Case 14760

Lissencephaly-pachygyria spectrum
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Section: Neuroradiology
Area of Interest: Neuroradiology brain
Procedure: Education
Technique: MR
Technique: CT
Special Focus: Pathology Case Type: Clinical Cases
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Patient: 2 months, male

Clinical History:

Two-month-old male patient with new onset seizure.

Imaging Findings:

CT brain parenchyma demonstrates no evidence of normal gray/white differentiation. There is diffuse flattening of the sulci with a single prominent sulcation in the region of the sylvian fissure. The ventricles are slightly dysmorphic in appearance, but normal callosal structures are present. There is complete visualisation of the septum pellucidum and normal hemispheric separation is present. The visualised brainstem is within normal limits. (Fig. 1) MRI shows a near complete lack of sulcation throughout the cortex, with thickening of the cortical grey matter in a uniform pattern. There is diffuse prominence of the lateral ventricles, with no evidence of hydrocephalus present. The third and fourth ventricles are normal in calibre. The corpus callosum is present, with no evidence for dysgenesis. (Fig. 2, 3 and 4)

Discussion:

The term lissencephaly is derived from the Greek for smooth ("lissos") and brain ("enkephalos"). Lissencephaly (LIS, which involve agyria and pachygyria), with subcortical band heterotopia (SBH), comprises a spectrum of malformations of cortical development caused by insufficient neuronal migration.

In severe lissencephaly, the cortex lacks surface folds (agyria) while milder manifestations include abnormally broad folds (pachygyria). [1]

The neuroblasts are generated through mitosis of neural stem cells in the ventricular zone (VZ) of the fetal brain between 5 and 22 weeks of gestation. Post-mitotic neuroblasts undergo radial migration outward from the VZ, guided by radial glial fibres, to populate the cortical plate—the embryonic cerebral cortex. Slow or arrested migration leads to a thickened cortex with reduced folding or the stranded neurons of SBH.

MRI remains the key investigation in the assessment of the lissencephalic patient. LIS is typically divided into type I or classic and type II or cobblestone complex, which differ in clinical presentation, genetic and imaging appearances.

Classical lissencephaly is distinguished from other forms of lissencephaly by the presence of an abnormally thick 4-layer cortex and, typically, by the absence of other major brain abnormalities. Classical lissencephaly is caused by mutations in three genes: PAFAH1B1, DCX, and TUBA1A [2]. The neuroradiological appearance of lissencephaly and SBH is often graded using a 6-point grading system based on the severity and anterior-posterior gradient of the abnormalities, from severe grade 1 (complete agyria) to mild grade 6 (SBH only) [3]. Around 65% of patients with isolated lissencephaly have deletions or intragenic mutations of PAFAH1B1. PAFAH1B1-related lissencephaly has some distinctive neuroradiological features. These include a smooth,
thickened cortex (typically 12–20 mm compared with a normal thickness of 3–4 mm. The multiple congenital anomaly syndromes with LIS include the Miller–Dieker and Baraitser–Winter cerebrofrontofacial syndromes, and X-linked lissencephaly with abnormal genitalia or XLAG.

Cobblestone cortical malformation (CCM), also known as "type 2" lissencephaly is clinical, genetically, histologically and neuroradiologically distinct from classical lissencephaly. CCM can appear agyric or pachygyric, although with higher quality brain imaging an irregular or pebbled aspect to the cortex becomes visible. The cortex in CCM is typically thinner than in classical lissencephaly. Irregularity in the grey-white boundary may also be present, similar to that seen in polymicrogyria. Histopathologically, CCM is due to over-migration of neurons (in contrast to the under-migration of classical lissencephaly).

**Differential Diagnosis List:** Lissencephaly-pachygyria spectrum, Polymicrogyria, Normal premature infant

**References:**


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