The presence of a large umbilical cord hernia containing intestinal viscera and liver with excessive abdominal skin folds has not been previously noted in this disease. The findings in this case suggest that the umbilical cord hernia arose as a secondary 'deformation' resulting from a combination of extrinsic forces from maternal factors (primigravida uterus and small pelvis) and a malformed fetus (bone dysgenesis and short thorax). The deformative process presumably occurred during the later stages of the pregnancy. The extrinsic forces acted on the malformed fetus and the abdominal contents of the fetus under increased pressure 'herniated' through the area of least resistance, the umbilical cord (fig 4). Adequate abdominal skin folds attest to the fact that there was no primary abdominal wall deformity. As the abdominal contents extruded into the hernial sac the testes were withdrawn from their well formed scrotal sacs (fig 5). It is also possible that the weakening of the connective tissue of the abdominal wall, because of the basic genetic defect, made it easier for the herniation to occur, given the external pressure.

A careful analysis of congenital malformation syndromes may help to distinguish those abnormalities which represent pleiotrophic manifestations of the abnormal gene from those arising as secondary deformative processes as a result of maternal and intrinsic fetal factors.

References


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Trisomy 14 mosaicism in a 2 year old girl

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SUMMARY Trisomy 14 mosaicism with 6% trisomic cells in blood and 16% in skin fibroblasts was found in a 2 year 2 month old girl with mild psychomotor retardation, craniofacial dysmorphism, pectus carinatum, curved fifth fingers, retarded bone age, and signs of an

FIG 4 Excessive abdominal skin folds of umbilical hernia and undescended testes with well formed scrotal sac.

FIG 5 Factors causing deformities.
ASD. These findings are consistent with the previously reported cases of trisomy 14 mosaicism and support the suggested existence of a distinctive syndrome. Non-disjunction studies showed that the extra chromosome 14 originated from either a second paternal meiotic error or an early mitotic error.

In a cytogenetic study of 1000 spontaneous abortions trisomy 14 was observed in five fetuses (0-5%). No cases of trisomy 14 mosaicism were found.1 Among liveborn infants only six cases with trisomy 14 or trisomy 14 mosaicism have been reported. One presumptive non-mosaic case confirmed by autoradiography was reported by Murken et al.2 The phenotype was similar to five cases of trisomy 14 mosaicism described previously.3-7 A distinct syndrome apparently exists for trisomy 14 mosaicism in spite of the proportion of trisomic cells in lymphocytes being low (approximately 10%) in three of the cases.3 4 7

Non-disjunction studies were not performed in any of the previously reported cases. To our knowledge this is the first report of a liveborn infant with trisomy 14 mosaicism, where the origin of the extra chromosome has been investigated.

Case report

The patient (fig 1) was a 2 year 2 month old girl who was born two weeks before term to an 18 year old mother. The pregnancy was uneventful and the delivery uncomplicated. The father was 25 years of age. Both parents and an older sister were normal. The birth weight of the child was 2700 g and the length was 46 cm.

The height remained below 2 SD of the mean of Danish children (age 2 years 2 months, height 76 cm, weight 10-1 kg). Microcephaly was not observed. The following anomalies were noted: high forehead, broad nasal bridge, hypertelorism, slight ptosis on the right side, low set ears, long philtrum, small mouth, microretrognathia, high arched palate, enamel hypoplasia of the front teeth, short neck, pectus carinatum, systolic murmur on auscultation of the heart, fifth fingers slightly curved, and a large clitoris at birth.

X-ray findings showed retarded bone age, hypoplasia of both middle phalanges of the fifth fingers, and a hypertrophic left ventricle. Echocardiography indicated an ASD. Serum steroid values, urinary amino acids, organic acids, and acid mucopolysaccharides were normal.

FIG 1 Proband at 2 years of age.

FIG 2 Chromosomes 14 from proband, father, and mother. a, b, c, and d are symbols and do not represent specific heteromorphisms.
Psychomotor development was somewhat retarded. She took her first steps at the age of 16 months. At 2 years 2 months she prattles and speaks a few understandable words. She is a smiling child who plays with toys suitable for her age.

**Cytogenetic Findings**

Chromosome analysis was carried out after QFQ banding on chromosomes from peripheral lymphocyte cultures. A total of 150 metaphases was analysed. Nine cells (6%) showed an extra chromosome 14 as the only numerical chromosome aberration observed. High resolution banding revealed no further anomalies, and the karyotype was thus 46,XX/47,XX,+14. A total of 50 skin fibroblasts was analysed after QFQ banding. Eight cells (16%) showed trisomy 14. The karyotypes of the mother, father, and older sister were normal.

Polymorphisms after QFQ banding and Ag-NOR staining were studied to determine the origin of the extra chromosome 14 (fig 2). The markers were consistent with a non-disjunction at paternal meiosis II with subsequent mitotic loss of one chromosome 14 (marker a) resulting in a normal diploid cell line in the majority of cells. With the markers a and d in the diploid cell line of the patient the other possible mechanism could be a diploid zygote exposed to mitotic non-disjunction in early embryogenesis.

**Discussion**

The observation of a trisomy 14 cell line in both skin fibroblasts and lymphocytes indicated that this was a case of true mosaicism. The clinical findings were similar to previously reported cases.2-7 thus supporting the suggestion of a trisomy 14 mosaicism syndrome. However, in this case the degree of malformation and psychomotor retardation did not appear as pronounced as that observed in five of the reported cases.2,3,5-7 The proportion of trisomic cells in the different mosaics ranged from 8 to 41% in lymphocytes. In the three cases where skin fibroblasts were examined too, the proportion of trisomic cells was less than or equal to the proportion in blood.3,4,7 However, we observed a higher proportion of trisomic cells in skin fibroblasts than in lymphocytes. The significance of this finding in relation to the phenotype and the origin of the trisomic cell line is unknown.

Non-disjunction studies by chromosomal markers were consistent with the extra chromosome 14 originating from the father. The mechanism of failure could be a mitotic non-disjunction in a diploid zygote. Another possibility would be a second paternal meiotic error followed by a mitotic loss of the extra chromosome 14, presumably due to anaphase lagging, thus establishing a diploid cell line. With the markers present it is not possible to rule out either of these two mechanisms.

Six of the seven reported cases were females. This is in accordance with the sex ratio of liveborn non-mosaic cases of trisomy 13 and trisomy 18.8 In contrast to this an excess of affected males has been reported in trisomy 21.8 Whether the distortion of the sex ratio in liveborn infants with trisomy 14 mosaicism is real or due to chance remains to be elucidated.

**References**


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