Holoprosencephaly: A Feature Of Patau Syndrome

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INTRODUCTION:

Holoprosencephaly is a group of disorders characterized by failure of diverticulation and cleavage of prosencephalon at the rostral end of primitive neural tube and hypoplasia or aplasia of premaxillary segment of face [1, 2]. Incidence of holoprosencephaly is 6-12/1000 live birth and 40/1000 in embryos with recurrence rate of 6% for non chromosomal form and 13% for autosomal dominant form.

It is most frequently seen in trisomy 13 & 18 and can be caused by teratogen as in infant of diabetic mother [3].

CASE REPORT:

Two neonates presented to the paediatric department with prematurity, hypotelorism, cleft lip & cleft palate (Fig-1). Both had delayed cry & low apgar score at birth. They were sent to our department for transfontanelle USG & then CT scan head.

(Fig-2). The thalami were partially separated by a rudimentary third ventricle (Fig-3). A large supratentorial dorsal cyst was seen extending between the occipital lobes (Fig-2). The small partly formed interhemispheric fissure and falx were seen only in high parietal region & were absent anteriorly (Fig-2, 3). Findings were suggestive of holoprosencephaly with a dorsal cyst.

RADIOLOGICAL EXAMINATION:

Case 1 (9 days male). Findings revealed by USG and further confirmed on CT scan were microcephaly with absent septum pellucidum & a single large ventricle in brain surrounded by thin rim of cortex showing pachygyria (Fig-2). The thalami were partially separated by a rudimentary third ventricle (Fig-3). A large supratentorial dorsal cyst was seen extending between the occipital lobes (Fig-2). The small partly formed interhemispheric fissure and falx were seen only in high parietal region & were absent anteriorly (Fig-2, 3). Findings were suggestive of holoprosencephaly with a dorsal cyst.

Fig 1

Fig 2

Fig 3

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Case 2 (1 month female) USG and CT scan head revealed similar findings as in case 1 i.e. a large monoventricle surrounded by thin rim of cortex showing pachygyria (Fig-4), partly fused thalami & rudimentary 3rd ventricle but the dorsal cyst was not seen in case 2 (Fig-5).

On karyotyping both children were shown to have trisomy 13. Thus the diagnosis of Patau syndrome was proved.

DISCUSSION :

Holoprosencephaly results from failure of diverticulation when primitive prosencephalon does not divide into telencephalon and diencephalon between 4th and 8th week of gestation. Another view is that holoprosencephaly is due to global lack of forebrain induction i.e. most rostral mid line section of the brain and face are not genetically induced and therefore do not develop [1&2].

The severity of brain and facial deformity varies widely in holoprosencephaly the clinical manifestation varies with amount of brain dysgenesis. Holoprosencephaly forms a continuum from most severe with no separation of telencephalon into hemispheres (Alobar holoprosencephaly) through moderately severe (Semilobar) to least severe with partial separation of dorsal aspect of brain (Lobar holoprosencephaly).

Alobar holoprosencephaly is characterised by nearly complete lack of ventricular and hemispheric cleavage with severe midline facial deformity and hypotelorism. Clinical manifestation in its most severe form are cyclopia [3], forehead proboscis and absent nose and in slightly less severe form are ethmocephaly, cebocephaly, midline cleft lip, cleft palate and hypotelorism.

Imaging studies shows single large crescent shaped ventricle without occipital and temporal horns surrounded by completely unsegmented rim of brain. Thalami are fused protruding into mono ventricle, there is absence of septum pellucidum, interhemispheric fissure, falx, corpus callosum, optic tract and olfactory bulb. A large posterior mid line cyst [5] occupying most calvarium is often seen communicating with the monoventricle. Prognosis is not good & infants die within first month or are stillborn.

Semilobar holoprosencephaly is intermediate in severity presenting with mild facial anomalies, midline and lateral cleft lip, hypotelorism and mental retardation. Imaging studies show H shaped monoventricles with partly developed occipital and temporal horns. Interhemispheric fissure and falx cerebri are usually formed posteriorly but absent anteriorly. The thalami are partially separated with rudimentary third ventricle. Septum pellucidum is always completely absent, splenium of corpus callosum may be formed. Dorsal cyst may or may not be seen. Pachygyria is commonly seen.

Lobar holoprosencephaly is the mildest form, clinically no facial anomaly or mild hypotelorism is seen. Mild mental retardation, spasticity and athetoid movements are seen. Imaging studies show nearly complete
separation of cerebral hemispheres with interhemispheric fissure and falx is seen extending into frontal area of the brain though the anterior falx is dysplastic and the frontal lobe fuse anteriorly across the mid line. Septum pellucidum is absent leading to square frontal horn. The basal ganglia and thalamus may be separated or fused. Pachygryria is present.

Recently another subset of holoprosencephaly has been described and is termed as syntelencephaly [4] in this form the interhemispheric fissure and falx cerebri are variably formed in both posterior and anterior part with deficiency in the high frontal convexity and hemispheric fusion seen in the same region. Septum pellucidum is absent. Heterotopic gray matter is seen inside the expected course of corpus callosum which is dysgenetic.

The incidence of Patau syndrome or trisomy 13 is 1/5000 births & it is characterised by abnormalities of brain, face, extremities and heart. It is the most severe of the trisomies that can lead to live born infants. The major abnormalities are reported in 91% affected fetuses & include holoprosencephaly, facial/ renal anomalies, cardiac defects, IUGR, ventriculomegaly, abnormal cisterna magna & cystic hygroma.

Neonate dies soon after birth & the rare survivor has profound mental retardation & seizures.

References:

6. Fitz CR : holoprosencephaly and related entities