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UNILATERAL GONADAL DYSGENESIS WITH BOTH TESTIS AND FALLOPIAN TUBE ON THE SAME SIDE IN A 45,X/46,X INV (Y) MOSAIC MALE

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Summary A 5-year-old male with ambiguous external genitalia, hypospadias and microphallus without an urethral orifice was referred for cytogenetic studies. Exploratory laparotomy revealed presence of an infantile uterus and unilateral gonadal dysgenesis with both testes and fallopian tube on the right side. The metaphase cells from peripheral blood culture showed both 45,X/46,X inverted Y (p11.2q11.23) cell-lines (98:2). The inverted Y was found to be of paternal origin. Maternal chromosomal pattern was normal 46,XX. The presence of a fallopian tube next to testis suggest absence of secretion of anti-Mullerian hormone by Sertoli cells. The absence of Wolffian duct derivatives suggest insufficient secretion of testosterone by Leydig cells.

Key Words cytogenetics, clinical findings, histopathology, mosaicism, unilateral gonadal dysgenesis

INTRODUCTION

The phenotype of patients with 45,X/46,XY or 45,X/46,X with structurally abnormal Y mosaicism, exhibits considerable variation ranging from normal male to normal female (Mailhes *et al.*, 1979). However, the gonadal tissue of these patients with 45,X/46,X normal or strucural abnormal Y depends on the frequency of cell-lines present in their genome. Majority of these individuals have Turner stigmata, ambiguous external genitalia, hypospadias, dysgenetic ovary, testes, or testis with ovarian stroma (Mailhes *et al.*, 1979; Ayuso *et al.*, 1984; Rosenberg *et al.*, 1987; Casperson *et al.*, 1971).

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MATERIAL AND METHODS

Karyotypes of the patient and his parents were prepared by blood cultures. G (GTG), Q (QFQ), and C (CGB) banding techiques were used to identify the chromosomes. In addition, ultrasonography, laparotomy of the case and histology of gonadal biopsies were carried out. Three hundred metaphase cells were analysed in the patient, and 100 metaphase cells each were studied in the case of parents.

CASE REPORT

A five-year-old proband with assigned sex male was the first child of healthy nonconsanguinous parents. The father and mother were 30 and 25 years old respectively when the child was born. The clinical findings were: height 75 cm; weight 12 kg; ambiguous external genitalia, hypospadias, palpable testis on the right side but absent on the left side (Fig. 1). No definite scrotal sac and a microphallus without an urethral orifice was observed, and also there were no symptoms of Turner syndrome.

Cytogenetic analysis

Two hundred buccal mucosa cells, each analysed for Barr body and Y chromatin, showed Barr negative and 3% Y-chromatin positive respectively. Examination of metaphase chromosomes showed both 45,X and 46,X inverted Y (p11.2q11.23) cell-lines. The 45,X cell-line comprised of about 98% of the total cells analysed. The remaining 2% of the cell-line was wih 46,X inverted (Y) (Fig. 2, A and B). Maternal chromosomal pattern was normal 46,XX. No mosaicism was detected in the parents.

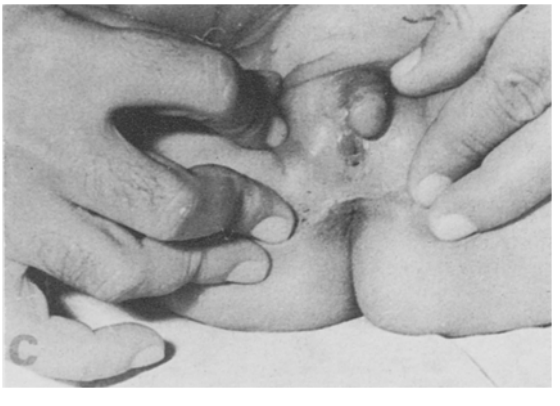

Fig. 1. The proband showing hypospadias, phallus, urethral and vaginal opening.

Laparotomy report

Exploratory laparotomy showed presence of uterus measuring approximately 40 mm. On the right side, a tube like structure and a testis measuring approximately 10–12 mm were observed. The reproductive organs on left side were completely absent (Fig. 3).

Histology report

Histology of gonadal biopsy showed the presence of testicular tissue with

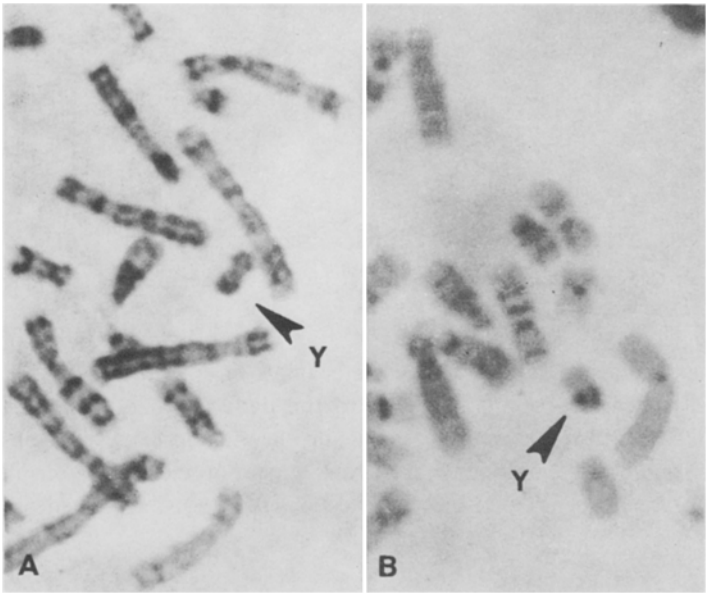

Fig. 2. A-B. Partial metaphase showing G and C-banded inv(Y) chromosome from proband's father.

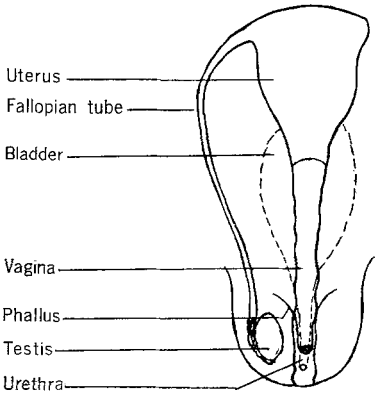

Fig. 3. Schematic presentation of the internal genitalia.

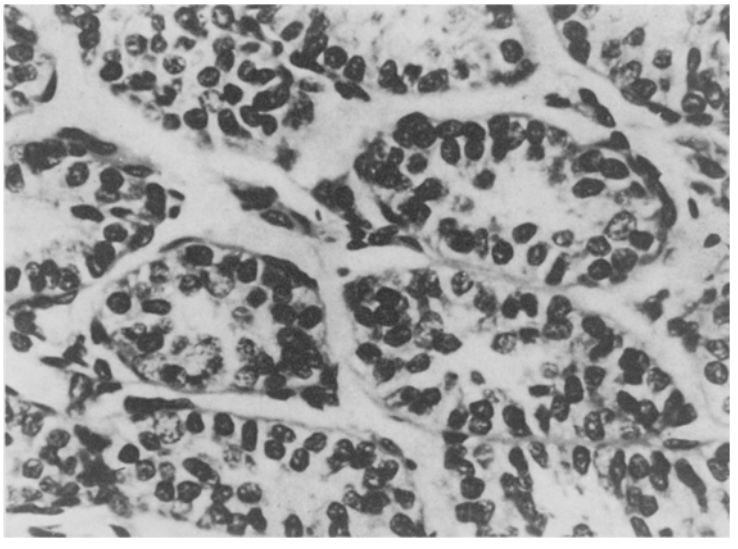

Fig. 4. Histological section of the gonadal biopsy of the proband showing infantile testicular tissue.

abundant seminiferous tubules which were small in size and were not hyalinized. The tubular lumen was obliterated due to the denudation of germinal cells. The intertubular interstitium was increased while the Leydig cells were observed to be less. The Sertoli cell population however were not clearly discernible (Fig. 4). The biopsy material present in-between testis and uterus appeared similar to fallopian tube.

DISCUSSION

A number of 45,X/46,XY or 45,X/46,X with structural abnormal Y have been reported earlier, but to the best of our knowledge, this may be the first case with 45,X/46,X inv (Y) (98:2) mosaicism associated with unilateral gonadal dysgenesis with both testis and fallopian tube on the same side. A patient having fallopian tube like structure next to the testis was reported by Williams *et al.* (1981) but the nature of the gonad was not confirmed histologically. The incidence of inverted Y chromosome in general population is 0.6–1 per 1,000 male births. No evidence existed regarding inverted Y (p11.2q11.23) chromosome associated with reproductive disadvantage and any phenotypic expression (Bernstein *et al.*, 1986). However, in the case under study, ambiguous external genitalia and hypospadias might be due to mosaicism with 45,X cell line and correlates with previous report (Yanagisawa, 1980). Majority of the earlier cases reported (Davis, 1981; Rosenberg *et al.*, 1987; Casperson *et al.*, 1971; Ayuso *et al.*, 1984; Wheeler *et al.*, 1988) showed neither normal male nor female external genitalia with gonads of either sex.

It could be concluded from these studies that fetal testis differentiation occurred in presence of Y chromosome present in the proband's genome which failed to induce Wolffian duct differentiation, probably due to insufficient secretion of testosterone by the Leydig cells of the fetal gonad. Moreover the presence of fallopian tube next to testis suggests absence of secretion of anti-Mullerian hormone by Sertoli cells.

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