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Case Report

Uncommon, but a Classic Case of Neonatal Encephalopathy

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Abstract

We report a rare case of Zellweger syndrome presenting in neonatal period as encephalopathy, poor feeding and with hepatic dysfunction. The diagnosis was not known initially but evolved later with imaging and lab workup, only to be confirmed by elevated Very Long Chain Fatty Acids in blood. Dysmorphic features in case of a neonatal encephalopathy having classic MRI findings, hepatomegaly with hepatic dysfunction and bilateral perinatal renal cysts should lead to a diagnosis of Zellweger Syndrome. This clinical case shows typical neuro-abdominal imaging findings of Zellweger's syndrome with a brief review of the literature.

Keywords: *Zellweger Syndrome; Germinolytic Cysts; Very Long Chain Fatty Acids (VLCA); Renal Cysts; Hepatic Dysfunction; Polymicrogyria*

Abbreviations

VLCA: Very Long Chain Fatty Acids; MRI: Magnetic Resonance Imaging; NICU: Neonatal Intensive Care Unit

Introduction

Inborn errors of metabolism are a cause of disease in the neonatal period that can present in many different ways. A high index of suspicion and a systematic approach are required to reach a diagnosis. The following case report is of a child that presented with encephalopathy that on a detailed work yielded a metabolic cause like Zellweger Syndrome. This case report aims to reiterate the classic imaging findings of Zellweger syndrome which is an infrequent cause of neonatal encephalopathy.

Case Report

A three-week-old neonate presented with hypotonia, feeding difficulty, and seizures since day ten of life. The baby was born at 40 weeks by vaginal delivery to non-consanguineous parents. Meconium stained liquor was noted. APGAR score was five at 1 minute and eight at 5 minutes. With repeated episodes of desaturation, the child required NICU admission. She was intubated and ventilated. Low set ears, wide open fontanelle and abnormal parietal bossing of the head were noted on physical examination. Antenatal ultrasound had shown lateral ventricular enlargement.

NICU work-up showed an increase in liver enzymes with hyperbilirubinemia. Increased plasma levels of Very Long Chain Fatty Acids were noted. Thyroid function tests, Plasma amino acid analysis, Acetylcholine receptor antibody test, Total creatine kinase estimation, serum glucose, CSF lactate and renal function test were unremarkable. TORCH panel and blood cultures were negative. A normal karyotype was reported. MRI examination of the brain and ultrasound examination of the abdomen were performed.

MRI showed a pattern resembling polymicrogyria of bilateral perisylvian cortex (arrows in figure 1A). Multiple shallow gyri appearing thick with poor differentiation of the cortex and white matter were noted in bilateral frontal lobes (arrowheads in figure 1A and 1B). Normal appearing cortical sulci and gyri were seen more posteriorly in occipital regions. Small periventricular CSF signal intensity germinolytic cysts were noted adjacent to the frontal horns at the caudothalamic interface (arrows in figure 1B). Bilateral, predominantly posterior ventricular dilation of lateral ventricles was observed (asterisk in figure 1B). Posterior limb of internal capsule showed loss of its normal linear bright signal on T1W images with corresponding loss of hypointense signal on T2W images suggesting impaired myelination (arrows in figure 2A and 2B). Similar, abnormal ill-defined increased signal intensity on T1W images is noted in bilateral globus pallidi (long arrows in figure 2A).

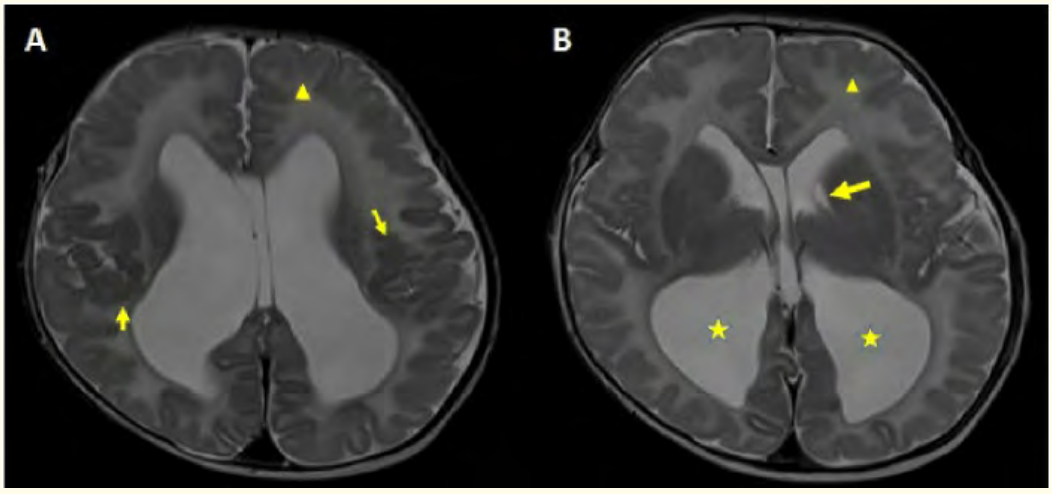

Figure 1: *T2W Axial MRI images of the brain at the level of the body of lateral ventricles (A) at the level of the caudothalamic interface (B).*

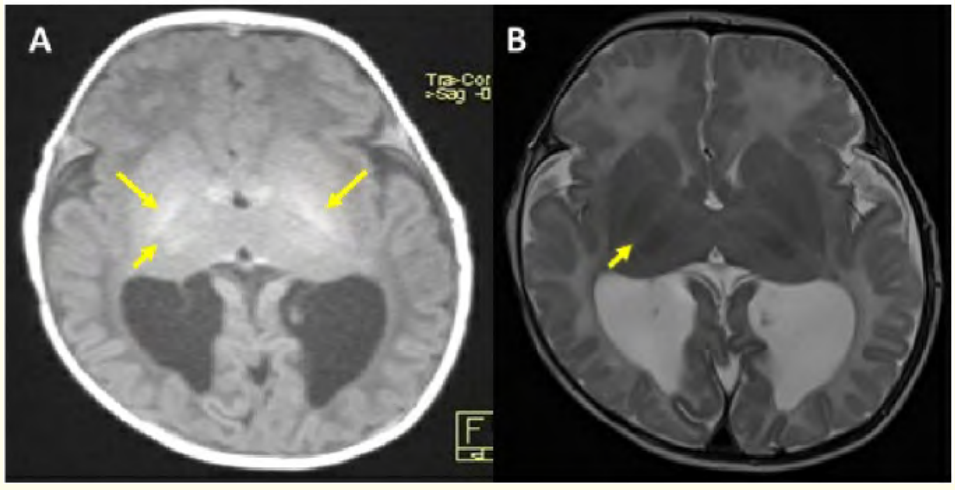

Figure 2: *(A) T1W and (B) T2W Axial MRI images of the brain at the level of the level of basal ganglia.*

Ultrasound scan of the abdomen showed normal sized kidneys with multiple small subcapsular cortical cysts in the renal parenchyma with a preserved corticomedullary difference (arrows in figure 3). Hepatomegaly was noted without focal lesions. There was no intrahepatic or extrahepatic biliary duct dilation.

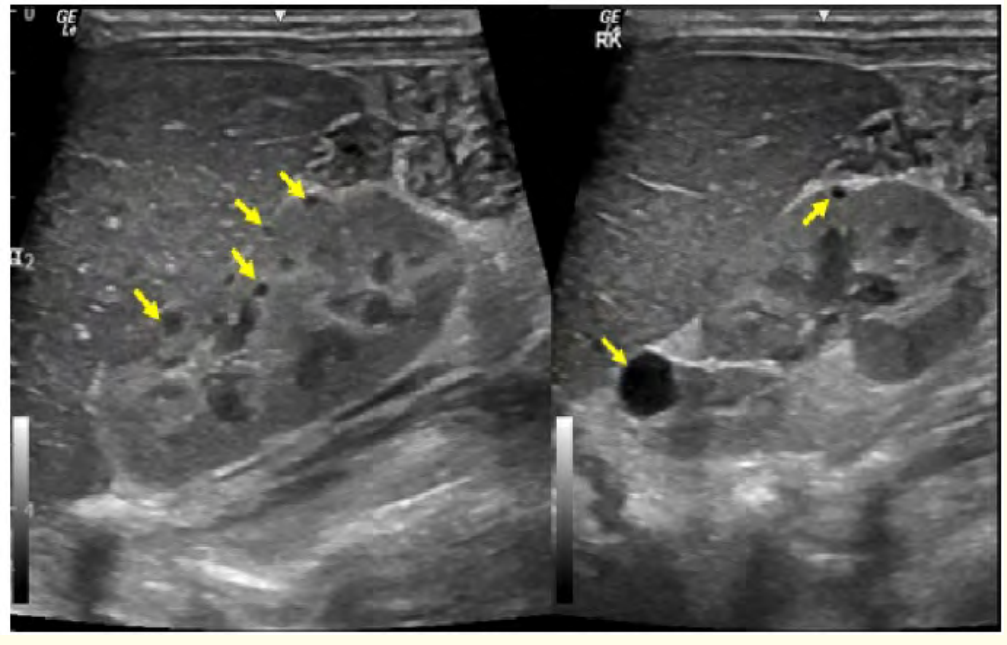

Figure 3: *Ultrasound images of right kidney in the long axis.*

The collective findings of MRI brain and abdominal ultrasound with hepatic derangement suggest Zellweger syndrome (Cerebro-Hepato-Renal degeneration). Although on further workup, the patient was negative for PEX1 gene, but the blood levels of Very Long Chain Fatty Acids (VLCA) were markedly elevated supporting the diagnosis.

Discussion

Zellweger syndrome is an autosomal recessive inherited disease caused by abnormal peroxisomes with variable loss of their function. It is the most common type among the peroxisomal disorders [1]. Peroxisomes are intracellular organelles, seen in all cells of human tissue except in mature red blood cells. Liver and kidneys have a rich store of peroxisomes. The peroxisomes are involved in lipid and amino acid metabolism, biosynthesis of cholesterol, free radicle scavenging and platelet activation [2].

Dysmorphic features, hypotonia, seizures, neurodevelopmental delay, hepatomegaly (in 80% of the cases) with raised liver enzymes, hyperbilirubinemia, bilateral renal cysts (in 70% cases) sensorineural deafness and retinopathy characterize the phenotype of Zellweger syndrome [2].

Finding of bilateral multiple renal cysts in perinatal period has a differential diagnosis. Autosomal recessive and dominant polycystic kidney disease, multicystic dysplastic kidney and bilateral obstructive renal dysplasia are well-known causes. Zellweger syndrome and Bardet – Biedl syndrome although rare should find a place in the list of differential diagnosis [3].

Laboratory diagnosis of peroxisomal disorders is supported by the finding of Very Long Chain Fatty Acids in blood. Skin fibroblast culture can also establish the diagnosis. Mutations involving the peroxisomal biosynthesis genes known as PEX genes permit correct identification [4].

Subependymal cysts on MRI can be either acquired or congenital. Acquired subependymal cysts are usually post-hemorrhagic sequelae. Congenital cysts are due to germinolysis. It is difficult to differentiate the cause of the cysts on ultrasound and by MRI. Germinolytic cysts are seen in various conditions like congenital viral infections, Zellweger syndrome, Fetal circulatory disorders, D2-hydroxyglutaricaciduria, pyruvate dehydrogenase E1-alpha deficiency, complex mitochondrial dysfunction, pontocerebellar hypoplasia, chromosomal abnormalities, and maternal cocaine abuse [5].

Conclusion

Although rare, Zellweger syndrome is a well-known cause of metabolic encephalopathy. Aggregate imaging findings of cerebral cortical abnormalities, ventricular dilation, germinolytic cysts, myelination abnormalities, when correlated with hepatic dysfunction and perinatal renal cysts in a neonate with encephalopathy should favor a radiological diagnosis of Zellweger syndrome.

Conflict of Interest

There are no conflicts of interest.

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