Female-to-Male Transsexual with 47,XXX Karyotype

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Background: There are few reports describing chromosomal abnormalities in transsexuals. In rare cases, transsexualism and sexual chromosomal multiplicity coexist. Six cases of male-to-female transsexuals with 47,XXY chromosomal pattern have been previously reported. We have not encountered any female transsexual cases with 47,XXX karyotype in the literature.

Methods: A 21-year-old female patient came to our outpatient department with depressive symptoms and suicidal thoughts. On psychiatric interview, she reported that she had feelings of discomfort with her gender identity and had desired to be male since her childhood. Then, we performed cytogenetic investigation using blood culture and G chromosome banding.

Results: Histology and DNA histograms of the patient revealed a chromosomal pattern of 47,XXX.

Conclusions: We conclude that sexual chromosomal abnormalities in some transsexuals may cause a vulnerability to development of a gender identity disorder.

Key Words: Transsexualism, sex chromosomal abnormality, gender identity disorder

Introduction

According to DSM-IV, gender identity disorder has two features: strong and persistent cross-gender identification and persistent discomfort about the patient’s assigned gender or a sense of inappropriateness in the role of that gender (American Psychiatric Association 1994). This disorder is manifested by cross-dressing and a search for hormonal and surgical reassignment of anatomic sex.

Chromosomal studies have shown that most transsexuals have no apparent abnormalities (Futterweit et al 1986). There are a few reports that have found chromosome abnormality in transsexuals. To our knowledge, six cases of male-to-female transsexuals with 47,XXY chromosome pattern were reported previously (Buhrich et al 1978; Haberman et al 1975; Snaith et al 1991; Taneja et al 1992; Wagner 1974); we did not find any female transsexual case with 47,XXX karyotype.

Case Report

SA, a 21-year-old, single, high school graduate, unemployed, female patient came to our outpatient clinic with depressive symptoms and suicidal thoughts. 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, and had predominantly been interested in masculine activities, such as playing football. It was revealed that she had feelings of discomfort with her own gender, and the desire to be male since her childhood. At the time of interview, she reported symptoms of depression, such as depressive mood, hopelessness, diminished interest in daily activities, insomnia, and suicidal thoughts. She stated that she had attempted suicide three times recently. She had some impulsive behaviors, such as self-injury and assaultiveness. She had a girlfriend, but their relationship was not stable. She had had a homosexual intimacy with her girlfriend once. She did not feel guilty. She wanted to have a sex-change operation, but she could not afford it. She did not receive any hormonal therapy.

Upon physical examination, she was 174 cm in height and 68 kg in weight. She had a muscular body in structure. In gynecological consultation, she was found to have normal female internal organs. Hormonal assays showed that estrogen and androgen levels were normal (estradiol: 245.73 pg/mL, normal: 55–256 pg/mL in luteal phase; total testosterone: 43 ng/dL, normal: 10–80 ng/dL). Her electroencephalogram was normal. Intelligence quotient test showed borderline intellectual functioning (IQ: 83). The Minnesota Multiphasic Personality Inventory revealed borderline personality features and refusing the female role. Her Hamilton depression score was 16, which
indicated moderate depression. Given all these symptoms, she was diagnosed as having gender identity disorder (transsexualism), according to DSM-IV (American Psychiatric Association 1994).

Cytogenetic investigation using blood culture and G chromosome banding revealed 47,XXX karyotype (Figure 1). All metaphases were found to have the same pattern. No mosaicism was detected.

We obtained the patient’s permission to participate in the laboratory procedures and informed consent for publishing. We guaranteed the confidentiality of the patient’s identity.

Discussion

The 47,XXX karyotype occurs in about 1 in every 1200 female newborns. Molecular studies revealed that 93.5% of the cases resulted from material nondisjunction with increasing maternal age being present in meiosis I (Robinson and de la Chapelle 1997).

47,XXX women have no specific phenotype as newborns or later. They have a higher than normal incidence of minor anomalies, such as epicanthic folds, ear anomalies, and clinodactyly. They are often retarded in their neuromotor development, and their mean IQ is 85 (Robinson and de la Chapelle 1997). In our case, there was no minor physical abnormality, and her IQ was 83.

There have hitherto been no recorded incidences of triple X with female-to-male transsexualism. Thus far, six cases of male-to-female transsexualism with a 47,XYY karyotype have been reported in the literature (Buhrich et al 1978; Haberman et al 1975; Snaith et al 1991; Taneja et al 1992; Wagner 1974). We do not routinely perform cytogenetic examinations in patients with gender identity disorder; but in our case, because she was physically unusual (e.g., she was taller than the mean height for the female Turkish population, and more muscular than usual), we referred her to the genetics department for cytogenetic investigation.

In rare cases, transsexualism and sexual chromosomal multiplicity coexist. One may speculate that there may be a causative relation between 47,XXX karyotype and gender dysphoria. It is pointed out that sexual differentiation of the brain occurs under the control of the gonadal steroid hormones at a later stage in fetal development than does the differentiation of the genitals. In transsexuals, a divergence might have developed between prenatal gonadal/genital sexual differentiation and subsequent sexual brain differentiation (Gooren 1990). It can be speculated that in the present case and other transsexual cases reported in previous studies, presence of the chromosomal abnormalities may lead to alterations at the gonadal hormonal levels in prenatal/perinatal period, and as a result, may affect the sexual brain differentiation. Thus, chromosomal abnormality may cause a vulnerability to disorder; but we have insufficient data to make such a conclusion.

In conclusion, although transsexuals usually have a normal chromosomal pattern, in some cases, sexual chromosomal abnormalities coexist with gender identity disorder. Because the 47,XXX karyotype occurs in approximately 1 in every 1200 female newborns, this present case may only represent a random association between 47,XXX karyotype and transsexualism; however, case reports of such atypical cases may contribute to the formulation of hypotheses for future scientific investigations. Controlled studies of sufficient numbers of cases will be necessary to definitively understand causal variables involved in the etiology of transsexualism.

References


