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Case report

Hyperactivity and autistic features in a child with lissencephaly-pachygyria complex with hypoxic ischemic encephalopathy

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Abstract

Lissencephaly–pachygyria complex or spectrum is a rare malformation of cortical development characterised by neuronal migration defect and abnormal formation of cerebral gyri or convolutions**.** The main features of lissencephaly are abnormally thick cortex along with absent (agyria) or abnormally developed (pachygyria) cerebral convolutions making the brain appear smooth. We present a case of nine-year-old girl with lissencephaly-pachygyria complex with hypoxic ischemic encephalopathy. She presented with severe intellectual disability, seizures, autistic features with marked sensory issues, self-stimulating behaviors, hyperactivity and aggression. We describe the clinical manifestations and highlight the role of non-pharmacological interventions that include family psycho-education, sensory and occupational therapy, functional behavior analysis and therapy, and addressing caregiver burn-out.

Keywords: autistic features, hyperactivity, intellectual disability, lissencephaly, neuronal migration defect, pachygyria

Introduction

Lissencephaly (LIS) is a rare malformation of cortical development characterized by neuronal migration defect and abnormal formation of cerebral gyri or convolutions. The term has been derived from the Greek words ‘lissos' meaning smooth and ‘encephalos' meaning brain. The main features of LIS are abnormally thick cortex along with absent (agyria) or abnormally developed (pachygyria) cerebral convolutions making the brain appear smooth. Lissencephaly (LIS) may occur due to various non-genetic and genetic factors such as intrauterine infection, fetal brain ischemia, and gene mutations [1]. Children born with LIS have feeding and swallowing problems, seizures (especially infantile spasms), and developmental delays, muscle tone anomalies with early hypotonia and subsequently limb hypertonia and spasticity. Most children are bed bound or severely retarded, with minimal contact with the environment. Hyperactivity is not the usual clinical feature [1-4]. In this background, we present a case of a nine-year old girl having LIS along with hypoxic ischemic encephalopathy (HIE). She presented with marked developmental delays, autistic features with sensory issues and notably, severe hyperactivity and aggression. We further discuss management issues and highlight the importance of non-pharmacological interventions.

Case History

Child A, firstborn of a non-consanguineous marriage from lower socioeconomic status family presented at age six. Maternal and paternal ages at conception were 18 and 28 years, respectively. Antenatal ultrasound revealed brain abnormality (documents were not available for verification). She was born at full-term through Cesarean section following suspected fetal distress. There was a history of a delayed cry after birth. The child had feeding difficulties during infancy along with marked delays in social, motor, speech, and language milestones since the first year. She developed seizures from the age of eight months, which

were controlled with Carbamazepine, but there was poor medication adherence. Besides the developmental delays, she had poor eye contact, showed almost no signs of emotional and social reciprocity; and had no stranger anxiety. Instead, the patient went to most people around her, touching them, trying to maintain physical contact by hugging or climbing over the other person for brief periods of 1-2 minutes, before moving away despite being reciprocated. This behavior was indicative of intrusive and inappropriate approach with poor reciprocity. She became irritable and aggressive if contact was prolonged. She frequently mouthed non-edibles and grated objects of rubbery texture against her teeth. She screamed, kicked, and banged her head or bit herself when stopped. The patient had significant levels of over-activity, moving purposelessly, and continuously around. She often fell and hurt herself. It was quite difficult for caregivers to feed, dress, or clean her. There was no meaningful play, and she constantly shifted her attention from one object to another. She had achieved no language and babbled almost continuously. Sleep was reduced and fragmented. Treatment history revealed worsening of behavioural problems with methylphenidate. On examination, the child had microcephaly (head circumference of 45 cm; below 3rd percentile), small forehead, hypertelorism, widely spaced teeth, and club-foot. The child was not co-operative for a complete neurological examination. There was no evidence of squint, drooling or facial asymmetry and ataxia. Muscle power was at least grade 3. Neurological examination revealed hypotonia in all limbs. Social quotient was 22 when assessed on Vineland Social Maturity Scale. Echocardiography done to rule out any cardiac malformation was normal. Ophthalmologic examination revealed mild temporal disc pallor. Magnetic resonance imaging (MRI) of the brain showed white matter (WM) loss in parieto-occipital region with dilatation of the posterior body and occipital horn of lateral ventricle. Sulci were relatively sparse in the parieto-occipital lobes with the relatively smooth appearance of the cortex. There was cortical thickening involving the frontal lobes. Posterior body and splenium of the

corpus callosum were thinned out, while anterior genu, anterior body, and rostrum were reduced in bulk likely consequent to perinatal hypoxic ischemic insult. In addition, patchy subcortical WM T2 hyperintensities were also noted in the frontal lobe. Rest of the cerebral hemispheres showed normal grey-white differentiation and signal intensity. Overall, the MRI revealed bilateral parieto-occipital lissencephaly-pachygyria complex with sequelae of perinatal hypoxic ischemic insult [Fig-1]. Genetic testing could not be undertaken due to financial constraints.

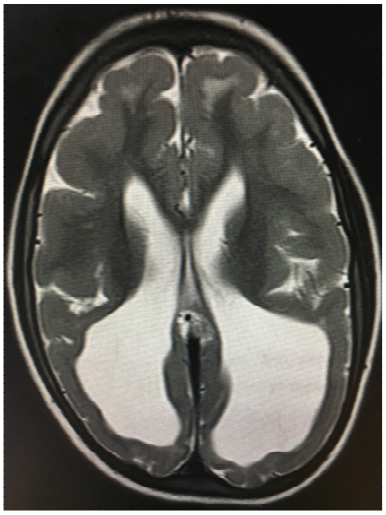

Figure-1 (A)

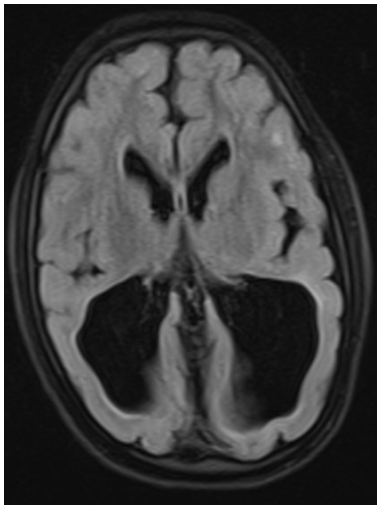

Figure-1 (B)

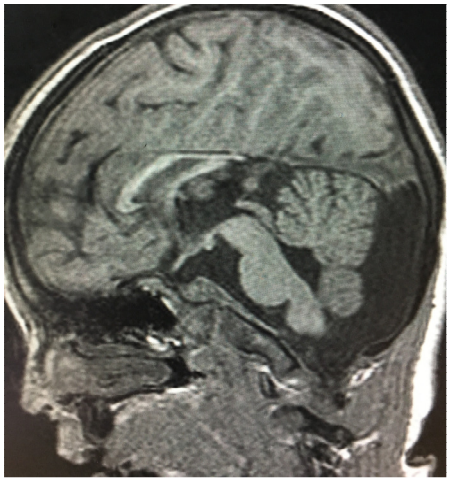

Figure-1 (C)

Figure-1: Axial T2 weighted image (A) and T1 weighted image (B) demonstrating smooth surface of the parieto-occipital lobe with periventricular WM volume loss and bifrontal subcortical WM hyperintensities. Mid-sagittal T1 weighted image (C) showing thinning of the posterior body and splenium of the corpus callosum signifying loss of commissural fibers.

Non-pharmacological interventions with child and family were the mainstay of treatment. Parent/ family Psycho-education was done. Caregiver burn-out issues and maladaptive family patterns were addressed. Detailed functional behavioural analysis was done with a special focus on sensory issues as well as environmental factors that either served as antecedents or reinforcers for problematic behaviors. Sensory stimulation and integration therapy and occupational therapy were started. Behavior therapy focusing on the functional aspects of behavior was implemented. For example, self-stimulating behaviors, including mouthing, were addressed by elements of sensory and occupational therapy. Mother's response of forcibly holding her down in her lap to rock her to sleep worsened child's behavior and increased mother's irritability. Advice to refrain from such a response and structuring the day around various therapies and free play reduced irritability and aggression. Low-dose risperidone 0.75 mg/day and clonidine 0.15 mg/day in divided doses were used adjunctively to control hyperactivity and aggression. Liaison with paediatrics, orthopaedics, and physiotherapy, cardiology, endocrinology and ophthalmology was established. Overall, there was 50% improvement at the time of discharge in view of her hyperactivity, aggression, self-injurious and mouthing behaviour; and sleep had improved. The child has been on follow-up for three years, though quite irregular in the last one year. Improvement in target behaviors was more sustained during the first two years. Aggression and self-injurious behaviors were seen more often when parents were not able to implement therapies or child was forcibly restrained and rocked to sleep. There was no improvement in speech or communication. Seizures occurred 1-2 times a year, and there was clear relation to non-adherence. Continued psycho-education and advice on non-pharmacological measures were given at every follow-up visit. Medication dosages were periodically adjusted with her increasing age and weight. The child could not be placed in a rehabilitative or educational setting due to the family's severe financial and logistical constraints.

Discussion

Our child had lissencephaly-pachygyria complex along with evidence of hypoxic ischemic encephalopathy. Lissencephaly-pachygyria complex may lead on to seizures which can be accentuated with hypoxic ischemic encephalopathy. The larger the volume of the brain that is involved, the poor is the prognosis. Our patient had microcephaly, severe intellectual disability, epilepsy, and muscle tone abnormalities as has been reported in the literature [1-4]. Additionally, there were distinctive sensory issues, especially in tactile and oral domains, and poor reciprocity. It has been described that these children are often not in touch with their environment. The autistic-like features in our child possibly highlight this difficulty. Overactivity can also be, to a large extent, explained by sensory issues seen in the child. Also, hypoxic ischemic encephalopathy may have contributed to the intellectual disability and hyperactivity [5].

Therapies for these children are directed towards symptoms and are supportive in nature [1]. Sensory-based therapy and occupational therapy helped reduce many of the behavioral problems secondary to sensory issues. In conjunction with functional behavior therapy and low dose pharmacotherapy, partial symptom control was achieved. This highlights the role and scope of non-pharmacological interventions in these children.

To conclude, lissencephaly-pachygyria complex with hypoxic ischemic encephalopathy can result in significant intellectual disability and seizures along with concomitant sensory issues and hyperactivity. Non-pharmacological management with judicious use of medications may provide symptomatic relief to some extent.

Conflict of interest: None declared

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