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Human Genetics

Trisomy 16q21→qter

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Summary. A case of trisomy 16q secondary to a paternal 16/18 translocation is described. A comparison of this case with the few other cases of trisomy 16q described in the literature indicates that trisomy for the long arm of chromosome 16 results in a severely affected phenotype and early death. Conversely, patient with trisomy 16p do not have gross abnormalities. We postulate that the prenatal lethality of full trisomy 16 is mainly due to the trisomy for the long arm.

Introduction

Partial trisomy 16 is rare and the phenotypic effects are difficult to study because most of them are secondary to chromosome rearrangements resulting concurrently in monosomies or trisomies for a second chromosome (reviewed by Roberts and Duckett, 1978).

We report on a partial trisomy 16q secondary to a 16/18 translocation, found in a child who died at 20 days of age, and we compare his phenotype with those of the other seven cases of partial trisomy 16q reported in the literature.

Case Report

MS was born on 16. 12. 1977 to a 27-year-old mother and a 30-year-old father, who already had a normal female child. The pregnancy, with threatened abortion at the second month, ended at term with a normal delivery. The child was registered as a female. The birth weight was 2470 g, length 40 cm, thoracic circumference 30.5 cm, and abdominal circumference 30 cm. After 7 days, when she was admitted to hospital because of ambiguous external genitalia, her weight was 2270 g. The child had a dysmorphic, flat facies with a high forehead, hypertelorism without epicanthus, small horizontal palpebral fissures, a broad flat nasal bridge and large nostrils, low-set, malformed ears, and a short neck. The thoracic cage appeared small and its motility seemed to be impaired. The scrotum bifidum was empty on the right, while the left side contained a pea-sized body with a consistency similar to that of testicular tissue. The penis was small. There was a single, apparently cloacal cavity at the opening to the urethra. There was flexion contracture of the elbows, valgus of both hands, and talus valgus of the left foot. A slight systolic murmur, with maximal intensity in the centrum cordis, was heard in all areas of auscultation. Hearts sounds were normal. Chest auscultation revealed coarse breath sounds. Chest X-rays gave normal findings. The abdominal organs were within normal limits. There was a diffuse muscular hypotonia and the infant was torpid with a poor sucking reflex; feeding was accomplished by means of nasogastric tube.

At the first examination all routine blood values were within normal limits except bilirubinemia (mg 15%) and BUN (mg 49%). Urobilinogen was present in the urine. After some days the patient developed edema. Diuresis decreased and BUN increased up to 71 mg%, while bilirubinemia and acidosis fell to within the normal limits.

Two days before death the infant began to vomit frequently and later the vomit became brown and fecal. Abdominal distension was observed, with bluish cutis around the umbilical and obvious pain on palpation. A right inguinal hernia that could not be reduced manually was noted. The patient was moved to a surgical department, dying when 22 days old of progressive respiratory distress, after manual reduction of the hernial boss. Permission for autopsy and photographs was refused.

Cytogenetic Findings

Chromosomes were investigated in cultured lymphocytes by means of G-R, Q-R and C banding. The patient had a 46,XY,−18,+der(18) karyotype. Unidentified extra material on the short arm of the abnormal chromosome 18 gave it a metacentric appearance. Chromosome examination of the parents revealed that the father carried a balanced translocation involving chromosome 16 and 18. His karyotype was: 16,XY, t(16;18)(16pter→16q21 : : 18p112→18pter ; 18qter→ 18p112 : : 16q21→16qter). Thus the infant was mono-

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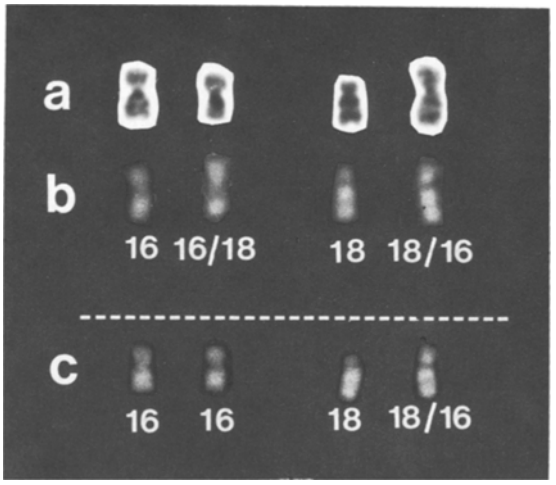

Fig. 1a–c. Partial karyotypes of the index patient's father in GT (**a**) and Q bands (**b**) and of the index patient (**c**) in Q bands

somic for the portion p112→pter of chromosome 18 and trisomic for the portion q21→qter of chromosome 16 (Fig. 1). The family refused further investigations and we were unable to karyotype to other members.

Discussion

We found seven cases of trisomy 16q in the literature (Pergament et al., 1970; Eriksson et al., 1971; Francke, 1972; Alfi et al., 1973; Machin and Crolla, 1974; Schmickel et al., 1975; Young et al., 1976). We do not consider the case of mosaic r(16) described by Pergament et al. (1970) informative, because although in 4% of the cells the ring was dicentric, the partial and total monosomy 16 found in the remaining cells makes it difficult to correlate phenotype and karyotype. Similarly, nor do we find the subject described by Machin and Crolla (1974) informative; this patient was trisomic for the same portion of 16q as was found in our case and had a concomitant partial monosomy 21p, but no phenotype description other than 'multiple malformations' was provided. The cases described by Francke (1972) and Schmickel et al. (1975) have a phenotype rather similar to that of our case, although the balanced translocations present in one parent of each of the three patients resulted in a simultaneous partial monosomy or trisomy for different chromosomes. The case of Schmickel et al. (1975) is the most informative, because their patient is trisomic for the entire 16q and for a portion of 15p, while partial monosomies 22q and 18p, respectively, are concomitant with the partial trisomy 16q in Francke's case and in our case. The features common to these three cases are low birth weight, early death, generalized hypotonia, heart abnormalities, prominent forehead, and flat nasal bridge. Furthermore, our case and that of Schmickel et al. (1975) have malformed ears, flexion contracture of elbows, and deformity of the feet in common. The two clinical histories are also similar, with frequent episodes of vomiting and abdominal distension due, in the case of Schmickel et al. (1975), to an abnormal bowel situation (duodenum and colon malrotation and midilial perforation). The case of Eriksson et al. (1971) was trisomic for a possibly smaller portion of 16q and also had a similar facial appearance, low birth weight, heart abnormality, and early death. This case also had partial monosomy 18q.

The cases described by Alfi et al. (1973) and Young et al. (1976), both of whom were trisomic for the telomeric portion of 16q, indicate that trisomy for this region does not result in early death, because both patients were still alive at the age of 21 months and 3 years, respectively. However, it should be noted that the patient of Alfi et al. (1973) had omphalocele and diaphragmatic hernia, symptoms that are not found in monosomy 9p, which is concurrent in this patient. It should be stressed that among the reported cases of trisomy 16q our case is the only one to show ambiguous external genitalia. In contrast to the liveborn cases with partial trisomy 16q, the four reported cases of partial trisomy 16p (Magnelli, 1976; Yunis et al., 1977; Roberts and Duckett, 1978; Dallapiccola et al., 1979) indicate that this condition does not result in a severely affected phenotype. In conclusion, we can postulate that since trisomy 16q invariably causes early death, while trysomy 16p does not, it is the trisomy of the long arm of chromosome 16 that is mainly responsible for the total prenatal lethality of full trisomy 16.

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Note Added in Proof

Two further cases of trisomy 16q have been published since this paper was submitted (Ridler and McKeown, J. Med. Genet. **16**, 317, 1979; Balestrazzi et al., Hum. Genet. **49**, 229, 1979). The first case was trisomic for the entire 16q, died at 12 days and had several features in common with our case. Conversely, the second case was trisomic for the portion 16q21→16qter and alive at the age of $3\frac{1}{2}$ years.