Trisomy E and T-E Fistula*

ANNEMARIE SOMMER and JAY L. GROSFELD

From the Department of Pediatric Medicine and the Division of Pediatric Surgery, Ohio State University, College of Medicine, and Children's Hospital, Columbus, Ohio, U.S.A.

One of the more common chromosomal abnormalities which has been well delineated and documented is trisomy of an E group chromosome. Since the first report of this syndrome by Edwards et al. (1960) and also by Patau et al. (1960), data on this anomaly have accumulated rapidly, and most cases are diagnosed on clinical features—only to be confirmed by chromosome analysis. The pitfalls in diagnosis have been recently described by Taylor (1968) who analysed 27 cases of E and 27 of D trisomy in detail. A high degree of overlap between the two conditions is evident, and in this report only one feature (webbed neck) finally emerged as one stigmata not found in D trisomy as well. One of the anomalies that has only rarely been reported in the E trisomy is tracheo-oesophageal (T-E) fistula.

We wish to report two cases of Edwards syndrome that were seen at Columbus Children’s Hospital in March 1969. These infants were referred to our surgical service because of multiple congenital anomalies, including oesophageal atresia and T-E fistulas. In both cases, the diagnosis of trisomy 18 was confirmed by chromosome analysis.

Case Reports

Case 1. This female child was born to a 33-year-old gravida 5 para 5 mother at 37 weeks’ gestation, at which time the infant was delivered by caesarian section because of placenta praevia. The pregnancy was complicated by polyhydramnios. The infant was given a one-minute Apgar score of 4 and needed respiratory assistance. The birthweight was 1474 g. At less than 24 hours of age, the infant was transferred to Columbus Children’s Hospital because of multiple congenital anomalies, respiratory distress, and suspected oesophageal atresia and T-E fistula. On physical examination she was found to be in moderate distress, with a pulse rate of 180/min. and respiration of 60/min. Crown-heel length was 46 cm. and head circumference 31 cm. The baby had ‘peculiar’ facies and a head which appeared round, with slightly prominent occiput. The palpebral fissures were small, and an epicanthal fold was present on the right medial canthus. The ears were small, poorly developed, and low set. The nose was beaked and a high-arched palate was observed. A thrill and very prominent systolic heart murmur were present. There was only a single umbilical artery. The baby had bilateral simian creases and flexed and overriding fingers. Oesophageal atresia was shown by inability to pass a nasogastric tube, and x-ray examinations revealed a blind upper pouch and air in the gastro-intestinal tract signifying an associated tracheo-oesophageal fistula (Fig. 1). In the operating room, oesophageal atresia and T-E fistulas were noted. Under local anaesthesia a Stamm gastrostomy was performed as the only initial procedure in a staged programme of management because of prematurity plus multiple anomalies. Post-operatively the infant did poorly and died 20 hours after operation. At necropsy, oesophageal atresia and T-E fistula were anatomically documented and the following additional anomalies were shown: a large persistent ductus arteriosus, incomplete fixation of the dorsal mesentery, and horseshoe kidney.

Case 2. This female child was born after an uncomplicated pregnancy to a 33-year-old gravida 5 para 5 mother after 36 weeks’ gestation. Labour was extremely rapid, and at delivery polyhydramnios was noted. The infant needed resuscitation. The birthweight was 1842 g. Because of multiple congenital anomalies, respiratory distress, and suspected oesophageal atresia and T-E fistula, the baby was transferred to Columbus Children’s Hospital. On physical examination the following anomalies were noted: the head shape was slightly elongated and the palpebral fissures were small, with apparent proptosis of the right eye. The ears were very small and low set—the helices being fused to the scalp; a pre-auricular tag was present just anterior to the atretic right external auditory canal. The infant had bilateral cleft lip with the left cleft extending into the alveolar ridge. The palate was intact. The heart was thought to be large, but no murmur was heard. The sternum was short and hip abduction was limited. Both hands exhibited camptodactyly and simian creases. Oesophageal atresia and T-E fistula were diagnosed by x-ray (Fig. 2) and documented at operation, where a Stamm gastrostomy was performed under local anaesthesia. This infant expired several hours after operation.

Received 22 September 1969.
* Supported in part by NIH Grant No. 1 F03 GM 39046-01A1.
due to cardiorespiratory complications. Necropsy showed the following additional malformations: the heart had a ventricular septal defect, an obturator band at the right ventricle, fenestration of the pulmonary valve leaflet, preductal coarctation of the aorta, and a large persistent ductus arteriosus. There was a small diaphragmatic hernia and uric acid deposits were noted in the kidneys. Incomplete fixation of the dorsal mesentery as well as a large Meckel's diverticulum were also present.

**Chromosome Analysis.** Peripheral blood specimens were taken from both infants and cultured by a modification of the method of Hirschhorn (1968, personal communication to Grand Island Biological Co., Grand Island, New York). Well-spread metaphases were photographed for chromosome analysis.

In both cases, most of the cells examined showed a chromosome count of 47 (Fig. 3), and the karyotype was that of females with, in addition, an extra submetacentric small chromosome of the size and configuration of the E
FIG. 3. Karyotype of patients (Case 1 (lower) and Case 2 (upper)) both showing trisomy E.
group chromosomes. A few cells with a chromosome component of less than 47 were found. Analysis of these losses showed them to be completely random.

A distribution of the chromosome count is presented in the Table.

<table>
<thead>
<tr>
<th>CHROMOSOME COUNT DISTRIBUTION</th>
</tr>
</thead>
<tbody>
<tr>
<td>43</td>
</tr>
<tr>
<td>-----</td>
</tr>
<tr>
<td>Case 1</td>
</tr>
<tr>
<td>Case 2</td>
</tr>
</tbody>
</table>

Discussion

The incidence of trisomy E has variously been estimated as 1 in 4000 (Lubs and Ruddle, 1969) live births to 1 in 6766 (Taylor, 1968). The postulated mechanism responsible for the occurrence of trisomy is meiotic non-disjunction.

The most frequent features (Butler et al., 1965) of this syndrome are hypertonia, antero-posterior elongation of the skull, webbed neck, a high-pitched cry (probably due to an abnormally shaped palate), and micrognathia. The ears are low set, malformed, and rotated, and the palpebral fissures are usually small. Camptodactyly of the fingers is seen and the thumbs are often distally implanted or rudimentary and retroflexible. The feet have a calcaneovalgus deformity or a prominent calcaneus (‘rockerbottom feet’), the halluces are often short, broad, and dorsi-flexed, and partial syndactyly of the toes is common. The toe-nails are often hypoplastic. The sternum is short and the chest may be narrow or shield-shaped. Abnormal hip and shoulder abduction is common. Other frequent findings include single umbilical artery, redundant downy hirsutism of the forehead and back, congenital heart disease, renal anomalies, inguinal hernias, and general mental and motor retardation with failure to thrive.

Necropsy findings show an even greater degree of overlap of the D and E trisomies (Taylor, 1968), but Meckel’s diverticulum, pyloric stenosis, and evagination of the diaphragm are more frequent in Edwards’ syndrome. The brain in trisomy E may be superficially normal or it may have abnormally few convolutions or dilated cerebral ventricles. In Patau’s syndrome, the olfactory nerves are usually missing and the optic nerves may be absent.

Our patients presented with several of the features mentioned for trisomy E, i.e. slightly elongated skull, small palpebral fissures, low-set malformed ears, congenital heart disease, camptodactyly, and single umbilical artery. Necropsy also did not reveal any features not previously reported in Edwards’ syndrome.

However, in addition, both infants had documented tracheo-oesophageal fistulas. These findings are not commonly included in the manifestation of trisomy 18.

This syndrome, though not compatible with long-term survival, as a rule is thought to be somewhat less severe in its manifestations as compared to trisomies of even larger autosomes, such as a D group chromosome. Most of the attention has been focused on the cranio-facial and limb anomalies in Edwards’ syndrome (Butler et al., 1965), but the clinical spectrum is growing rapidly. The amount of genetic information carried on the extra number 18 autosome, while presumably having specific effect, has not been fully defined. The autosomal trisomies known to date have some stigmata in common, leaving only a narrow range of clinically distinguishing features. All defects seen do essentially correspond to disturbance occurring at the embryological anlage during the fourth through to the seventh weeks of gestation in man (Rhode, Hodgman, and Cleland, 1964). The action of environment on the genetic material has not been established for the trisomies of the larger autosomes, though some causal relation between the occurrence of hepatitis and Down’s syndrome has been suggested (Stoller and Collmann, 1965).

A review of all cases of trisomy E seen in our hospital, including the present two cases, did not uncover any unusual disturbances during pregnancy.

Summary

Two infants with trisomy E, oesophageal atresia, and T-E fistulae are reported. T-E fistula has only rarely been reported in this syndrome, but these cases might warrant inclusion of this malformation in the clinical spectrum for suspecting this chromosomal disorder.

We are grateful to Dr. H. William Clatworthy, Jr. for allowing us to study his patients and for his advice in the preparation of this report.

References


Trisomy E and T-E fistula.

A Sommer and J L Grosfeld

*J Med Genet* 1970 7: 70-74
doi: 10.1136/jmg.7.1.70

Updated information and services can be found at:
http://jmg.bmj.com/content/7/1/70.citation

**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

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/