The OEIS complex (omphalocele-exstrophy-imperforate anus-spinal defects): recurrence in sibs

N M Smith, H M Chambers, M E Furness, E A Haan

Abstract

The OEIS complex comprises a combination of defects including omphalocele, exstrophy of the cloaca, imperforate anus, and spinal defects. It may represent the most severe manifestation of a spectrum of birth defects, the exstrophy-epispadias sequence. The OEIS complex affects 1 in 200 000 to 400 000 pregnancies and is of unknown cause. The purpose of the current report is to document the occurrence of OEIS in sibs from separate pregnancies and suggest that some cases may have a genetic basis.

(J Med Genet 1992;29:730-2)

In 1978 Carey et al gave the name OEIS complex to a combination of defects comprising omphalocele, exstrophy of the cloaca, imperforate anus, and spinal defects. This combination had been reported previously by authors using a variety of terminologies such as ectopia cloacae, vesico-intestinal fissure, exstrophia splanchnica, and cloacal exstrophy, though the first report was that of Littré in 1709 (quoted by Spencer). The OEIS complex is rare, affecting 1 in 200 000 to 400 000 pregnancies. It may represent the most severe end of a spectrum of birth defects, the exstrophy-epispadias sequence, which, in order of increasing severity, includes phallic separation with epispadias, pubic diastasis, exstrophy of the bladder, cloacal exstrophy, and OEIS complex.

Very few reports have documented recurrence in sibs or offspring, of defects within the exstrophy-epispadias sequence. This argues against monogenic causation in most cases but does not exclude a monogenic, multifactorial, or environmental basis for some. In this report we document the features of two sibs born with the features of OEIS and briefly discuss the possibility that some cases of this association of malformations may have a genetic basis.

Case reports

The first child of a non-consanguineous couple, the mother aged 21 and not diabetic, and the father aged 38, was noted at routine ultrasound scan at 18 weeks' gestation to have several abnormalities. There was a raised maternal serum α-fetoprotein level. Detailed ultrasound scan at 22 weeks' gestation showed a single fetus with severe kyphoscoliosis, poorly defined lumbar spine, small thorax, deficient anterior abdominal wall, and fluid filled spaces at the back of the neck, extending inferiorly on to the back. The amniotic fluid volume was normal. The parents elected to continue the pregnancy. A glucose tolerance test was normal. A stillborn infant was delivered at 30 weeks' gestation after spontaneous membrane rupture.

At necropsy the fetus weighed 1110 g and was of indeterminate sex. The anterior abdominal wall was absent, the viscera being partly covered by a thin walled omphalocele sac. The bladder was exstrophied and connected to normal kidneys via narrow and ill-defined ureters and the external genitalia were absent. The anus was imperforate and a spinal defect comprising a meningocele from mid-thorax to perineum was present. Other abnormalities included small thoracic cavities, particularly on the right, associated with lung immaturity and hypoplasia, fluctuant oedema in the soft tissue of the posterior neck, severe distortion of the lower limbs with partial syndactyly of the second and third toes, and a single umbilical artery. The face and head were normal. The diaphragms were intact and the heart was caudally positioned but normally formed with normal arterial and venous connections. Histologically normal testes were present. There were no amniotic bands. The karyotype was 46,XY.

Postmortem radiological examination showed, in addition, fusion of the right 11th and 12th ribs, of the right T12 and L1 neural arches, and of the right L2 to 5 neural arches. There were two sacral vertebral bodies. The pelvis was distorted and the femora were dislocated posteriorly, and were below the 5th centile in length for age (fig 1).

Fifteen months after the death of this fetus, the mother gave birth to a normal female.

The mother became pregnant for the third time four months later. Ultrasound scan at 13 weeks' gestation showed a major anterior abdominal wall defect, causal displacement of the heart, and fluid filled spaces at the back of the head, neck, and thorax. Normal ossification centres at the distal spine could not be identified, and there was a sac lying posterior to this area. The amniotic fluid volume was normal. Pregnancy continued until 24 weeks' gestation when spontaneous membrane rupture occurred. A stillborn fetus weighing 329 g was delivered.

At necropsy (fig 2) a large omphalocele was noted, there were no demonstrable internal or external genitalia, and the urinary bladder was exstrophied and connected via narrow ureters
The OEIS complex (omphalocele-extrophy-imperforate anus-spinal defects): recurrence in sibs

Figure 1 AP x ray of case 1. Arrow on right, meningocele. Arrow on left, extruded abdominal viscera.

Figure 2 Lateral view of external appearance of case 2.

rotation and distortion of the lower spine and pelvis, with the femora lying posterior to the trunk. They were at the 5th centile in length for age.

Discussion
Carey et al in 1978 reported 10 patients with OEIS and stated that "no familial cases have been described" and that "since there have not been any families who had had more than one affected child in the literature or in our series, there is no evidence that the OEIS complex is an inherited entity". The purpose of this report is to document the occurrence of OEIS in sibs from separate pregnancies and thereby to suggest that some cases of this association of malformations may have a genetic basis.

Both of the cases described above showed omphalocele, exstrophy of the cloaca, imperforate anus, and spinal defects (severe kyphoscoliosis and meningocele). The presence of large postnuchal fluid collections in both cases is of interest and is considered to represent jugular lymphatic obstruction sequence. There were no amniotic bands on the placental surface and none of the craniofacial defects typically found in early amnion rupture sequence. No history of maternal diabetes mellitus, or of hydantoin administration, both of which have been associated with OEIS, was obtained in our cases. An OEIS-like complex can occur in trisomy 18, but the karyotypes in the current cases were normal male 46,XY and normal female 46,XX. Recurrence of omphalocele or bladder exstrophy in sibs has been documented, with a risk of less than 1%. OEIS (referred to as cloacal exstrophy) has been reported in both of a pair of monozygotic twins on two occasions, but recurrence in sibs born in separate pregnancies has not been previously reported.

Defects within the epispadias-extrophy sequence (extrophy of the bladder, cloacal exstrophy, OEIS complex) do recur but this is clearly uncommon. The point has been made, however, that the published rates of occurrence and recurrence of conditions within this spectrum, some based on surgical data, are likely to be spuriously low, as some of the patients may die without treatment shortly after birth or be stillborn or be classified as omphalocele only, where this is the most prominent abnormality.

Part of the definition of OEIS is exstrophy of the cloaca. Opinions differ about the possible existence of a continuum of abnormalities ranging from epispadias to bladder exstrophy to cloacal exstrophy. Carey et al, in their original article, clearly separated OEIS from exstrophy of the bladder. Some writers suggest that there may be a spectrum of defects ranging from penile epispadias, through bladder exstrophy, and cloacal exstrophy, to OEIS. Kutner et al are clearly of the latter view when saying that the definition of OEIS includes exstrophy of the bladder.

The occurrence of exstrophy of the bladder appears to be more frequent at 1:30,000 to 40,000 births than exstrophy of the cloaca at
1:200 000 to 250 000,4,5 or OEIS at 1:200 000 to 400 000.6 Markedly different rates of occurrence are suggested for cloacal extrophy by Gosden and Brock7 at 1:10 000 to 15 000. Clearly, precise definition of terms remains a problem.

Given the lack of certain knowledge regarding the aetiology of either bladder extrophy or cloacal extrophy, it seems reasonable to accept that an event such as failure of cloacal septation or cloacal membrane breakdown during the fourth to sixth week of intrauterine life may have the potential to cause abnormalities in the adjacent lumbarosacral somites, depending upon the severity of the original abnormality.8,9 Notwithstanding the differing views on the presence or absence of an epispadias-OEIS spectrum, the appearances in the two cases we describe are in accord with the original description of Carey et al.1

Possible explanations for the recurrence include autosomal recessive inheritance, multifactorial inheritance, gonadal mosaicism for a dominant mutation, an environmental factor, or subclinical maternal disorder. The latter possibility, while speculative, has a parallel in recent evidence that periconceptional folic acid supplementation can reduce the risk of recurrence of neural tube defects for couples who have had an affected child.10 The mother of the sibs described is not known to have been exposed to a potential teratogen and the sibs were conceived two years apart, making an environmental cause unlikely. There is no compelling evidence that genetic factors have a role in the causation of OEIS complex and related birth defects, but our cases indicate that they may do so in some instances.

The OEIS complex (omphalocele-exstrophy-imperforate anus-spinal defects): recurrence in sibs.
N M Smith, H M Chambers, M E Furness and E A Haan

doi: 10.1136/jmg.29.10.730

Updated information and services can be found at:
[http://jmg.bmj.com/content/29/10/730](http://jmg.bmj.com/content/29/10/730)

**Email alerting service**

Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

**Notes**

To request permissions go to:
[http://group.bmj.com/group/rights-licensing/permissions](http://group.bmj.com/group/rights-licensing/permissions)

To order reprints go to:
[http://journals.bmj.com/cgi/reprintform](http://journals.bmj.com/cgi/reprintform)

To subscribe to BMJ go to:
[http://group.bmj.com/subscribe/](http://group.bmj.com/subscribe/)