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Partial trisomy 17q and a generalised bone dysplasia in a 12 week fetus

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SUMMARY A fetus, which was spontaneously aborted at 12 weeks' gestation, was found to have a generalised bone dysplasia and an unbalanced karyotype with trisomy for 17q23.1→qter due to a maternal translocation: 46,XX,t(5;17)(p15.3;q23.1)mat.

We present the clinical details of a fetus, spontaneously aborted at 12 weeks' gestation, which had an unbalanced translocation between chromosomes 5 and 17 and a generalised bone dysplasia.

Case report

The fetus was the product of the third pregnancy of a non-consanguineous Scottish couple. The pedigree is shown in fig 1. Their first pregnancy was terminated at 20 weeks' gestation when anencephaly was diagnosed in the fetus by ultrasound examination. The second pregnancy aborted spontaneously at eight weeks' gestation. No pathological or cytogenetic studies were performed on either abortus. Chromosome analysis was performed on both parents and the proband was found to be the carrier of a balanced reciprocal translocation, 46,XX,t(5;17)(p15.3;q23.1) which she had inherited from her mother (fig 1). The present fetus aborted spontaneously at 12 weeks' gestation. Macroscopic examination revealed abnormally short limbs and a cleft palate and the phenotypic sex was male (fig 2).

Received for publication 29 January 1986.

Revised version accepted for publication 16 June 1986.

FIG 1 Family pedigree.

histological examination was uninformative because of autolysis of the tissues, but radiological examination was grossly abnormal (fig 2). Ossification was retarded in some bones but not in others and there was undermineralisation of the cranial vault. The clavicles were short and broad, the scapulae were hypoplastic, and the ribs were short. The spine was

FIG 2 Macroscopic and radiological appearance of the fetus.

completely ossified, but in the pelvis only hypoplastic iliac wings were visible. The long bones of the upper and lower limbs were short, hypoplastic, and misshapen. Both femora had an unusual hooked configuration in their proximal portion. There was a double ossification centre indicating preaxial polydactyly of the right hand. Cytogenetic studies on cultured fetal fibroblasts revealed an unbalanced karyotype, 46,XY,-5,+der(5),t(5;17) (p15.3;q23-1) mat (fig 3).

Discussion

There have been 12 previous cases of duplication of the distal portion of 17q and the main clinical features of nine of these cases were summarised recently.¹ All cases resulted from unbalanced segregation in a balanced translocation carrier. The size of the duplicated segment has varied in different cases with breakpoint in bands 17q21, q22, q23, and q25-1. The reported clinical features include psychomotor retardation, short stature, microcephaly, narrow palpebral fissures, flat nasal bridge, cleft palate, low set malformed ears, proximal limb shortening, post-axial polydactyly, and ligamentous laxity. The unusual extreme prematurity in our case makes it difficult to compare with previously published cases, but it is notable that a cleft palate was present in our

case and six of the previous 12 cases also. In one case the x ray report suggested the presence of a generalised skeletal dysplasia.² Direct comparison of the x rays of that case with our own, taking into consideration the difference in gestational age, revealed shared features. Both had broad clavicles, an undermineralised cranial vault, and a poorly ossified pelvis. However, the long bones were much more abnormal in our case and, after expert review of the x ray films of both cases, it was adjudged that the changes in each case were dissimilar. Moreover, the radiological features in our case did not resemble those of a known bone dysplasia.

Other bone dysplasias which share features with our case are hypophosphatasia, achondrogenesis, and lethal osteogenesis imperfecta. In these conditions there is reduced ossification of the fetal skull but cleft palate and polydactyly are not recognised features. These two abnormalities may occur in the short rib-polydactyly syndrome which is a heterogeneous condition comprising at least three types of neonatally lethal dwarfism.³ Our case also had short ribs, but without pathological evidence of characteristic visceral abnormalities or bone histology this diagnosis cannot be confidently suggested.

The association of trisomy 17q and an apparently unique bone dysplasia may be coincidental or the dysplasia may be due to the unbalanced translocation. The assignation of the locus for the pro

FIG 3 Partial karyotypes of (a) the proband 46,XX,t(5;17)(p15:3;q23:1), (b) an ideotype showing breakpoints, (c) the fetus 46,XY,-5,+der(5),t(5;17)(p15:3;q23:1)mat. Derivatives are on the right of each pair.

$\alpha 1(I)$ collagen gene (*COL1A1*) has been confirmed at 17q21-31,⁴ which is close to the breakpoint (17q23) in our case. Different mutations in this gene have been reported in cases of lethal and non-lethal osteogenesis imperfecta,^{5,6} and although the polydactyly and cleft palate in our case make this diagnosis unlikely, the unbalanced chromosome constitution may be making the phenotype atypical.

We cannot exclude the possibility that a recessive gene has been 'unmasked' on the segment of chromosome 5p for which the fetus is monosomic; however, no candidate genes have been mapped to this region and a generalised bone dysplasia has never, to our knowledge, been reported with the 5p- syndrome.

Many different skeletal dysplasias have been diagnosed in the second and third trimesters of pregnancy by detailed ultrasound examination and measurement of fetal limb lengths.⁷ As this case showed visible evidence of disturbed limb growth at the end of the first trimester, it can be anticipated that as expertise and equipment improves very early diagnosis of some dysplasias may be possible and more knowledge will be gained about the classification and natural history of these disorders.

We are grateful to Professors D Rimoin, R Lachman, and J Spranger for evaluating our case and comparing it with that of Gallien *et al.*² to Dr H Richmond, Consultant Pathologist, and the Department of Medical Illustration, Raigmore Hospital, Inverness for advice and preparation of the illustrations.

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