Patient report

Elif Ozsu, Gul Yesiltepe Mutlu*, Filiz M. Cizmecioglu, Gulsen Ekingen, Bahar Muezzinoglu and Sukru Hatun

Ovotesticular disorder of sexual development and a rare 46,XX/47,XXY karyotype

Abstract: Ovotesticular disorder of sexual development (DSD) is characterized by the presence of both ovarian and testicular tissues in the same individual. The most common karyotype is 46,XX. Here, we report the case of a boy with a 46,XX/47,XXY karyotype diagnosed as ovotesticular DSD by gonadal biopsy. A 5-month-old boy presented with hypospadias, unilateral cryptorchidism, and a micropenis. Pelvic magnetic resonance imaging revealed a suspicious gonad tissue that is solid in structure in the right scrotum and a suspicious gonad that is cystic in structure in the left inguinal canal. He underwent a diagnostic laparoscopy. Cytogenetic analysis of peripheral blood revealed a 46,XX/47,XXY karyotype. Histopathologic examination of the left gonad showed ovarian tissue containing primordial follicles with ipsilateral undifferentiated tuba uterina. The right gonad showed immature testis tissue. He underwent left gonadectomy and hypospadias repair, and was raised as a male. Through this rare case, we highlight the importance of histological and cytogenetic investigation in DSD.

Keywords: biomarker; calprotectin; feces; inflammatory bowel disease; point-of-care test.

Introduction

Ovotesticular disorder of sexual development (DSD) is characterized by the presence of both ovarian and testicular tissues in the same individual. Diagnosis can only be established by histologic examination of the gonads. The most common karyotype is 46,XX (1). To our knowledge, there are only four cases of ovotesticular DSD with Klinefelter’s syndrome mosaic karyotype reported in the literature. Here, we report the case of a 5-month-old boy with a 46,XX/47,XXY karyotype diagnosed as ovotesticular DSD by gonadal biopsy.

Patient and methods

A 5-month-old boy presented with hypospadias, unilateral cryptorchidism, and a micropenis. Pelvic ultrasound revealed left inguinal hernia, and the left testis could not be visualized. Pelvic magnetic resonance imaging (MRI) showed a suspicious gonad tissue, solid in structure, in the right scrotum and a suspicious gonad, cystic in structure, in the left inguinal canal. He underwent a diagnostic laparoscopy. Cytogenetic analysis of peripheral blood revealed a 46,XX/47,XXY karyotype. Histopathologic examination of the left gonad showed ovarian tissue containing primordial follicles with ipsilateral undifferentiated tuba uterina. The right gonad showed immature testis tissue. He underwent left gonadectomy and hypospadias repair, and was raised as a male. Through this rare case, we highlight the importance of histological and cytogenetic investigation in DSD.

Keywords: biomarker; calprotectin; feces; inflammatory bowel disease; point-of-care test.

*Corresponding author: Gul Yesiltpe Mutlu, Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics, Medical School, Kocaeli University, Kocaeli, Turkey, E-mail: gulyesiltpe@gmail.com

Elif Ozsu, Filiz M. Cizmecioglu and Sukru Hatun: Division of Pediatric Endocrinology and Diabetes, Department of Pediatrics, Medical School, Kocaeli University, Kocaeli, Turkey

Gulsen Ekingen: Department of Pediatric Surgery, Medical School, Kocaeli University, Kocaeli, Turkey

Bahar Muezzinoglu: Department of Pathology, Medical School, Kocaeli University, Kocaeli, Turkey
and his sitting height/height ratio and arm-height difference were normal. He had a bifid scrotum and a micro-penis (the stretched penile length was 3.5 cm), his right testis was palpable in the scrotum, and a 3 mL external urethral meatus was at the tip of the penis (his external genitalia is shown in Figure 2). He had normal intelligence and no typical features of Klinefelter’s syndrome. His laboratory findings are shown in Table 1. Pelvic MRI showed a tubular formation resembling a vagina. Scrotal ultrasound revealed microlithiasis and epididymal cyst in the right testis. He is being followed up owing to the risk of malignancy and will begin sex steroid replacement therapy in puberty.

Discussion

Ovotesticular DSD is a type of sexual disorder that can be diagnosed by histopathological methods, showing the presence of both ovarian tissue with follicles and testicular tissue with seminiferous tubules in the same individual (1). Ovotesticular DSD constitutes 3%–10% of all sexual disorders. Commonly, the patients present with ambiguous genitalia in the neonatal period; however, it is well known that ovotesticular DSD may have a large spectrum ranging from a complete female phenotype to a complete male phenotype. Both Wolffian and Mullerian structures can exist depending on the maturity of the testicular tissue (2). In patients who have a male phenotype, micropenis, scrotal hypoplasia, cryptorchidism, hypospadias, and labioscrotal fusion may be observed. A complete male phenotype was rarely reported, such that only 10% of the all ovotesticular DSD cases reported had complete or near-complete male external genitalia (3). Kanaka-Gantenbein et al. (4) reported a case of ovotesticular DSD in which the patient had a complete male phenotype and presented with scrotal hemorrhage due to corpus luteum rupture. In a case series, six patients with ambiguous genitalia, one patient with cliteromegaly, and one patient with hypospadias were reported by Yordam et al. (5). As in the cases reported in the literature, our patient did not have a complete male phenotype, although his external genitalia had an incompletely masculinized appearance with a bifid scrotum and unilateral cryptorchidism.

The histological types of the gonads are highly variable in ovotesticular DSD. Krob et al. (6) examined the histopathological structures of the gonads in 283 ovotesticular DSD cases. They found that the most common gonad type was ovotestis (44%), followed by ovary (21%) and testis (12.5%). Testicular tissue was often seen at the right side and the ovarian tissue was observed to be left sided. Despite the more functional ovarian structures, the testes were immature and spermatogenesis was insufficient. Furthermore, 21 pregnancies were reported versus only one fertile man. Our patient had a
gonad with an ovarian structure containing primordial follicles at the left side and a gonad with immature testicular structure at the right side. Nevertheless, the sufficient testosterone result in the classic human chorionic gonadotropin (hCG) test and the normal level of anti-Mullerian hormone suggested a more functional testis tissue than expected. Therefore, we planned to protect the testis by means of watchful waiting in terms of malignancy. Although ovotesticular DSD is a sexual disorder with low malignancy risk, careful follow-up is recommended owing to the risk of malignancy in patients with preserved gonads (7).

A testis was observed in the labioscrotum and an ovary was observed in the lower part of the inguinal canal in our patient. He also had vaginal tissue, which is commonly reported in ovotesticular DSD. The position of the ovary was a rare finding but the finding of testicular tissue in the scrotum is relatively common. In a large series consisting of 111 cases, only 2% of the gonads located in the inguinal canal were ovaries. In the same study, it was shown that 15% of the gonads that were located in the scrotum were testis (8).

The most common genotype in ovotesticular DSD cases is 46,XX (70%) followed by 46,XX/46,XY mosaicism (20%) and 46,XY (7%). True hermaphroditism occurs with sex chromosome mosaicism, chimerism, Y-X chromosomal translocations, and mutations of the sexual genes (6). A case of true hermaphroditism was first reported in 1967 and showed typical Klinefelter’s syndrome characteristics (9). Thereafter, Barta et al. (10) reported an ovotesticular DSD case with a 46XY/46XX/47XXY mosaicism in 1976; however, there was no genotype-phenotype correlation in this case. Isguven et al. (11) also reported a patient with both Klinefelter’s syndrome and true hermaphroditism who was admitted with cyclic hematuria and gynecomastia and had a 46,XX /47,XXY karyotype. The peripheral blood karyotype (30 metaphases) of our patient was 46,XX (20)/47,XY; however, the cytogenetic analysis of both of the two gonad materials revealed a 45,X/46,XX/47,XXY mosaicism. Despite the rare Klinefelter’s syndrome mosaicism in his karyotype, he had no clinical findings suggesting Klinefelter’s syndrome. To our knowledge, this is the fifth case in the literature of ovotesticular DSD in which the patient has the Klinefelter mosaic karyotype; furthermore, it is the first ovotesticular DSD case in the literature in which the patient had gonads with the 45,X/46,XX/47,XXY karyotype.

Conclusion

Although the most common genotype in ovotesticular DSD is 46,XX, Klinefelter’s mosaic karyotype is rarely seen. By this rare case, we highlight the importance of histological and cytogenetic investigations in DSD.

Received December 4, 2012; accepted March 7, 2013

References