in diagnosis of Fructose 1,6 bisphosphatase deficiency.

Results Five (4 male) children (age range 7 days – 6 yrs old) were identified. The majority (3/5) had presented with hypoglycaemia and lactic acidosis which responded to dextrose infusion. Two patients (twin siblings) presented with lactic acidosis only. Urine organic acids were measured at the initial presentation in only one patient. In 1/5 patients, urine was obtained at the time of hypoglycaemia but was stored for toxicology due to a lack of clarity on specimen request form regarding patient’s clinical presentation. In 4/5 patients,
subsequent urine analysis demonstrated glyceruria and white cell enzyme analysis confirmed the diagnosis of Fructose 1,6 bisphosphatase deficiency in all. Lack of appropriate screening resulted in 4/5 patients presenting with repeated episodes of decompensation with an average of 3.4 episodes per patient. In these patients, average time period between initial presentation and diagnosis with Fructose 1,6 bisphosphatase deficiency was 13.25 months.

**Conclusion** Our case series emphasise the importance of obtaining urine for organic acid analysis at the time of hypoglycaemia and/or lactic acidosis to avoid delay in diagnosis and initiation of appropriate therapy. Timely diagnosis and treatment can prevent morbidity and potential mortality associated with repeated episodes of decompensation. Fructose 1,6 bisphosphatase deficiency is a treatable metabolic disorder that can be identified with prominent glyceroluria during an acute episode; which might not be seen after recovery from illness. It is important to be aware of false positive results due to contamination from nappy creams and to ensure repeat organic acid analysis in these situations. Management involves avoidance of prolonged fasting and emergency regimen during illnesses which includes administration of glucose polymer and avoiding drinks with higher fructose content.

**G473** PRIMARY CARNITINE DEFICIENCY: VARIABLE IN ITS PRESENTATION, TREATABLE IN ITS COURSE AND THE IMPORTANCE OF FAMILY SCREENING. A CASE SERIES

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**Background** Primary carnitine deficiency (PCD) is an autosomal recessive disorder of fatty acid oxidation, caused by mutations in the SLC22A5 gene encoding for the carnitine transporter OCTN2. Carnitine uptake deficiency prevents the body from using certain fats for energy, particularly during periods of fasting or illness. The first manifestation of PCD can be at any age, where patients can present with hypoglycaemia, hyperammonaemia, encephalopathy, skeletal myopathy and cardiomyopathy.

**Case Review** We report on a previously well 15 year old boy who participated in a challenging Duke of Edinburgh expedition. The following morning he was found drowsy and subsequently admitted to hospital with worsening encephalopathy, hypoglycaemia and hyperammonaemia. This, along with rising CK and troponin levels meant PCD was included in the early differential and carnitine supplementation was commenced. Unfortunately his cardiac failure was too advanced and he had a cardiac arrest, dying after an hour of CPR. Genetic testing confirmed the diagnosis of PCD. On family cascade screening his asymptomatic sister was also diagnosed with PCD, started on oral carnitine supplements and continues to be well.

A retrospective analysis of a total of thirteen diagnosed patients from one centre illustrates the variability of first presentation of PCD. Five children (ranging between 2 months and 7 years) presented with cardiac symptoms; four with cardiomyopathy, one with a cardiac arrest. Two children presented between 1 year and 3 years with hypoketotic hypoglycaemia. Two children presented with muscle fatigability at 7 months and 7 years of age. Another presented at 10 months old with motor regression, failure to thrive and an abnormal ECG. Two children were diagnosed at birth, either by newborn or sibling screening.

**Conclusion** This case series illustrates that PCD can present at any age with variable symptoms. Although rare, PCD should always be considered in patients with unexplained symptoms including encephalopathy. It is potentially lethal, but also extremely treatable, as early carnitine supplementation equates to excellent prognosis. Lastly, our case highlights the importance of family screening in preventing potential fatalities.

**G475** CENANI-LENZ SYNDACTYLY IN SIBLINGS WITH A NOVEL HOMOZYGOUS LRP4 MUTATION AND RECURRENT HYPOGLYCAEMIA

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Cenani-Lenz Syndactyly (CLS) is a rare autosomal recessive syndrome characterized by disorganized oligosyndactyly of upper and lower limbs as well as radioulnar synostosis. Structural renal abnormalities are also common. We report two affected brothers, born to orthodox Jewish parents, in whom we found a novel homozygous missense variant c.4910G>A; p.(Cys1637Tyr) in LRP4 situated in an EGF-like domain between the 4th beta-propeller and transmembrane domains. Both brothers have had recurrent ketotic hypoglycaemia which has not been associated previously. We present 3D-CT imaging illustrating the limb abnormalities in detail.

**G476** AMINOACYLASE 1 DEFICIENCY, A CLINICAL PROSPECT

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Background Aminoacylase-1 deficiency (OMIM 609924) is a rare form of inborn error of metabolism (IEM) (Van Coster et al.2005 Sass et al. 2006) inherited by autosomal pattern characterized by increased urinary excretion of specific N-acetyl amino acids. Most patients demonstrate neurologic abnormalities such as intellectual disability, seizures, hypotonia, and motor delay. In this case series we describe four patients from diverse ethnic origins with slightly variable clinical phenotypes.

**Methods/Case Report** This retrospective case note review was conducted in a single metabolic centre at a tertiary care hospital in the UK. Clinical, biochemical, molecular genetic and neuro-imaging parameters were gathered from the clinical records, with a focus on the neurologic symptoms and signs.

**Results** Four patients were identified. Three were female in the age between 4–17 years at time of review and one male

A170

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