Case Report

An infant with isolated Lissencephaly

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ABSTRACT

Lissencephaly or agyria is a prototype of disorders of neuronal migration, a rare type of hereditary malformation of the brain, which manifests with smooth cerebral surface, poorly defined sylvian fissures with thickened cerebral cortical mantle. A case of an infant with isolated variety is presented highlighting some of the major associated clinical features, which include profound intellectual impairment, seizures and hypotonia that later evolves to spasticity in the 2nd year of life. Morbidity is usually high and mortality is dependent on associated deficits.

Keywords: Infant, lissencephaly.

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Congenital structural defects of the central nervous system (CNS) constitute part of the 3% of severe malformations encountered in newborns. Whereas some may be due to hereditary abnormal development; others may arise from iatrogenic factors such as infections and teratogens. They may be classified broadly as 1. Developmental neural tube defects. 2. Cleavage and differentiation defects. 3. Cerebellar malformations. 4. Post neuronal migration defects and 5. Disorders of neuronal migration. A prototype of the disorders of neuronal migration is lissencephaly or agyria. The term was first coined in the 19th century and literally means smooth brain. Currently, it is defined as a brain malformation manifested by a smooth cerebral surface, thickened cortical mantle with microscopic evidence of incomplete neuronal migration. The absence of the usual cerebral convolutions and the poorly formed sylvian fissures portray the appearance of a 3 to 4-month fetal brain. Lissencephaly is classified into 2 types mainly: type I, which is referred to as classical lissencephaly and the type II, which is a more complex malformation consisting of polymicrogyria or polymicrogyri with a pebble-like surface, a thickened cortex, edematous or cystic white matter with infrequently hydrocephalus. A case of an infant with isolated lissencephaly is presented with the aim of highlighting the structural nature and some of the clinical features of this anomaly.

Case Report. A 5-month-old male infant was referred to the Pediatric Outpatient Department because of generalized body weakness that had persisted from birth. Parents had also observed brief episodes of contractions of the neck and trunk over a period of 7 days prior to presentation. A brief history revealed that he was the product of a full term normal delivery. Birth weight was 3.2 kg, length 54 cm, and occipito fronto circumference (OFC) 34 cm. Feeding was appropriate for age. Parents are not consanguineous and have a healthy 5-year-old daughter. There was no history of congenital microcephaly or other CNS disorders in the immediate or extended family. On physical examination, he appeared well nourished with a weight of 6 kg, OFC 40 cm. He had a micrognathia, high arched palate and large ears. The cardiovascular, respiratory, digestive and urogenital systems were grossly normal. Central nervous system revealed that vision and auditory perception were intact. Fundoscopy revealed normal optic discs. There was no social smile, no cooing and no babbling. Muscle tone was reduced in all the limbs.
and head lag was marked. He was unable to sit up even with support. Deep tendon reflexes were exaggerated, ankle clonus sustained and Babinski sign elicited. From the above findings, a clinical impression of psychomotor delay with infantile spasms was entertained.

**Investigations.** The complete blood count (CBC), serum electrolytes and urea, thyroid and liver function tests, serum ammonia, lactate and creatine phosphokinase were normal. The toxoplasma, rubella virus, cytomegalovirus, herpes virus (TORCH) screening test was negative. An MRI of the brain (Figure 1a and 1b) reveals a hypoplastic brainstem, enlarged lateral ventricles, smooth and flat brain surface with a thin outer cortical layer. There is also a thick layer of subcortical gray matter corresponding to arrested migrating neurons. The electroencephalogram (EEG) (Figure 2) shows a suppression burst pattern.

**Clinical course.** Regular physiotherapy was commenced and treatment with vigabatrin and clonazepam was started because of the infantile spasms. After 4 months of anti-epileptic drug treatment, the EEG was no longer hypsarrhythmic and the suppression burst pattern during sleep had disappeared. At the age of 10 months, the neurological status had not improved much; although the flexor attacks had ceased. The OFC was 42 cm and below 2 standard deviation. There was marked drooling, inadequate social smile and rarely any babbling. He appeared slightly less floppy but could neither roll over on a lying position, nor sit without support. Head control was still poor.

**Discussion.** The normal duration of gestation, absence of grotesque dysmorphic features and development of microcephaly in the first year of life, are suggestive of Lissencephaly type I. As with the case being presented, a large majority of patients with lissencephaly have seizures during the first year of life and more than half of these present with infantile spasms. Other neurological manifestations include profound mental retardation and hypotonia that evolves to spasticity with time. Lissencephaly occurs in several syndromes like the Miller-Dieker syndrome which is associated with prominent forehead, short nose with upturned nares, protuberant upper lip and small jaw. It may be found in the Norman-Roberts syndrome with grotesque physical features and Fukuyama congenital muscular dystrophy. The overall minor facial changes in this case with brain MRI findings are suggestive of an isolated type I lissencephaly. Etiologically, there are non-genetic causes due to intrauterine cytomegalovirus infection and intrauterine perfusion failure. An autosomal-recessive mode of inheritance has also been observed in some families and in some others an X-linked variety with small penis. Treatment of children with lissencephaly is
essentially symptomatic. This may consist of physiotherapy, use of appropriate antiepileptic drugs and introduction of affected children to appropriate rehabilitative programs. Genetic evaluation and counseling are indicated for families of children with lissencephaly. For the X-linked variety, the recurrence risk is 50% for brothers. Morbidity is generally high and mortality is dependent on associated deficits.

References


