101

INHERITED AUTOINFLAMMATORY ENCEPHALOPATHY IN THE DIFFERENTIAL DIAGNOSIS OF CONATAL VIRAL INFECTIONS- NEWBORN WITH AICARDI-GOUTIÈRES SYNDROME

¹Dora Bulić*, ²Tea Škorić, ^{1,3}Tamara Žigman, ⁴Goran Krnjak, ^{1,5}Goran Tešović, ^{1,3}Nina Barišić, ^{1,3}Ivo Barić, ^{1,3}Danijela Petković Ramadža. ¹University of Zagreb, School of Medicine, Zagreb, Croatia; ²Department of pediatrics, Požega General County Hospital, Požega, Croatia; ³Pediatric clinic, University Hospital Centre Zagreb, Zagreb, Croatia; ⁴Department of pediatrics, Varaždin General County Hospital, Varaždin, Croatia; ⁵University Hospital for Infectious Diseases, Dr. Fran Mihaljević, Zagreb, Croatia

10.1136/archdischild-2021-europaediatrics.101

Aicardi-Goutières (AGS) syndrome is a rare early-onset subacute encephalopathy, usually inherited by autosomal recessive trait. The disease commonly manifests in the first year of life. It is genetically heterogeneous disorder associated with mutations of seven different genes. The pathogenic mechanism is disturbed metabolism of endogenously produced nucleic acids and type I interferon upregulation that activates an immune system response. The main clinical features are encephalopathy, irritability, seizures, truncal hypotonia, peripheral spasticity, dystonic posturing, microcephaly, and intellectual impairment. Some patients have episodes of aseptic febrile illness and chilblain-like skin lesions on fingers and earlobes. In 20% of patients, clinical presentation mimics congenital viral infection (hepatosplenomegaly, elevated aminotransferases, thrombocytopenia); for which the syndrome was previously described as pseudo-TORCH. Characteristic findings on neuroimaging are basal ganglia calcifications, cystic leukodystrophy, brain atrophy, and lymphocytosis in the cerebrospinal fluid (CSF). The disease is progressive with lethal outcome during early childhood in 40% of the cases. No etiological treatment is available, but there are ongoing clinical trials with antiretroviral and immunomodulatory agents. The objective of this case report is to increase awareness of AGS in the differential diagnosis of early-onset encephalopathies with basal ganglia calcifications and leukodystrophy and in newborns with suspected congenital viral infections.

Case Presentation The male patient is the first child of non-consanguineous healthy parents. Delivery was on term, but newborn was small for gestational age (BW 2320 g, BL 46 cm, HC 31 cm), and also had truncal hypotonia, tremor, and splenomegaly. Laboratory results showed thrombocytopenia and pleocytosis in the CSF. Brain ultrasound showed ventriculomegaly and periventricular and basal ganglia calcifications. PCR and serology tests for viral infections were negative. Brain MRI revealed polymicrogyria, leukodystrophy, parenchymal and subependymal calcifications, ventriculomegaly, and cerebellar hypoplasia. AGS was suspected and the diagnosis was confirmed by genetic test. Patient was homozygous for common pathogenic mutation c.314G>A (p.Arg114His) in the TREX1 gene. In the further course, the patient was irritable and encephalopathic, with nystagmus, tremor, hyperkinesia, hypotonia, microcephaly, and severe psychomotor retardation.

Conclusion AGS is a rare autoinflammatory encephalopathy with a broad phenotypic spectrum, including perinatal-onset disease that mimics congenital viral infection. Early clinical suspicion followed by genetic testing can shorten the diagnostic odyssey. The correct diagnosis is required to provide information about the expected course of the disease, genetic counseling of the family, and to offer prenatal diagnosis in subsequent pregnancies.

102

EMANUEL SYNDROME – CASE REPORT OF A RARE UNBALANCED TRANSLOCATION SYNDROME

Lorita Mihovlović Prajz*, Lucija Debeljak Poslek, Rebeka Ribičić, Jasna Tumbri, Iva Kuliš, Snježana Gverić-Ahmetašević. Klinički bolnički centar Sestre milosrdnice

10.1136/archdischild-2021-europaediatrics.102

Emanuel syndrome is a rare syndrome characterized by prenatal and postnatal growth retardation, hypotonia, severe mental retardation, microcephaly with characteristic facial features including micrognathia, protruding forehead, broad and flattened nasal root, long and pronounced philtrum, ear deformities with preauricular pits and/or appendages, high or cleft palate and congenital heart defects, kidney anomalies and genital anomalies in men. It is an unbalanced translocation syndrome caused by a 3:1 meiosis I malsegregation during gametogenesis in a phenotypically normal, balanced translocation carrier parent. The exact incidence of the syndrome is unknown but it is estimated that there are about 500 patients worldwide with this syndrome. We report a male newborn from the mother's 4th pregnancy and 1st birth in which a diagnostic process, done due to intrauterine growth retardation, raised a suspicion of Dandy Walker malformation. After birth, specific characteristics were noticed that raised suspicion of Emanuel syndrome. The diagnosis of Emanuel syndrome is made by detecting duplication 22q10-22q11 and duplication 11q23-qter on the supernumerary derivative chromosome 22 [der (22)], so extensive diagnostics was performed on our patient, including genetic analysis. Genetic analysis confirmed the karyotype 47, XY, + der (22) t (11; 22) (q23, q11.2) mat; CMA and FISH confirmed that it indeed was Emanuel syndrome. Cytogenetic analysis of family members revealed that the mother was a carrier of a balanced translocation between the long arms of 11th and 22nd chromosome that she inherited from her father, and we found the same translocation in one of the mother's sisters. The outcomes of future pregnancies of a parent who is a carrier of balanced translocation t(11; 22) are varying from the possibility of having a healthy child, a child who has Emanuel syndrome, a child who is a carrier of balanced translocation t(11; 22), but also having repeated spontaneous miscarriages. Prenatal diagnosis in these cases is highly recommended. It is necessary to make a diagnosis as soon as possible in order to improve the quality of life and prolong the survival of the patient but also to give timely genetic counselling advice to family members.

Metabolic Disease

103

ENT CONDITIONS AND DISORDERS IN CHILDREN WITH HUNTER SYNDROME

Irina Zelenkova*, SG Gubanova, TA Polunina, ND Vashakmadze, LS Namazova-Baranova. The Research Institute of Pediatrics and Child Health of the Central Clinical Hospital of the Russian Academy of Sciences of the Ministry of Science and Higher Education of the Russian Federation

10.1136/archdischild-2021-europaediatrics.103

Objective to describe the features of the ENT conditions and disorders in children with Hunter syndrome. Hunter syndrome, also known as mucopolysaccharidosis type II (MPS II),

is a rare X-linked recessive disease. The MPS II is a hereditary metabolic disorder caused by accumulation of glycosaminoglycans (GAG) in organs and tissues due to mutations in the genes, which encode intralysosomal hydrolysis of macromolecules. Hunter syndrome is a progressive, multisystem disease. At the same time a child may have mental retardation and speech development delay, skeletal bone deformities, loss of vision, hearing loss.

Patients and Methods The study included 17 boys aged from 2 to 12 years old with genetically confirmed Hunter syndrome. All patients underwent examination by otolaryngologist, also tympanometry, diagnostic nasopharyngolaryngoscopy, registration of otoacoustic emission, audiometry, cardiorespiratory monitoring were performed.

Results The accumulation of GAG leads to a gradual narrowing of the nasopharynx and larynx lumen, a thickening of the tongue and vocal folds, laryngeal cartilages deformation, an enlarged of pharyngeal, palatine and lingual tonsils.

11 children (64.7%) had chronic inflammation of the nasal mucosa and pharyngeal tonsil with frequent exacerbations. Pharyngeal tonsil hypertrophy was detected in 10 patients (58.8%).

14 children (82%) had a wide, thickened tongue. Hypertrophy of the tonsils was diagnosed in 8 children (47%).

The voice had changed (hoarseness) in 16 children (94%). Deformation of the epiglottis was detected in 4 people (23.5%), tracheomalacia – in 1 child (5.8%).

Among the complications acute sinusitis and exudative otitis media were detectable in 52.9% of patients. 10 children (58.8%) had obstructive sleep apnea (OSA) syndrome, two of them (11.7%) had a severe degree of the disease, which was an indication for adenotonsillectomy. Hearing loss was found in 10 boys (58.8%).

In most patients (82%) a combined pathology of the ear, throat and nose was detected, 2 children (11.7%) had only adenoid hypertrophy, and only 1 child

(5.8%) did not have any pathology of ENT organs.

Conclusion Functional disorders and diseases of the ear, throat and nose are found in most children with Hunter syndrome, which could be one of its early manifestations. An ENT specialist may suspect MPS type II according to the presence of an ENT pathology that is difficult to treat in a standard manner, combined with the pathology of other organs and systems.

Early diagnosis and the possibility of enzyme replacement therapy can control the disease progression and avoid early disability.

104

HYPOKETOTIC HYPOGLYCEMIA AND HYPERAMMONEMIA AS PRESENTING FEATURES OF EARLY ONSET MULTIPLE ACYL-COA DEHYDROGENASE DEFICIENCY

Vanja Ille*, Danijela Petković Ramadža, Tamara Žigman, Boris Filipović-Grčić, Ruža Grizelj, Dorotea Ninković, Dorotea Bartoniček, Ana Škaričić, Iva Bilandžija Kuš, Nikola Mesarić, Goran Krmjak, Ksenija Fumić, Ivo Barić. *Department of Pediatrics, University Hospital Centre Zagreb, Zagreb, Croatia*

10.1136/archdischild-2021-europaediatrics.104

Introduction Multiple acyl-coenzyme A dehydrogenase deficiency (MADD) or glutaric aciduria type II is a rare, autosomal recessive disorder of fatty acid and amino acid oxidation. Disease is caused by pathogenic mutations in ETFA or ETFB

genes, which encode two subunits of electron transfer flavoprotein (ETF), or ETFDH gene, encoding for ETF-dehydrogenase. Phenotype is heterogenous, from severe neonatal acute metabolic decompensation, with or without congenital anomalies, to milder, late onset forms. Diagnosis is made by acylcarnitine and urinary organic acid analysis, and gene testing. Treatment is based on restricted fat and protein intake, high carbohydrate diet, with carnitine, riboflavin and CoQ10 supplementation.

Case Report Patient is a second child of unrelated parents. Family history unremarkable. Pregnancy was complicated by oligohydramnios. Delivery was on term, uneventful, BW 3740 g, BL 53 cm, AS 10,10. Tremor occurred as manifestation of hypoglycemia (BG 1.8 mmol/L), corrected with 10% oral glucose, on the first day of life. The newborn was euglycemic until 20 hours of life when irritability and somnolence were noticed in hypoglycemia (capillary glucose 2.3 mmol/L, venous glucose was immeasurably low). Glucose infusion was started but patient deteriorated to bradypnea and bradycardia.

Cardiopulmonary reanimation lasted 40 minutes. Upon admission in NICU, patient was cardio-respiratory stable, but unconscious, hypertonic and soon developed seizures. Laboratory findings revealed metabolic acidosis (pH 7.3, BE -15.6), hyperlactatemia (14 mmol/L), hyperammonemia (230 µmol/L), increased aminotransferases and CK, normal blood glucose and positive urinary ketones. Brain MRI revealed cortical cytotoxic edema, restricted diffusion in corticospinal tracts and pons, and temporal atrophy. Ammonia normalized following high caloric intake, nitrogen scavengers, L-arginine, L-carnitine and vitamin B12. Urgent metabolic work-up revealed typical plasma acylcarnitine and urine organic acid profile for MADD. We started low protein and fat, high carbohydrate diet, continued with L-carnitine and added CoQ and riboflavin in therapy. Ultrasound showed mild hypertrophic cardiomyopathy and no malformations of other organs. Gene analysis revealed homozygous mutation c.1250C>A (p. Thr266Met) of the ETFB gene. In further course patient was stable, but with severe developmental delay, epilepsy and impaired vision.

Conclusion Beta oxidation defects, even with positive ketones, should be in differential diagnosis of neonatal hyperammonemia, as treatment is different than for other diseases. Lipid infusions, used to provide adequate caloric supply in other disorders, are contraindicated. Urgent metabolic work-up is mandatory for early diagnosis and optimal patient management. Clinical course with early acute cardio-respiratory failure, hypoglycemia and moderate hyperammonemia may be indicative for beta-oxidation defects.

105

ALG6-CDG- CONGENITAL DISORDER OF GLYCOSYLATION WITH RECOGNIZABLE PHENOTYPE

Marina Kokić Golub*, Tamara Žigman, Danijela Petković Ramadža, Maja Jurin, Duška Tješić Drinković, Stanko Čavar, Sanja Džida, Jelena Nikolić, Andrija Miculinić, Ernest Bilić, Ksenija Fumić, Ivo Barić. *Dom zdravlja Krapinsko-zagorske županije/Kliničko bolnički centar Zagreb*

10.1136/archdischild-2021-europaediatrics.105

Congenital disorders of glycosylation (CDG) is a large group of genetic metabolic diseases that usually affects many different organ systems. Glycosylation is a complex process