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CASE REPORT

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Holoprosencephaly in identical twin neonates: An extremely rare case report

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Abstract: Holoprosencephaly (HPE) is a rare congenital brain malformation which results from complete or incomplete separation of the forebrain and diencephalon or horizontal separation of the optic and olfactory structures. The septum pellucidum is always absent and patients usually present with gross facial abnormality. HPE has an incidence of 1 in 10,000-16,000 births. It is quite uncommon in twin gestations, and when it occurs, usually only affects one of the twins. This study is however presenting the occurrence of HPE in presumably identical set of twins. The twins were a product of assisted reproduction (IVF) and uneventful pregnancy: they were delivered preterm and of low birth weight. Twin one was microcephalic and had facial hypoplasia, while twin two had an associated hydrocephalus. Both were hypoglycaemic. Chest radiographs and abdominal ultrasound scans were normal. Echocardiography showed mid-muscular ventricular septal defect in twin two. Brain CT scans showed semi-lobar holoprosencephaly in both twins, with hydrocephalus in twin two.
This case report is being made to document an extremely rare occurrence of holoprosencephaly in both identical twins who were products of assisted reproduction.

Keywords: Holoprosencephaly, identical, twin, preterm, assisted-reproduction, semi-lobar

Introduction

Holoprosencephaly (HPE) is a congenital brain deformity in which there is partial or complete lack of cleavage or lateral diverticulation of the forebrain and cleavage of the diencephalon or horizontal separation of the optic and olfactory structures. This is usually due to arrest of lateral ventricular growth in the sixth week of gestation. The growing brain cortex subsequently covers the mono -ventricle and fuses in the midline. The posterior ventricular portion thus becomes enlarged and cystic. The Septum pellucidum is always absent.[1] HPE has an incidence of about 1: 10,000-16000 births, with variable sexual preference.[1,2] Patients usually present with gross facial anomalies as the major feature.[1,3,4] There are three fundamental variants of HPE, namely: Alobar, Semilobar and Lobar. The Alobar type is the extreme form in which there is no separation of the forebrain. This subtype presents with variable ventricular configuration, such as pancake, cup or ball. They have a single ventricle with absence of the occipital and temporal horns. [1]

The Semilobar is the intermediate type in which there is a partial cleavage of the prosencephalon and presents with mild facial anomalies. Lastly, the lobar subtype, being the mildest form has two definite cerebral hemispheres and two lateral ventricles. The frontal lobe might be dysplastic. Both semilobar and lobar subtypes frequently survive into adulthood, unlike the alobar which is known for infant and perinatal mortalities.[1] Holoprosencephaly in twin pregnancies is quite uncommon and when it occurs, usually only affects one of the two babies.[3,5] The possible aetiologies of HPE are heterogeneous, as multiple environmental and genetic factors have been implicated.[6,7] There is a high prevalence with increasing maternal age and urban centres.[2] Most cases of HPE have other associated anomalies.[2,8]

Case Report

This set presumably identical twins (same gender and shared placenta) were delivered to a 30yr old mother at an estimated gestational age of 35 weeks + 4days via an elective caesarean section on account of twin gestation, breech leading twin and IVF conception. There was polyhydramnios, but liquor was clear. Apgar scores were 7 and 9 (Twin 1) and 5 and 9 (twin 2) at one and five minutes respectively. Both babies required vigorous tactile stimulation, prolonged suctioning and free flowing oxygen.

Mother's antenatal history was eventful. She had a threatened miscarriage at 18 weeks and had multiple admissions for preterm contractions and urinary tract infections. Her genotype is AC and blood group is O negative. She had a negative screen for HIV/Hepatitis B/ Syphilis.

Birth weights were 1900g (Twin 1) and 2200g (Twin2). Birth lengths were 43cm (twin 1) and 45.5cm (twin 2). Intramuscular Vitamin K (1mg stat) was given to each neonate. Other routine care was also offered.
Twin 1 had an occipito-frontal circumference of 25.5cm (microcephaly), with abnormally shaped face (hypotelorism), strong cry, optimal rooting and sucking reflex and a sub-optimal muscle tone; while twin 2 had occipito frontal circumference of 37cm (macrocephaly), with cranio-facial disproportion, sun setting eye appearance; initially weak cry, optimal rooting and sucking reflex and optimal tone globally. There were no abnormalities or anomalies in other systems and vital signs including oxygen saturation in room air were within normal ranges. Random blood glucose was 0.6mmol/L (10mg/dl) for Twin 1 and 1.7mmol/L (30mg/dl) for Twin 2.

Laboratory investigations showed metabolic acidosis, anaemia and thrombocytopenia. White blood cell count was within normal ranges for both infants. Blood cultures grew no organisms. Echocardiography revealed a structurally normal heart with good biventricular function in twin 1. Twin 2 had a small mid muscular ventricular septal defect and good biventricular function. There was no pulmonary arterial hypertension.
Care received included respiratory support (oxygen and continuous positive airway pressure), intravenous fluids (glucose containing solutions, electrolytes, amino acids infusions), blood transfusions (packed red blood cells and platelets concentrates) and antibiotics.
The neonates spent 14 days on admission and were referred to paediatric neurosurgery clinic at the tertiary health institution for follow up, the parents did not attend clinic for personal reason. The twins were however being seen in at a private paediatric facility where they were managed for severe symptomatic anaemia in the fourth week of life. They were stable when seen at the immunization clinic at six weeks. Twin 2 however deteriorated and died at 9weeks + 3 days of life.

Both twins had normal chest radiographs and abdominal ultrasound sans. The CT scan however showed gross pathologies depicting semilobar holoprosencephaly of variable patterns in both twins. For twin 1, it showed: Fusion of the frontal lobe with absence of the anterior part of the falx cerebri, absence of the septum pellucidum and corpus callosum. There was partial separation of the lateral ventricles, giving rudimentary temporal and occipital horns. The third ventricle appeared slit-like, as the thalami were partially fused. The fourth ventricle was preserved. There was cortical atrophy and some subcortical white matter hypodensities (Figure A). Twin 2 had non-communicating hydrocephalus. There was fusion of the frontal lobes, absence of the falx cerebri, septum pellucidum and corpus callosum. The lateral ventricles were partially separated and showed rudimentary temporal horns. The remaining components of the lateral ventricles appeared like a grossly dilated monoventricle which appeared cystic posteriorly. The third ventricle was slit-like, as the thalami were partially separated. The fourth ventricle was however preserved (Figure B).

Fig A: CT brain: Absent anterior cerebral falx, absent septum pellucidum, fused lateral ventricle and partially fused thalami

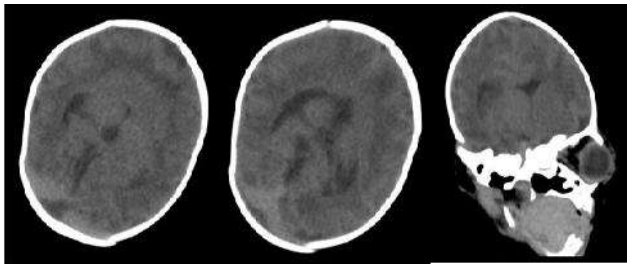
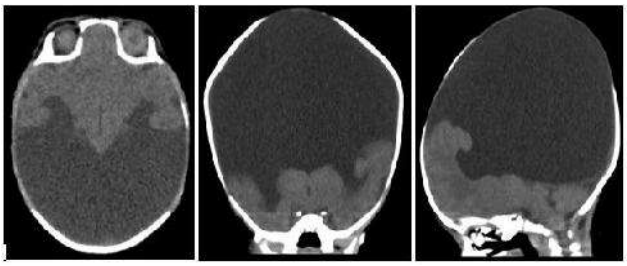


Fig B: CT brain: Absent anterior cerebral falx, absent septum pellucidum, fused lateral ventricle with gross hydrocephalus (non– communicating) and partially fused thalami



Discussion

This is a unique occurrence of semilobar holoprosencephaly in a set of identical twins.
Maternal age 30years and above has been established as a significant factor for HPE and the patients are often females, just as in the index case.[2,5,9,10] It has also been reported to be commoner in urban centres than the rural settlements.[2]
Many publications have presented assisted conception as a risk factor for HPE, just as in this particular case.[9,11]
The set of twins demonstrates similar facial deformities, as documented in Ibadan and other parts of the globe.[1,3–5,12–14]

Gross genetic abnormalities have been noted in HPE. These include trisomies, deletions, and other non-specific genetic abnormalities.[6,7] Cytogenetic analysis could however not be done in our cases due to cost and personal reasons.

HPE has been reported in multiple pregnancies, especially dizygotic. Most of the reported HPEs however affect only one of the twins, as the other is usually healthy.[5,15] Some cases of HPE in monozygotic twins have also been reported in which only one of the set had holoprosencephaly.[13,16] There had however being a documentation of HPE in both monozygotic fetuses however with discordance, in which one was mild, while the other was of the alobar type.[17] A case of congenital anomalies in identical twins of HPE in one of the set and Down's syndrome in the other has also been docu-

mented.[9] Trisomy 13 has been severally documented as the most common associated chromosomal abnormality.[18]

Conclusion

The occurrence of holoprosencephaly in these presumably identical twins emphasizes the strong role attributable to genetic composition. The variable presentation and early demise of twin 2 however suggest the possibility of other subtle secondary factors, which might have predisposed the deceased to a more severe variant (presence of hydrocephalus) and co-existing ventricular septal defect. The unavailability of cytogenetic analysis serves has a limitation to this particular report.

Informed consent

Verbal consent was obtained from the parents while on admission, as they were assured of confidentiality.

Conflicts of interest: None
Funding: None

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