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Rare Triad of Midline Craniofacial Defects: A Case Report

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ABSTRACT

Midline craniofacial anomalies are rare malformations that may occur in isolation or as part of syndromic associations. Among them, the coexistence of basal encephalocele, agenesis of the corpus callosum, and Morning Glory Syndrome (MGS) is exceptionally rare, with only a handful of cases described in the literature. We report the case of a 7-year-old female with hypertelorism, cleft lip and palate, and an intraoral swelling. MRI demonstrated sphenoethmoidal encephalocele, complete agenesis of the corpus callosum, right ocular coloboma, and a posterior fossa arachnoid cyst. Fundus examination revealed characteristic features of MGS in the right eye. Genetic testing including whole-exome sequencing, mitochondrial sequencing, and chromosomal microarray was normal, supporting a sporadic occurrence. The patient underwent staged surgical interventions, including Millard's rotation–advancement cheiloplasty and transcranial repair of the basal encephalocele. Supportive visual management with refractive correction and multidisciplinary rehabilitation was initiated. Basal encephaloceles account for less than 1.5% of all encephaloceles and are frequently associated with midline craniofacial anomalies. MGS, although typically sporadic, may coexist with midline craniofacial and intracranial defects, reflecting a common embryological pathway of failed midline closure. The presence of this triad resembles features of the Sakoda complex. Despite normal genetic results in our case, prior studies implicate genes such as PAX6, OTX2, and SOX2 in similar overlapping phenotypes. MRI remains the gold standard for evaluating intracranial extension and associated anomalies, while CT is essential for delineating the bony defect for surgical planning. This report adds to the scarce literature on the rare triad of sphenoethmoidal encephalocele, corpus callosal agenesis, and MGS. Comprehensive imaging, early surgical repair, supportive ophthalmic care, and multidisciplinary follow-up are essential for optimizing long-term outcomes.

Keywords: Basal encephalocele; Agenesis of corpus callosum; Morning glory syndrome; Craniofacial malformations; Sakoda complex.

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Introduction

Midline craniofacial malformations are among the most common congenital anomalies detected both prenatally and postnatally, ranging from 1 in 600 to 1.4 in 1000 live births [1][2][3]. They may occur as isolated defects or as part of genetic syndromes. Brain anomalies associated with facial malformations are relatively rare, present in only about 1% of cases [4]. Hypertelorism is a well-recognized clinical marker that often points to midline brain and craniofacial defects, such as corpus callosal dysgenesis/agenesis, cranium bifidum, basal encephaloceles, dermoids, and rare anomalies like duplicated pituitary stalk [5]. It can also be associated with ocular pathologies including retinal and optic nerve dysplasias, persistent hyperplastic primary vitreous (PHPV), and morning glory syndrome (MGS). Conversely, hypotelorism is frequently associated with holoprosencephaly or septo-optic dysplasia. We present a rare case of a child with sphenoethmoidal encephalocele, agenesis of the corpus callosum, and morning glory syndrome - an rare triad of midline craniofacial anomalies.

Case Report

A 7-year-old female, born to non-consanguineous parents with unremarkable antenatal and birth history, presented with a history of respiratory distress during the neonatal period. On physical examination, the child exhibited frontal bossing, hypertelorism, and cleft lip and palate. A fluctuant swelling was noted on the roof of the mouth (Figure 1). Given the constellation of findings, a syndromic craniofacial malformation was suspected and MRI was done. MRI showed coloboma of the right eye with a tortuous right optic nerve (Figure 2A), agenesis of the corpus callosum (Figure 2B, 2C), a midline defect involving the sphenoid, ethmoid bones, and tuberculum sella, with herniation of brain tissue (encephalocele) (Figure 2D) and finally a posterior fossa arachnoid cyst. Fundus examination revealed a funnel-shaped excavation of the right optic disc with peripapillary pigmentary changes and radially oriented vessels—features diagnostic of Morning Glory Syndrome (MGS). The left eye was normal. A provisional diagnosis of Sakoda complex was made. Although the Sakoda complex is considered a developmental malformation sequence rather than a primary chromosomal or genetic abnormality. Genetic evaluation was done to rule out variant in the EFNB1 gene associated with craniofrontonasal dysostosis. Whole exome sequencing, mitochondrial sequencing, and microarray (Cyto-One Advanced) were performed, all of which yielded normal results.

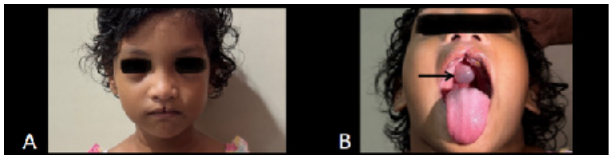

Figure 1. Clinical images of a 7-year-old female with midline craniofacial anomalies. (A) Photograph showing frontal bossing, hypertelorism, and cleft lip. (B) Intraoral photograph demonstrating a fluctuant swelling on the roof of the mouth (black arrow) in association with a cleft palate.

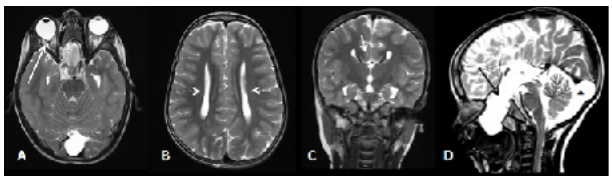

Figure 2. MRI of the same patient depicting agenesis of the corpus callosum, sphenoethmoidal encephalocele, and right-sided ocular anomalies. (A) Axial T2-weighted image demonstrating a coloboma of the right eye with a tortuous optic nerve (white arrow). (B, C) Axial and coronal T2-weighted images showing parallel orientation of the lateral ventricles ("racing car" sign, dotted arrow) and "Viking helmet" appearance (white arrow), characteristic of corpus callosal agenesis. (D) Sagittal T2-weighted image depicting a bony defect involving the sphenoid and ethmoid bones with herniation of brain parenchyma forming an encephalocele (black arrow). An incidental posterior fossa arachnoid cyst is also noted (asterisk).

Discussion

Basal encephaloceles are rare congenital anomalies that account for less than 1.5% of all encephaloceles and are frequently associated with midline craniofacial defects such as hypertelorism, cleft lip, and cleft palate [7]. The coexistence of agenesis of the corpus callosum with midline facial clefts has been described in the Sakoda complex, a rare constellation of midline anomalies that underscores the shared embryologic origin of these malformations [5]. Morning Glory Syndrome (MGS) is a congenital anomaly of the optic disc characterized by funnel-shaped excavation, peripapillary pigmentary changes, and radially oriented vessels [6]. While most cases are sporadic, MGS can be associated with midline craniofacial defects, basal encephaloceles, and rarely with transsphenoidal encephaloceles [8,9]. This reflects the common developmental

pathway involving failure of embryonic closure along the midline during early gestation. Abnormal interactions between the neuroectoderm, mesenchyme, and surface ectoderm have been postulated as the underlying mechanism [9,10]. Genetic contributions to these anomalies remain an area of ongoing research. Whole exome sequencing in our case was normal, supporting a sporadic occurrence. However, previous studies have suggested that mutations in genes regulating forebrain and optic nerve development, such as PAX6, OTX2, and SOX2, may contribute to overlapping phenotypes that include optic nerve colobomas, corpus callosal agenesis, and craniofacial malformations [10,11]. Mitochondrial dysfunction has also been implicated in some optic nerve malformations, though no specific mitochondrial variants were identified in our case. The normal genetic results highlight that many such presentations may arise from non-genetic developmental disturbances rather than identifiable monogenic syndromes. From a clinical perspective, recognition of this rare triad has important implications. First, the presence of a basal encephalocele necessitates cross-sectional imaging for surgical planning.

MRI delineates the intracranial extent of herniation and associated anomalies, while CT confirms and delineates the osseous defect [7,8]. Second, ocular anomalies such as MGS should be carefully evaluated, as they may be associated with reduced visual acuity, amblyopia, or strabismus. Third, corpus callosal agenesis can result in neurodevelopmental delay, seizures, or subtle cognitive and social impairments, necessitating long-term neurodevelopmental follow-up [6]. A thorough literature search identified just eight previously reported cases exhibiting the complete triad (Sphenoethmoidal encephalocele, corpus callosal agenesis and Morning glory syndrome) [8,9,10,11,12,13,14,15] highlighting the uniqueness of our case.

Our patient underwent Millard's rotation–advancement cheiloplasty for cleft lip repair, which achieved satisfactory restoration of lip form and function. The associated basal encephalocele was surgically corrected through a transcranial fronto-orbital approach with dural repair and skull base reconstruction, preventing cerebrospinal fluid leakage and risk of infection. For the ocular anomaly, supportive management of Morning Glory Syndrome was initiated with prescription of refractive glasses to optimize residual visual acuity in the affected eye. The patient continues to be followed in a multidisciplinary setting, including speech therapy, orthodontics, and neuro-ophthalmology, for long-term rehabilitation and surveillance.

Conclusion

This case highlights the importance of comprehensive clinical evaluation and cross-sectional imaging in evaluating midline craniofacial malformations. MRI not only delineates the extent of encephalocele and associated intracranial anomalies but also aids in surgical planning, prevents unnecessary biopsies, and facilitates detection of associated ocular abnormalities such as MGS. Such thorough evaluation contributes to better prognostic assessment, long-term management, and avoidance of potentially harmful interventions.

Conflict of Interest

There is no conflict of interest to declare.

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