CASE REPORT

Klinefelter's syndrome with unilateral absence of vas deferens

Numan Baydilli, M.D.,[a] *Ahmet Gökçe, M.D.,*[a] *Sevda Yesim Karabulut, M.D.,*[b] *and Oguz Ekmekcioglu, M.D.*[a]

[a] Department of Urology; and [b] Department of Medical Genetics, Erciyes University Medical Faculty, Kayseri, Turkey

Objective: To report a case of Klinefelter's syndrome with unilateral absence of vas deferens.
Design: Case report.
Setting: Tertiary-care infertility clinic.
Patient(s): A 28-year-old man with the complaint of infertility.
Intervention(s): None.
Main Outcome Measure(s): Physical examination, genetic and hormonal evaluation.
Result(s): Both testicles were approximately 2 mm, and unilateral vas deferens was not palpable. Hormonal evaluation revealed hypergonadotropism, and genetic studies revealed a 47,XXY karyotype and delta F508 mutation of the cystic fibrosis gene.
Conclusion(s): To our knowledge there are no previous reports of both conditions (Klinefelter's syndrome and unilateral absence of vas deferens) existing simultaneously. A detailed physical examination seems mandatory for patients seeking treatment for infertility, to determine any possible deleterious health-related condition(s) for both themselves and offspring. (Fertil Steril® 2010;94:1529.e1–e2. ©2010 by American Society for Reproductive Medicine.)

Key Words: Klinefelter's syndrome, vas deferens, agenesia, cystic fibrosis

Klinefelter's syndrome is the most common known genetic cause of azoospermia among men. Klinefelter's syndrome is characterized by X chromosome polysomy, with X disomy being the most common variant (47,XXY). Ninety percent of men with Klinefelter's syndrome have nonmosaic X chromosome polysomy (1). Internal or external genital abnormality is rare in Klinefelter's syndrome. Leiba et al. (2) first reported a case of mosaic Klinefelter's syndrome with bilateral absence of the vas deferens. Thereafter one case of nonmosaic Klinefelter's syndome with bilateral absence of vas deferens was reported, by Fuse et al. (3). Here we report the first case of 47,XXY Klinefelter's syndrome with unilateral absence of vas deferens and with heterozygous mutation in the *CFTR* (cystic fibrosis transmembrane conductance regulator) gene.

CASE REPORT

A 28-year-old man presented to our clinic with the complaint of infertility. On physical examination, left vas deferens was not palpable, and both testicles were approximately 2 mm. He had pubic hair of male type. He was 177 cm tall and weighed 59 kg. There was no gynecomasty. Hematologic test results were within normal range. The LH, FSH, and total T levels in the blood were 26.1 mIU/mL, 50.1 mIU/mL, and 574 ng/dL, respectively. Semen analyses showed pellet-negative azoospermia with low ejaculate volume (0.5 and 0.6 mL). On transrectal ultrasonographic evaluation, left seminal vesicula could not be seen. His kidneys were present with normal localization and size on abdominal ultrasound evaluation. Cytogenetic analysis showed a 47,XXY karyotype (Fig. 1), and on *CFTR* gene mutation analysis he had heterozygous delta F508 mutation. There were no *AZF* gene deletions on the Y chromosome. His wife was his first-degree cousin, but she had no *CFTR* gene mutation.

DISCUSSION

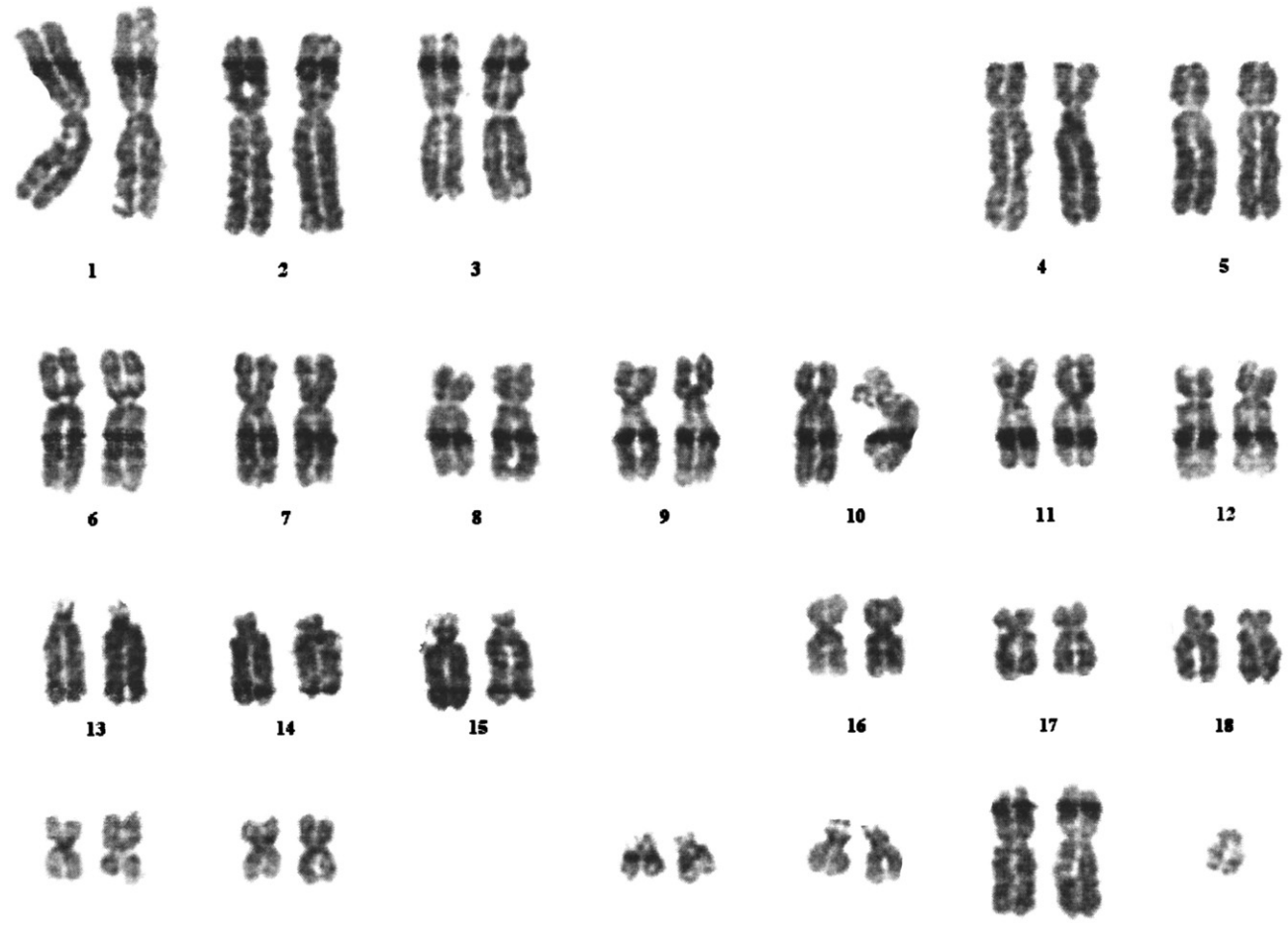
The prevalence of XXYs has risen from 1.09 to 1.72 per 1,000 male births (4). Cystic fibrosis (CF) is a fatal autosomal recessive exocrinopathy that affects approximately 1 in 2,000 individuals in Caucasian populations (5). Congenital absence of the vas deferens (CBAVD) is a genital form of CF that is responsible for 2%–6% of male infertility (6). The incidence of CF varies in different populations; therefore, the incidence of CBAVD will also vary in different populations. Generalized Wolffian duct anomalies, unrelated to *CFTR* gene mutations, can also result in CBAVD. These patients constitute 10% of men with CBAVD (7).

Patients with congenital unilateral absence of the vas deferens (CUAVD) represent another male infertility phenotype associated with *CFTR* mutations (8). The incidence of CUAVD can not be known exactly because these patients have the chance of spontaneous conception.

Received January 17, 2010; revised February 2, 2010; accepted February 4, 2010; published online March 21, 2010.
N.B. has nothing to disclose. A.G. has nothing to disclose. S.Y.K. has nothing to disclose. O.E. has nothing to disclose.
Reprint requests: Ahmet Gökçe, M.D., Department of Urology, Erciyes University Medical Faculty, 38060 Kayseri, Turkey (FAX: 90-352-437-76-13; E-mail: aagokce@yahoo.com).

FIGURE 1

Chromosome analysis of patient (47,XXY).



Baydilli. Klinefelter's syndrome and unilateral vasal agenesia. Fertil Steril 2010.

Infertility is not only the inability to have a child but also might be a health issue, as seen in our case. A physician dealing with infertility must be suspicious for every possible condition that might interfere with both the patient's fertility and general health status. Presently it is possible for a 47,XXY male to have children. In the case presented here, the presence of consanguinity with his wife and a *CFTR* gene mutation might result in a baby with a higher chance of having the same or a worse defect. The couple must be informed adequately. Fortunately the woman did not have the same mutation in the detected regions.

Renal ultrasound should be performed on all men with CBAVD and CUAVD to evaluate for renal abnormalities, findings that have implications for the likelihood of associated *CFTR* mutations (9).

In conclusion, a detailed physical examination seems mandatory for the patients seeking treatment for infertility, to determine any possible deleterious health-related condition(s) for both themselves and offspring.

REFERENCES

1. Lanfranco F, Kamischke A, Zitzmann M, Nieschlag E. Klinefelter's syndrome. Lancet 2004;364:273–83.
2. Leiba S, Ber A, Joshua H, Lazebnik J, Ben-Bassat M. A case of XY-XXY mosaicism and bilateral absence of the vas deferens. Acta Endocrinol (Copenh) 1969;62:498–504.
3. Fuse H, Shiseki Y, Shimazaki J, Katayama T. A case of Klinefelter's syndrome with bilateral absence of the vas deferens. Urol Int 1990;45:181–2.
4. Herlihy AS, Halliday J. Is paternal age playing a role in the changing prevalence of Klinefelter syndrome? Eur J Hum Genet 2008;16:1173–4.
5. Dörk T, Dworniczak B, Aulehla-Scholz C, Wieczorek D, Böhm I, Mayerova A, et al. Distinct spectrum of CFTR gene mutations in congenital absence of vas deferens. Hum Genet 1997;100:365–77.
6. Radpour R, Gourabi H, Dizaj AV, Holzgreve W, Zhong XY. Genetic investigations of CFTR mutations in congenital absence of vas deferens, uterus, and vagina as a cause of infertility. J Androl 2008;29:506–13.
7. McCallum T, Milunsky J, Munarriz R, Carson R, Sadeghi-Nejad H, Oates R. Unilateral renal agenesis associated with congenital bilateral absence of the vas deferens: phenotypic findings and genetic considerations. Hum Reprod 2001;16:282–8.
8. Mickle J, Milunsky A, Amos JA, Oates RD. Congenital unilateral absence of the vas deferens: a heterogeneous disorder with two distinct subpopulations based upon aetiology and mutational status of the cystic fibrosis gene. Hum Reprod 1995;10:1728–35.
9. Walsh TJ, Pera RR, Turek PJ. The genetics of male infertility. Semin Reprod Med 2009;27:124–36.