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Case Report

AN AZOOSPERMIC MALE WITH AN UNBALANCED AUTOSOMAL-Y TRANSLOCATION

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Summary An azoospermic male with an unbalanced translocation between the Y chromosome and chromosome 15 was examined in the present study. Testicular biopsy found only Sertoli cells only within the seminiferous tubules of the 35-year-old patient. Chromosome analysis, using the techniques of G and C banding and fluorescent *in situ* hybridization revealed an abnormal karyotype of 46,XY,der(15)t(Y;15)(q12; p11). Deoxyribonucleic acid (DNA) analysis confirmed the presence of the genes such as DAZ and YRRM1 which are known to control spermatogenesis. The cause of spermatogenetic dysfunction in this particular patient therefore.

Key Words chromosome abnormalities, male infertility, azoospermic factor gene, Y chromosome, autosome

INTRODUCTION

The incidence of major chromosomal abnormalities among azoospermic males, is approximately 15.2% according to recent reports. A majority of these serious abnormalities which include cases of 47,XXY (Klinefelter syndrome), 46,XX male, inversions of the Y chromosome, dicentric Y chromosomes, translocations between the Y chromosome and autosomal chromosomes, occur among the sex chromosomes (Yoshida *et al.*, 1996). It was also reported by Nagafuchi *et al.* (1993) that 13% of the azoospermic males whose Y chromosomes were found to be cytogenetically normal, have been observed to have deletions of the azoosper-

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mic factor (AZF). The genes, such as AZF, which control spermatogenesis are found on the distal region (interval 6) in the long arm of the Y chromosome (Tiepolo and Zuffardi, 1976), whereas the genes which play a fundamental role in controlling testis differentiation are located on the short arm of the Y chromosome (Su and Lau, 1993). The present report describes an azoospermic male exhibiting an abnormal karyotype with an unbalanced translocation between the Y chromosome and chromosome 15.

CASE REPORT

A 35-year-old male patient first came to the Reproduction Center of Toho

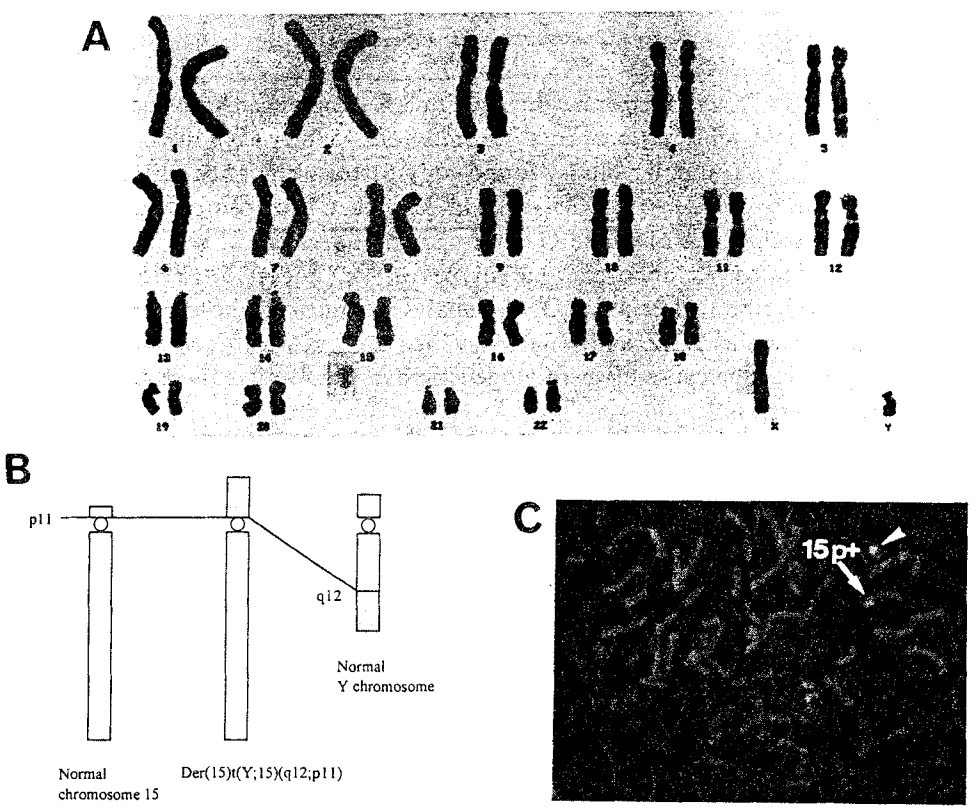

Fig. 1. A) The karyotype of 46,XY,der(15)t(Y;15)(q12;p11); G-band. B) A rough sketch of a normal Y chromosome and a normal chromosome 15 as compared to der(15)t(Y;15)(q12;p11). C) Fluorescent *in situ* hybridization (FISH) shows fluorescence illumination of the long arm of the Y chromosome and the short arm of the derivative chromosome 15 using a DYZ1 probe (q12 of the Y chromosome).

University School of Medicine in February of 1995 for infertility evaluation promoted by a 113-month history of fruitless unprotected sexual intercourse. The patient had a height of 158 cm and weighed 78.0 kg. Preliminary evaluation did not reveal any evidence of varicocele or genital infection. His sexual function was categorized as normal with a frequency of sexual intercourse of 8 times per month. His right and left testicular volumes were 10 ml and 8 ml, respectively.

His total semen volume was measured at 2.0 ml. Subsequent semen analysis led to the diagnosis of azoospermia. His serum FSH, LH, testosterone and prolactin values were 17.1 mIU/ml (normal range 1.8 to 13.6), 5.6 mIU/ml (normal 1.1 to 8.8), 5.31 ng/ml (normal 2.7 to 10.7) and 40.0 ng/ml (normal 4.4 to 30.0), respectively.

Chromosome analysis were performed using peripheral blood lymphocyte cultures. A total of 20 metaphases were analyzed by the G banding method. Analysis of each of the 20 chromosome sets revealed an unbalanced translocation between the Y chromosome and chromosome 15, resulting in a karyotype of 46, XY,der(15)t(Y;15)(q12;p11) (Fig. 1A, 1B). Fluorescent *in situ* hybridization (FISH) using a DYZ1 probe (q12 of the Y chromosome) resulted in fluorescent illumination of the long arm of the Y chromosome and the short arm of the derivative chromosome 15 (Fig. 1C).

Testicular biopsy, performed after obtaining informed consent, revealed Sertoli cells only (Fig. 2).

DNA analysis was then performed on a total of 17 Y-specific loci (PABY, SRY, AMGL, DYZ3, DYS139, DYS132, SMCY, YRRM1, DAZ, DYS232, DYS233, DYS1, DYS236, DYS237, DYS239, DYS240, DYZ1) (Fig. 3). None of the Y-specific DNA fragments were found to have been deleted. Because deletions

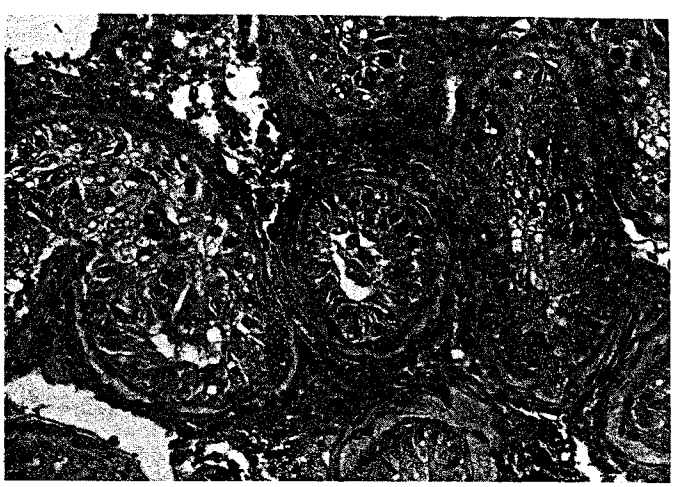

Fig. 2. Testicular histology revealed Sertoli cells only. Reduced from ×200.

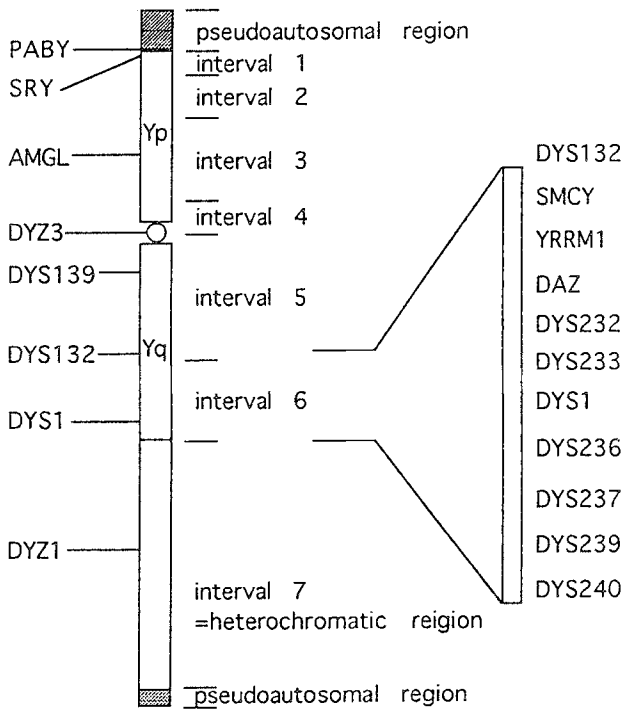

Fig. 3. Seventeen loci on the Y chromosome analyzed in this study.

of the spermatogenesis controlling genes did not occur, the cause of spermatogenesis dysfunction is still unclear.

DISCUSSION

Smith *et al.* (1979) reported that Y/autosome translocations in postpubescent males with normal phenotypes could be divided into two basic categories: (1) balanced reciprocal translocations between the Y chromosome and an autosomal chromosome, or (2) unbalanced non-reciprocal translocations of the heterochromatic region of the long arm of the Y chromosome onto the short arm of an acrocentric chromosome. The case described in this report however, does not fall into either of the two categories described above. This particular patient exhibited an abnormal karyotype in which he possessed one normal Y chromosome, one normal 15 chromosome and an unbalanced translocation derivative 15 chromosome which was seen as an acrocentric chromosome with Yq12→15p11→15cen→15qter.

A gene which is involved in controlling spermatogenesis is located on the distal euchromatic segment of the long arm of the Y chromosome. Recently Reijo

et al. (1995) reported that a deletion of this AZF region is associated with highly variable testicular defects, ranging from complete absence of germ cells to spermatogenic arrest with the occasional production of condensed spermatid. Although our patient was diagnosed as being Sertoli cells only, the genes which are responsible for controlling spermatogenesis such as DAZ (Reijo *et al.*, 1995) and YRRM1 (Ma *et al.*, 1993), were present as indicated by DNA probe analysis.

Because the case described in this report deviates from the generally observed examples of chromosomal abnormalities, the cause of spermatogenesis dysfunction is still not well understood. However, we surmise that spermatogenesis dysfunction in our patient may attributed to defects in autosomal genes required for spermatogenesis (Yen *et al.*, 1996) or partial deletions of the Y chromosomal genes which are responsible for controlling spermatogenesis, such as DAZ.

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