ORIGINAL RESEARCH PAPER

Paediatrics

A CASE REPORT OF ZELLWEGER SYNDROME WITH GLOBAL DEVEOPMENTAL DELAY

KEY WORDS: seizures, global developmental delay, hypotonia

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ABSTRACT

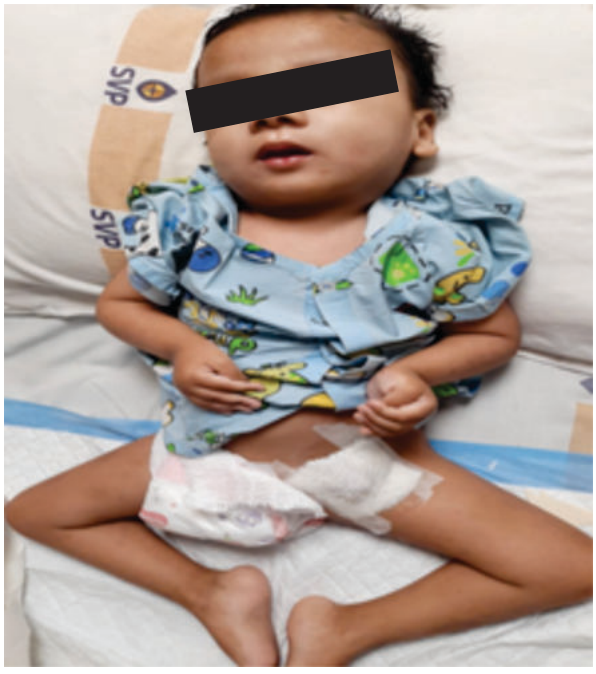
Peroxisome biogenesis disorder are related to spectrum of genetic diseases that range from severe Zellweger syndrome to milder infantile Refsum disease. Zellweger syndrome is characterized by dysmorphic features, severe hypotonia, seizures, failure to thrive, liver dysfunction and skeletal defects. We report a case of Zellweger syndrome, confirmed by clinical, biochemical and molecular findings, diagnosed in context of dysmorphism, and seizures.

INTRODUCTION

The Zellweger Syndrome is a rare peroxisome biosynthesis disorder (incidence: 1 in 50,000 to 100,000 live births), characterized by a generalized loss of peroxisomal functions. This is a fatal hereditary autosomal recessive disorder, whose features include craniofacial dysmorphism and profound neurologic abnormalities. ZS is commonly caused by mutations in PEX1 and PEX6 genes. Zellweger syndrome (ZS) is a severe manifestation of disease within the spectrum of peroxisome biogenesis disorders(PBDs) that include neonatal adrenoleukodystrophy, infantile Refsum disease, and rhizomelic chondroplasia punctata. Patient with Zellweger syndrome in the neonatal period often presented with typical dysmorphic features, severe neurological dysfunction with hypotonia and occasionally seizures, failure to thrive. During the first month of life, predominant symptoms may include hepatomegaly, prolonged jaundice, and sometimes, liver failure but may also manifest as non specific gastrointestinal problems such as anorexia, vomiting, diarrhea, leading to FTT.

CASE STUDY

We report the case of Zellweger syndrome. The patient was first born male child born through vaginal spontaneous delivery at 37 weeks of gestational age with birth weight of 2400 g and cried immediately after birth with normal prenatal and perinatal history. Patient was discharged with routine newborn care. There was no history of neonatal jaundice. Patient had first episode of GTCS seizure with fever at 2 months of age and was treated as per standard protocol and discharged. Again patient had 2nd attack of seizure at 4 months of age. At that time patient presented with fever, refusal to feed, lethargy and GTCS seizure. On examination patient had hypotonia, and dysmorphic features (flattened facies, broad nasal bridge, micrognathia, thin lips), hepatomegaly , skeletal deformities, and also developmental delay was present in form of patient was not able to hold neck, no social smile. Patient was further investigated. Cranial magnetic resonance imaging was done which suggested ill defined asymmetric MR signal abnormality involving bilateral parietal subcortical white matter as compared to adjacent unmyelinated white matter P/O encephalopathic changes. EEG suggestive of multifocal discharge, predominantly occipital, and Absence of sleep spindles. CSF examination was normal. TMS report was done which was normal. Exome sequencing suggested homozygous mutation of PEX3 gene on EXON 2 of Chromosome 6 and Heterozygous mutation of AP3B2 gene in EXON 14 of Chromosome 15 which suggestive of Early infantile epileptic encephalopathy. On the basis of clinical phenotype the hypothesis of PBDs was considered. Patient treated with appropriate AEDS. Patient discharged on AED and advised regular physiotherapy. Hearing assessment was done which was normal. At present patient is seizure free since 4 months on two AEDS with developmental milestones not achieved as per age.



CONCLUSION

Patients with ZS present in the neonatal period with a characteristic phenotype of distinctive facial stigmata, pronounced hypotonia, poor feeding, hepatic dysfunction, and often seizures and bony abnormalities.

Prenatal diagnosis can be achieved through assays of peroxismal enzymes activity(di hydroacetone-phosphat acyltransferase), peroxismal metabolites and molecular screening techniques. Analysis of cerebral gyration and myelination in MRI performed during 3rd trimester also facilitates the prenatal diagnosis. Biochemical prenatal testing for ZS is possible in chorionic villus biopsy material, cultures chorionic villus cells or culture amniocytes.Despite an absence of treatment options, prompt diagnosis of ZS is important for providing appropriate symptomatic care, definitive genetic testing, and counseling regarding family planning.

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