A Case Series of Holoprosencephaly

Bir Holoprosensefali Olgu Serisi

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ABSTRACT

Holoprosencephaly is congenital brain anomaly due to incomplete separation of two cerebral hemispheres. It has three subtypes which are alobar, semilobar and lobar. Degree of severity is decreased from alobar, semilobar then lobar holoprosencephaly. The embryogenesis incidence rate is 1:250. Because of spontaneous abortion, the lower occurrence rate is seen at 1:16000 in a live birth. The patient's survival rate depends on the extent of the deformity and also the type of holoprosencephaly. In this case series, we include radiological descriptions of the holoprosencephaly of all three subtypes.

Key Words: Holoprosencephaly, alobar, semilobar, lobar

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ÖZET

Holoprosensefali, iki serebral hemisferin eksik ayrılmasına bağlı doğuştan beyin anomalisidir. Alobar, semilobar ve lobar olmak üzere üç alt tipi vardır. Alobar, semilobar ve ardından lober holoprosensefaliden şiddet derecesi azalır. Embriyogenez insidans oranı 1: 250'dir. Spontan abortus nedeniyle, canlı doğumda daha düşük görülme oranı 1: 16000'de görülmektedir. Hastanın hayatta kalma oranı, deformitenin boyutuna ve ayrıca holoprosensefali tipine bağlıdır. Bu vaka serisinde, üç alt tipin hepsinin holoprosensefalisinin radyolojik tanımlarını dahil ediyoruz.

Anahtar Sözcükler: Holoprosensefali, alobar, semilobar, lobar

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INTRODUCTION

The medical terminology of a case due to incomplete separation of the two cerebral hemisphere is called holoprosencephaly (HPE). Alobar, semilobar and lobar are the three main subtypes which alobar are most severe form followed by semilobar then lobar. A Mild type of HPE is a middle interhemispheric variant (MIHF).

It happened during the period of embryogenesis, between 18th to 28th weeks of gestation. Patient with holoprosencephaly usually associated with craniofacial deformity manifestation. The ratio of occurrence for holoprosencephaly in a live birth is 1:16000 and in conceptuses is 1:250 (1). Multiple factor that contributes for the cause of holoprosencephaly. One of the leading causes is maternal diabetes or teratogenic exposure during pregnancy (2).

Magnetic resonance imaging (MRI) of brain is the best choice of imaging that performed on survive patient to visualize the brain structure. It is crucial for the diagnosis and management of the disease (3). Based on the subtype of holoprosencephaly, the survival rate and prognosis are poor especially in alobar holoprosencephaly and with those who have more severe type of craniofacial deformity. For all sort of this anomaly, the patient will be managed conservatively (2). We will present a serial case of holoprosencephaly with reviewed literature in this case report.

CASE REPORT

Case 1

A borderline preterm baby was born at 36 weeks gestational age with a birth weight of 1900 grams. The routine antenatal ultrasound demonstrates the incidental findings of a large central monoventricle. No facial deformity detected during the detail scan.

Antenatally, the mother, was diagnosed as gestational diabetes mellitus requiring subcutaneous insulin. The blood sugar control was good throughout the pregnancy. No family history of genetic disorder.

Upon delivery, the baby was not vigorous with Apgar score of 3/10. The further examination noted, enlarged head circumference with limp muscle tone. Subsequently, neurosurgeon inserted a ventriculoperitoneal shunt at day 14 of life.

MRI brain (Figure 1) in the first month of life showed monoventricle with absence of septum pellucidum, interhemispheric fissure and corpus callosum. The final diagnosis was alobar holoprosencephaly with neuropathic arthrogryposis.

Case 2

A term baby was born with a birth weight of 2500 grams via elective caesarean section for breech presentation. The detailed scan at 32 weeks gestation showed absent corpus callosum. Antenatal history of the mother is unremarkable.

Upon delivery, the baby had facial dysmorphism with enlarged head circumference. A chromosomal study is consistent with trisomy 21. Computed tomography (CT) of the brain (Figure 2) showed monoventricle with partially developed occipital and temporal horns of bilateral lateral ventricles. The frontal horn of lateral ventricles and septum pellucidum is absent. However, posterior falx and interhemispheric fissure are well-formed. Overall features are compatible with semilobar holoprosencephaly.

The child now is one year old, suffered from global developmental delay with growth development is below 5th centile. The patient is having hypotonia in all four limbs and unable to walk.

Case 3

A mother with gestational diabetes mellitus on diet control was referred to a fetomaternal specialist for detail scan at 36 weeks of gestation. Ultrasound shows bilateral ventriculomegaly with fused thalami. No facial deformities detected. The baby was born at 38 weeks gestation with a birth weight of 2700 grams via emergency caesarean section. Upon delivery, the baby was not vigorous, thus require immediate intubation. On further examination of the back revealed spina bifida.

MRI Brain (Figure 3) showed, absent septum pellucidum and partially fused thalami. Presence of corpus callosum dysgenesis (absent splenium part with fusion of rostrum, genu and body of corpus callosum with cingulate gyrus). Otherwise, the interhemispheric fissure is normal. MRI whole spine revealed a feature of lumbar myelomeningocele. The final diagnosis was lobar holoprosencephaly with lumbar myelomeningocele.

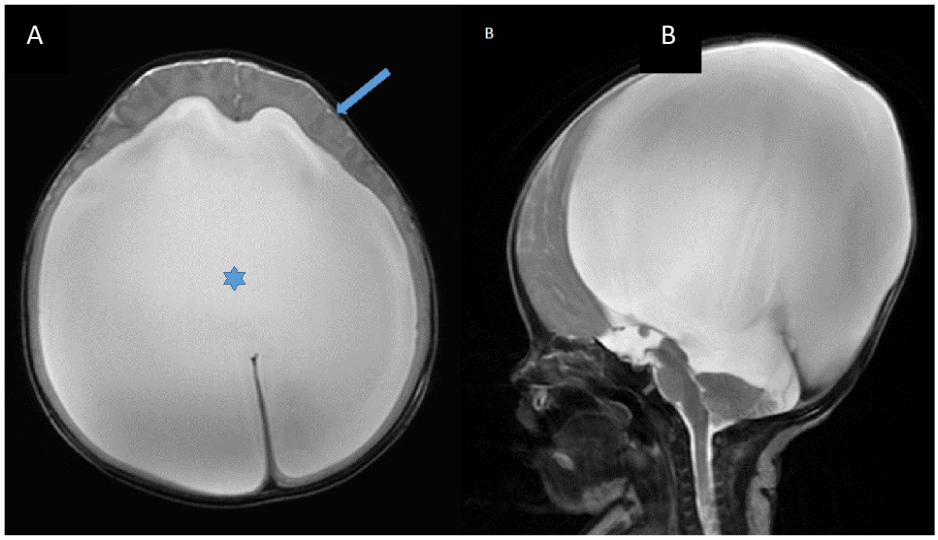

Figure 1: MRI brain in (a) axial T2W and (b) sagittal T2W shows monoventricle (star) with thin frontotemporal cerebral cortex (solid arrow). Absent of midline structures (septum pellucidum and corpus callosum). Features are of alobar holoprosencephaly.

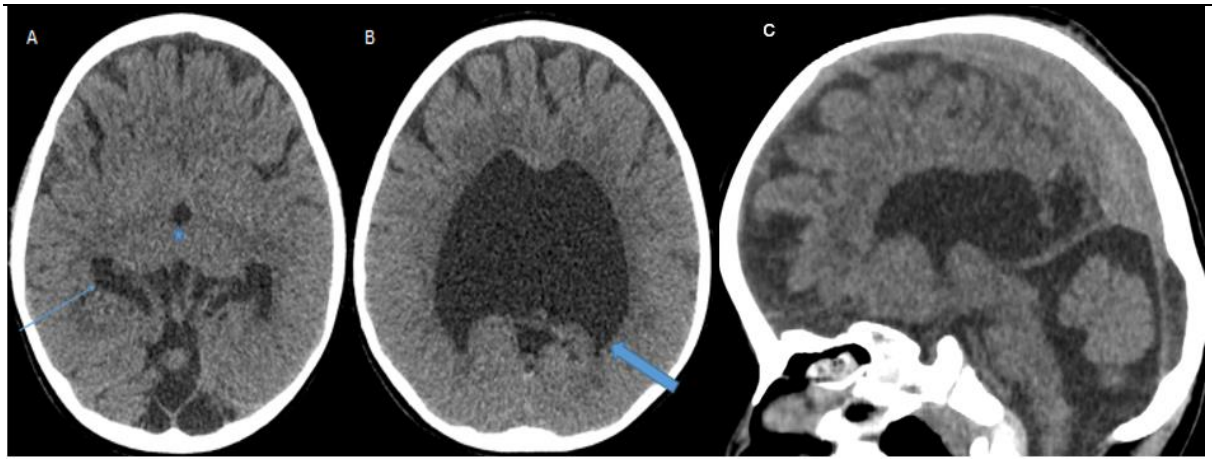

Figure 2 : CT scan of brain in (a and b) axial view and (c) in sagittal view shows the monoventricles with partially developed occipital horns (solid arrow) and temporal horns (line arrow). No frontal horns of lateral ventricle. Incomplete anterior interhemispheric fissure. Absent septum pellucidum. The thalami partially fused (star). Features are of semilobar holoprosencephaly.

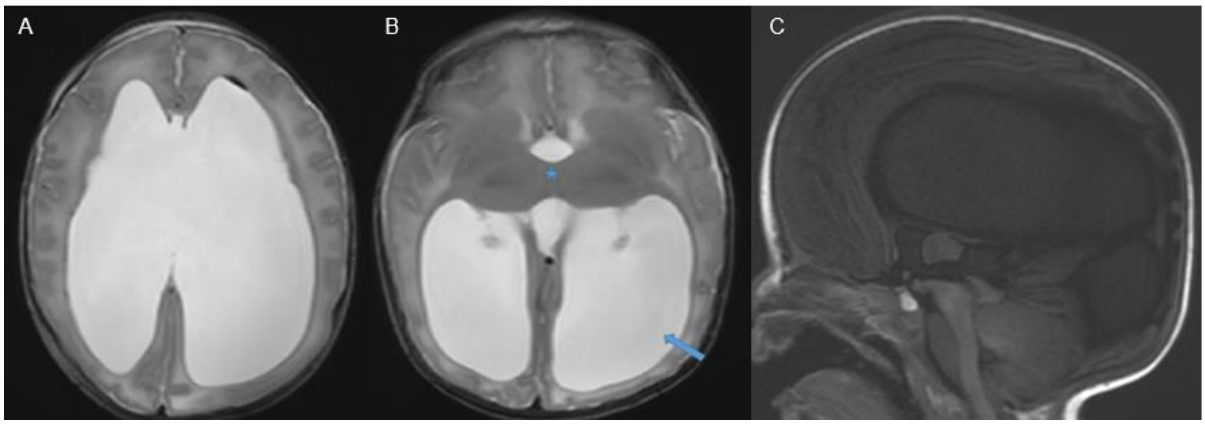

Figure 3(a) and (b): MRI brain in axial T2W shows dilated and abnormal configuration of the lateral ventricles with deficient anterior horns. Partially fused thalami (star) and absent septum pellucidum as well as disproportionally dilated temporal and occipital horns (solid arrow) of lateral ventricles. 3(c) MRI brain in sagittal T1W shows corpus callosum dysgenesis (absence of splenium part and fusion of rostrum, genu and body of corpus callosum with cingulate gyrus). The features in keeping with lobar holoprosencephaly.

DISCUSSION

Holoprosencephaly(HPE) occurs due to failure of prosencephalic/forebrain cleavage, therefore causing incomplete separation of the cerebral hemispheres and midline structures (3,4). The incidence rate of HPE is 1:250 in conceptuses and 1:16000 in a live birth (1). Teratogen, chromosomal and genetic abnormalities are the cause of HPE. The most common teratogens to fetuses are maternal diabetes (5). Few genetic syndromes are associated with HPE, most commonly trisomy 13 (Patau syndrome) and less commonly trisomy 18 (Edward syndrome) (2, 5). Three subtypes of HPE are recognised, in decreasing severity; alobar, semilobar and lobar HPE. The mildest type of HPE is middle interhemispheric variant (MIHF) or also known as syntelencephaly (1).

During embryogenesis, the cephalic part of neural tube formes into three primary vesicles, which are hindbrain, midbrain and forebrain (4). These formations happened in the fifth week gestation (6). Prosencephalon or forebrain development will take three sequence events, firstly formation followed by cleavage and then midline development.

Pathogenesis of three HPE subtypes is different. Alobar HPE happened due to the complete absence of prosencephalon division; meanwhile, for semilobar HPE, it happened due to incomplete separation of the cerebral hemisphere. The least severe type of HPE is lobar form, and it occurs due to the midline fusion of the cingulate gyrus (7).

The patients with holoprosencephaly frequently have dysmorphic faces and neurological deficits (8). There are variable craniofacial deformities observed. The commonly observed abnormalities include cyclopia, cebocephaly and premaxilla agenesis with median cleft lip (9). Cyclopia is an abnormal single median eye. It contains a single lens with two sets of lens fibres (9). Besides, hypotelorism with single nostril meant cebocephaly (7).

Antenatal sonography is very helpful in detecting craniofacial abnormalities as early as 18th to 20th weeks gestation (6). After birth, MRI brain is the imaging tool of choice to demonstrate the structural abnormalities of HPE (3). Several distinct radiological features can differentiate between these three HPE subtypes. Alobar HPE demonstrates the monoventricle (absent lateral and third ventricles division), absence of interhemispheric fissure and corpus callosum. The thalami and cerebral hemispheres are fused. Meanwhile, in semilobar HPE, the interhemispheric fissure may present but incomplete, particularly at the anterior portion associated with partial fusion of thalami. The basal ganglia and hypothalami are still primarily fused with the absence of septum pellucidum. It can appear as a monoventricle, but has partially developed occipital and temporal horns. Corpus callosum may be absent or hypoplastic (1, 3, 7).

On the other hand, lobar HPE shows complete interhemispheric fissure. Frontal horns of lateral ventricles appear communicating and disfigured. The temporal and occipital horns are better defined, with normal third ventricle. Septum pellucidum is still absent. The corpus callosum is present and can be normal, incomplete, or hypoplastic. Basal ganglia are usually separated, but the thalami can be fused or not (1, 3, 7).

The outcome of HPE patient is mostly related to neurological deficits such as seizures, epilepsy, motor impairment, oromotor dysfunction, pulmonary and gastrointestinal problems and hypothalamic dysfunction (4). Supportive management based on deformities and deficits will be the primary treatment for HPE cases. In term of prognosis, the alobar type is lethal (7). Around 20% of alobar patient can survive up to 12 months. Semilobar HPE may survive longer, in which more 50% survived more than one year (2). Meanwhile, in lobar HPE, the patient will survive longer than the former subtypes, but most of the patient suffer from mental retardation, visual disorders and spastic quadriplegia (7). The attending doctor must counsel parent with prior history of HPE to perform chromosomal study in later pregnancy. Early detailed antenatal ultrasound is compulsory as the risk of recurrence is around 25 to 35% (4).

CONCLUSION

In these case reports, we illustrate the radiological findings of each HPE subtypes. Imaging, in combination with clinical findings, is essential for recognition of HPE spectrum. Early and accurate diagnosis is important for family counselling, in terms of pregnancy management, risk of fetal demise, understanding of the ongoing needs of the surviving children and future recurrence risk.

Conflict of interest
No conflict of interest was declared by the authors.

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