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Case Report

Lobar holoprosencephaly with associated meningocele: A rare case report of a 25-year-old patient with multiple seizures ☆,☆☆

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ABSTRACT

Lobar holoprosencephaly (HPE) represents the mildest form of HPE, featuring an interhemispheric fissure extending along most of the entire midline, with the thalami remaining unfused. Lobar HPE is usually diagnosed in the prenatal stage or infancy; however, cases of adult-onset are exceedingly rare. Here, we present a 25-year-old patient who was presented with multiple episodes of seizures and was subsequently diagnosed with lobar HPE accompanied by a meningocele. By shedding light on this rare brain malformation, we hope to raise awareness among healthcare professionals and stimulate further research into the pathogenesis, clinical course, and management of adult-onset HPE.

Introduction

Holoprosencephaly (HPE) is a rare brain malformation where an incomplete separation of the cerebral hemispheres occurs during the early embryonic stage. HPE is typically classified into 3 subtypes in decreasing order of severity — alobar (no separation of the cerebral hemispheres), semi lobar (interhemispheric fissure recognizable only posteriorly), and lobar (hemispheres for the most part being separated) — other

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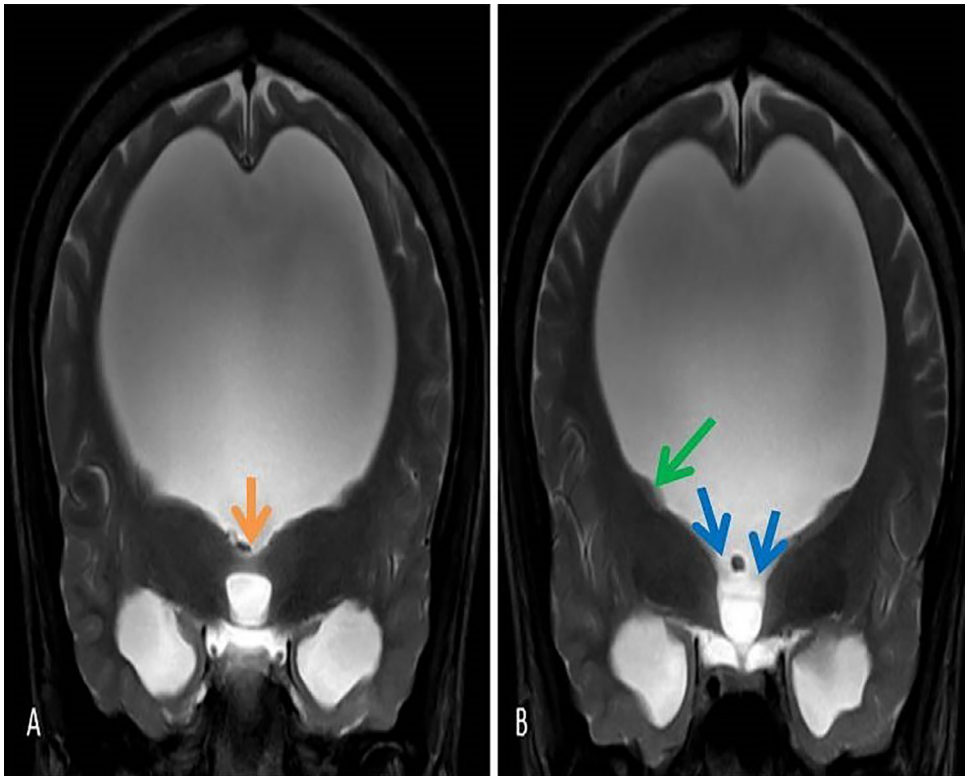

Fig. 1 – Magnetic resonance imaging of brain T2 weighted imaging coronal sections (A and B) shows nonfusion of bilateral thalami with interthalamic adhesion—Massa intermedia (orange arrow). Gross hydrocephalus with nonvisualization of cavum septum and wide communication of bilateral lateral ventricles with third ventricle (blue arrows). Subependymal nodule (green arrow).

milder forms of HPE include middle interhemispheric variant and microform variant [1]. The etiology of HPE is multifactorial, involving genetic, environmental, and teratogenic factors. The severity of clinical manifestations varies widely, ranging from mild facial anomalies and intellectual disability to severe neurological deficits incompatible with life. Typically lobar HPE diagnosed in the prenatal period or infancy, adult-onset cases are exceedingly rare and present unique diagnostic and management challenges [2,3]. Herein, we present a case of lobar HPE accompanied by a meningocele, a sac-like protrusion of the meninges through a skull defect, in a 25-year-old patient with a history of multiple episodes of seizures.

Case

A 25-year-old male patient presented to the outpatient department (OPD) of our hospital for brain magnetic resonance imaging (MRI) following complaints of multiple episodes of seizures for the past 5 years. The patient's birth history indicates that he was the first child born to his mother when she was 25 years old, and the delivery was through normal vaginal birth. No pregnancy-related issues were reported. The patient's birth weight was within the normal range. After birth, he showed stable vital signs, with an Apgar score of over 8 at both 1 and 5 min. He was born to healthy, non-consanguineous parents, and his family history did not reveal any incidence of HPE among his relatives, including distant ones. Upon physical examination, the patient exhibited hypertelorism, characterized by an increased distance between the eyes. Due to this facial dysmorphic feature, high-resolution karyotyping was performed, and the results were normal. A cardiac ultrasound was also conducted, which showed no abnormalities. Following birth, there were no additional clinical issues noted, such as developmental delays or feeding difficulties. The patient had no significant medical or surgical history prior to the age of 20. At the age of 20, he began to experience generalized symptoms, including poor sleep quality (erratic sleep patterns), constipation, and irritability. Around this time, he also started having frequent seizure episodes. During his visit to our OPD, routine biochemical and hematological tests were conducted, and all values were within normal limits. An MRI was planned to further investigate the cause of his seizures. MRI showed non-fusion of bilateral thalami with interthalamic adhesion (Figs. 1 and 4). Additionally, gross dilatation of the lateral and third ventricles was evident. However, the fourth ventricle appeared normal. T2 weighted imaging coronal sections showed partial fusion of the frontal and occipital horns of the lateral ventricle, along with gross hydrocephalus, non-visualization of the cavum septum, and wide communication between bilateral lateral ventricles and the third ventricle. The imaging also revealed the presence of a subependymal nodule (Figs. 1–4) and the absence of sep-

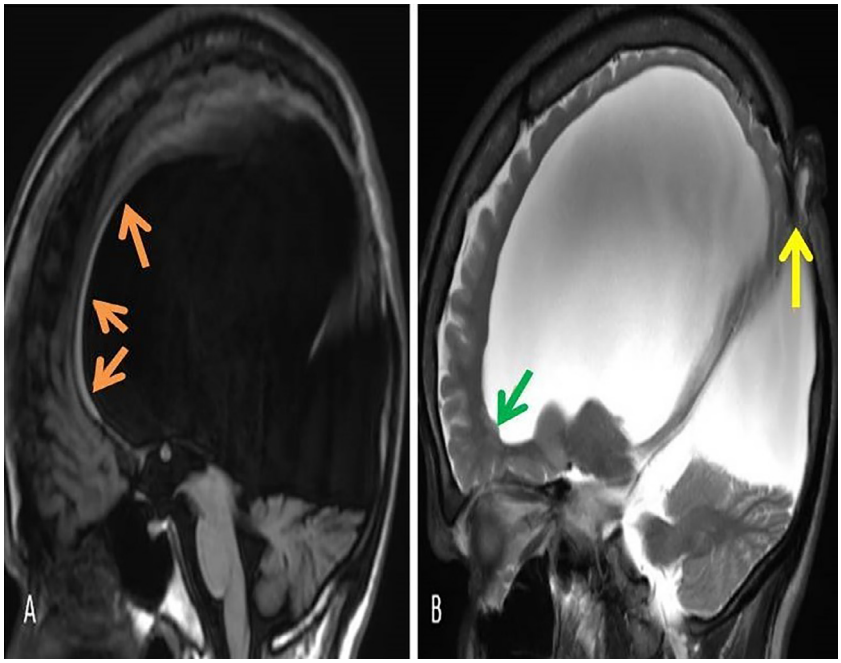

Fig. 2 – Magnetic resonance imaging of brain sagittal sections T1 weighted imaging (A) and T2 weighted imaging (B) shows hypoplastic corpus callosum, ie, genu and body, with non-visualization of splenium (orange arrows). A bony defect is seen in the posterior parietal bone with herniation of cerebrospinal fluid and meninges through the defect (yellow arrow). Subependymal nodule noted (green arrow).

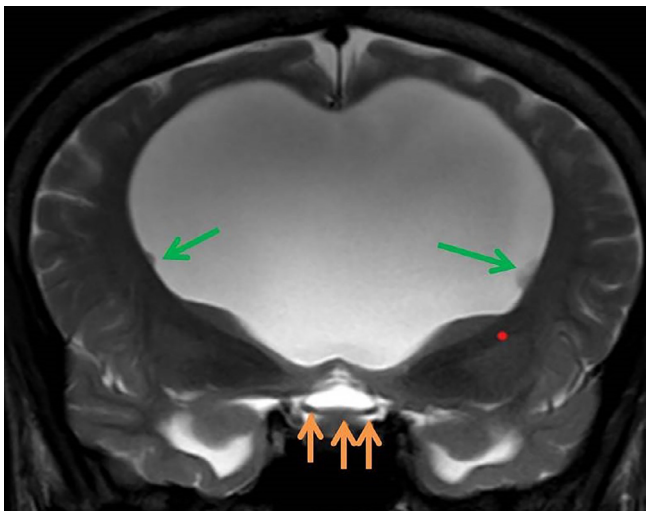

Fig. 3 – Magnetic resonance imaging of the brain T2 weighted imaging coronal section shows hypoplastic optic chiasm (orange arrows). Subependymal nodules noted (green arrows).

tum pellucidum. T1 and T2 weighted brain sagittal sections showed thinning of the corpus callosum (genu and body), non-visualization of the splenium, inferior displacement of the cerebellum, and absence of tonsillar herniation. The bone defect was noted in the right posterior parietal bone with herniation of CSF and meninges in the extra-calvarial region (Figs. 2 and 4). The findings also indicated smaller-than-usual optic chiasma (Fig. 3). Midline structures, including the falx, pituitary fossa, and infundibulum, appear normal. Gangliocapsular regions, brainstem, basal cisterns, sella, parasellar region, and visualized paranasal sinuses were also normal. Due to its exceptional therapeutic impact and tolerability, the patient was effectively treated for seizures with sodium valproate (250mg twice daily). Up until the first year of patient follow-up, no seizure recurrence was noticed, and the patient is on regular follow-up.

Discussion

To the best of our knowledge, we presented a rare occurrence of lobar HPE in a 25-year-old patient, detailing their clinical presentation, diagnostic assessment, and management approach. The presence of a meningocele further complicated the clinical presentation and management of HPE in this case.

Utilizing a therapy approach and a 9-month subsequent follow-up, Gawrych et al. [4] disclosed an exceptional instance of an infant with lobar HPE and the average cleft lip and palate. They eventually concluded that HPE can indicate a variety of craniofacial malformation features that do not always correspond with the degree of brain defects. The case also stated that individuals may live into childhood and beyond if they have modest to severe abnormalities in the brain. However, our case had dysmorphic features of hypertelorism, which is also 1 of the features of lobar HPE. The occurrence of seizures is a prevalent clinical feature in patients diagnosed with HPE [5]. Similarly, the lobar HPE case in this study is presented with

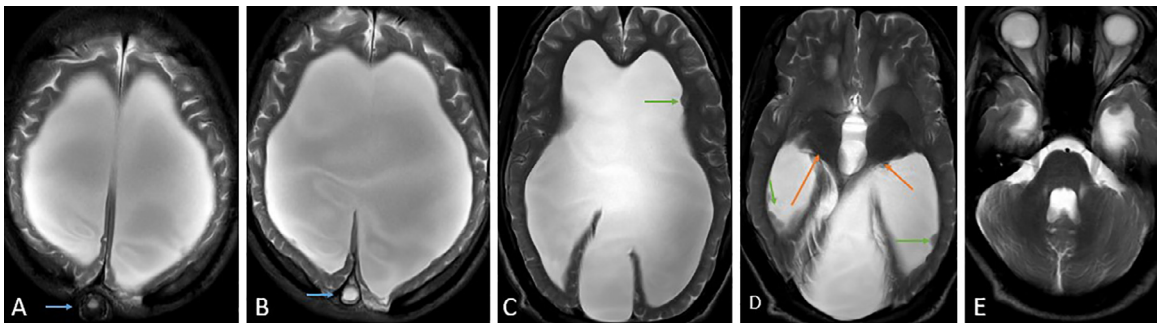

Fig. 4 – Magnetic resonance imaging of brain T2 weighted imaging sequential axial sections (A, B, C, D, and E) shows nonfusion of bilateral thalami (orange arrow). Gross hydrocephalus with nonvisualization of cavum septum and wide meningocele (blue arrows) with normal appearance of the fourth ventricle. Subependymal nodule (green arrow).

multiple seizures to the OPD. It was generally reported that HPE children with severe forms of the condition characterized by craniofacial anomalies such as cyclopia, ethmocephaly, or chromosomal anomalies will not survive beyond early infancy [6]. In line with our case, a retrospective study carried out at Carter Center on 104 children with HPE revealed a mean age of 4 years, with 15% of patients aged between 10 and 19 years [7]. These findings underscore the importance of considering HPE as a potential differential diagnosis in adult patients presenting with seizures.

Cranial ultrasonography and computed tomography scans serve as valuable tools for evaluating patients with HPE [8]. As patients transition to older age groups, consideration may be given to employing computed tomography or MRI. However, CT potentially leads to excess radiation exposure, and MRI poses a risk of excess sedation [9]. Although, MRI is the preferred imaging choice for the accurate diagnosis and classification of HPE.

In a 9-month-old patient, cranial computed tomography and MRI scans revealed a fronto-ethmoidal defect with meningoencephalocele, absent interhemispheric fissure, fused cerebral hemispheres, horseshoe-shaped mono ventricle, and absent septum pellucidum indicative of alobar HPE. Additionally, perisylvian grey matter surrounded by cerebrospinal fluid consistent with type I schizencephaly further supported the diagnosis of alobar HPE [10]. In this case, MRI findings suggested septo-optic dysplasia due to optic nerve abnormalities, thinning of the corpus callosum, and the absence of septum pellucidum. However, the characteristic features of HPE — nonfusion of thalami, partial fusion of lateral ventricles, absence of septum pellucidum, inferior displacement of the cerebellum, and thinning of the corpus callosum and the severity, strongly inclined towards a diagnosis of lobar HPE. Furthermore, a bone defect in the right posterior parietal bone indicated the presence of a meningocele. However, genetic testing is necessary to rule out underlying chromosomal anomalies commonly associated with HPE [11] Waghmare et al. [12] described a case of alobar HPE associated with Meningomyelocele and Omphalocele in a male child born to a 28-year-old female at 34 weeks of gestation, but the association of meningomyelocele and meningocele with lobar HPE either in pediatric or adult patients has not been witnessed in the past published literature. A liveborn child was delivered at term to a 19-year-old woman (G1P0) who had lumbar myelomeningocele and Chiari II malformation associated with lobar holoprosencephaly (HPE), as described by Rollins et al. (1998) [13]. Other examples of HPE linked to spinal abnormalities include a stillborn female new born with lumbar meningocele, cebocephaly, and alobar HPE, as well as a liveborn male infant delivered at term that had caudal regression, renal, and cardiac abnormalities, along with lobar HPE [14,15]. However, our case has not demonstrated the previously proposed association between these diseases, with the exception of meningocele. Therefore, as far as our researchers are aware, this is the first case report of meningocele with adult lobar HPE.

Surgical intervention may become necessary to repair the meningocele and address any associated hydrocephalus or neurological deficits. However, the presence of HPE might complicate surgical planning and heighten the risk of complications. Hence, managing patients with lobar HPE demands a multidisciplinary approach aimed at addressing their intricate medical, developmental, and psychosocial needs [16].

Marques et al.[17] emerged to the conclusion that the smallest daily sodium valproate dose in monotherapy that could control seizures for the majority of epilepsies patients was up to 700mg. This value can be used as a low dose criterion in studies evaluating the therapeutic sodium valproate ranges in support of treatment performed for seizure control in our case like Gawrych et al. [4].

There are alternative approaches that are available. According to a study, an overall ventriculostomy (ETV) success rate of 72%, with a significant difference in the success rate of infants younger than 6 months of age (12.5% success rate) compared to those over 6 months of age (80% success rate) [18]. One more technique, which is the standard surgical treatment for myelomeningocele-associated hydrocephalus, is ventricular CSF shunt drainage. However, malfunction rates range from 14.7% to 64%, and shunt infection rates range from 2.9% to 15.3% [19].

In this case, our patient received management through the administration of antiepileptic medications to control seizures, consultation with neurosurgery for the meningocele, and provision of multidisciplinary rehabilitation to address any cognitive and functional deficits. Long-term follow-up is essential to monitor treatment response and disease progres-

sion. Overall, this case emphasizes the necessity of ongoing collaboration among healthcare professionals to ensure comprehensive care for patients with lobar HPE. Additionally, this case highlights the need for further research and the development of tailored therapeutic approaches to optimize outcomes in patients with lobar HPE.

Conclusion

This case represents the first detailed description of lobar HPE in an adult patient, which is a rare occurrence. Clinicians should remain vigilant and consider the possibility of lobar HPE, even in adult populations, particularly when presented with atypical symptoms. The case exhibits neuroradiologically typical, albeit mild, findings of lobar HPE accompanied by meningocele. The case report emphasizes the significance of MRI in the differential diagnosis of adult patients presenting with seizures. Overall, the case underscores the necessity for further research to enhance understanding of the pathogenesis and optimal management strategies for lobar HPE with associated meningocele.

Patient consent

An informed verbal and written consent was obtained from the patient.

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