

A female with XO/XY mosaicism and partial trisomy 9p

The proband was born when the mother was 27 and the father 32 after a normal pregnancy and delivery. The parents and an older brother are healthy with normal karyotypes. At 13½ years she had severe mental and physical retardation, general muscular hypotonia, hyperactivity, and trichotillomania. Height and weight were below the 3rd centile, ossification was delayed, and she had brachycephaly, a wide fontanelle, deep-seated ears, hypertelorism, and antimongoloid slants. Bilateral cleft lip and palate had been treated surgically. Hands and feet were short, Dubois sign was positive, there was bilateral clinodactyly, and syndactyly between fingers 2 and 3, and more markedly between toes 2, 3, and 4. There were single transverse palmar creases on both hands and diastasis of the rectus abdominis muscle. X-ray examination showed asymmetry of the os sacrum and spina bifida occulta. Chronic constipation, gastroesophageal reflux, and disturbed micturition were reported. The external genitalia were normal, no testes were palpable, and there was no onset of puberty.

G banding of the proband's lymphocytes revealed an aberrant chromosome 9 which is interpreted as an inverted tandem ('mirror') duplication of 9p (figure a). Of 100 metaphases investigated, 97 showed, in addition to a single X chromosome, a small acrocentric chromosome which was identified as a Y by Q and C banding and distamycin A pretreatment¹ (figure b, d). Presence of Y heterochromatin specific repeated sequences was confirmed by Hae III restriction endonuclease analysis of the DNA of the proband, father, and brother. The remaining three metaphases lacked a Y chromosome. After staining preparations of the proband with quin-

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acrine mustard, C banding showed an extremely large block of constitutive heterochromatin in one chromosome 7 (figure c). This particular chromosome was also seen in the mother and brother. Using a cytotoxicity assay technique, the proband was found to be negative for the H-Y antigen.

The karyotype of the proband is therefore 45,XO,inv dup(9)(pter → p24 :: p21 → p24 :: p21 → qter)/46,XY,inv dup(9)(pter → p24 :: p21 → p24 :: p21 → qter). Trisomy 9p could not be confirmed by gene dosage measurements (eg galactose-1-P-uridyl transferase), nor could the internal genitalia be explored, since the proband's parents refused any further examination. However, the phenotype of the proband clearly shares features with previously reported cases of XY gonadal dysgenesis² and trisomy 9p.³ The phenotypic sex is as expected from the H-Y constitution.

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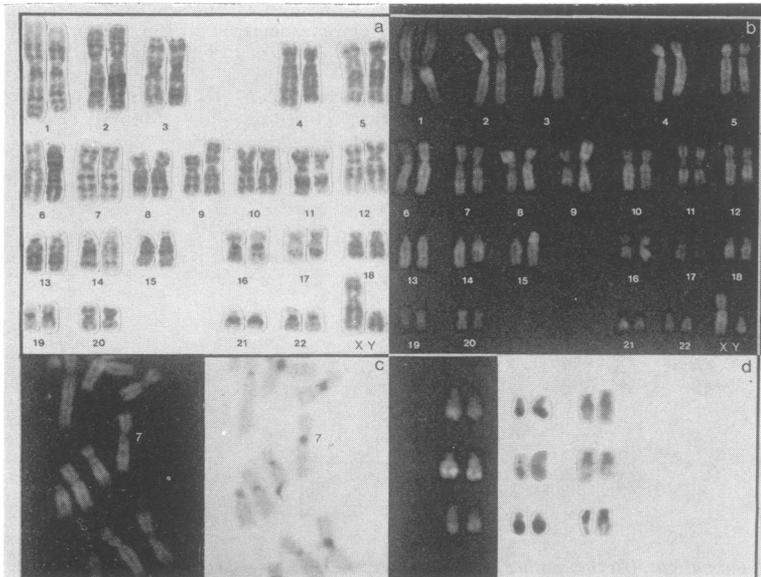


FIGURE G banded (a) and Q banded (b) karyotype of proband, showing presumptive inverted tandem duplication of 9p and presumptive Y chromosome. (c) Parial metaphase of proband, prestained with quinacrine (left) and then restained after the C banding method. Note very large centric heterochromatin in chromosome 7. (d) Identification of the Y chromosomes of the father (top), proband (middle), and brother (bottom), stained with quinacrine mustard (left), C banded (centre), and stained with aceto-orcein after pretreatment with distamycin A (right).