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LETTER TO THE EDITOR

A 47,XXY Female with Gender Identity Disorder

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According to DSM-IV-TR, gender identity disorder (GID) (also known as transsexualism) has two features: a strong and persistent cross-gender identification and persistent discomfort about one's assigned gender or a sense of inappropriateness in the role of that gender. It is reportedly a rare disorder, with prevalence rates between 1:12,000 and 1:40,000 in western countries (Landén, Wålinder, & Lundström, 1996). Though the etiology is largely unknown, genetic factors have been reported to play an important role, based on reports of twin concordance and families with several affected members (Green, 2000). Although chromosomal abnormalities have not been reported to occur at an increased rate in these patients, rare reports of chromosomal abnormalities in GID have been reported (Table 1).

Klinefelter's syndrome (KS) is the most common sex chromosome disorder and the second most common condition caused by the presence of extra chromosomes. The condition exists in roughly one out of every 1,000 males and is characterized by chromosomal abnormality in the form of 47,XXY karyotype with a male phenotype. Males with KS may have a mosaic 47,XXY/46,XY constitutional karyotype and varying degrees of spermatogenic failure. Mosaicism 47,XXY/46,XX with clinical features suggestive of Klinefelter syndrome is very rare. Thus far, only about 10 cases have been described in the literature (Velissariou et al., 2006).

Few reports of sex reversal in KS have been reported. Mutations in the *SRY* or *SOX* gene have been implicated in sex reversal (Cameron & Sinclair, 1997). As per our knowledge, so far there are only three reports of complete sex reversal in this syndrome searchable on PubMed (Rottger et al., 2000; Saavedra-Castillo, Cortés-Gutiérrez, Dávila-Rodríguez, Reyes-Martínez, & Oliveros-Rodríguez, 2005; Thangaraj, Gupta, Chakravarty, & Singh, 1998).

We present a rare case, probably the first of its kind, in which a XXY female presented to us with transsexualism.

X, a 24-year-old, single, graduate, employed female patient was referred to our department for psychiatric evaluation in view of her request for sex reassignment surgery. She introduced herself to us as a male. On psychiatric interview, she reported that, since her childhood, she had experienced sexual interest in girls, preferred dressing like a boy, played mainly with boys, would take the role of boys in games, and had been predominantly interested in masculine activities, such as playing football. She would find it difficult to use female restrooms and would often be teased by people around her. She could not understand what and who she was and, at times, would even consider herself a hermaphrodite. It was revealed that she had feelings of discomfort with her own gender, and the desire to be male since her childhood. Birth history revealed that she was a full term, normal vaginal delivery. Parents had no doubt regarding the anatomical sex of her and reared her like a female. There were no family conflicts or any difference in her rearing as compared to her other siblings. There was neither significant family history nor any history suggestive of mental subnormality or psychosis.

Menstrual history revealed that her first and only menstruation occurred at the age of 15–16 years. This was very scanty. She was started on hormonal therapy, but did not resume menstruation. She has homosexual contact with a female and was not guilty of the same.

The Gender Identity/Gender Dysphoria Questionnaire for Adolescents and Adults (Deogracias et al., 2007) was applied. It is a scale designed to assess gender identity (gender dysphoria)

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Table 1 Reports of chromosomal abnormalities in patients with gender identity disorder

Author and year	Chromosomal abnormality	Sex assigned at birth	Type of transsexual
Wagner (1974)	47XYY	Male	Male-to-female
Haberman et al. (1975)	47XYY	Male	Male-to-female along with schizophrenia
Buhrich et al. (1978)	2 cases with 47XYY	Male	Male-to-female
Snaith et al. (1991)	47XYY	Male	Male-to-female
Taneja et al. (1992)	47 XXY	Male	Male-to-female
Turan et al. (2000)	47XXX	Female	Female-to-male
Wylie and Steward (2008)	47XYY	Male	Male-to-female

dimensionally. It consists of 27 items, each rated on a 1–5 point scale, pertaining to gender identity and dysphoria. It captures a range of subjective, social, somatic, and sociological indicators of gender dysphoria that can be answered in parallel form by both males and females. The scale revealed a score of 2.00, indicating marked dysphoria for one's gender. Given all these symptoms, she was diagnosed as having gender identity disorder, according to DSM-IV-TR.

Upon physical examination, she was 165 cm in height and 58 kg in weight. She was dressed in a shirt and a pair of trousers. Her hair was cut and combed like a man. In gynecological consultation, she had small breasts. Vagina was small while the clitoris was enlarged. Her hymen was intact. In laboratory examinations, routine hematological investigations were within normal limits. Her endocrinological profile (including Thyroid function test, testosterone, progesterone, prolactin, LH, FSH, and estradiol) was within normal limits. Pelvic ultrasound test showed normal female internal organs (uterus $74 \times 32 \times 50$ mm and bilateral ovaries $\sim 40 \times 22$ mm).

Her karyotyping was done, which revealed a 47,XXY karyotype. The patient did not consent for subsequent genetic tests, which is a main limitation of our report. However, exploration of the abdomen was done, revealing presence of normal fallopian tubes, uterus, and ovaries. A search for testes was made but none were found. Biopsy of ovary also ruled out presence of ovotestes. The patient was subsequently counseled and referred back to the surgery department. The patient was then lost to our follow up.

Initially, KS was identified in males with gynecomastia, small testes, and infertility. Jacobs and Strong (1959) reported these men to have an extra X sex chromosome resulting in a genotype of 47,XXY. Although the 47,XXY aneuploidy is the most common sex chromosome disorder, the 47,XXY mosaics have been infrequently reported in the literature. Thus, phenotypically KS is a male but there are a few cases with genital anomaly. This may range from complete sex reversal to presence of minor genital anomalies. These have generally been associated with complete or partial androgen insensitivity syndrome or testicular feminization (Lee, Cheng, Ahmed, Shaw, & Hughes, 2007). Complete sex reversal is rare in the syndrome.

Our case is another instance of complete sex reversal in KS. Further study regarding the presence of specific genes responsible for sex determination was not done, as the patient was not willing to do this. This is a major limitation of our report.

There have hitherto been no recorded examples of XXY with female-to-male transsexualism. In rare cases, transsexualism and sexual chromosomal multiplicity coexist. One may speculate that there may be a causative relation between 47, XXY karyotype and gender dysphoria. Among the various theories proposed for gender dysphoria, presence of chromosomal abnormalities is one of them. Genetic factors and hormones are current issues for future research in this field. Our case probably also had partial androgenization, though her endocinological profile was within normal limits. Both the chromosomal abnormality and the partial androgenization could have played role in the etiopathogenesis of GID in our case. Case reports of such atypical cases may contribute to the formulation of hypotheses for future scientific investigations. There is a dire need of more studies on genetics of patients with GID to better understand the etiology of this complex disorder and help in the proper evaluation and management of such patients.

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