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Holoprosencephaly in An 11-Month Old Nigerian Male and Review of Literature

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Background: Holoprosencencephaly is a rare congenital abnormality of the brain that presents diagnostic challenges to the radiologist and the paediatrician because of many mimics.

Aim: To report a case of holoprosencephaly seen in University of Port Harcourt Teaching Hospital

Key Words: Holoprosencephaly, Congenital brain anomaly, Magnetic resonance imaging

INTRODUCTION

Holoprosencephalies are a group of disorders characterized by failure of cleavage of the telencephalon and diencephalon.[1]This disease has a world wide distribution, but a study by Lewis *et al*[2]. suggests an increased incidence in individuals of Hispanic ancestry. This disease is present in 1 in 10,000-20,000 neonates at birth and occurs at a rate of l in 250 during embryogenesis. The age of onset is 3-4 weeks of gestation. Depending on the severity of the disorder, alobar, semilobar and lobar varieties have been documented.[1]

Females tend to have the severe forms of holoprosencephaly compared to males i.e, in a lobar holoprosencephaly; the female-to-male ratio of occurrence is 3:1, whereas in lobar holoprosencephaly, the ratio is I: I. Females also have more severe facial anomalies compared to males.[3]

Holoprosencephaly arises from disruption of the normal induction and pattering of the rostral neural tube during early embryogenesis. Prenatal factors associated with the development of holoprosencephaly are low calorie diet, antiepileptic medication exposure, sulfasalazine, cytomegalovirus infection, and gestational diabetes.[3-7] However, most cases are sporadic and familial cases have been described.[8] This case is reported because of its rarity in our environment.

CASE REPORT

Baby S.E is an ll-month- old male delivered to a 30-year-old para I+1 woman. The patient presented at the paediatric outpatient clinic of the University of Port Harcourt Teaching Hospital on 20/3/2007 with history of poor developmental milestone and abnormal shape of the head.

Pregnancy and birth were uneventful. The mother was not diabetic or hypertensive. There was no history of maternal febrile illness, alcohol consumption by the mother during pregnancy or congenital chromosomal defect in maternal or paternal pedigree. On examination, the skull was microcephalic with flat nasal bridge and hyperteloric eyes. He was not pale, febrile or jaundiced. Central nervous system examination revealed moderate global hypotonia of the upper and lower limbs, and primitive reflexes such as grasp reflexes were still present. The chest was clinically clear, and the abdomen was not contributary. Laboratory investigations of the blood and urine were not remarkable. Karyotyping was not done because of lack of the materials.

Plain skull radiograph showed small and abnormally shaped skull with normal cranio-facial ratio (see fig. 1). Magnetic resonance image showed a single brain ventricle (monoventricle), rudimentary cerebral cortex, absent corpus

callosum, septum pellucidum and rudimentary falx cerebri (see figs.2-4).
The parents were counseled on how to support the child.

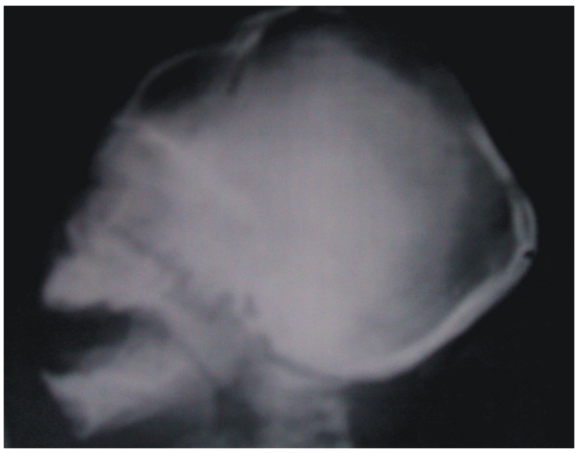


Fig.1 Plain lateral skull radiograph showing small and abnormal shape of the skull

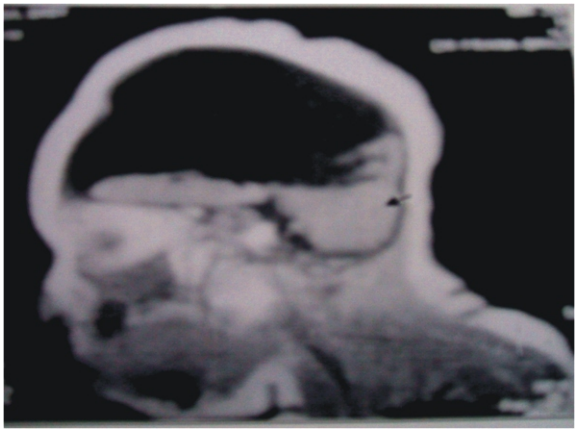


Fig. 2 Saggital slice of cranial Magnetic Resonance Image (T1-weighted), showing a large amorhous, hypo-intense area filling the cranium(long arrow], with rudimentary brain tissue in the base and posterior fossa (short arrow)

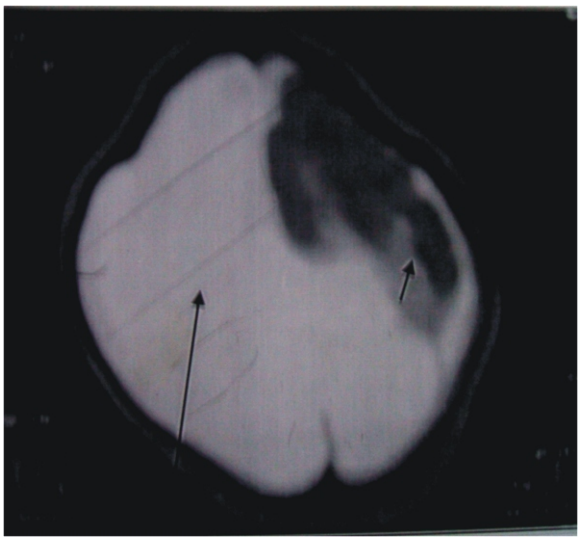
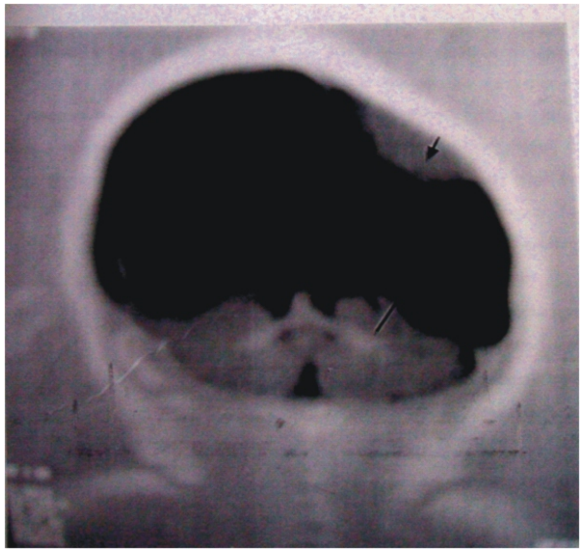


Fig.3 Axial slice of cranial MRI (T2-weighted),showing a large,amorphous hyperintense
Area (monoventricle)-(long arrow) and cerebral



mantle(short arrow)

Fig.4 Coronal slice of MRI (T1-weighted),showing a hypo-intense area-monoventricle (long arrow),and a rudimentary cerebral mantle(short arrow)

DISCUSSION

Classically, the spectrum of this holoprocencephaly can be divided into four major categories namely alobar, semilobar, lobar and middle hemisphere variant. These are based on gross morphologic abnormalities involving the telencephalon and diencephalon. Our patient had the alobar type of holoprosencephaly, which is made up of a single brain ventricle (monoventricle) without formation of an interhemispheric fissure, i.e. fused cerebral hemispheres, fused thalami, absent corpus callosum, septum pellucidum and fornix[9] . In semilobar holoprosencephaly, there is partial formation of the interhemispheric fissure, particularly posteriorly. A rudimentary falx may be present and a primitive occipital horn may be seen. In lobar holoprosencephaly, there is almost complete formation of the interhemispheric fissure and only focal areas of cortical continuity across the interhemispheric fissure, usually interiorly. Sometimes, lobar holoprosencephaly is limited to an absence of the septum pellucidium.[10] .The middle interhemispheric fusion variant is a recently described anatomic entity that some authors consider to be part of the spectrum of holoprosencephaly. This variant denotes incomplete cleavage of the posterior, frontal and parietal lobes with varying degrees of incomplete cleavage of the basal ganglia and thalami and absent body of the corpus callosum[11]

Lewis *et al*.[2] reported the incidence of holoprosencephaly as 1 in 10,000-20,000.Croen *et al*.[12] reported that the incidence of the disease is 5-12/1 00,000 live birth. The literature search shows that there is paucity of published data on the incidence of holoprosencephaly in Nigeria. Females are affected three times more than males i.e ratio of 3:1.[12] Our patient is a female.

Characteristic facial anomalies correlate with the degree of holoprosencephaly and have prognostic relevance.[12] According to the severity of holoprosencephaly, clinical presentation include cyclopia, ethmocephaly, cebocephaly, occular hypotelorism, midline clefting, and bilateral clefting. More subtle facial dysmorphic features may also be present. Microcephaly is usually associated with holoprosencephaly and the presence of macrocephaly suggests hydrocephalus. Some developmental delay is usually noted, which often presents as mental retardation. Generally, this finding is directly correlated with the severity of holoprosencephaly. Our patient had delayed developmental milestone, abnormally shaped skull and hypertelorism. Other clinical presentations in patients with holoprosenaphaly include seizures, hypotonia, dystonia, chorea, and dysphagia.[13] Our patient had hypotonia in all the limbs. For this disease, visceral abnormalities affecting the cardiovascular, gastrointestinal, genitourinary and skeletal systems have been described.[14] There was no associated visceral abnormality that was demonstrated in our patient.

The imaging modality of choice is Magnetic Resonance Imaging (MRI), followed by Ultrasonography and Computed Tomography. Plain skull radiograph is the least useful. Our patient was investigated with MRI and plain skull x-ray. **In** alobar holoprosencephaly, MRI usually shows a horse shoe-shaped monoventricle, an absent falx, agenesis of the corpus callosum, absent septum pellucidum and olfactory bulbs, abnormal cerebral cortex and migration anomalies; this would be demonstrated in T_1 and T_2 weighted sequences.[15] In our patient, there was an amorphous shaped monoventricle, rudimentary falx cerebri and little cerebral mantle.

In semilobar holoprosencephaly, MRI will demonstrate a partial ventricular cavity seen as hypointense area on T_1, hyper intense on T_2, a partial interhemispheric fissure and falx cerebri, partial or incomplete formation of the anterior corpus callosum, and a variable degree of thalamic fusion. The olfactory bulbs are often absent in lobar type. MRI will show partial fusion of the frontal lobe with an otherwise normally formed inter hemispheric fissure, lateral ventricular formation, variable and incomplete absence of the anterior corpus callosum and /*or* septum pellucidum, and separate thalami. The olfactory tracts are usually present.[15] .The middle interhemispheric fusion variant appears as incomplete cleavage of the posterior, frontal and parietal lobes and incomplete cleavage of the basal ganglia and thalami. The body of the corpus callosum is absent which coincides with the site of failure of cerebral separation.[2,11] .

Computed tomography will demonstrate the different types of holoprosencephaly, but provides less details of the brain parenchyma than MRI. CT does not provide good images of the posterior fossa and brain stem therefore, some cases of mild holoprosencephaly and associated central nervous anomalies may be missed on CT.[11,13] Plain skull radiograph may show microcephaly or abnormally shaped skull. Our patient had abnormally shaped skull as demonstrated by plain skull radiograph.

Differential diagnosis of holoprosencephaly are hydrancephaly, hydrocephalus, porencephalic cyst, pseudotrisomy 13, Smith-Lemli-Optiz-Syndrome, septo-optic dysplasia, trisomy 13, trisomy18 and ventriculomegaly.

Management of holoprosencephaly is primarily symptomatic and supportive. In hydrocephalus, or dorsal cyst for example, a ventriculoperitoneal shunt may be necessary, a gastrostomy tube may be useful in managing dysphagia and fundoplication may be indicated because of gastroesophageal reflux and aspiration. The risk of recurrence in subsequent babies from parents of an individual with holoprosencephaly depends on the aetiology.[15,16] The emperic risk of occurrence from non-specific aetiology is 60%. If holoprosencephaly is due to trisomy 13 or 18, then the risk is increased with advancing age of the mother and if holoprosencephaly is due to an inherited single gene mutation in Shh, ZIC2, SIZ3 or TGIF, then the risk is up to 50%. Recurrence risk will be 25% if holoprocencephaly is due to an inherited autosomal recessive condition .[15,16] We could not do karyotyping on our patient to identify the aetiology of this disease because of unavailability of necessary materials.

CONCLUSION:

Holoprosencephaly is rare congenital disorder of the brain that presents challenge of diagnosis in the midst of myriad of differential diagnosis and management.

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