SHORT REPORT

Omphalocele in three generations with autosomal dominant transmission

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J Med Genet 2002;**39**:184–185

We report a family with nine subjects over three generations affected with an omphalocele requiring surgical intervention within the first few days of life. Because of the vertical transmission and male to male inheritance in our family, we conclude that an autosomal dominant gene caused the omphalocele in the affected family members. The paternal great grandfather of the proband was not clinically affected but produced two children with omphaloceles with different spouses.

An omphalocele is a herniation of abdominal contents through a defect in the anterior abdominal wall.¹ The incidence has been reported to be as low as 1 in 3800² and as high as 1 in 2000.¹ Isolated omphalocele is generally regarded as a sporadic malformation with a negligible recurrence risk.³ However, an omphalocele can present as either an isolated anomaly or as a feature of a syndrome. As many as 50% of patients with omphalocele have other associated abnormalities.¹ Numerous chromosomal abnormalities and other genetic syndromes may be associated with omphalocele including Beckwith-Wiedemann syndrome⁴ and trisomy 13, 18, or 21.⁵ Various modes of genetic transmission have been suggested from pedigree analysis of families with isolated omphalocele, including autosomal dominant, autosomal recessive, and X linked recessive.⁶

Here, we report a large family with nine subjects affected over three generations with isolated omphalocele requiring surgical intervention during the first few days of life.

CASE REPORTS

The proband was a 37 week gestation white male infant born to a G4 P3, 31 year old female, with a birth weight of 2600 g (25th centile), head circumference 33 cm (50th centile), and length of 46.25 cm (50th centile). He was born by caesarean section because of the omphalocele identified by prenatal ultrasound. Apgar scores were 7 at one minute and 9 at five minutes. The child was transferred to the neonatal intensive care unit. There were no other obvious anomalies noted. Because of her previously affected child, a maternal serum alpha fetoprotein measurement was offered but declined by the subject's mother. During his stay in the neonatal intensive care unit, an echocardiogram was preformed. Two myocardial echobright densities were noted. One was near the tricuspid leaflet and was 8 mm × 5 mm. The second density was in a tricuspid valve papillary muscle and noted to be 3 mm × 2 mm. These areas were thought to represent rhabdomyomas. He had surgery to repair his omphalocele on day 2 of life. He is the ninth member of the family to have this condition. All members of the family have had surgery to correct the omphalocele within the first few days of life. Neither the proband nor any other affected family members had evidence of hypoglycaemia, macroglossia, seizure disorder, or birth defects. As can be seen in the pedigree (fig 1), he was born to an unaffected mother (III.8) and an affected father (III.7). The proband also has a sister (IV.4) who was affected. She had a normal female karyotype (46,XX). There are two other sibs, one full (IV.3) and one half (IV.6), who were unaffected. The paternal grandfather (II.4) was also affected. Surprisingly, the paternal great grandfather (I.2) was not affected yet had two affected children (II.2 and II.4) with different spouses (I.1 and I.3). The paternal great half uncle (II.2) had three affected

Figure 1 Pedigree showing nine affected subjects with omphalocele over three generations. The paternal great grandfather (I.2) was unaffected but had two affected children (II.2 and II.4) from two different spouses (I.1 and I.3).

children (III.1, III.2, and III.4) and two unaffected children. One of the affected offspring (III.4) died at birth from complications of the omphalocele. The proband's paternal half first cousin (IV.1) was also affected.

DISCUSSION

Our family with nine affected subjects in three generations represents the most extensive family published to date with vertical transmission of an omphalocele. The largest kindred previously reported involved seven affected subjects.⁷ The paternal great grandfather in our report was unaffected but produced two affected children with different spouses, indicating possible non-penetrance of the gene. We propose a 50% recurrence risk for other affected members in our family. As can be seen from our pedigree, both males and females are affected and there were at least three occurrences of male to male transmission, which rules out X linked recessive inheritance. To date, there are five previous reports of pedigrees with vertical transmission of isolated omphalocele consistent with autosomal dominant inheritance.³ Five families were reported with horizontal transmission consistent with autosomal recessive inheritance.³

An additional observation seen in our proband included echobright densities which may represent rhabdomyomas. These could be explained by the inheritance of a second autosomal dominant gene (for example, tuberous sclerosis). However, no other family members were reported with cardiac tumours, seizures, or mental retardation, which may be present in patients with tuberous sclerosis. In particular, an echocardiogram was performed on the affected sister (IV.4) and no cardiac lesions were seen. There were also no skin

findings identified upon examination with a short wave spectrum light (Wood's lamp). Therefore, the cause of the echobright densities are unexplained.

We would be interested in receiving information about other families with several affected subjects with omphalocele to pursue further genetic testing and to search for an autosomal dominant gene for this congenital malformation.

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REFERENCES

- 1 **Seashore MR**, Wappner RS. *Genetics in primary care and clinical medicine*. Stamford, CT: Appleton & Lange, 1996:123-4.
- 2 **Havalad S**, Noblett H, Speidel BD. Familial occurrence of omphalocele suggesting sex-linked inheritance. *Arch Dis Child* 1979;**54**:142-51.
- 3 **Pryde PG**, Greb A, Isada NB, Johnson MB, Klein M, Evans MI. Familial omphalocele: considerations in genetic counseling. *Am J Med Genet* 1992;**44**:624-7.
- 4 **Osuna A**, Lindham S. Four cases of omphalocele in two generations of the same family. *Clin Genet* 1976;**9**:354-6.
- 5 **Rott HD**, Truckenbrodt H. Familial occurrence of omphalocele. *Humangenetik* 1974;**24**:259-60.
- 6 **Kapur S**, Higgins JV, Scott-Emuakpor AB, Dolanski EA. Omphalocele in half siblings. *Clin Genet* 1980;**18**:88-90.
- 7 **Steele K**, Nevin MC. Familial omphalocele. *Ulster Med J* 1968;**54**:214-15.