A CASE OF LISSENCEPHALY

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Abstract: we report a case of lissencephaly who presented with intractable neonatal seizure, microcephaly, dysmorphic facies, diagnosed by MRI brain.

Keyword: neonatal seizure, lissencephaly, microcephaly.

Twenty eight days old baby admitted in our hospital with multiple episodes of seizure since day one of life. Seizures were tonic in nature, multiple episodes per day, each episode lasting for < 5 min, inbetween seizures baby was normal. Baby was admitted in Stanley medical college hospital in status epilepticus. Seizures were controlled with phenobarbitone, phenytoin and with midazolam infusion. Baby was mechanically ventilated for 3 days and after weaning from ventilator, baby was seizure free with maintenance antiepileptic drugs. On examination baby had microcephaly head circumference was 30.5 cm (< 3rd percentile of WHO growth chart), hypertelorism, depressed nasal bridge, upturned nares, bitemporal grooving, anterior fontanel wide open, posterior fontanel open, tall forehead, central nervous system examination revealed no evidence of cranial nerve palsies, tone increased in all four limbs, exaggerated deep tendon reflexes, extensor plantar response. There was a small mass 0.5 cm just above posterior fontanel with underlying bony defect, nonpulsatile, firm, not increasing in size on crying, and mass was found to be strectic encephalocele. Spine was normal. Other systems were normal on examination. Antenatal period was uneventful. Mother had previous two spontaneous abortions at 3rd and 4th month of gestation. Term baby born of nonconsanguinous marriage with birth weight of 2.3 kg, spontaneous vaginal delivery with no birth asphyxia developed seizure on day one of life. Baby was evaluated further with a differential diagnosis of 1) structural anomalies of brain, 2) TORCH infection, 3) inborn error of metabolism. Investigation revealed: complete blood count - normal, plasma sugar - 72 mg%, serum calcium - 8.6 mg%, CRP - negative, TORCH screening - negative, serum CPK - 93 IU (within normal limits) chest xray - normal study, ultrasound abdomen - normal study, urine for metabolic study - negative for all, blood pH 7.34. CT brain plain and
contrast-thickening of cortex, paucity of sulci and gyri with atretic encephalocele in occipital region. MRI brain - paucity of sulci and gyri, thickening of cortex, thinning of corpus callosum. EEG showed bursts of sharp waves suggestive of bilateral epileptiform activity. Ophthalmological evaluation done- Left optic discs mild pallor otherwise normal, and advised regular follow-up. No other abnormality detected in both eyes. Baby was followed-up till 2 months of age and lost in further follow-up.

DISCUSSION:
Lissencephaly is a rare congenital malformation of the brain with characteristic clinical and radiological features. Lissencephaly in strict terminology means agyria - complete absence of gyri - in actuality it is a spectrum of brain abnormality ranging from agyria to pachygyria (1). Lissencephalic brains also lack secondary sulci and major fissures. Certain forms of lissencephaly have dysmorphic facies which bring them to medical attention. Most forms of lissencephaly do not have dysmorphic facies where CT / MRI brain are used to diagnose the condition (1). All forms of lissencephaly have poor prognosis only length of survival varies. Abnormality in lissencephaly is in the development of cortex of the brain. It is secondary to the derangements occurring during the stage of neuronal migration in the developing brain of the fetus (1). Development of central nervous system is complicated and it is organised in following pattern. 1. primary neurulation (3-4 weeks of gestation), 2. prosencephalic development (2-3 months of gestation), 3. neuronal proliferation (3-4 months of gestation), 4. neuronal migration (3-5 months of gestation), 5. organization (5 months - after birth), 6. myelination (after birth). Neuronal migration consist of nerves moving from site of origin in the ventricular and subventricular zone to their final location (2). Neurons originating from cortical ventricular zone migrate radially to form the cortical plate and mainly become projection neurons. The first post- mitotic neurons produced in the ventricular zone migrate to form subpialpreplate or primitive plexiform zone (2). Subsequently produced neurons which will form cortical plate migrate into
preplate and split into superficial molecular layer(layer-1) and deep subplate.with subsequent migration remaining 5 layers are formed (2,5).children with lissencephaly have 4 layered cortex with total or near total absence of sulci and gyr(1).For simplification lissencephaly is classified into three types.Type-1 dysmorphic facies and microcephaly. Type-2 hydrocephalus, ocular anomalies, congenital muscular dystrophies, but without characteristic facial features. Type-3 microcephaly without characteristic facial features. **TYPE 1 LISSENCEPHALY**: It includes Miller-Dieker, Norman-Roberts, Neu-Laxova syndromes. It occurs both due to tangential and radial migrational disorder of neurons. Affected children have early developmental delay, mental retardation, and spastic quadripareisis(2). The prognosis is poor most of them die at birth or within a year (1). Seizures are present in almost all patients with 80% infantile spasms with or without hypersarhythmia on EEG. Multiple seizure types including focal seizure, tonic, atypical absence, atonic seizures were observed. EEG shows diffuse fast rhythms with high amplitude is considered peculiar of this condition(6).

**TYPE 2 LISSENCEPHALY**: It includes Walker-Warburg disease, muscle-eye-brain disease, Fukuyama type congenital muscular dystrophy. These patients are macrocephalic because of associated hydrocephalus. They do not have characteristic facial features, but have ocular anomalies (retinal dysplasia), muscular dystrophy, posterior fossa cyst, posterior cephalocele. Their life expectancy is shorter than type 1 because of complexity of brain anomalies. In this condition, the association of epilepsy and atretic seizures disorder have been reported in 50% of patients. Seizures were febrile and afebrile such as GTCS, complex partial seizure, Lennox-Gestaut syndrome. 30% of them were intractable. **TYPE 3 LISSENCEPHALY**: It includes isolated lissencephaly and cerebr-cerebellar lissencephaly. They have hypotonia and microcephaly without any facial dysmorphism. Both the condition are autosomal recessive, later condition invariable immediately after birth because of associated posterior fossa defect. Isolated lissencephaly have longest survival and may live up to 6 years of age.

**GENETICS OF LISSENCEPHALY**: To date six genes have been identified in causing lissencephaly, these include LIS1, DCX, TUBA1A, RELN, VLDLR AND ARX. Whereas co-delition with YWHAE & LIS1 appears to act as modifier locus. **NEUROIMAGING IN LISSENCEPHALY**: The imaging finding in lissencephaly vary with severity of mutation. When very severe cortex is markedly thickened and almost no sulci are formed, in less severe cases the cortex is less thickened and variable number of shallow sulci separate broad gyri(3).

**CONCLUSION**: In our case the patient had features suggestive of type-1 lissencephaly with atretic posterior encephalocele (feature found in type-2 lissencephaly), genetic studies could not be done for this patient as facility was not available in our hospital. Over the past decade, molecular biological and genetics of brain development have widely increased our knowledge about regulation of neuronal migration during development. Identification of genetic defects help genetic counseling and occurrence in future pregnancy. It is hoped that accumulating data of developmental mechanism underlying the expanded network formation in the brain will lead to development of therapeutic option for neuronal migration disorder.
References:


