

SHORT COMMUNICATION: Coexistence of ovotestis and testicular regression in a boy with 46,XX/46,XY chimerism and sex ambiguity

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ABSTRACT

We report on a boy with ambiguous genitalia (hypospadias and cryptorchidism), a 46,XX/46,XY karyotype, complete Wolffian differentiation and no Müllerian derivatives, a left ovotestis, and no gonadal tissue on the right side. True hermaphroditism and regression of testicular tissue in this case indicate that chimerism may not only disturb gonadal differentiation but also arrest its development.

INTRODUCTION

Hermaphroditism is defined as coexistence of ovarian and testicular tissue in the same subject. It can arise both in individuals with a normal chromosomal constitution, 46,XX or 46,XY, and in those with various chromosomal aberrations, including 46,XX/46,XY chimerism (Simpson, 1990).

In turn, testicular regression syndromes are included among causes of male pseudohermaphroditism and are characterized by surgically verified absence of gonads in 46,XY individuals, with great variability in

differentiation of internal and external genitalia depending on the timing of testicular insult during the embryonic development (Bergada *et al.*, 1962; Clearly *et al.*, 1977).

We examined a boy with 46,XX/46,XY chimerism who exhibited ambiguous external genitalia, a left ovotestis, and evidence of testicular regression on the right side.

CASE REPORT

EPS, a 12-year old boy, was referred because of cryptorchidism and scrotal hypospadias (Figure 1). He was born at term by normal delivery after an uncomplicated pregnancy to nonconsanguineous parents: 24-year old mother and 31-year old father. He was the 5th child in a sibship of eight (five boys and three girls), and family history was unremarkable. Except for genital anomalies, he was a healthy child

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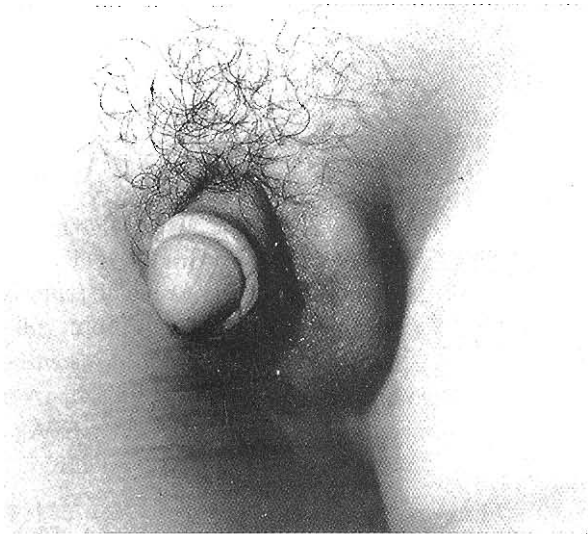


Figure 1 - External genitalia of the patient.

with normal neuromotor and mental development. Prior to his evaluation in our service, he had had an unsuccessful operation to correct hypospadias.

On examination, his height was 153.2 cm (75th centile) and weight 32.3 kg (25th centile). He had a 4.0-cm length phallus with two acquired fistulae on the transition of the penis and scrotum, mild shawl scrotum, a 2.5-cm diameter gonad palpable on left inguinal region, absence of palpable right gonad, and pubic hair on Tanner stage P II. No other physical abnormalities were noted.

Abdomen and pelvic ultrasonography did not reveal any abnormality, while radiological examination of the chest disclosed a hypoplastic right 12th rib.

He had pubertal serum gonadotropins, low testosterone level, and normal prolactin and estradiol levels. The G and Q banding karyotype in cultured peripheral blood lymphocytes was 46,XX/46,XY (9:23) and chimerism could be demonstrated by a different Q-banding polymorphism between the two cell lines (a 3qh+ in the 46,XY cell line which is absent in the 46,XX cell line) (Figure 2). Unfortunately, the parents were not available for laboratory investigations which could determine the origin of this disorder.

On surgical examination, there were normal male internal ducts and no Müllerian derivatives. The left gonad was fixed in the scrotum, while the right abdominal gonad, which looked like an atrophic testis, was removed. Biopsy of the left gonad revealed prepubertal developing testis, while the right gonad consisted of fibro-adipous tissue (Figure 3).

The possibility of an undiagnosed left ovotestis and risk of malignancy in 46,XX/46,XY true hermaphrodites (Verp and Simpson, 1987) was discussed with the parents, who agreed to gonadectomy. A thorough histological examination revealed, besides testicular tissue with arrest of development at the primary spermatocyte stage, ovarian tissue with primordial and Graafian follicles in a small area near the hilus (Figure 4), thus making the diagnosis of true hermaphroditism.

DISCUSSION

Van Niekerk and Retief (1981) reviewed gonadal distribution in 409 true hermaphrodites; in 90.5% of cases hermaphroditism was lateral (an ovary

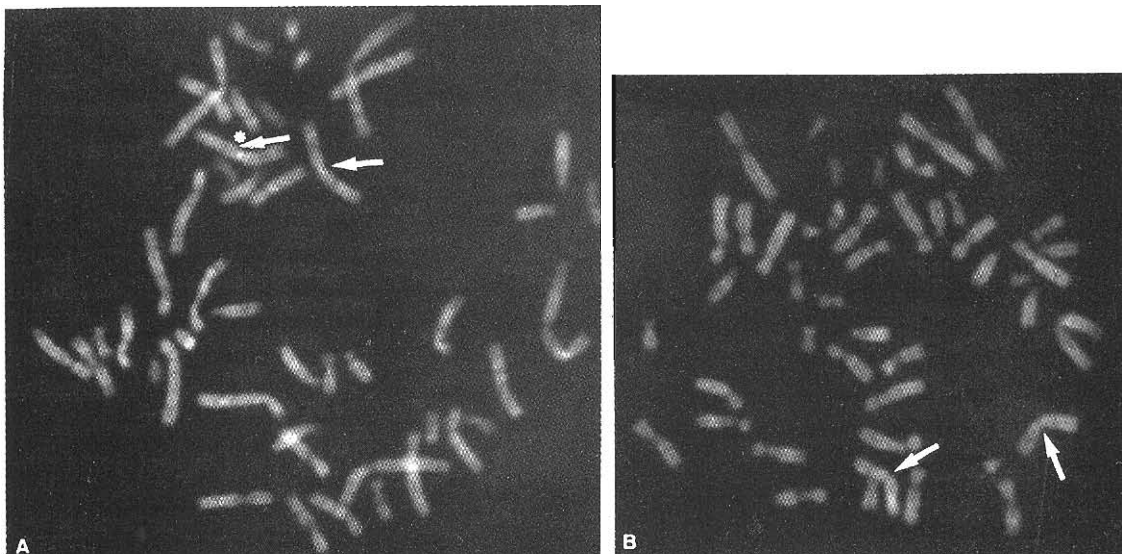


Figure 2 - Partial karyotype of the propositus showing a different Q-banding polymorphism. A - 46,XY cell line with a 3qh+ which is absent in B (46,XX cell line).

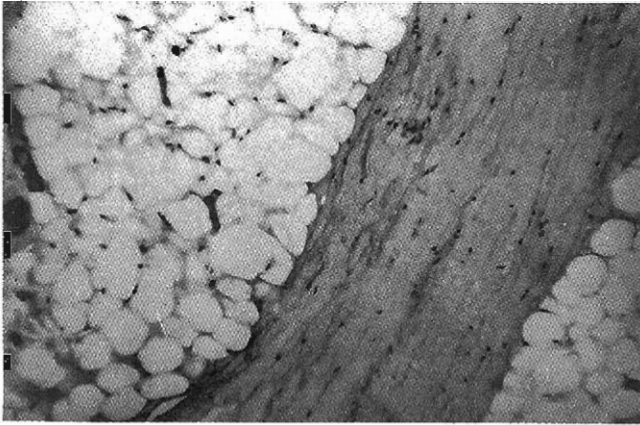


Figure 3 - Right gonad from the patient showing fibroadipous tissue (160*X magnification, H and E stain) (*in the negative, before ampliation).

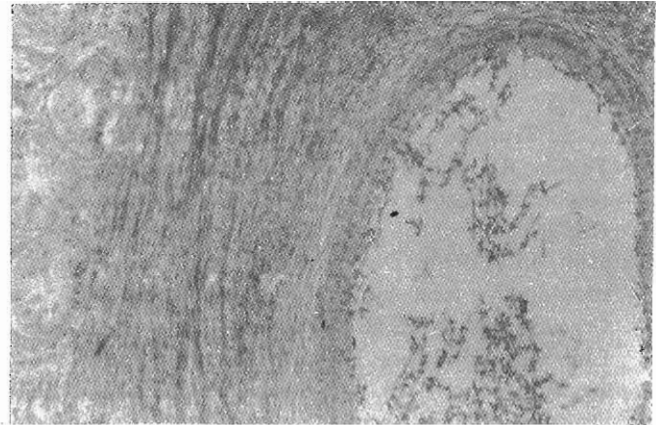


Figure 4 - Left gonad from the patient showing transition between testicular (left) and ovarian (right) tissues. Note Graafian follicle (100*X magnification, H and E stain) (*in the negative, before ampliation).

on one side and a testis on the other side), unilateral (an ovotestis on one side and an ovary or testis on the other) or bilateral (with ovotestes on both sides). In 3.9% of cases there was an ovotestis on one side and there was no information about the other gonad; "other combinations" (not described) were seen in 5.6% of cases.

A 46,XX/46,XY karyotype was found in 12.8% of the cases reviewed by Van Niekerk and Retief (1981). This chromosomal aberration may be a mosaicism (cell lines derived from a single zygote in which a cell - or cells - has undergone mutation or nondisjunction) or chimerism (cell lines derived from two different zygotes). A 46,XX/46,XY chimerism may arise from transfusion of blood stem cells from a dizygotic twin through common blood vessels, fusion of two embryos, or fertilization of the ovum and one of the polar bodies. In our patient, the finding of a different Q-banding polymorphism in chromosome 3 in 46,XY cells indicates a different genetic contribution from at least one of the parents to each cell line.

In cattle, chimerism is responsible for cases of abnormal sexual development known as freemartins, i.e., genetically female cows with fraternal male twins who are sterile and exhibit atrophic gonads, hypoplastic female internal genitalia, and enlarged clitoris. The sex differentiation of the male partner seems to be quite normal, but fertility problems do occur (Dunn *et al.*, 1979), indicating that the presence of XX primordial germ cells in testes (Ohno *et al.*, 1962; Teplitz *et al.*, 1967) could lead to abnormal spermatogenesis.

In the present case, the finding of an ovotestis and an atrophic gonad which had been able to induce complete Müllerian regression and full development of Wolffian derivatives indicate that coexistence of cell

lines with different sex chromosomes can lead to a broad spectrum of abnormal sex differentiation.

ACKNOWLEDGMENTS

We are grateful to Dr. Christine Hackel for assistance in the cytogenetic analysis. We are also indebted to the Departamento de Anatomia Patológica, Faculdade de Ciências Médicas, Universidade Estadual de Campinas. Publication supported by FAPESP.

RESUMO

Descreve-se o caso de um menino com genitália ambígua (hipospádia e criptorquidia) e quimerismo 46,XX/46,XY. Apresentava diferenciação completa dos dutos de Wolff, ausência de derivados de Müller, um ovotestis à esquerda e ausência de tecido gonadal à direita. Neste caso, a existência de hermafroditismo verdadeiro e regressão de tecido testicular indicam que o quimerismo possa não só perturbar a diferenciação gonadal como também inibir o seu desenvolvimento.

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(Received April 4, 1994)