CASE REPORT

Dicentric Y chromosome in an azoospermic male

Atsumi Yoshida, Yutaka Nakahori, Yoko Kuroki, Mitsuhiro Motoyama, Yasuhisa Araki, Kazukiyo Miura and Masafumi Shirai

First Department of Urology, Toho University School of Medicine, 6-11-1, Omorinishi, Ota-Ku, Tokyo 143, Department of Public Health, School of Medicine, The University of Tokushima, 3-18-15, Kuramoto-cho, Tokushima-city, Tokushima 770, and Institute of Advanced Medical Technology Central Clinic, Minamikawachimachi Kawachi-gun, Tochigi-ken, Japan

We describe a 28 year old male with a pseudodicentric Y chromosome who suffered from azoospermia attributed to maturation arrest of the primary spermatocyte, as diagnosed by testicular biopsy. Chromosome analysis, using G, Q and C banding techniques, revealed an abnormal karyotype of 45,X[7]/46,X,psu dic (Y)(pter→q11.2::q11.2→pter)[33]. Polymerase chain reaction (PCR) DNA analysis did not detect the absence of DAZ and RBM1 which are candidates for azoospermic factor (AZF) genes. Therefore, it is suggested that the maturation arrest of the primary spermatocyte in this patient was caused either by a pairing dysfunction between the X and Y chromosomes during meiosis or by deletions in the autosomal or the Y chromosomal spermatogenesis controlling genes, excluding DAZ and RBM1.

Key words: azoospermic factor gene/chromosome abnormalities/male infertility/testicular biopsy/Y chromosome

Introduction

As reported in a recent review, the incidence of major chromosome abnormalities among azoospermic males is 15.2%. The majority are abnormalities that are related to abnormalities of the sex chromosomes, including cases of 47,XXY (Klinefelter’s syndrome), 46,XX males, inversions of the Y chromosome, dicentric Y chromosomes, etc. The incidence of abnormal karyotypes with dicentric Y chromosomes was 0.3% among 1523 azoospermic males (Yoshida et al., 1996).

The short arm of the Y chromosome is known to play a fundamental role in testis differentiation (Su and Lau, 1993), whereas the azoospermic factor (AZF) gene is located on the distal region (interval 6) of the long arm (Tiepolo and Zuffardi, 1976). The stature determinants in the long arm of the Y chromosome are presumed to be proximal to the AZF gene (Cohen et al., 1983).

Deletions of the region, including the AZF which controls spermatogenesis, have also been observed in 13% of the azoospermic males with cytogenetically normal Y chromosomes (Nagafuchi et al., 1993). Recently, two genes, RBM1 (RNA-binding motif 1) and DAZ (deleted in azoospermia), have been shown to map to a small region of the long arm of the human Y chromosome which is deleted in azoospermic males (Ma et al., 1993; Reiho et al., 1995). Vereb et al. (1997) detected deletions involving DAZ in five out of 43 (11.6%) azoospermic males. Reiho et al. (1996) found Y chromosome deletions, involving DAZ, in two of 35 (5.7%) severely oligozoospermic males, while no Y chromosome deletions were detected in their fathers. Moreover, Vogt et al. (1996) found Y chromosome deletions in 26 of 370 (7.0%) idiopathic azoospermic or severely oligozoospermic males.

We present a case of an azoospermic male with an abnormal karyotype of Y chromosome mosaicism, exhibiting dicentric Y chromosomes in the majority cell line. The Y chromosome deletions were analysed using 17 Y-specific loci.

Case report

A 28 year old male patient and his 28 year old wife first came to the Institute of Advanced Medical Technology Central Clinic in June, 1994, for infertility evaluation following a 24-month history of unsuccessful unprotected sexual intercourse. His wife exhibited regular ovulation and salpingography revealed normal reproductive function. His height was 156 cm and his weight was 68.0 kg. There was no evidence of varicocele or genital infections. His sexual function was normal, engaging in sexual intercourse four times per month. The right and left testicular volumes were 8 and 10 ml respectively.

Semen analysis revealed azoospermia and the semen volume was 3.5 ml. Serum follicle stimulating hormone (FSH), luteinizing hormone (LH), testosterone and prolactin values were 7.3 mIU/ml, 2.4 mIU/ml, 2.6 ng/ml and 7.3 ng/ml respectively.

Chromosome analysis was carried out following peripheral
blood lymphocyte culture. A total of 40 metaphase cells was analysed by the G-banding method. Two cell lines with different chromosome complements were found within the patient with Y chromosome abnormalities in 33 of the cells (Figure 1A,C). Brilliant fluorescence of the heterochromatic region was not seen by Q-banding. C-banding revealed two bands of which one was darker than the other. The remaining seven lymphocytes exhibited a karyotype of 45,X (Figure 1B). Therefore, the karyotype of the patient is described as 45,X[7]/46,X,psu dic (Y)(pter→q11.2::q11.2→pter)[33].

Testicular biopsy, performed after informed consent, revealed maturation arrest of the primary spermatocytes (Figure 2).

The presence or absence of 17 Y-specific loci was analysed (PABY, SRY, AMGL, DYZ3, DYS139, DYS132, SMYC, RBM1, DAZ, DYS232, DYS233, DYS1, DYS236, DYS237, DYS239, DYS240, DYZ1) (Figure 3). Among them, DYZ1 was absent while the remaining 16 loci were present. This finding was consistent with the cytogenetic observation and also indicated that the region responsible for spermatogenesis was intact.

Discussion

The phenotype of the carriers of 46,X,dic(Y) range from Turner-like females to normal males, most of whom are azoospermic (Therman, 1993). A lag in anaphase is usually seen in the patients with 46,X,dic(Y), probably because the presence of two centromere disturbs the normal segregation of chromosomes in meiosis. In this particular patient, the ratio of 45,X cells to 46,X,dic(Y) cells was 7:33. Since the proportion of 45,X cells in this patient was low (17.5%), the patient might have developed as a male, as previously reported by Taniuchi et al. (1991). The presence of other cell lines, particularly 45,X, may influence the phenotype.

A gene 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 the AZF region is associated with highly variable testicular defects, ranging from complete absence of germ cells to spermatogenic arrest with occasional production of condensed spermatids. Moreover, Vogt et al. (1996) demonstrated the presence of not one but three spermatogenesis loci in Yq11 and showed that each locus is active during a different phase of male germ cell development. Mulhall et al. (1997) showed that the rates of fertilization and embryo development were similar when testicular spermatozoa extracted from azoospermic males with DAZ deletions were compared with those obtained from azoospermic men without deletions. We performed a testicular biopsy to ascertain the feasibility of intracytoplasmic sperm injection using testicular spermatozoa. However, the testicular biopsy revealed the absence of spermatozoa in all seminiferous tubules. Although testicular biopsy in this patient revealed maturation arrest of the primary spermatocyte, the presence of spermatogenesis-related genes, such as DAZ and RBM1, was confirmed by DNA analysis. The maturation arrest seen in this patient therefore, may be attributed to a pairing dysfunction between the X and Y chromosomes during meiosis or to deletions in the autosomal (Yen et al., 1996), or the Y

Figure 1. (A) The karyotype of 46,X,psu dic(Y)(pter→q11.2::q11→pter); G-band. (B) The karyotype of 45,X; G-band. (C) An approximation of the rough sketch of the 46,X,psu dic(Y)(pter→q11.2::q11→pter) region.
Dicentric Y chromosome in an azoospermic male

Figure 2. Testicular histology revealed maturation arrest of the primary spermatocyte. Original magnification ×200.

Figure 3. The 17 loci analysed in this study.

Chromosomal spermatogenesis controlling genes (Vogt et al., 1996) excluding DAZ and RBM1.

Takihara et al. (1993) have described a male with a similar dicentric Y chromosome whose height was 147 cm. The short stature was assumed to have been caused by a deletion of the stature determination gene. In the present case, it is suggested that the slightly decreased height in our patient was caused as the mixed result of the presence of 45,X cell lines and the presence of the dic(Y) which caused the number of Y-growth genes to double (Ogata et al., 1995).

Acknowledgements

The authors are extremely grateful to Mr Hiro Sung for his assistance in the preparation of this manuscript.

References


A. Yoshida et al.


Received on April 14, 1997; accepted on June 18, 1997