Case Series of Classical Type-1 Lissencephaly

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Abstract: Lissencephaly (LIS) is a cortical development malformation characterised by impaired neuronal migration and abnormal formation of cerebral convolutions or gyri. Agyria, pachygyria, and subcortical band heterotopia are all part of the LIS spectrum. The main difference between LIS and SBH is that LIS has an abnormally thick cortex with reduced or absent formation of cerebral convolutions, whereas SBH has abnormal bands of neurons beneath a normal cortex, though the cerebral gyri may be separated by unusually shallow sulci. A few lissencephaly patients have severe congenital microcephaly, which is known as microlissencephaly (MLIS). Miller-Dieker and Baraitser-Winter cerebrofrontofacial syndromes, as well as X-linked lissencephaly with abnormal genitalia, are examples of congenital anomaly syndromes associated with LIS. Lissencephaly is a rare genetic condition that is distinguished by a lack of cortical convolutions. It has been linked to mutations in the lissencephaly-1 (LIS1) (Reiner et al., 1993), doublecortin (DCX) (des Portes et al., 1998), and tubulin alpha 1A (TUBA1A) genes most frequently.

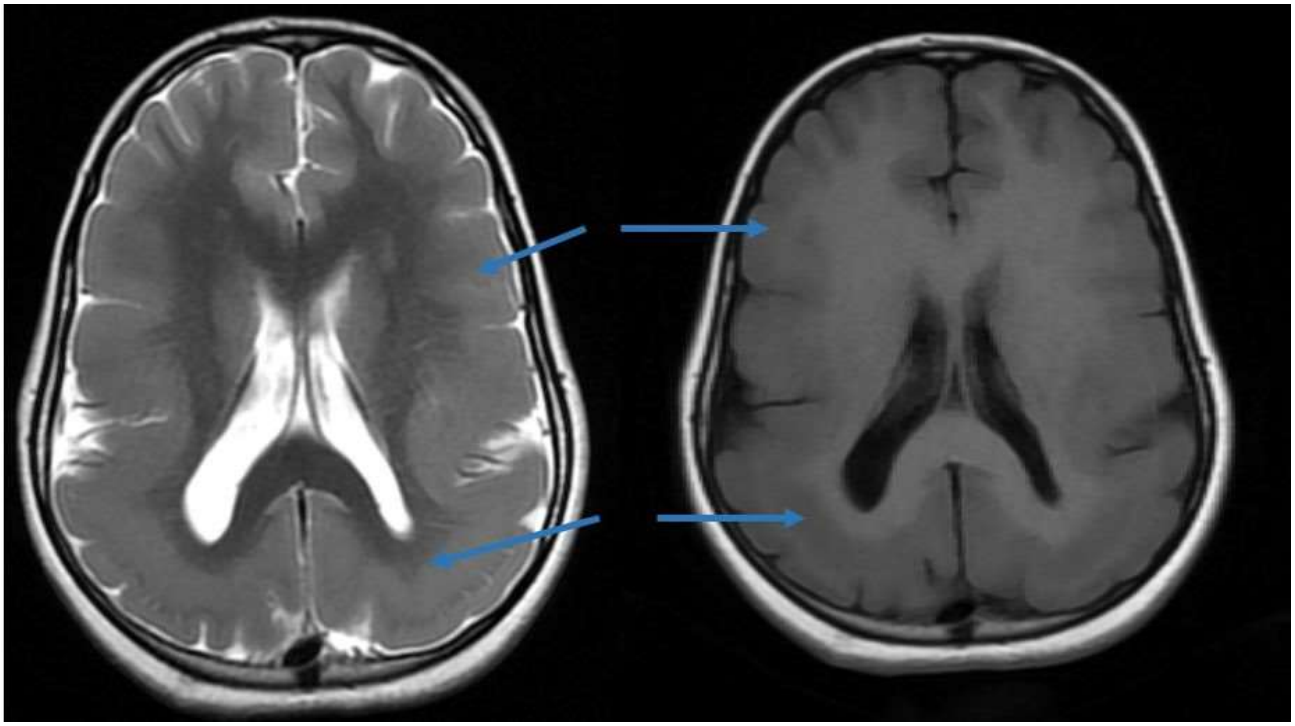
Clinical statement:

3 episodes of seizures, no birth insult, developmental delay

MRI FINDINGS:

Abnormal gyration in the form of reduction in number of gyri with broadening and thickening of cortex seen in bilateral cerebral hemipsheres, prediminant in parieto-occipital lobes-Pachygyria-lissencephaly complex

Lobar band heterotopia is seen in bilateral parieto-occipital lobes.



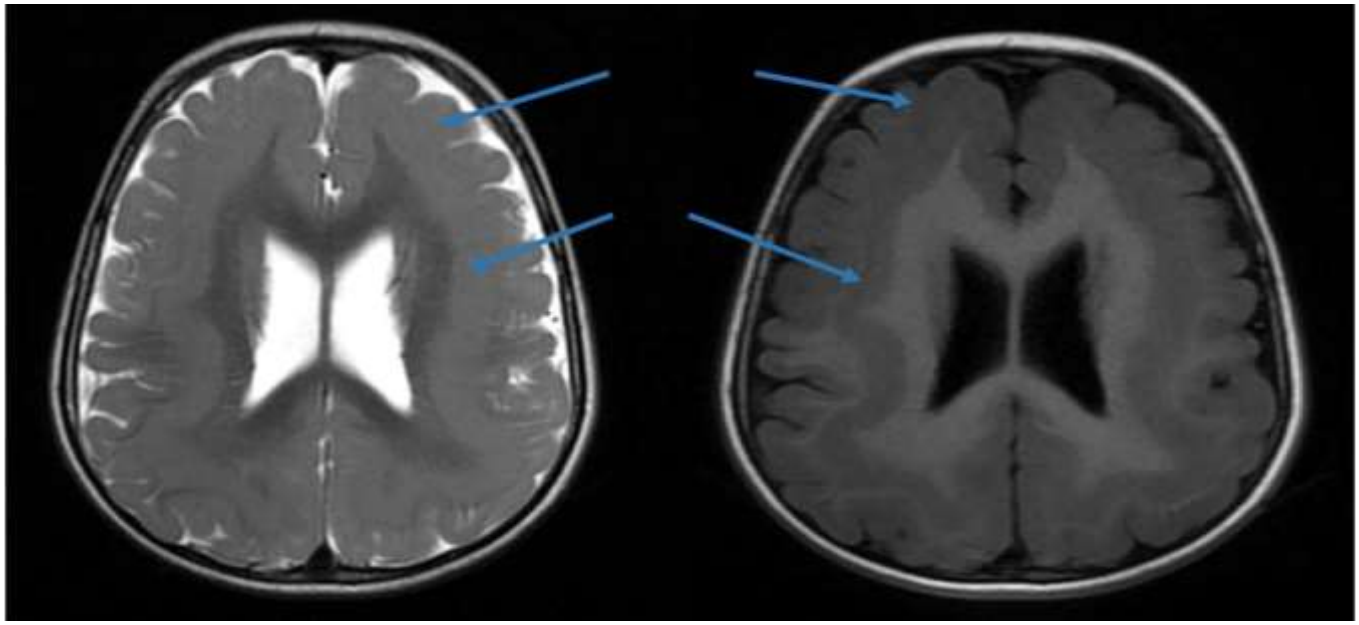
Case 2:

4 episodes of seizures, no birth insult, no developmental delay - ? Infantile spasms.

MRI FINDINGS:

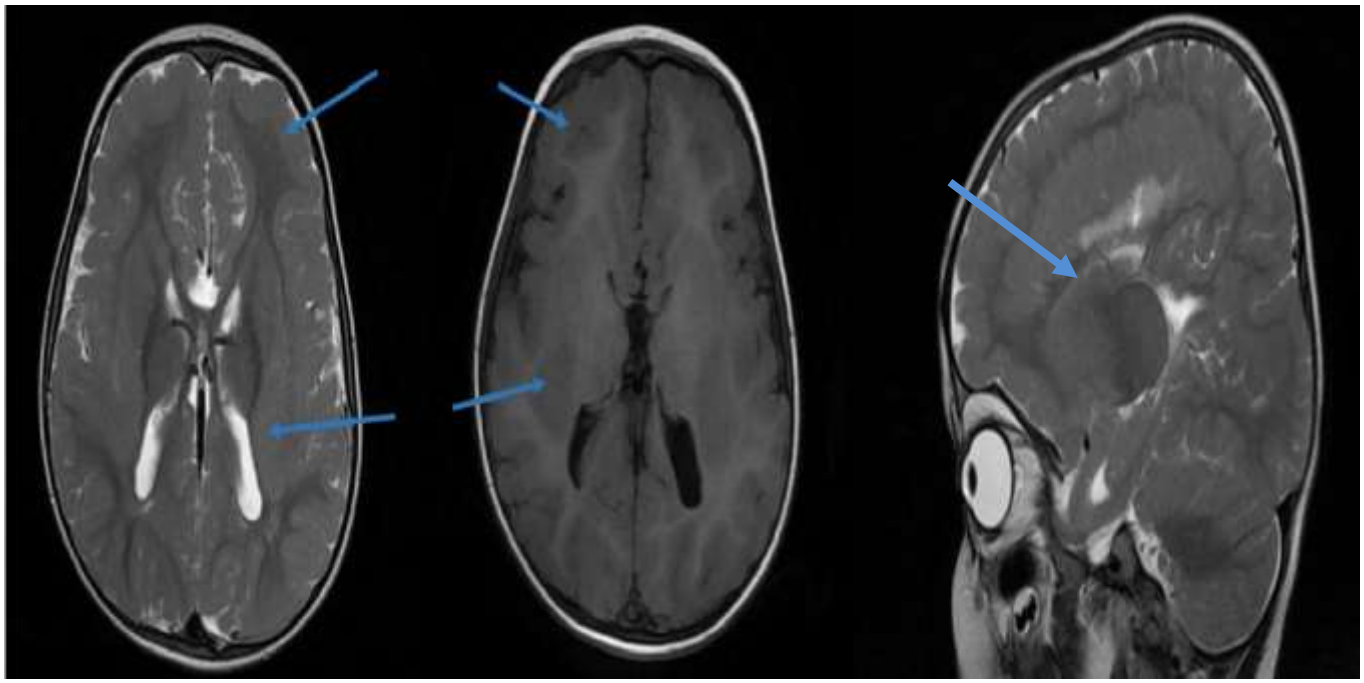
Abnormal gyration in the form of reduction in number of gyri with broadening and thickening of cortex (maximum thickness of 7mm) and shallow sulcal spaces seen in bilateral cerebral hemipsheres, predominantly in parieto- occipito-temporal lobes.

Lobar band heterotopia in the form of hyperintense signal on T1 images and hypointense signal on T2 images is seen in bilateral cerebral hemispheres.



Case 3:

Global developmental delay. NICU admission for 3 days. Antenatal history of hydrocephalus.



On MR Imaging Abnormal gyration in the form of broadening and thickening of cortex (maximum thickness of 7mm) and shallow sulcal spaces seen in bilateral cerebral hemipsheres.
Abnormal band like gray matter noted along the periventricular and deep white matter regions in bilateral cerebral hemispheres.
Near total absence of corpus collosum.

DISCUSSION:

Lissencephaly is caused by insufficient neuronal migration at the cellular level. LIS1 lissencephaly is distinguished by a "four-layered cortex," whereas DCX lissencephaly has a cerebral cortex with six layers. This is significant because the appearance of cortical convolutions has been linked to the intensity of neurogenic processes such as the development of radial glial scaffolding used for radial migration of neurons , differences in the rate of increasing supragranular thickness and differences in the rate of increasing supragranular thickness I-III) vs. infragranular layers (V-VI), sequential cortical fibre ingrowth, increases in brain volume, and accelerated white matter growth compared to grey matter are all indicators of connectivity development.Recently, phenotypic differences in subjects with mutations in a single lissencephaly-associated gene were reported (1).

Pachygyria is considered a subtype of lissencephaly which, in turn, is a spectrum of disorders caused by abnormal neuronal migration. Clinical presentation in this disorder may be varied including microcephaly, developmental delay, facial dysmorphism, seizures, and mental retardation. Magnetic resonance imaging (MRI) of brain identifies the exact nature and extent of the disease and helps in delineating further plan of management. A Tigroid pattern on axial MRI scan and leopard pattern on a sagittal plane has been classically reported in disorders of myelin formation such as metachromatic leukodystrophy and Pelizaeus–Merzbacher disease(2).

There are over 20 different types of lissencephaly, with the majority of them falling into one of two categories: Type 1 lissencephaly and Cobblestone lissencephaly (Type 2)

- Classic lissencephaly (type 1)
- LISX1 is a DCX gene mutation. DCX has a six-layered cortex rather than four in LIS1 lissencephaly.Isolated lissencephaly with no other known genetic defects
- Cobblestone lissencephaly (type 2)
- Walker-Warburg syndrome
- Fukuyama syndrome
- Muscle-eye-brain disease
- Other types cannot be classified into either of the two previously mentioned groups.
- LIS2: Norman-Roberts syndrome, which is similar to type I lissencephaly or Miller-Dieker syndrome but does not involve a chromosome 17 deletion.
- LIS3LISX2
- Microlissencephaly:It is caused by a lack of normal cerebral cortex folding as well as an abnormally small head. At birth, children with typical lissencephaly have a normal head size. Microlissencephaly is typically diagnosed in children who have a smaller head size at birth.(3)

Classical lissencephaly:

In the complete form, patients with classic lissencephaly have a smooth brain surface; in the incomplete form, they have a smooth surface with some gyral formation along the inferior frontal and temporal lobes. This anomaly is caused by a halt in the migration process. In the complete form, patients present with seizures and developmental delay; in the incomplete form, patients present with complex seizures, hypotonia, microcephaly (50%), and facial dysmorphism (30%).Complete agyria in the complete form or parieto-occipital agyria with frontotemporal pachygyria in the incomplete form characterises the malformation. The cortex is thick because it encompasses the arrested cells' radial columns. The subcortical white matter is thin, with no gray-white matter interdigitation as is typical. A circumferential band exists which shows high signal intensity on T2-weighted images, most prominent in the parieto-occipital cortex, corresponding to a sparse cell zone with increased water content. Due to a lack of or incomplete operculization, the cerebral configuration is oval or hourglass with shallow Sylvian fissures. The malformation is classified into several subtypes based on the underlying genetic abnormality. The LIS1 gene mutation affects both men and women equally, causing gyral abnormalities primarily in the form of parieto-occipital agyria and, less frequently, frontal pachygyria. The doublecorten gene is typically found in females, with gyral abnormalities primarily in the frontal lobes. The relin gene causes a rare form of lissencephaly with a small cerebellum, hypoplastic brain stem, and mild reduction of the cortical gyri. The ARX gene causes lissencephaly, which is characterised by frontal pachygyria and parieto-occipital agyria, agenesis of the corpus callosum, and ambiguous genitalia.(4)

References:

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