

A Case of Lissencephaly Type 1 in a 11 Month Old Infant

Dr. Shrasta Soumya¹, Dr. Ipsita Vashishtha², Dr. Ravi Prakash Naulakha³, Dr. Neelu Elon⁴,
Dr. Prithi Inamdar⁵, Dr. Rajesh Kumar Rai⁶

Abstract: *Lissencephaly means smooth brain, i.e., brain without convolutions or gyri, rare and severe cortical malformation. It results from a defect in neuronal migration with four rather than six layers in cortex and the onset of this disorder is presumed to be before 9 weeks of gestation. The spectrum ranges from complete absence of gyri (agyria) to broad gyri with reduced sulci (pachygyria), with an abnormally thick cortex. [1] Here, we report a 11 months old male baby with failure to thrive, spasticity, global developmental delay, microcephaly and cortical visual impairment. MRI brain was done which was suggestive of diffuse gyral thickening involving bilateral cerebral hemispheres with broad flat gyri and shallow sulci suggestive of Agyria – Pachygyria complex (Lissencephaly) and mild dilatation of bilateral lateral ventricles and widening of bilateral sylvian fissures.*

Keywords: Lissencephaly, neuronal migration, agyria, pachygyria, microcephaly, sylvian fissures

1. Introduction

Lissencephaly is a rare congenital malformation in which infants present with smooth brain surface [2]. The term lissencephaly came from the Greek words "lissos" (smooth) and "encephalus" (brain) [3]. The distinct features of this condition are smooth cerebral surface, thickened cortex and incomplete neuronal migration microscopically which results in abnormal layers of cells. In a healthy normal adult brain, six layers are found in the cerebral cortex but lissencephalic brain has only four layers [4]. In lissencephaly two main distinctive types (type I and type II) exist, both with subconditions [5]. The first observations of Miller-Dieker syndrome, a type I lissencephaly, was made by Miller in 1963 [6] and Dieker [7] in 1969. This chromosomal defect can be so discrete that DNA analysis is necessary to detect it [8]. Type 1 is associated with minimal hydrocephalus, but without any brain malformation. Type II lissencephaly is associated with hydrocephalus, cerebellar malformations and congenital muscular dystrophy, i.e., Walker Warburg syndrome. Synonyms of Lissencephaly are Agyria and Lissencephaly, type I.

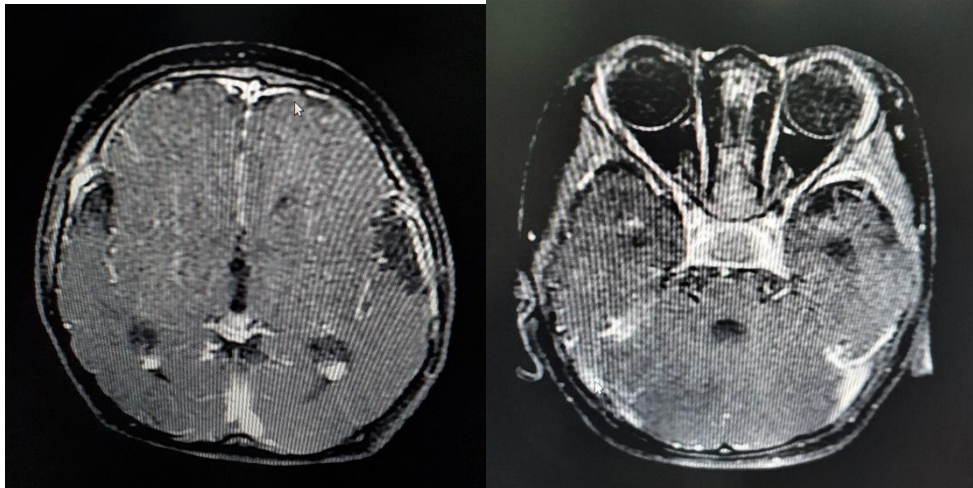
2. Case Report

A 11 months old male child was brought to our hospital in view of delayed milestones since birth and marked global developmental delay. History of Varicella infection in mother at 2 months of period of gestation. Baby was born out of non-consanguineous marriage at full-term delivered at home with immediate crying. Mother came with the complaint that the child is not able to roll over or able to sit

even with support unlike other children, child had achieved neck holding at around 10 months age with continuous fisting of thumb, only cooing present achieved at 9 months of age. Abnormal posturing of the bilateral upper and lower limbs with scissoring of lower limbs present when child is pulled to stand. On examination, it was found that child didn't respond to any visual or sound stimulus. Physical examination revealed weight –6.8 kg (expected 9.5 kg i.e. <3rd percentile), Head circumference was 37 cm (microcephaly, expected- 46 cm i.e. <3rd percentile) and length was 60 cm (expected- 75 cm i.e. <3rd percentile). Failure to thrive present. There was hypertonia and range of movements were decreased. On cranial nerve examination, Pupillary and Menace reflex was absent. Other systemic examinations were within normal limits.

Routine investigations were normal. Cortical visual impairment was present. MRI brain was done which was suggestive of diffuse gyral thickening involving bilateral cerebral hemispheres with broad flat gyri and shallow sulci suggestive of Agyria – Pachygyria complex (Lissencephaly) and mild dilatation of bilateral lateral ventricles and widening of bilateral sylvian fissures. Our is a case of lissencephaly type 1 with global developmental delay with microcephaly with failure to thrive most probably secondary to congenital varicella infection.

Baby was started on supportive management, started on physiotherapy and tablet Baclofen and the dose was gradually increased which was explained to the mother and was asked to followup.



MRI Brain Showing Diffuse Gyral Thickening With Broad Flat GYRI and Shallow Sulci , widening of B/L sylvian fissure and mild dilatation of B/L lateral ventricles.

3. Discussion

Lissencephaly is clearly a heterogeneous disorder with several loci involved in neuronal migration. Lissencephaly is usually diagnosed with MRI or CT-scan of the brain. Even at 27 weeks a certain differentiation of the cortex is expected and thus in this case the total lack of sulci and gyri development was significant. The course of lissencephaly is invariably poor in spite of the etiological type and so has an influence on obstetrical management.

Abnormalities of neuronal migration at any stage give rise to a group of congenital malformations comprising lissencephaly (agyria-pachygyria), pachygyria, schizencephaly, heterotopia and polymicrogyria. Cytoarchitectonic analysis of the agyric cortex suggests a disorder of neuronal migration between the 9th and 13th fetal week while the pachygyric cortex shows attenuated and later disorder acting in the Rakic and Sidman stage IV after the 13th fetal week. Therefore, there is a gradient from the agyric to the normal six-layered cortex. Polymicrogyria presumably results from events after the 16th fetal week when the migration has terminated. [9]

The possible causes of neuronal migration disorders may be acquired or genetic. The acquired etiologies include viral infections such as varicella, cytomegalovirus and toxoplasmosis infections, exposure to toxins such as ethanol, carbon monoxide, isotretinoic acid and cytotoxic drugs, effects of ionizing radiation and intrauterine circulatory disturbances. [10] Classical lissencephaly occurring either as an isolated lissencephaly sequence or in association with the Miller-Dieker syndrome (MDS), has been found to be associated with visible or submicroscopic deletions of chromosome 17p 13.3 (in upto 90% of MDS patients). [10] [11] [12] The identification of unbalanced translocations and inversions is of particular importance because of the risk of recurrence, while deletions and ring chromosomes are mainly sporadic. Syndromes featuring lissencephaly type II are most probably autosomal recessively inherited though the location of the gene and the nature of the mutations are not known.

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. [13] Lissencephaly associated with abnormalities of the LIS1 gene usually results in severe clinical sequelae. These include severe or profound mental retardation, early-onset intractable epilepsy, early and persistent hypotonia that may progress to mild spastic quadriplegia, and major feeding problems. Early data suggested that lifespan is usually shortened with few patients surviving beyond the first decade, the major causes of death being aspiration pneumonia and sepsis. [14] Lissencephaly is a neurological disorder, which carries a bad prognosis because of poorly controlled seizures and mental retardation. [15]

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