Multicystic Brain and Refractory Neonatal Seizures

Pedro Maneira Sousa[1], Teresa Campos[2], Luísa Sampaio[3], Ana Vilan[1]

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A term male infant, second child of first-degree consanguineous parents presented myoclonic jerks at 6 hours of life. The neonatal transition was uneventful. Sepsis workup, metabolic neonatal screening as well as ammonia, lactate, amino acid profile, and organic acid were unremarkable. He had a peculiar face with prominent cheeks, axial hypotonia, and absence of gaze fixation (normal fundi and lens). He required tube feeding and seizures became refractory. Head ultrasound on day 2 of life was normal and on day 10 of life showed cystic lesions confirmed in brain magnetic resonance imaging at 14 days of age (Fig. 1). Molybdenum cofactor deficiency was considered. Homocysteine was markedly reduced, and uric acid was undetectable in serum. Urinary sulfites were positive by dipstick. The genotype analysis identified the pathogenic variant diagnosed p.Lys180Argfs*31(c.539_540 del AA) mutation in the homozygosity of the molybdenum cofactor synthesis (*MOCS*) 2 gene. He had a rapid neurological deterioration and, therefore, he was redirected to palliative care.

Molybdenum cofactor deficiency is a rare autosomal recessive metabolic disorder caused by mutations in four genes: *MOCS1*, *MOCS2*, *MOCS3,* and gephyrin (*GEPH*). Molybdenum is an essential cofactor to xanthine dehydrogenase, sulfite oxidase, and aldehyde oxidase function.[1] Neonatal onset presents with feeding difficulties, refractory seizures, progressive destruction of neuronal structures, and subcortical cystic changes, due to sulfite accumulation leading to death in early childhood.[2-4] Facial dysmorphisms and lens dislocation have been reported.[1] Recognizing the rapid progressive cystic changes with a head ultrasound was an important clue to consider molybdenum cofactor deficiency. Although the brain magnetic resonance findings could mimic hypoxic-ischemic encephalopathy, low plasma homocysteine and elevated urine sulfite was decisive in the diagnosis. Currently, there is no effective therapy for patients with an *MOCS2* gene mutation, but establishing early diagnosis, delineating the phenotypic spectrum will be crucial in future target treatment to change the neurological outcome.[5]

Keywords: Brain Diseases, Metabolic/diagnosis; Genetic Diseases, Inborn/diagnosis; Infant, Newborn; Metabolic Diseases/diagnostic imaging; Seizures

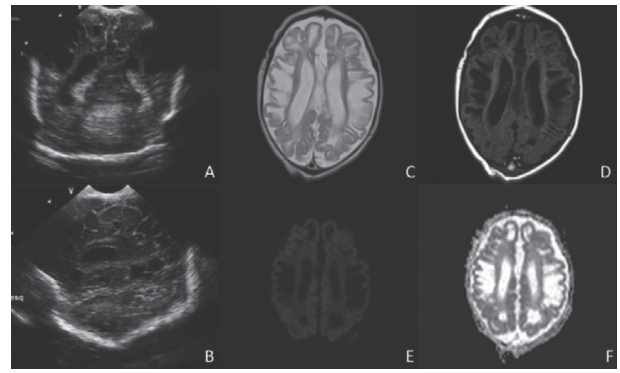

Figure 1. Head ultrasound, coronal (A) and parasagittal left (B) view, at 10 days of age shows subcortical cystic lesions and a wider interhemispheric fissure. Brain magnetic resonance, T2-weighted image (C), T1-weighted image (D), diffusion and apparent diffusion coefficient map (E/F), at 14 days of age shows extensive multicystic leukoencephalopathy in both hemispheres, predominantly subcortical.

WHAT THIS REPORT ADDS

- A genetic-metabolic cause of neonatal seizures should be suspected when there is consanguinity in the family history, seizure semiology - myoclonic seizure, refractory seizure, and seizure associated with a syndromic phenotype.
- Cranial ultrasound as a key tool at the bedside, allowing for the recognition and monitoring of the progressive cystic changes, later confirmed in magnetic resonance imaging.
- Uric acid as an important screening marker to detect inborn errors of metabolism.

Conflicts of Interest

The authors declare that there were no conflicts of interest in conducting this work.

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1. Neonatology Department, Centro Hospitalar de São João, Porto, Portugal
2. Reference Center of Inherited Metabolic Diseases, Centro Hospitalar de São João, Porto, Portugal
3. Neuroradiology Department, Centro Hospitalar de São João, Porto, Portugal
Corresponding Author
Pedro Maneira Sousa
https://orcid.org/0000-0001-7372-5916
pedromaneirasousa@gmail.com
Centro Hospitalar de São João, Alameda Prof. Hernâni Monteiro, 4200-319 Porto, Portugal
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