P429 GITELMAN SYNDROME – REPORT OF THE FIRST PEDIATRIC PATIENT FROM MACEDONIA

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Background and aims Gitelman syndrome (GS) is a rare renal channelopathy with an autosomal recessive type of inheritance, caused by homozygous or compound heterozygous mutations in *SLC12A3* gene. The disorder causes metabolic abnormalities and may be overlapped with Barter type 3 syndrome.

Methods A 7 year-old boy presented with a history of several episodes of carpopedal spasms and muscle aches in the last few months. The boy has been a relatively healthy child previously. His auxological parameters were within normal range for his sex and age. Diagnostic assessment was achieved by characteristic symptoms, imaging technics, biochemical, hormonal and molecular analyses.

Results The biochemical analyses revealed hypokalemia (3.0–3.4 mmol/l), hypomagnesemia (0.64–0.66 mmol/l), hypocalcemia (<0.79 mg/kg/d) without metabolic alkalosis. The parathyroid and thyroid hormones were within reference range. The measured Q-T interval (0.36 sec) in the electrocardiogram was also within normal range. No abnormalities were found in the audiogram and the electroencephalogram. The molecular analyses have shown that the patient was heterozygous for the *SLC12A3* c.1805_1806del and c.2660+1G>A pathogenic variants and also heterozygous for the *SLC12A3* c.2944 A>T (p.Ile982Phe) likely pathogenic variant. His mother was a heterozygous for the c.2944 A>T (p.Ile982Phe) mutation, but his father was heterozygous for the other 2 variants (*SLC12A3* c.1805_1806del and c.2660+1G>A).

Conclusions Herein we present a first child from Macedonia with clinical manifestations and electrolyte imbalances typical for a GS. The results of the molecular analyses were consistent with the diagnosis of GS. The boy is on a high salt diet and oral potassium and magnesium supplements.

P430 IDENTIFYING RARE DISEASE RESEARCH PRIORITIES THROUGH (RAINDROP) A RARE DISEASE RESEARCH PARTNERSHIP

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Background To date, the rare disease research community is largely fragmented in Ireland without a coherent programmatic focus. All too often, priorities for research are decided by one group of stakeholders. The James Lind Alliance (JLA) model allows us to challenge this dynamic through the Rare Disease Research Partnership (RAInDRoP) Workshop which will enable clinicians, patients and carers to work together to identify and prioritise uncertainties that could be answered by research. The RAINDRoP is a truly collaborative effort in which everybody has a voice, and it refocuses the research on the patients rather than the disease.

Objectives To identify and prioritise topics and questions in the three research areas: (1) Route to Diagnosis (2) Living with rare diseases (3) Integrated care or Holistic care.

Design A modified nominal group technique.

Setting Republic of Ireland

Participants Anyone with experience of care for patients with rare diseases including patients, carers and healthcare professionals.

Results This workshop is scheduled to take place on the 04th of April 2019. The result is not available at the time of submission.

Conclusions This study is the first national prioritisation exercise to identify patient and healthcare professional priorities for rare diseases research. The research priority partnership will identify a range of important gaps in the existing evidence to inform (1) Pathway to Diagnosis, focusing on facilitating early, accurate diagnosis and the communication/informational challenges associated with a rare disease diagnosis (2) Supporting management and self-management of rare disease and (3) Integrated care pathways.

P431 WHEN SICK ISN'T SEPTIC – METABOLIC CRISIS PRESENTING IN THE EARLY NEONATAL PERIOD

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Introduction Metabolic crisis in the neonatal period is an infrequently encountered, but potentially devastating presentation of an inborn error of metabolism. Due to the rarity of these disorders, diagnosis may be delayed. Furthermore, presentation may closely mimic neonatal sepsis, a much more frequently encountered condition. We describe the case of a neonate who presented at day nine with non-specific symptoms and signs. Careful evaluation of biochemical abnormalities led to a timely diagnosis of a rare, potentially life threatening metabolic disorder – Argininosuccinic Aciduria.

Clinical Case A nine day old female infant presented with three days of poor feeding, lethargy and reduced urine output. Examination identified hypothermia (34.5°C), tachypnoea, and a decreased level of consciousness. She was the first child of non-consanguineous Irish parents, with no family history of metabolic disorders. She was delivered at term by spontaneous vaginal delivery to non-consanguineous Irish parents, following an uncomplicated pregnancy. There were no septic risk factors or concerns at discharge on day 3. Blood glucose and inflammatory markers were normal. She was fluid resuscitated and commenced on broad-spectrum antibiotics. Despite treatment, she deteriorated. Venous blood gas showed respiratory alkalosis (pH 7.458, pCO₂ 3.92, HCO₃ 20.8, BE -2.4, lactate 1.0) prompting further investigation. Serum ammonia was 562. Retrospective review of investigations identified an unrecordable urea (<0.4 mmol/L), and a diagnosis of urea cycle defect was considered. She was referred to the National Centre for Inherited Metabolic Disorders, and transferred to a tertiary intensive care unit for specialty input. Intravenous sodium benzoate, sodium phenylbutyrate and L-arginine were administered, alongside 10% dextrose. Further investigation revealed elevated glutamine of 2213µmol/L (0–960), citrulline 565µmol/L (0–63), and

argininosuccinate 1014 $\mu\text{mol/L}$, consistent with a diagnosis of argininosuccinic aciduria, subsequently confirmed on molecular genetic testing. She was discharged on oral sodium phenylbutyrate, sodium benzoate and L-arginine, with an appropriate dietary plan. To date, there is no evidence of neurological sequelae, likely attributable to prompt diagnosis and treatment.

Conclusion Argininosuccinic aciduria is a rare, autosomal recessive disorder of urea cycle metabolism caused by deficiency of argininosuccinic lyase. Clinical and biochemical manifestations depend on the severity of enzyme deficiency. In the neonatal variant, it typically presents with hyperammonaemia, encephalopathy and respiratory alkalosis. This case highlights the importance of considering inborn errors of metabolism in the assessment of a sick neonate.

P432 ENCEPHALOPATHY IN TEENAGERS – A CHALLENGING ETIOLOGIC DIAGNOSIS

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Introduction Inherited metabolic disorders due to intoxication provoked by highly toxic endogenous compounds are among the causes of encephalopathy. That is the case of urea cycle disorders in which ammonia's great neurotoxicity can frequently be lethal. Ornithine Transcarbamylase (OTC) Deficiency is an X-link genetic disorder and the most common disorder of the urea cycle. Presentation in heterozygote females is variable and can go from being asymptomatic to having mild chronic symptoms with severe exacerbations in any age.

Case report Fifteen year old female with sporadic headache since the age twelve without other relevant medical history. Due to persistent frontoparietal headache for two weeks, she was given topiramate. Despite medication, the headache worsened and dizziness, blurred vision, dysarthria, aphasia, asterix, motor incoordination and lethargy developed. Trauma, recent infections or toxic ingestions were denied. Diagnostic workup in a private hospital with laboratory studies including urine toxic screening, complete blood count, hepatic and renal function and cerebral MRI were normal. On account of a suspected iatrogenic cause for encephalopathy, topiramate was suspended after two days and the patient was referred to a Pediatric Emergency Department. On admission CSF study was normal but blood tests showed hyperammonemia (229 $\mu\text{mol/L}$) with latter increase to (359 $\mu\text{mol/L}$) despite treating measures (endovenous fluids and discontinuation of protein intake); She was given sodium benzoate, sodium phenylbutyrate and arginine resulting in blood levels of ammonia returning to normal. The demonstration of elevated urinary orotic acid led to the probable diagnosis of OTC deficiency which was later confirmed by molecular diagnosis.

Discussion Serum ammonia levels could be measured in every patient with unexplained altered mental status. Primary (urea cycle disorders) and secondary hyperammonemia alike are considered emergency situations therefore, treatment should never be delayed by diagnostic tests. On the other hand, both treatment and exacerbation preventions have an impact in prognosis regardless of age.

P433 AN INTERESTING CASE DIAGNOSED AS BOTH PHENYLKETONURIA AND MATERNAL PHENYLKETONURIA

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Introduction Phenylketonuria (PKU) is the most common and autosomal recessively inherited metabolic disease due to the deficiency of phenylalanine hydroxylase (PAH). Elevated levels of phenylalanine are not only toxic for the children but also teratogenic for the fetus. Clinical findings of maternal phenylketonuria (MPKU) are intrauterine growth retardation, microcephaly, significant developmental delay, congenital cardiac anomalies, and some other structural defects. Poorly diet control and high levels of blood phenylalanine causes to this severe but preventable clinical syndrome.

Case report A seven-day-old girl admitted to the pediatric metabolism clinic with a suspicion of PKU after newborn screening program. She was born at 40 weeks of gestation with a 2300 gr birth weight and hospitalized for 2 days. Her parents were first degree cousins and the family history was unremarkable for an inherited metabolic disease, however the mother had two miscarriages. Physical examination revealed microcephaly, mild facial dysmorphism, and cardiac murmur in addition to intrauterine growth retardation. Her blood phenylalanine level was 1140 $\mu\text{mol/dL}$ and she was diagnosed as moderate phenylketonuria. As a ventricular septal defect was detected with echocardiography and the mother was born before the national newborn screening program was available, the mother's blood Phe concentration was measured. Surprisingly her blood Phe level was 1614 $\mu\text{mol/dL}$. The mother was a 25 years old woman be able to graduate from primary school and. complained about only concentration problems and forgetfulness. She had also blond hair and blue eyes on physical examination.

Conclusion Maternal phenylketonuria is a preventable public health problem which causes undesirable results like mental-motor retardation and cardiac defects. Although maternal phenylketonuria is not completely coped with, after newborn screening program the incidence is decreased. A strict Phe restricted diet beginning before the pregnancy together with frequent controls of blood Phe levels are essential for management. Here, we report this case, as she was diagnosed both phenylketonuria and maternal phenylketonuria and in order to emphasize thinking MPKU in the presence of microcephaly, developmental delay, and cardiac defects.