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Case Report Open Access

Agenesis of the Corpus Callosum Associated with a large Ocular Lipodermoid in a Neonate: A Case Report and Literature Review

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Abstract

Agenesis of the corpus callosum is the most common brain malformation. It may be an isolated malformation or a component of a malformation syndrome. Associated Central Nervous System (CNS) and non-CNS malformations have been broadly reviewed. However, the coexistence of a large ocular lipodermoid has never been mentioned. We reported a female newborn with multiple congenital anomalies, including complete agenesis of the corpus callosum with intracranial midline lipoma, a large epibulbar lipodermoid over the entire left cornea and a large Ventricular Septal Defect (VSD). No clinical neurological or cardiac symptoms or signs were noted during admission. She received an ocular tumor excision with amniotic membrane transplantation on the left eye at 10 days old. Limbal dermoids/lipodermoids are hallmarks of Goldenhar syndrome; however, our patient did not have preauricular tag, microtia, or vertebral anomalies. In addition, a chromosome study and comparative genomic hybridization array in this patient revealed no significant abnormalities. To the best of our knowledge, this is the first report of a case with a combination of agenesis of the corpus callosum, an ocular lipodermoid, and VSD.

Keywords: Agenesis of the corpus callosum; Lipodermoid; Intracranial lipoma

Introduction

Agenesis of the Corpus Callosum (AgCC) is the most common Central Nervous System (CNS) congenital malformation, and literature suggests that dysregulation during embryogenesis causes a neural migration disorder. Structural changes within the affected corpus callosum may include a lipoma, midline meningioma, dermoid cyst, or hamartoma and the prevalence is around 3-7/10,000 [1]. Clinically, agenesis of the corpus callosum is frequently accompanied by multiple systemic anomalies. Among ocular anomalies, strabismus, nystagmus, chorioretinopathy, bilateral iris coloboma, and bilateral anophthalmia have all been mentioned [1]. Goldenhar syndrome, which is a characteristic of a defect of the 1st and 2nd branchial arch derivatives, may include agenesis of the corpus callosum and ocular segmental lipodermoids [2,3]; however, a lipodermoid large enough to cover the whole cornea has never been reported, especially in cases without other symptoms associated with Goldenhar syndrome.

The prognosis of agenesis of the corpus callosum may rely on the associated anomalies and the causes of agenesis of the corpus callosum. Study by Lu et al. [4] reveals that vital organs, such as the heart, may be a flagging indicator, and emphasized the importance of thoroughly surveying for systemic anomalies while facing a patient with agenesis of the corpus callosum. Here, we reported a patient with the agenesis of the corpus callosum, an ocular lipodermoid and Ventricular Septal Defect (VSD), which is a combination that had not been reported before.

Case Report

This female newborn was born to a 34-year-old mother at a gestational age of 37+6 weeks. She was delivered by Caesarean section due to prolonged labor. The Apgar score was 8 at 1-minute and 9 at 5-minutes. Her birth weight was 2680 gm (10-25th percentile), length 47 cm (10-25th percentile) and head girth 33 cm (25-50th percentile). There was no premature rupture of the membrane or other perinatal insult. According to the family's statement, regular prenatal examinations revealed no abnormalities. The mother denied history of diabetes mellitus, taking any medication or having radiation exposure before and during pregnancy. No family members had congenital anomalies. However, one yellowish soft tissue mass covered on the whole left eyeball was noted after birth. Thus, the baby was transferred to our hospital for further evaluation.

After admission, this infant had stable vital signs and could tolerate oral feeding well. A physical examination revealed bilateral palpable eyeball with normal light reflex in the right eye. Bilateral eyelids were normal; however, one yellowish soft tissue mass with several thin hairs, which covered the whole left eyeball, was found (Figure 1a and 1b). A grade I/VI systolic murmur over the left sternal border was also noted. No periauricular pit, cutaneous hyperpigmentation or lipoma, or hypotonia was noted. We consulted an ophthalmologist for further evaluation and treatment concerning the left eye mass. Ocular ultrasonography revealed an intact posterior segment of bilateral eyes with a thick pre-corneal mass on the left eye. Ocular Magnetic Resonance Imaging (MRI) revealed a thick membrane-like lesion overlying the left cornea, most likely a lipodermoid. Besides, serial image and genetic studies were performed, to check for other congenital malformations. Subsequently, brain ultrasonography showed one hyperechogenic lesion over the interhemispheric area and a complete absence of the corpus callosum. The brain MRI showed

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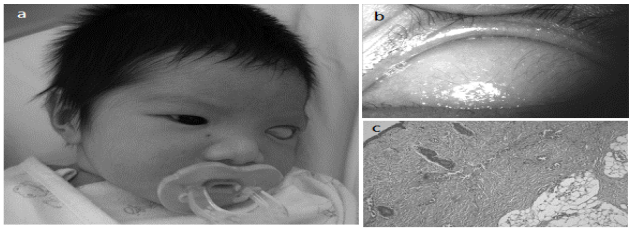

Figure 1: Ocular lipodermoid. (a) One yellowish soft tissue fully covering the left eye. (b) Some thin hairs were visible on the surface of the epidermis-like mass which covered the whole cornea and extended to the fornix. (c) Histopathology demonstrated the copious amout of mature fibro-adipose tissue underlying the keratinized epidermis and dermis. Some hair follicles and sebaceous glands were distributed in the middle-level of the dermis.

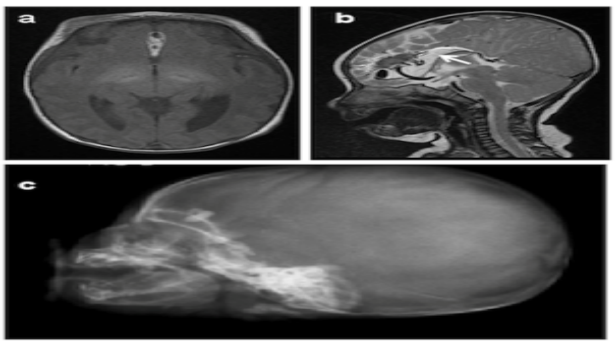

Figure 2: (a) Axial view of brain MRI showed agenesis of the corpus callosum and ventricular dilatation of bilateral posterior horns; (b) sagittal view showed agenesis of the corpus callosum and an intracranial lipoma (arrow) near the midline region; (c) a Skull X-ray also revealed a dense opaque nodular shadow near the midline region of the inferior frontal area.

an intracranial lipoma near the midline region with calcification, and agenesis of the corpus callosum with ventricular dilatation of bilateral posterior horns (Figure 2a and 2b). Other than these findings, there were no other remarkable structural changes within the posterior fossa or definite focal signal changes at the brain parenchyma. A Skull x-ray also revealed a dense opaque nodular shadow near the midline region of the inferior frontal area (Figure 2c). In addition, cardiac ultrasonography was performed because a heart murmur was noted and it showed a 5.2 mm perimembranous trabecular type ventricular septal defect. For her multiple systemic anomalies, we performed a Comparative Genomic Hybridization (CGH) array study and a TORCH survey, but the results of both were negative. The audiologic examination was normal bilaterally. She then received a lamellar keratectomy to excise this pre-corneal tumor and amniotic membrane transplantation to cover the residual corneal stromal bed at 10 days old. Neovascularization was found on the stromal surface of the remaining translucent cornea. The removed elastic tumor (2.5 cm×1.5 cm) had an epidermis-like surface and contained copious amount of underlying adipose tissue. A histopathological examination revealed lobules of mature adipose tissue admixed with fibrotic tissue which is compatible with a lipodermoid (Figure 1c). She recovered smoothly after the operation and was discharged at 19 days old. At 1.5 months old, she began having feeding intolerance and taking digoxin and furosemide to control for heart failure.

Discussion

The corpus callosum is the major connective structure of the brain. Clinically, AgCC is the most common congenital malformation [5]. Prevalence is around 3-7/10,000, but in children with developmental disability the estimated incidence is around 2-3/100 [1]. It can be an isolated malformation or a component of malformation syndromes. The cause of AgCC is thought to be the dysregulation of embryogenesis, causing neural migration defects in which may be due to genetic, infectious, vascular, or toxic causes. Retrospective chart reviews and cross-sectional cohort studies have shown that 30-45% of cases of AgCC have identifiable causes [6]. Approximately 10% have chromosomal anomalies and the remaining 20-35% has recognizable genetic syndromes, including acrocallosal syndrome, Aicardi syndrome, cerebro-oculo-facio-skeletal syndrome, FG syndrome, Mowat-Wilson syndrome, septo-optic dysplasia, Toriollo-Carey syndrome, Walker-Warburg syndrome [6]. Clinical severity varies. It can be asymptomatic, or presented with mental retardation, visual problems, speech delay, seizure, or feeding problems. These above symptoms may be associated with other combined CNS anomalies. Malformation of cortical development resulting from altered neural proliferation and migration and cerebellar defects are the most commonly reported anomalies. Isolated AgCC may have a favorable outcome, so further studies for genetic factors and structure lesion are indicated [7,8]. In our patient, there was no evidence of any associated CNS malformation, including heterotopia, pachygyria, or other cerebellar vermis hypoplasia. But further follow-up of her neurological development is still warranted.

Intracranial lipoma is believed to be a congenital malformation that results from abnormal persistence and mal-differentiation of the meninx primitiva during the development of the subarachnoid cisterns [9]. Most lipomas occur at or near the midline. Jabot et al. [10] reported that interhemispheric lipomas are the most common type (45%), followed by quadrigeminal/superior cerebellar cistern lipoma (25%), suprasellar/interpeduncular cistern lipoma (14%), cerebellopontine angle cistern lipoma (9%) and sylvian cistern lipoma (5%). The most commonly associated CNS anomaly is dysgenesis of the corpus callosum, just like in our case. Since the meninx primitiva is fused with the borders of lamina reuniens, as one component for differentiation of the corpus callosum, it may interfere with the normal development of the corpus callosum [11,12]. Lipoma over the pericallosal area is classified into two groups: anterior and posterior lipoma. The former is classified as tubulonodular type, usually bigger than 2 cm and is frequently associated with hypogenesis/agenesis of the corpus callosum, frontal lobe anomalies, frontal encephalocele, calcifications, and/or ocular anomalies. However, an associated ocular lipodermoid with lipoma has never been reported. Posterior lipoma is classified as curvilinear type and usually thin and lay on the splenium; they are less frequently associated with other anomalies [13]. Intracranial lipoma does not usually require surgical intervention.

A conjunctival dermoid is a congenital well-circumscribed yellow-white solid mass that involves the bulbar or limbal conjunctiva. It characteristically occurs inferotemporally and may extend to the central cornea or be located in other quadrants. In rare situations, it can be extensive and involve the full thickness of the cornea, anterior chamber, and iris stroma. Dermoids usually occur in the early stage of embryogenesis [3]. Dermoids are thought to be a hallmark of Goldenhar syndrome, which is also called oculo-auriculo-vertebral spectrum, resulting from defects of 1st and 2nd branchial arch derivatives. It is characterized by anomalies of the ear (mostly microtia), hemifacial microsomia, and defects of the vertebral column. Some case reports also found that Goldenhar syndrome may also be associated with agenesis of the corpus callosum and congenital heart disease [14]. However, in our case, there were no anomalies of the ears or vertebra, which are the primary defects of Goldenhar syndrome. Jakobiec et

al. [15] reported a case of a corneal polypoidal lipodermoid lacked of any of the characteristics associated with Goldenhar syndrome, which is similar to our patient. Therefore, they concluded that the central corneal lesions lacked association with Goldenhar syndrome.

Encephalocraniocutaneous Lipomatosis (ECCL), described by Haberland and Perou [16] as a new example of ectomesodermal dysgenesis, is characterized by profound mental retardation, early onset of seizures, unilateral temporofrontal lipomatosis, ipsilateral cerebral and leptomeningeal lipomatosis, cerebral malformation and calcification, and lipomas of the skull, eye, and heart. Prontera et al. [17] had reported a patient having bilateral epibulbar dermoid, moderate tricuspid valve insufficiency, hypoplastic corpus callosum, and intracranial lipomas, but also with additional anomalies including lipomas on the face, alopecia areata, coloboma of iris, chorioretinitis, leptomeningeal angiomatosis, arachnoid cyst, microgyria, osteolytic lesion in the right jaw and odontogenic jaw tumor. Lipomatosis and cutaneous manifestations are key features in this syndrome. However, our patient had no other cutaneous lesion except the epibulbar dermoid. We considered the patient may have ectomesodermal dysgenesis, but not totally fit the clinical features of ECCL.

As mentioned above, multiple factors, especially genetic defects, may be responsible for the malformation of the corpus callosum and associated anomalies in other organ systems. Our patient received a chromosome study and CGH array to survey microdeletion; however, the results showed normal karyotype without any microdeletion. In summary, this infant presented with a large ocular lipodermoid combined with agenesis of the corpus callosum and a ventricular septal defect, though no currently known syndrome can be considered a perfect fit. We will continue to pay special attention to the further visual rehabilitation of her right eye and to the possibility of heart failure due to the ventricular septal defect while growing up.

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