

Omphalocele, exstrophy of bladder, imperforate anus and spinal defect (OEIS complex) – autopsy and prenatal ultrasound findings

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SUMMARY

Omphalocele, exstrophy of bladder, imperforate anus and spinal defect (OEIS complex) is a rare congenital anomaly with varied clinical presentation. A case report in a spontaneously aborted fetus of 20 weeks gestation and diagnosed on autopsy is discussed. External omphalocele sac, imperforate anus, kyphoscoliosis, ambiguous genitalia and bilateral congenital talipes were present. Omphalocele sac contained liver, coils of small intestine, spleen and stomach. The sac also contained right testis and right kidney. The presence of kidney and testis in the omphalocele sac is a very rare finding in this complex. Antenatal ultrasound at 18 weeks of gestation had demonstrated omphalocele, deformed spine, club feet, non-visualization of bladder and polyhydramnios. Imperforate anus could not be detected prenatally. Occasionally, Two-Dimensional (2-D) ultrasound (US) may fail to detect the full spectrum of the complex. For definitive and differential diagnoses, Three-Dimensional (3-D) ultrasound, color Doppler and fetal Magnetic Resonance (MR) can be used.

Key words: OEIS complex – Omphalocele – Exstrophy of cloaca – Bladder exstrophy – Imperforate anus

List of abbreviations used: Ultrasound (US),

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Two-Dimensional (2-D), Three-Dimensional (3-D), Magnetic Resonance (MR), Cloacal exstrophy (CE).

INTRODUCTION

The complex occurrence of omphalocele, exstrophy of bladder, imperforate anus and spinal defect (OEIS complex) is very rare. Reported incidence is 1:200,000 to 1:400,000 (Smith et al., 1992; Lee et al., 1999). OEIS complex was first described by Carey et al. in 1978. OEIS complex describes a combination of birth defects involving most organ systems with case-to-case anatomical variability (Yang, 2007). Most of the cases are sporadic and their etiology is unclear (El-Hattab et al., 2010). OEIS complex arises from a localized defect in early development of mesoderm. Those defects later contribute to the formation of infra-umbilical mesenchyme, cloacal septum and caudal vertebrae (Chen et al., 1997). The complex may be associated with renal, genital and limb malformations (Kallen et al., 2000). Association is also reported with mutations (Keppler-Noreuil, 2001), chromosomal abnormalities, environmental exposures, twinning and in vitro fertilization (El-Hattab et al., 2010).

Though fetal Two-Dimensional (2-D) ultrasound (US) examination is the modality of choice to detect the condition prenatally (Ben-Neriah et al., 2007), differential diagnosis of OEIS complex may be difficult by US. Combination of Three-

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Dimensional (3-D) ultrasound and fetal Magnetic Resonance (MR) imaging is beneficial in diagnosing the condition antenatally (Tonni et al., 2011).

A case of OEIS complex diagnosed on autopsy in a spontaneously aborted fetus of 20 weeks gestation is discussed.

CASE REPORT

A fetus fixed in formalin was received by the Anatomy department for autopsy. The gestational age was around 20 weeks. The mother was 24 years old, and she was primigravida. Her body mass index (BMI) was 22.2. She did not have any history of infection, medication, recreational drug use or consanguineous marriage.

Parental consent for autopsy was taken. On external examination the ventral abdominal wall in the umbilical region had a defect and a large sac was projecting out through it. Externally, the sex of the abortus could not be determined, because the genital swellings were not able to be distinguished

with the presence of malformations at the present stage of development. Only a rudimentary genital tubercle was seen. Kyphoscoliosis of thoracolumbar spine and bilateral congenital talipes (Fig. 1A) was observed. Postnatal radiogram demonstrated kyphoscoliosis (Fig. 1B). Vertebrae were normal. Imperforate anus with a small dimple in perineum was noted (Fig. 1C).

On removing the membrane, liver, coils of small intestine, spleen, stomach, right kidney and right testis were seen within the sac (Fig. 2A, B). The infraumbilical part of the defect showed ureteric opening and bladder mucosa (Fig. 2A). Left kidney and suprarenal glands were at normal location. Each testis was situated lateral to the respective kidney along with vas deference. The colon was present in the form of a coiled blind tube. The terminal part of the small intestine was seen below the colon. No other associated anomalies were observed.

Antenatal ultrasound was done at 18 weeks of gestation. Ultrasound was performed using a

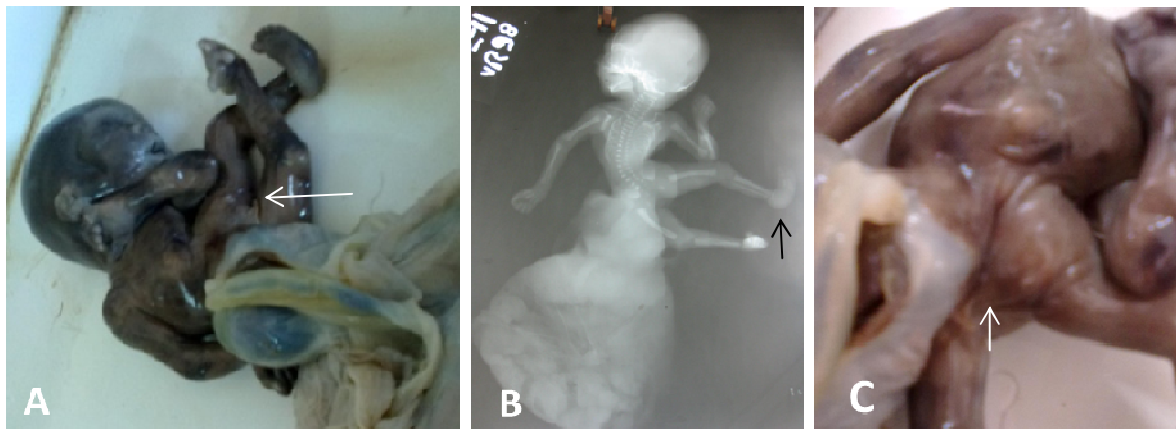


Fig. 1. (A) Abortus showing thick sac containing abdominal organs, bilateral congenital talipes and small phallus (arrow). (B) Radiogram showing kyphoscoliosis and bilateral congenital talipes (arrow). (C) Abortus showing imperforate anus (arrow).

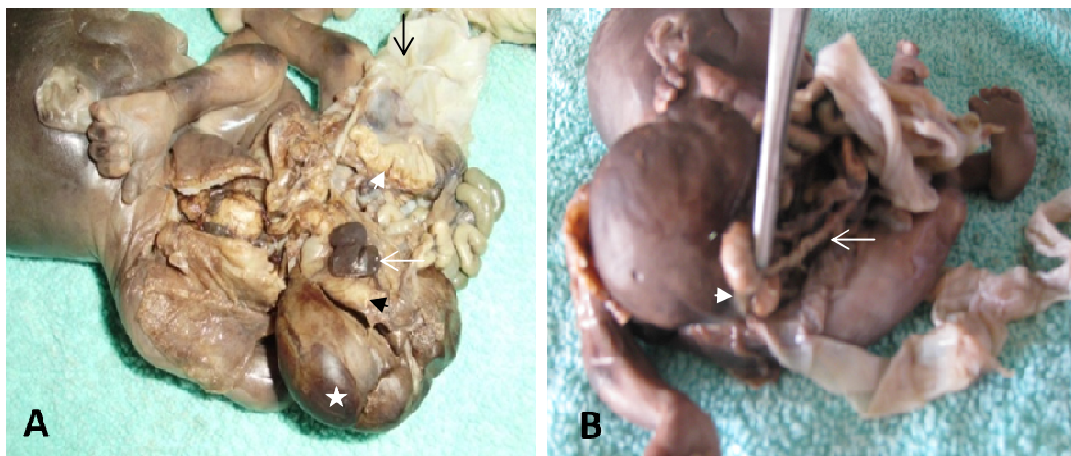


Fig. 2. (A) Autopsy showing omphalocele, bladder exstrophy (black arrow), colon (white arrowhead), spleen (white arrow), stomach (black arrowhead) and liver (star). (B) Right testis (arrowhead) and vas deference (arrow) lateral to right kidney.

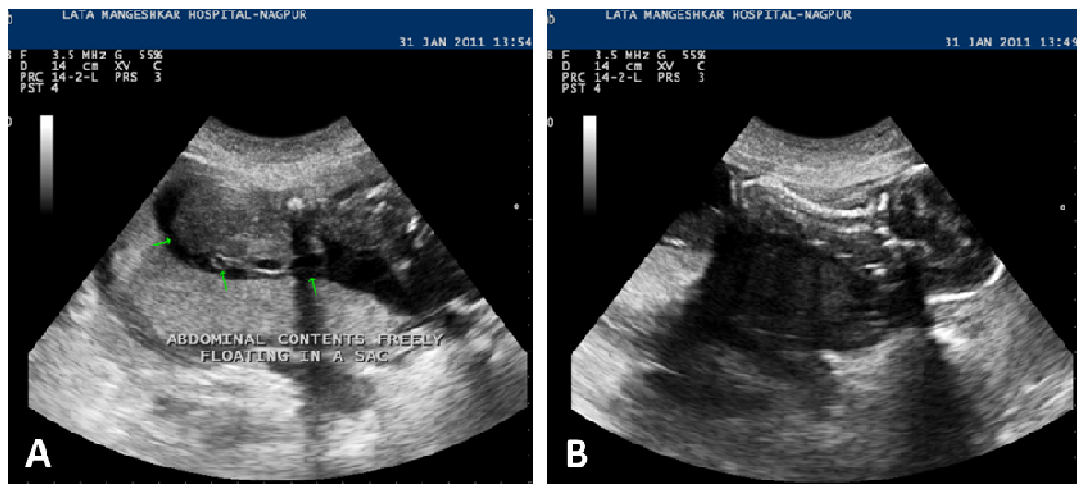


Fig. 3. Ultrasound images showing abdominal wall defect (A) and kyphoscoliosis (B).

MyLab 50 XVision Ultrasound System (M/S Esaote, Milano, Italy) with a 3.5-5 MHz broadband convex probe. It revealed a single fetus with polyhydramnios, omphalocele (Fig. 3A) spinal deformity (Fig. 3B), bilateral congenital talipes and non visualization of urinary bladder. All findings are summarized in Table 1. Parents were informed and counseled about the anomalies. The fetus aborted spontaneously after two weeks.

DISCUSSION

It is suggested that the terms exstrophy of cloaca and OEIS complex should be used as synonyms, since both are caused by the same insult in early blastogenesis (Bohring, 2002). Epidemiological analysis of characteristics in infants with cloacal exstrophy (CE) and infants with bladder exstrophy (BE) to determine if they constitute two different entities was done by Martinez-Frias et al. (2001). The study indicated that OEIS complex tend to occur together in the same child with a higher frequency if the child has the CE defect than in infants with multiple congenital anomalies patterns that did not include CE or BE. They concluded that CE and BE are two different expressions of a primary polytopic developmental field defect. The

primary polytopic developmental field defects are pathogenetically related and are of blastogenetic origin. Factors associated with CE included pre-term low birth weight, multiple birth and female sex. Infant mortality was found to be greater in the CE (Caton et al., 2007).

The exact etiology is unclear. OEIS complex has also been reported in siblings from separate pregnancies (Smith et al., 1992) and in patients with a family history of same malformations (Keppler-Noreuil, 2001). OEIS complex is also observed with maternal obesity, diabetes mellitus, and exposure to valproic acid (Keppler-Noreuil et al., 2007). In this case, maternal BMI was within normal limits. Usually, the karyotyping is normal. However, chromosomal anomalies like 1p36 deletion (El-Hattab et al., 2010), 22q11.1 deletion (Tonni et al., 2011) have been reported. A mutation in homeobox gene, retinoic acid or its receptor has been demonstrated in etiogenesis (Keppler-Noreuil, 2001). OEIS complex is also seen in monozygotic (Lee et al., 1999) and dizygotic twins (Noack et al., 2005), suggesting disturbances early in embryogenesis.

The basic defect arises in week three of development during gastrulation of the caudal part of the

Table 1. Summary of findings in this case

S no.	Examination	Finding
1	External	Ventral abdominal wall defect with large sac protruding out, rudimentary genital tubercle, kyphoscoliosis of thoraco-lumbar spine and bilateral congenital talipes, imperforate anus with small dimple in perineum.
2	Radiogram	kyphoscoliosis
3	Internal	Liver, coils of small intestine, spleen, stomach, right kidney and right testis in the sac, ureteric opening and bladder mucosa in infraumbilical part of defect, left kidney and suprarenal glands normal, testis lateral to the respective kidney along with vas deference, colon was present in the form of coiled blind tube.
4.	Antenatal ultrasound	Omphalocele, spinal deformity, bilateral congenital talipes, non visualization of urinary bladder, polyhydramnios.

embryo, which then affects tail folding of the gastrula leading to exstrophy of cloaca. Omphalocele results due to lack of mesoderm in the infraumbilical abdominal wall. CE precludes development of proctodeum and hence imperforate anus. Caudal dysgenesis affects somite formation in the embryo and results in vertebral defects, although these were not found in this case. The effects of teratogens during the late third and early fourth weeks of embryogenesis may cause these defects (Keppler-Noreuil, 2001).

Different authors have quoted the different incidence of OEIS complex. The estimated incidence is 1:200-400,000 live births (Smith et al., 1992; Lee et al., 1999) and 1:200-250,000 by Martinez-Frias et al. (2001).

US is the non-invasive modality used for prenatal diagnosis. In this case, the gestational age at the time of antenatal 2-D Ultrasound was around 18 weeks (second trimester) when the possibility of OEIS complex was indicated. Ultrasound diagnosis of the complex can be made as early as 16 weeks of gestation (Ben-Neriah et al., 2007). Ultrasound did not detect abnormal external genitalia, bladder exstrophy and imperforate anus. None of the 15 cases studied by Keppler-Noreuil et al. (2007) had prenatal detection of the all four key features of this complex. Similar observations were made by Ben-Neriah et al. (2007) while studying nine cases. On ultrasound OEIS complex should be differentiated from other midline anterior abdominal wall defects like Limb body wall complex and Pentalogy of Cantrell (Tonni et al., 2011).

Oligohydramnios is usually found with OEIS complex (Tonni et al., 2011). Oligohydramnios is also reported in cloacal anomalies in female fetuses (Patrikovosky et al., 1988). Polyhydramnios was noted on US in this case. The cause could not be found.

Additional findings like depiction of urine flow in direct communication with the abdominal cavity by Color Doppler has been proved to be helpful in diagnosis of BE (Noack et al., 2005). Pre natal 3-D ultrasound has also been used as useful adjunct to 2-D ultrasound (Chen et al., 2008).

When conventional ultrasound findings are inconclusive, fetal MR can detect omphalocele, absent bladder, ambiguous external genitalia and spinal defect, and is a useful tool for prenatal diagnosis of OEIS complex. MR helps in prenatal counseling and planning of postnatal early treatment strategy (Goto et al., 2012). Fetal MR should be advised if the bladder exstrophy is observed on US prenatally (Goldman et al., 2013).

On autopsy omphalocele was the most con-

spicuous feature in this case. It contained liver, coils of small intestine, spleen, stomach, right kidney and right testis. Omphalocele was found in all the 15 cases reported by Keppler-Noreuil et al. (2007) on autopsy.

Right kidney and right testis were seen outside the abdominal cavity within omphalocele sac in this case. This is a very rare finding in this complex and has been reported by Ben-Neriah et al. (2007). They observed similar findings in one of the nine cases studied on autopsy. Ureteric opening and bladder mucosa were seen in the infraumbilical part of the defect. There was a small dimple in the perineum along with an imperforate anus. This is commonly found in the complex. Keppler-Noreuil et al. (2007) studied 15 cases and found bladder exstrophy in 13 cases and imperforate anus in all cases on autopsy/postnatally.

The colon was present in the form of a coiled blind tube in this case. It may be a closed tube or is missing in most of the cases (Ben-Neriah et al., 2007).

There was kyphoscoliosis of the thoracolumbar spine in this case. Spinal abnormalities range from open neural tube defects to angulations (Keppler-Noreuil et al., 2007). Additionally, there was bilateral congenital talipes. This is the most common limb abnormality found with this complex (Ben-Neriah et al., 2007). The lower limb anomalies range from talipes equino varus (club feet), calcano valgus deformity (rocker bottom foot) to congenital dislocation of the hip (Schober et al., 2002).

OEIS complex has been reported to occur with glomerulocystic kidney disease, supernumerary kidney, major cardiac defect, open neural tube defect and craniofacial anomalies (Tonni et al., 2011). No any other anomaly was found in this case.

Prognosis of OEIS complex is variable. It depends upon the severity of the defect and associated other structural malformations (Tonni et al., 2011). Very few postnatal live cases are known. The postnatal management aims at multiple deformity correction which includes multiple surgeries. The complications include recurrent urinary tract infections, failure to thrive and the individual suffers from psychosocial problems (Tiblad et al., 2008).

OEIS complex is a rare congenital anomaly with unknown etiology and varied presentation. Most cases are diagnosed on autopsy. Chromosomal abnormality, though rare, should be sought for whenever possible. OEIS complex must be ruled out in case of omphalocele and non-visualization of bladder on antenatal US. 3-D ultrasound, Doppler and fetal MR are comple-

mentary techniques that may aid the prenatal diagnosis or detection of the congenital disease.

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