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Case Report

Corpus callosal agenesis with gray matter heterotopia and bilateral eye coloboma in an infant: A case report ☆,☆☆

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ABSTRACT

Corpus callosal agenesis (CCA) is a rare congenital disorder characterized by the partial or complete absence of the corpus callosum, a structure crucial for interhemispheric communication. CCA can occur in isolation or be associated with other anomalies such as heterotopia, holoprosencephaly, cerebellar hypoplasia, coloboma, and hydrocephalus. The prevalence of CCA ranges from 0.020% to 0.025%, though some reports suggest higher rates. This case report describes a 1-year-old male with developmental delays and no significant antenatal or family history. MRI revealed a complete absence of the corpus callosum, asymmetrically dilated lateral ventricles, subependymal gray matter nodules suggestive of gray matter heterotopia, and bilateral posterior globe defects with vitreous herniation, indicating severe ocular anomalies. The child received supportive care including physical therapy and special education services, with regular follow-ups for developmental and ophthalmologic evaluation. This case report details the rare occurrence of CCA, accompanied by gray matter heterotopia and bilateral posterior eye coloboma in a pediatric patient. The combination of these congenital anomalies presents unique diagnostic and management challenges requiring multidisciplinary care. We discuss the clinical presentation, radiological findings, and implications for supportive care and improving the prognosis.

Introduction

Corpus callosal agenesis (CCA) is a rare congenital disorder characterized by the partial or complete absence of the corpus callosum, the structure that connects the 2 cerebral hemispheres. It can occur in isolation or in association with other anomalies, including heterotopia, holoprosencephaly, cerebellar hypoplasia, coloboma, abnormal cerebral fissures,

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porencephalic cysts, and hydrocephalus [1]. Heterotopia refers to an abnormal collection of neurons in an anomalous location other than the cortical gray matter. It is believed to be secondary to an arrested migration of neurons from the germinal matrix toward the cortical ribbon along the radial glial path [2]. Coloboma is a developmental anomaly that results from incomplete closure of the embryonic choroidal fissure, resulting in ectasia and herniation of vitreous into the retro-ocular space [3]. This defect in ocular structure may coexist with CCA but is rarely reported together. The prevalence of congenital absence of corpus callosum ranges from 1 in 5000 to 1 in 4000 (0.020%-0.025%), with some reports indicating a higher prevalence of 0.2%-0.7% [4,5].

This case report aims to contribute to the limited literature on this combination of anomalies, emphasizing the importance of thorough radiological and clinical evaluation in the diagnosis and management of similarly affected patients.

Case presentation

A 1-year-old male presented to the pediatric neurology clinic with a history of developmental delay. The patient's parents reported that the child was not developing as per his peers. The child's antenatal, natal, and postnatal history were uneventful. His mother did not consume alcohol or other illicit drugs during pregnancy. Furthermore, there was no family history of developmental delays. On examination, the patient exhibited normocephaly, normal tone in extremities, and without dysmorphic facial features. Vital signs were within normal limits. On assessment, the patient displayed global developmental delays, i.e. not being able to sit without support and not being able to speak even a single word, apart from coos and babbles.

His biochemical and hematologic investigations were within normal limits. Therefore, imaging with MRI (Magnetic Resonance Imaging) brain was sought to look for any structural defects. A T1-weighted sagittal MRI image showed a complete absence of the corpus callosum (Fig. 1). This finding was further corroborated by a T2-weighted coronal image, which confirmed the absence of the corpus callosum, but distinct Probst bundles, indicative of re-routed white matter tracts, and also revealed asymmetrically dilated lateral ventricles (Fig. 2). Additionally, T2-weighted axial images displayed subependymal gray matter nodules along the right lateral ventricular wall, indicative of gray matter heterotopia (Fig. 3). Furthermore, axial T1-weighted images identified bilateral defects in the posterior globe, with herniation of the vitreous humor through these defects, suggesting severe ocular anomalies (Figs. 4A and B).

The patient's parents were counseled about the findings of imaging. The patient was managed with conservative and supportive measures including physical therapy, and special education services. Regular follow-ups were scheduled to monitor developmental progress. Ophthalmologic follow-ups were also arranged to look for visual impairment and potential complications related to coloboma.

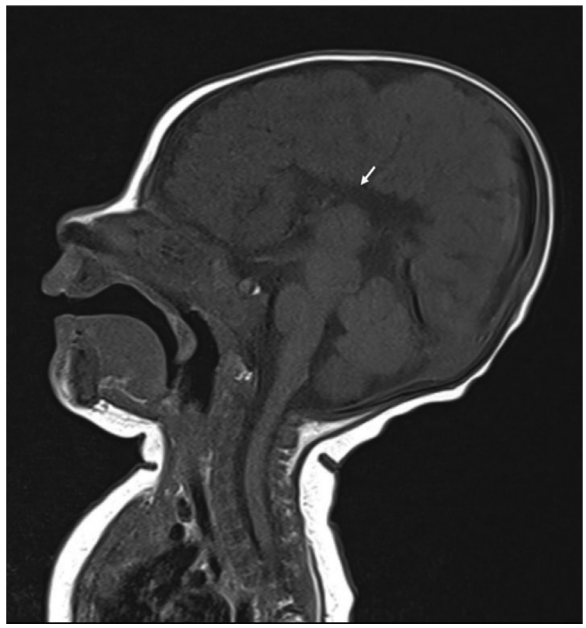

Fig. 1 – T1 weighted sagittal image shows a complete absence of the corpus callosum (white arrow).

Discussion

CCA refers to the partial or complete absence of the corpus callosum, the major commissural structure connecting the 2 cerebral hemispheres. This condition may be congenital or acquired and can manifest in isolation or alongside other neurological anomalies, including heterotopia, microgyria, and hydrocephalus [1,6]. Embryologically, the corpus callosum forms between the eighth and 20th weeks of gestation, and its agenesis is often linked to complex telencephalic or posterior fossa malformations [7]. During this time the corpus callosum forms through a sequence of developmental steps, including midline patterning and axon guidance across the hemispheres [8].

Structural brain abnormalities, including CCA, occur in approximately 1 to 2 per 1000 births, with genetic disorders, being key contributors [9]. Estimates suggest it occurs in approximately 1.8 per 10,000 in the general population, with higher rates of 230-600 per 10,000 in children with neurodevelopmental disabilities [10]. CCA is notably more prevalent in males, and its detection often occurs within the first year of life, especially when associated with other neurological or cognitive deficits [11]. Our case was also male in the first year of life when the CCA got detected.

The etiology of CCA is complex and multifactorial. It reflects a mix of genetic and environmental factors, with up to 70% of cases having an unclear cause even after comprehensive clinical evaluation [12,13]. While genetic factors account for 30–45% of CCA cases, with 10% linked to genetic mutations and chromosomal abnormalities such as trisomies 18, 13, and 8 [1,14], environmental factors also play a significant role [15].

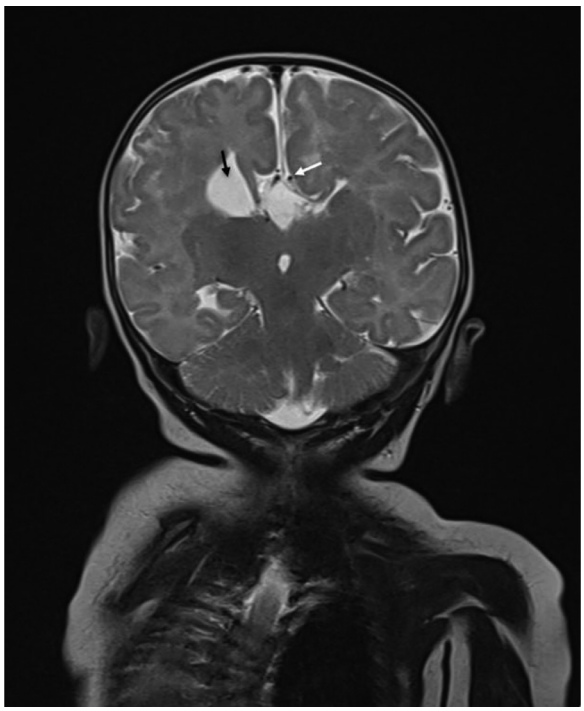

Fig. 2 – T2 weighted coronal image shows the absence of corpus callosum (white arrow) with asymmetrically dilated lateral ventricles (black arrow).

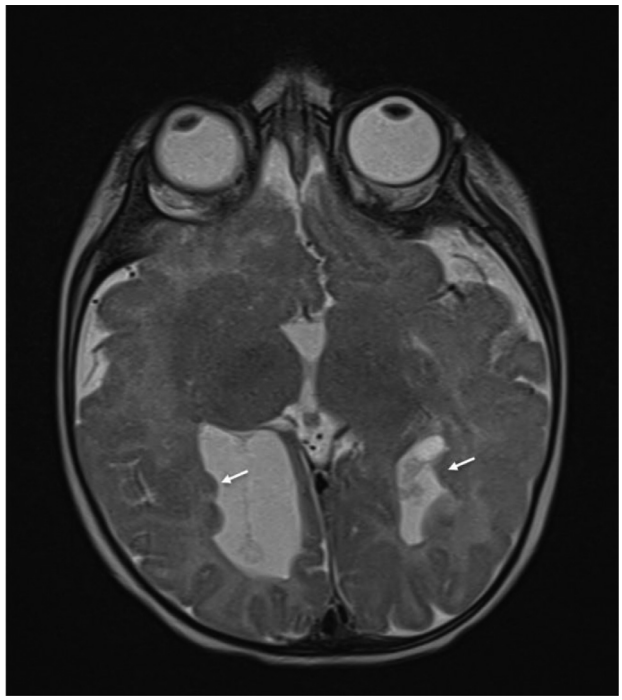

Fig. 3 – T2 weighted axial image shows subependymal gray matter nodules in the lateral ventricular wall suggestive of gray matter heterotopia (white arrow).

Genetic defects, such as haploinsufficiency of the AKT3 gene, have also been identified as contributing factors, particularly in cases associated with microcephaly [16]. Fetal alcohol syndrome, advanced maternal age, premature birth, maternal diabetes, and infections like rubella have all been implicated in CCA development [17,18]. However, our patient did not have in-utero exposure to any identifiable insults. His mother was nondiabetic and did not have infections. Chromosomal microarray analysis (CMA) and exome sequencing can help identify the genetic basis of CCA in some cases [14] though it was not pursued in our case due to unavailability.

Clinical manifestations of CCA vary widely, ranging from severe developmental delays to being asymptomatic, depending on the presence of other abnormalities and the extent

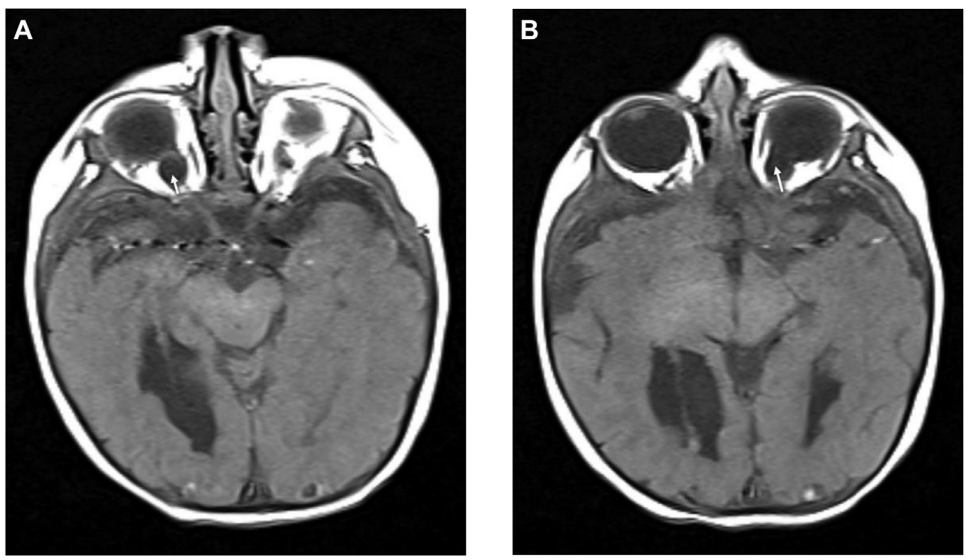

Fig. 4 – (A and B) Axial T1 weighted images show the defect in the posterior globe bilaterally with herniation of the vitreous through the defect (white arrow).

of the agenesis [15]. Our patient had associated heterotopia and presented with global developmental delay, which is in line with the established literature. The absence of the corpus callosum disrupts interhemispheric communication, which is crucial for sensory, motor, and cognitive integration [19]. Agenesis can lead to developmental delays and seizure disorders, particularly in cases associated with heterotopia [6]. However, no seizures were presented in our case.

CCA is associated with over 100 congenital syndromes [19]. It is often accompanied by other central nervous system (CNS) abnormalities, including Dandy-Walker malformation, holoprosencephaly, and cerebellar hypoplasia. Our case has heterotopia and bilateral coloboma in eye. Bilateral involvement often indicates a more widespread developmental issue, which may be associated with syndromes such as CHARGE syndrome. These associations highlight the disrupted early cerebral development processes leading to CCA. Structural anomalies such as interhemispheric cysts, hydrocephalus, and cortical malformations are common in CCA, reflecting the malformation's role as part of broader syndromic conditions like Aicardi syndrome and Andermann syndrome [14,20]. Additionally, extracerebral abnormalities may affect the eyes, heart, and kidneys, indicating a systemic developmental issue [19,21]. However, our patient did not have any facial or other characteristics to suggest syndromic occurrences.

Diagnosis of CCA is primarily established through neuroimaging, often prompted by evaluations for developmental delay or epilepsy [7]. Ultrasound is useful for early detection, but its ability to fully assess CCA is limited compared to MRI, and it is best used as a preliminary screening tool [19]. Ultrasound findings associated with CCA include absence of the CSP(Cavum Septi Pellucidi), teardrop-shaped lateral ventricles with enlarged occipital horns and reduced frontal horn size, Increased separation of the lateral ventricles and upward displacement of the third ventricle [14,22]. Magnetic resonance imaging (MRI), particularly in the sagittal plane, is the preferred method for diagnosing CCA, as in our case, due to its ability to visualize the brain in multiple planes, assessing associated anomalies, and a low false positive rate compared to USG [23]. MRI findings for CCA include the absence of the corpus callosum, an elevated third ventricle, and the presence of Probst's bundles [6]. The presence of Probst bundles, which are longitudinally oriented neuronal fibers, is a hallmark of CCA, indicating abnormal commissure formation [7,15,24]. These typical findings are present in the MRI imaging of our case, except for elevated third ventricles. CT is less favored than MRI due to lower resolution and limitations in detecting partial agenesis, but it is an alternative when MRI is unavailable [1].

Treatment and prognosis for CCA vary widely, particularly because CCA often occurs with other brain anomalies. There is no universal treatment for all cases; instead, interventions are tailored to individual needs. Effective management of CCA involves a multidisciplinary approach, including genetic counseling, early intervention programs, and ongoing neurodevelopmental assessments to support optimal outcomes [25]. Common therapies include physical therapy, speech therapy, and occupational therapy, with early intervention crucial for addressing developmental delays [18]. Regular monitoring and support are recommended to address developmental and educational needs as they arise [18,21]. Genetic counseling and prenatal imaging are essential in assessing recurrence risks and planning for future pregnancies [25].

Children with CCA present with a broad spectrum of neurodevelopmental outcomes. Approximately 76.04% of children prenatally diagnosed with isolated complete CCA exhibit normal neurodevelopment, though developmental delays and other issues are frequently reported by parents [15]. However, isolated CCA, particularly when identified incidentally, often carries a better prognosis, with many individuals showing no significant neurological symptoms [6,10].

Conclusion

Agenesis of the corpus callosum may present with diverse clinical manifestations influenced by multiple factors. The patient's presentation of CAA with heterotopia and coloboma on MRI underscores the rarity and complexity of such cases, adding to the understanding of clinicians about active evaluation of associated anomalies in the case of corpus callosum agenesis. The condition's clinical presentation, genetic diversity, and association with other brain anomalies underscore the need for comprehensive diagnostic evaluation and management tailored to each case.

Provenance And peer review

Not commissioned, externally peer-reviewed.

Authors contributions

Saubhagya Dhakal, Saroj Kumar Jha, Alisha Adhikari: Led data collection, and contributed to writing the case information. **Saubhagya Dhakal, Saroj Kumar Jha, Alisha Adhikari:** Contributed to the process of original draft preparation and introduction and discussion. **Saroj Kumar Jha, Alisha Adhikari, Pinky Jha, Srijana Katwal:** Contributed to conceptualization and discussion. **Saubhagya Dhakal, Saroj Kumar Jha, Alisha Adhikari, Pinky Jha, Srijana Katwal:** Revised it critically for important intellectual content, and contributed in review and editing. **Saroj Kumar Jha, Alisha Adhikari:** Edited the rough draft into the final manuscript.

Patient consent

Written informed consent was taken from the patient for the publication of the case report and the images. A copy of it is available for review by the editor-in-chief of this journal on request.

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