CASE REPORT

A rare case of a neonate with agenesis of the corpus callosum and severe laryngomalacia

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Abstract
Background: Agenesis of the corpus callosum (ACC) is a rare congenital anomaly often associated with other congenital anomalies, syndromic, chromosomal, or genetic disorders. ACC may be detected antenatally. The postnatal diagnosis usually arises following neuroimaging evaluation for neurodevelopmental disorders during the first years of life.
Case description: We report a case of a neonate with complete ACC, presenting with serious feeding-swallowing difficulties and respiratory symptoms. Coexisting severe laryngomalacia was diagnosed. ACC was detected on routine cranial ultrasound. Molecular karyotype revealed pericentric inversion of chromosome 9, inv(9)(p23q22.3), and whole exome sequencing was negative.
Conclusion: The reported case presented unusual clinical manifestations. Laryngomalacia is an extremely rare associated anomaly in infants with ACC, with only a few cases reported in the literature. Moreover, to our knowledge, this is the first reported case of ACC and laryngomalacia associated with the polymorphism inv(9)(p23q22.3). HIPPOKRATIA 2022, 26 (3):118-120.

Keywords: Corpus callosum agenesis, associated anomalies, infants, laryngomalacia

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Introduction

Agenesis of the corpus callosum (ACC) is a rare congenital anomaly with a prevalence of approximately 1.4 per 10,000 live births and reported male predominance[1,2]. ACC is classified as partial or complete and isolated or complex[1,3]. Complex forms are associated with other central nervous system (CNS) and/or extracranial anomalies and/or syndromic, chromosomal, or genetic disorders[1,3,4]. CNS is the most commonly affected system, followed by the musculoskeletal, cardiovascular, urogenital, and gastrointestinal systems[2]. We report a rare case of a neonate with complete ACC who presented serious feeding difficulties and respiratory symptoms and a definitive diagnosis of severe laryngomalacia. Associated respiratory system anomalies in infants with ACC are extremely rare, and only a few, mainly syndromic cases, are reported in the literature[2,5,6].

Case description

A male neonate of 32 1/7 weeks gestation and birth weight 2,010 gr was born to a 41-year-old gravida 2 para 2 mother by an emergency cesarean section due to placental abruption. Both parents were healthy, non-consanguineous, and their first child was healthy. Fetal karyotyping due to advanced maternal age revealed pericentric inversion of chromosome 9, inv(9)(p23q22.3).

ACC was diagnosed on routine cranial ultrasound in the first week of life (Figure 1). Brain magnetic resonance imaging confirmed complete ACC, with no detection of other brain abnormalities (Figure 2). Ultrasonographic investigation for possible extracranial anomalies revealed thoracic spina bifida occulta and mild hydronephrosis. He had no dysmorphic features, and his neurologic examination was normal.

Initially, he was mechanically ventilated for five days due to respiratory distress syndrome. After the second week of life, he was noted to have inspiratory stridor, chest retractions, and cyanotic spells, gradually worsening, requiring supplemental oxygen and non-invasive respiratory support. He had severe feeding difficulties due to the inability to coordinate suck-swallow sequences and regurgitations. Laryngomalacia type C was diagnosed by flexible laryngoscopy. Computed tomography revealed segmental stenosis in the trachea and left main bronchus, indicative of trachea/bronchomalacia. He was treated conservatively with nasogastric tube feeding, anti-regurgitation milk formula, acid suppression therapy (esomeprazole), supplemental oxygen, and respi-

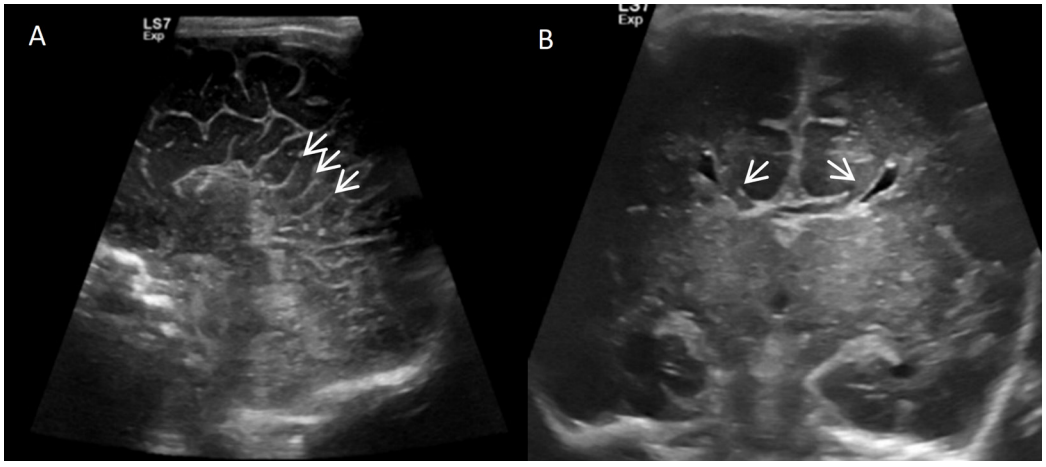

Figure 1: Ultrasound brain images of the male neonate with agenesis of the corpus callosum. A) Midsagittal view: absence of the corpus callosum with "cartwheel appearance" of the sulci and gyri (arrows). B) Coronal view: the crescentic appearance of the lateral ventricles with visibility of the bundles of Probst (arrows). Dilatation of the temporal horns, more prominent on the right.

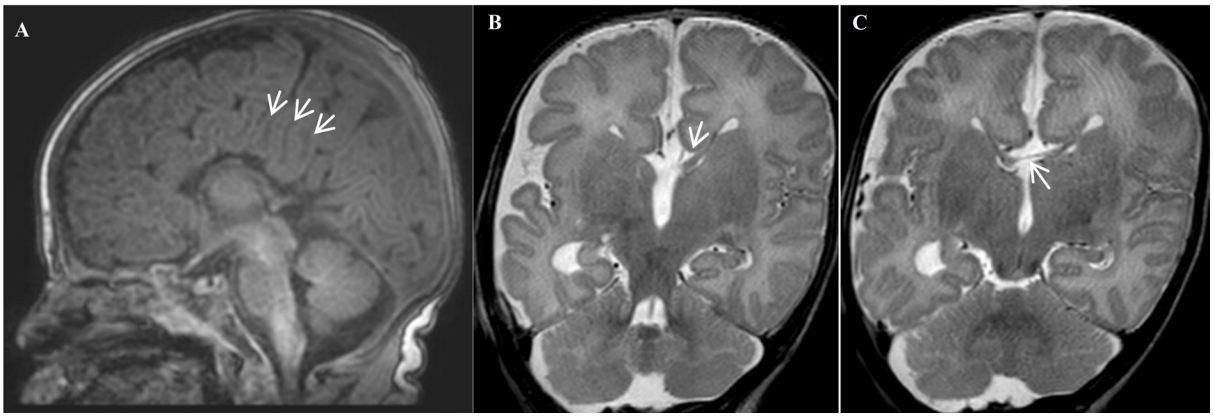

Figure 2: Magnetic resonance brain imaging of the male neonate with agenesis of the corpus callosum. A) Axial T1-weighted image shows an absence of the corpus callosum with a "cartwheel appearance" of the sulci and gyri (arrows). B) Coronal T2-weighted image shows the bundles of Probst (arrow). C) Coronal T2-weighted image shows the hippocampal commissure (arrow).

ratory support with a high flow nasal cannula (HFNC). Clinical improvement was shown after the fifth month of life, confirmed by laryngoscopy. The infant was gradually weaned from oxygen, and weaning from HFNC was achieved. Successful oral feeding attempts have been achieved, and a speech therapy feeding program was applied. Genetic testing was performed using whole exome sequencing (WES), and no clinically significant variant relevant to the patient's phenotype was identified. His neurodevelopment and growth were normal during his hospitalization, apart from the feeding-swallowing problems. He was hospital discharged at seven months of age. Multidisciplinary follow-up was recommended. An early intervention program has been initiated, including physiotherapy and occupational therapy. The last neurodevelopmental assessment was performed at 15 months of corrected age (17 months of chronological age) and was within the normal range in all domains. The infant no longer has any feeding or shallowing difficulties and respiratory symptoms.

Discussion

ACC is detected antenatally in about 75 % of the cases[1-3]. The diagnosis during infancy is usually made after evaluation for neurodevelopmental disorders, seizures, or dysmorphology[2,3,7]. In our case, ACC was diagnosed postnatally by routine cranial ultrasound. The rarity and complexity of the case lie in the association of multiple congenital anomalies, the unusual clinical presentation, and the coexistence of chromosome 9 polymorphism.

ACC and laryngomalacia were the cardinal congenital anomalies. Spina bifida and hydronephrosis, as well as trachea/bronchomalacia are considered associated anomalies of ACC and laryngomalacia, respectively[2,7,8].

Children with ACC can present feeding difficulties, including an inability to coordinate suck-swallow-breathing patterns in the newborn period and oral/pharyngeal sensory disorder or dysphagia afterward. Some cases are transiently dependent on tube feedings after birth, as in this case[9]. Associated respiratory system defects are extremely rare in infants with ACC, and only a few cases

have been reported[2,5,6]. In the Chandra et al series[5], three out of nine infants who underwent surgery for severe laryngomalacia had ACC. Moreover, some individual cases with the rare Toriello-Carey syndrome presented with ACC and laryngeal/tracheal anomalies[6]. Finally, in recently reviewed data from thirteen case series with ACC, respiratory system anomalies were reported in only one fetal autopsies series (80 % of these fetuses were syndromic)[3]. The above data indicate that respiratory system defects are rare, mainly diagnosed in syndromic conditions associated with ACC. In the current case, laryngomalacia was the most remarkable clinical finding. Although serious respiratory and feeding-swallowing difficulties are demonstrative of severe disease, which may require surgical intervention[8], in this case, significant improvement was observed with maturation and conservative treatment.

Over 200 different genetic syndromes are associated with ACC[3,4]. The reported case did not have "typical" features of a distinct syndrome. Further genetic investigation (WES) reveal no clinically significant variant relevant to the patient's phenotype. In a recent population-based study, only 40 % of the cases with ACC and associated anomalies could be classified into a recognizable malformation syndrome or pattern[2].

Chromosomal anomalies are detected in 16-18 % of the cases[1,2,4]. The pericentric inversion inv(9)(p23q22.3), detected prenatally in our patient, is a novel one found in individuals of Southeast European origin, mainly in the Greek population, that has been associated with miscarriages and fetal anomalies such as growth retardation, ventriculomegaly, and agenesis of the vermis[10]. Rearrangements of chromosome 9, particularly pericentric inversions, are not uncommon structural polymorphisms in the general population. The evidence for their pathogenicity is inconclusive[10,11].

The neurodevelopmental outcome of individuals with callosal agenesis is variable. According to the current literature, 73-85 % of individuals with isolated ACC have a normal outcome. Complex forms are usually associated with a significantly worse prognosis[3]. In our case of complex callosal agenesis, neurodevelopment up to 15 months of corrected age was within the normal range. Long-term neurodevelopmental surveillance is of great importance in these patients.

In conclusion, ACC is a rare clinically and genetically heterogeneous condition. The reported case presented with unusual clinical manifestations since laryngomalacia is an extremely rare coexisting anomaly reported in a few mainly syndromic cases in the literature. Furthermore, to our knowledge, this is the first description of ACC and laryngomalacia associated with the polymorphism inv(9)(p23q22.3).

Conflict of Interest

Authors declare no conflicts of interest.

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