CASE REPORT

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Prenatal diagnosis of omphalocele, cloacal exstrophy, imperforate anus and spinal anomalies complex (OEIS complex)

Diagnóstico prenatal del complejo onfalocele, extrofia cloacal, ano imperforado y defecto de la columna vertebral (complejo OEIS)

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ABSTRACT

Omphalocele, cloacal exstrophy, imperforate anus and spinal anomalies complex (OEIS complex) is a combination of severe and extremely rare congenital malformations. Its incidence is estimated at 1 per 200,000 - 400,000 live births. The occurrence of cases is sporadic and has no known etiology. Some have been associated with environmental exposures, genetic causes, and in vitro fertilization procedures. The mechanism of development appears to be associated with alterations in early blastogenesis or defect in mesodermal migration during the embryonic period. Prenatal diagnosis can be made at 16 weeks of gestation, although earlier diagnosis is sometimes possible. Definitive diagnosis is made necropsy findings. Most surviving newborns require multiple surgeries with potential complications and the desired results are not always achieved. A case of prenatal diagnosis of omphalocele, cloacal exstrophy, imperforate anus and spinal anomalies (OEIS complex) is presented.
Key words: Cloaca exstrophy, Anus imperforate, Spine, Prenatal diagnosis, OEIS complex.

RESUMEN

El complejo onfalocele, extrofia de la cloaca, ano imperforado y anomalías de la columna vertebral (Complejo OEIS) es una combinación de malformaciones congénitas severas y extremadamente raras. Su incidencia es estimada en 1 por cada 200.000 – 400.000 nacidos vivos. La aparición de los casos es esporádica y no tiene una etiología conocida. Algunos han sido asociados a exposiciones ambientales, causas genéticas y procedimientos de fertilización in vitro. El mecanismo de desarrollo parece asociado a alteraciones de la blastogénesis temprana o defecto de la migración mesodérmica durante el período embrionario. El diagnóstico prenatal puede realizarse a las 16 semanas de gestación, aunque en ocasiones es posible un diagnóstico más temprano. Su diagnóstico definitivo se realiza con los hallazgos de la necropsia. La mayoría de los recién nacidos supervivientes necesitan múltiples cirugías con complicaciones potenciales y no siempre se alcanza los resultados deseados. Se presenta un caso de diagnóstico prenatal de onfalocele, extrofia de la cloaca, ano imperforado y anomalías de la columna vertebral (complejo OEIS).
Palabras clave. Cloaca, extrofia, Ano imperforado, Columna vertebral, Diagnóstico prenatal, Complejo OEIS.

Introduction

Cloacal exstrophy was described by Litre in 1709 as a condition with poor prognosis associated with other malformations of skeletal, renal and gastrointestinal systems[1]. The OEIS complex (omphalocele, cloacal exstrophy, imperforate anus and spinal anomalies) is a rare congenital midline defect[2]. The acronym was initially used by Carey et al.[3], in a report of a case series with fetal body development anomaly. In addition to the findings of the acronym, there are descriptions of several associated anomalies, including genital defects (from complete absence of external genitalia to ambiguous genitalia) and limbs (arthrogryposis of knees, elbows and clubfoot or clubfoot secondary to neural tube defects)[2].

The estimated frequency of OEIS complex is 1: 200,000 to 400,000 live births with a female to male ratio of 2:1. Most cases are sporadic with no obvious etiology[5]. The diagnosis can be made during the prenatal period using conventional ultrasound, but the anatomical alterations can be confused with other conditions, such as limb-body wall complex, due to overlap of fetal anomalies found in the evaluation[6,7]. A case of prenatal diagnosis of omphalocele, cloacal exstrophy, imperforate anus and spinal anomalies is presented.

Case report

A 33-year-old primigravid pregnant women with a 22-week pregnancy who was referred to high-risk prenatal clinic for presenting multiple fetal malformations during routine ultrasound evaluation. Patient denied any significant personal and/or family history.

During fetal anatomical evaluation, a single fetus was found in breech presentation with an amniotic fluid index of 14, with evident hypoplasia of thoracic cage together with alterations of lumbosacral vertebrae with displacement of the conus medullaris and an echo-free zone of 9.3 × 5.0 millimeters with spinal cord in the region of distal spine (Figure 1A). Part of bowel and liver had a partially encapsulated lesion within an omphalocele measuring approximately 35 × 23 millimeters on the anterior abdominal wall toward amniotic cavity, immediately to the right of the insertion of the umbilical cord, extending to the lower edge and reaching the perineum (Figure 1B). Ultrasound assessment of the four cardiac chambers was normal, as were the outflow tracts.

During prenatal evaluation in the following week, absence of cardiac activity was verified, so the patientwas transferred to the emergency room for dilatation and uterine curettage. A stillborn female neonate with macroscopically normal placenta was obtained. Fetal necropsy showed a narrow thorax, thoracolumbar spine with signs of kyphoscoliosis and lumbosacral myelomeningocele of approximately 6 centimeters in diameter, which in section contained serous fluid with neural and medullary tissue. Abdominal wall showed a muscular defect, compatible with omphalocele and containing liver, spleen and intestinal loops, accompanied by anal agenesis (Figure 2A). Bladder exstrophy with common cloaca was also observed, with opening of the ileum and meconium outflow through vesico-colonic fistula. Genitalia were ambiguous with prominent folds and insertion of umbilical cord directly above these (Figure 2B). The right kidney showed a large hydroureter but no hydronephrosis. The left kidney and ureter were normal. Both the heart and the great vessels showed no alterations. There was no evidence of tracheoesophageal anomaly/duodenal atresia.

Radiographic evaluation showed anomaly in vertebral segmentation in the mid-thoracic, lumbar and sacral region, elements that supported the diagnosis of OEIS complex. The kariotype analysis was 46XX with no chromosomal or karyotypic abnormalities.

Figure 1. Fetal ultrasound images at 22 weeks. A) Alterations of the lumbosacral spine. B) Omphalocele with part of the fetal liver inside.

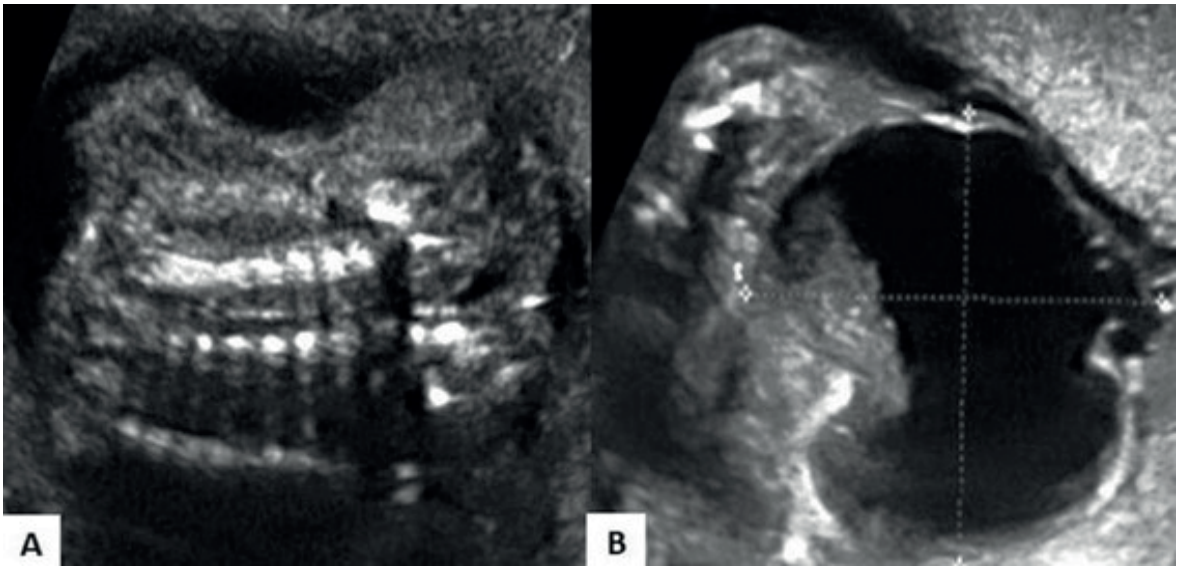
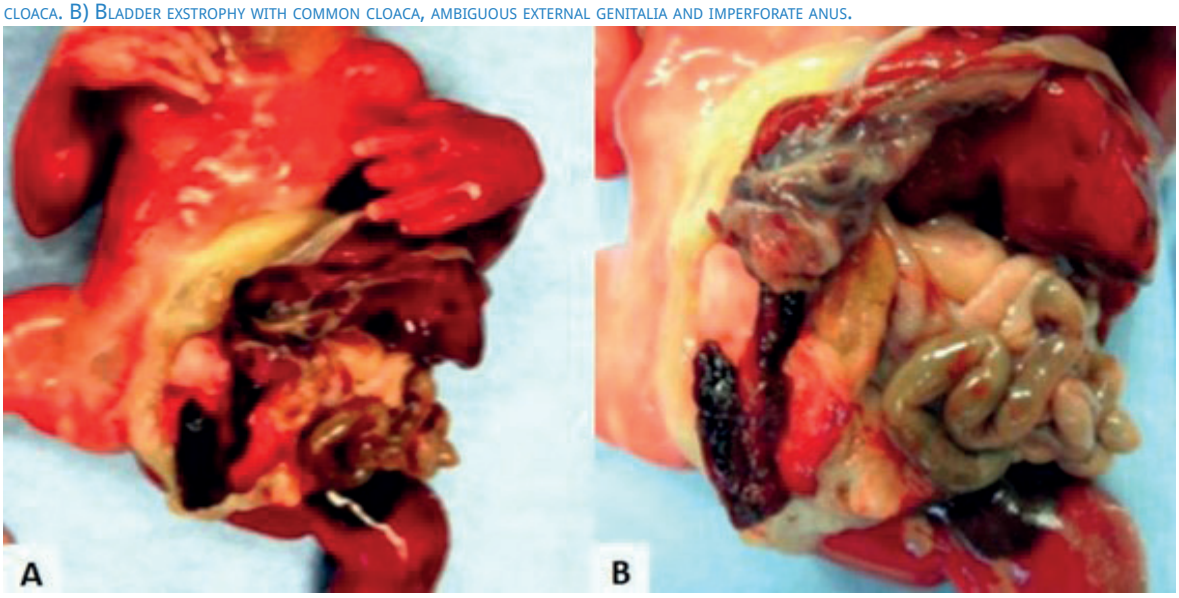


Figure 2. Findings of OEIS syndrome. A) Fetal omphalocele containing liver, spleen and small intestine, bladder exstrophy with common cloaca. B) Bladder exstrophy with common cloaca, ambiguous external genitalia and imperforate anus.



Discussion

The OEIS complex is a severe and rare type of malformation. In addition to the findings indicated in the acronym, there are descriptions of a variety of associated central nervous system anomalies and urinary, reproductive and skeletal malformations[2,5]. Some authors suggest that it may be part of a spectrum of alterations that includes bladder and cloacal exstrophy. However, the complex has a distinct pattern of fetal anomalies[6-9].

The cloaca is the primitive structure from which both the rectum and urogenital sinus appear. At the caudal end, ectoderm is directly overlying the endoderm, forming the cloacal membrane. By the fourth week it forms the ventral wall of the urogenital sinus and at the sixth week the mesoderm grows towards the midline, forming the infraumbilical abdominal wall. At the same time, the urorectal septum extends caudally towards the cloacal membrane, and the lateral folds are above midline. During the seventh week, the cloaca divides into an anterior chamber (primitive urogenital sinus) and a posterior chamber (rectum). The cloacal membrane ruptures at the end of eighth week of fetal development[9].

The OEIS complex occurs as a consequence of early mesenchymal abnormalities of the structures forming the infraumbilical mesoderm, urorectal septum and lumbosacral somites. The infraumbilical mesoderm gives rise to the infraumbilical abdominal wall, genital tubercle and pubic branches. Tissue alterations lead to premature rupture of the cloacal membrane, causing omphalocele, cloacal exstrophy and altered fusion of the genital tubercles. This leads to genital anomalies and separation of the pubic branches and distancing of the notochord from the neural tube, inhibiting differentiation and causing myelomeningocele. Abnormalities in the development of the urorectal septum produce alterations of the cloacal septum, resulting in persistent cloaca, rudimentary bowel and imperforate anus. In addition, alterations of the lumbosacral somites lead to incomplete development of the spine[9,10].

OEIS complex is a heterogeneous and generally sporadic condition. Most cases lack obvious etiology, although it may be associated with both genetic (1p361 deletion, 9q34.1-qter, 3q12.2-3q13.2 and trisomy 18) and environmental causes[11]. In addition, homeobox genes (especially HLXB9), retinoic acid or its receptor may play a role in its occurrence[12,13]. Similar fetal alterations are also associated with maternal exposure to diphenylhydantoin, diazepam, valproic acid, methamphetamine, smoking, maternal obesity, diabetes mellitus, in vitro fertilization procedures and multiple uterine fibroids[12].

Prenatal diagnosis of OEIS complex can be performed by conventional ultrasonography and allows it to be distinguished from other fetal syndromes and malformations. However, the

challenge of prenatal counseling is to identify all fetal ultrasound findings as accurately as possible[7]. The main findings include omphalocele with large midline infraumbilical anterior wall defect and lumbosacral myelomeningocele, usually covered by skin, low umbilical cord insertion, lack of visualization of the urinary bladder and external genitalia, along with limb defects, including alterations in the position or absence of limbs. In addition, urogenital anomalies are marked and have an impact on prognosis[6,7]. Maternal serum alpha-fetoprotein concentrations are variable and directly proportional to the extent of exposure of abdominal defects to amniotic fluid through defect, as omphalocele is usually covered by a thick membrane and myelomeningocele by skin[14].

There are reports of association between OEIS complex with increased nuchal translucency. The most likely cause of increased nuchal translucency is probably vascular or hemodynamic, although the exact mechanism remains unclear. Some authors have proposed that the changes in umbilical artery blood flow are a consequence of the alterations of an abnormally extended abdominal wall and increased intrathoracic compression due to severe anatomical alterations of the spine[12].

Differential diagnoses for the combination of abdominal wall and neural tube defects diagnosed prenatally, in addition to the OEIS complex, include cloacal exstrophy sequence, limb-body wall complex and schisis association[15]. Although there is significant clinical overlap between all of these conditions, they may belong to a spectrum of embryologic/fetal developmental field defects of unknown etiology[16,17].

Newborns diagnosed with complex OEIS should receive care by a multidisciplinary medical team. Most cases require multiple surgeries with potential complications, which may include renal failure, sexual dysfunction and infertility, gait disturbance secondary to spinal damage or bone malformations. In a large proportion of cases, this approach does not always achieve the desired results. In the absence of neural tube closure defects, cognitive development is normal[14].

In conclusion, OEIS complex is a rare condition of unknown cause, although it may be associated with environmental or genetic causes. The embryologic mechanism seems to be associated with a defect in early blastogenesis or mesodermal migration in the embryonic period. Ultrasonography allows the diagnosis to be made during the prenatal period, but these findings must be confirmed with necropsy evidence in order to identify them from other conditions with alterations of the abdominal wall and spine.

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