Sex Chromosome Abnormality in Chronic Renal Failure

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Dear Sir,

Sex chromosome abnormality is one of the representative causes of male infertility. Previously, various types of the abnormality have been reported [1, 2]. Patients with the abnormality usually show gonadal dysfunction [3]. Similar dysfunction was often found in male patients with chronic renal failure [4, 5]. However, little attention has been paid to sex chromosome abnormality in men with end-stage renal disease. Herein, we report a case of Klinefelter's syndrome with chronic renal failure undergoing hemodialysis.

A 47-year-old Japanese man, on maintenance hemodialysis for 5 years, was referred to our hospital because of his infertility. He was a well-developed male weighing 68 kg and 184 cm in height. A female-type distribution of the pubic hair was noted. Neither malformations nor gynecomastia were seen. The penis, epididymides and spermatic cords were normal, but the prostate was barely palpable. His testes were only about 3 ml in volume with an orchidometer. Repeated spermatograms revealed the absence of spermatozoa.

A hemogram disclosed leukocytes of 8,400/mm³ (normal, 4,000-9,000), erythrocytes 231×10^6 /mm³ (normal, 430-570 $\times 10^4$), hemoglobin 6.8 g/dl (normal, 14.0-18.0), hematocrit 21% (normal, 40-54) and platelet count 375,000/mm³ (normal, 130,000-340,000). Serum sodium was 138 mEq/l (normal, 135-145), potassium 5.1 mEq/l (normal, 3.2-4.5), chloride 94 mEq/l (normal, 96-110), calcium 5.7 mg/dl (normal, 8.8-10.2) and phosphorus 5.3 mg/dl (normal, 2.9-4.7).

Blood urea nitrogen was 81 mg/dl (normal, 9-25), serum creatinine 14.3 mg/dl (normal, 0.5-1.5) and uric acid 7.6 mg/dl (normal, 2.0-7.6). Liver function test and immunological examinations were all within the normal range.

Plasma-luteinizing hormone (LH), follicle-stimulating hormone (FSH) and testosterone were 18.8 mIU/ml (normal, 1.8-5.2), 51.0 mIU/ml (normal, 2.9-8.2) and 0.3 ng/ml (normal, 2.8-8.2), respectively. Chromosome analysis of peripheral lymphocytes with 26 cells showed 47, XXY (96.2%) and 46, XY (3.8%) mosaicism (fig. 1, 2).

The patient was treated with intramuscular injection of 250 mg testosterone enanthate every 3 weeks. Twelve weeks after the initiation of testosterone replacement therapy, LH, FSH and testosterone were 22.5 mIU/ml, 45.3 mIU/ml and 1.1 ng/ml, respectively.

Klinefelter et al. [1] described a clinical syndrome characterized by gynecomastia, azoospermia and elevation of urinary gonadotropin excretion titers in 1942. Following recent development in the field of chromosome analysis, this syndrome was subsequently found to be associated with the presence of more than 2 X chromosomes and more than 1 Y chromosome [6] and other types of sex chromosome abnormality have been reported [2, 7].

Patients with sex chromosome abnormality usually show gynecomastia, abnormality of external genitalia, reduced libido and azoospermia [3]. Endocrinologically, they show hypergonadotropic hypogonadism and have an abnormality in the hypothalamic-pituitary-gonadal axis [8]. In our case, too, testicular atrophy, elevation of plasma gonadotropins and reduction of plasma testosterone were seen. Impaired sexual function has been observed among male patients with end-stage renal disease [4]. Impotence, reduced libido, oligo- or azoospermia and gynecomastia are prevalent in these patients. Chronic renal insufficiency is characterized by an elevated level of plasma gonadotropins, an abnormally low level of plasma testosterone and an abnormality in the hypothalamic-pituitary-gonadal axis [5,9].

These findings suggest that male patients with sex chromosome abnormality and chronic renal failure have similar clinical and hormonal characteristics.

Testosterone replacement is widely applied to patients with sex chromosome abnormality. In male hypogonadism the administration of testosterone usually resulted in a sustained suppression of plasma gonadotropins within the normal range or slightly above [10]. However, patients with an abnormality have an altered pituitary response associated with a long period of hypersecretion of the pituitary gonadotropins. A failure of suppression of plasma gonadotropin levels by exogenous testosterone administration is occasionally observed [11]. In our case, the administration of testosterone did not suppress plasma gonadotropins. For early and adequate treatment of gonadal dysfunction in sex chromosome abnormality, we should bear in mind the possibility of the abnormality in male patients with chronic renal failure and it is advisable to perform chromosome analysis.

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Fig. 1. Chromosome analysis reveals a karyotype of 47, XXY (96.2%).

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Fig. 2. Chromosome analysis shows a karyotype of 46, XY (3.8%).

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