Case Report

Ovotesticular Disorder of Sexual Development with Rare Karyotype

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ABSTRACT

Ovotesticular disorder of sexual development (OT-DSD) is a rare disorder of sexual differentiation. It is associated with variable genotype of which the most common karyotype is 46,XX. A 2 year-old boy presented with severe penoscrotal hypospadias and unilateral right side cryptorchidism. The right gonad was atrophic , present in the right inguinal region and showed presence of ovarian tissue with mature ovarian follicles and testicular tissue with distinct seminiferous tubules in the same gonad (ovotestis) on histopathology and a 45,XO/46,XY karyotype.

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Introduction

Ovotesticular disorder of sexual development (OT-DSD) is a rare disorder of sexual differentiation . It is characterized by the presence of ovarian tissue with mature ovarian follicles and testicular tissue with distinct seminiferous tubules in the same gonad (ovotestis).[1] It constitutes 3% – 10% of all sexual disorders. Both Wolffian and Mullerian duct derivatives are seen, and most affected individuals commonly present with ambiguous external genitalia as neonates or infants.[2] In individuals with OT-DSD, the ovotestis is the most common histological gonad type. There is an increased risk of developing germ cell tumor is the gonads of such individuals.[3,4,5] OT-DSD is also associated with variable genotype of which the most common karyotype is 46,XX. [1]

Case Report

A 2 year-old boy presented with severe penoscrotal hypospadias .Physical examination revealed unilateral right side cryptorchidism with left gonad palpable in left hemi scrotum and normal in size. No other physical abnormality was noted.

Ultrasound examination showed a heterogenous ovoid structure present in the right inguinal region. Left gonad had homogenous echotexture .Pelvic ultrasound examination showed no evidence of a uterus or ovaries. The testosterone levels were measured both were in the normal range (3-10ng/ml). Cytogenetic analysis performed on peripheral blood lymphocytes revealed a 45,XO/46,XY karyotype.

Right sided gonadectomy and hypospadias repair was performed. The right gonad was submitted along for histopathological evaluation.

Histopathological findings: Gross examination revealed a tubular grey white structure measuring 3.5x1x0.5 cms. Histopathologic examination of the right gonad showed the ovarian and testicular tissue. Ovarian tissue consisted of ovarian stroma with primordial follicles along with ipsilateral fallopian tubal lumen and endometrial stromal tissue. The testicular tissue consisted of numerous solid seminiferous tubules filled with immature sertoli cells and a few primitive germ cells. The immature sertoli cells had a regular, round to ovoid nucleus with inconspicuous nucleoli. The germ cells were found adjacent to the basement membrane and those were distinguishable from the immature sertoli cells because of their larger nuclei and abundant cytoplasm. Also identified was vas deferens. A histopathological diagnosis of ovotestis was given.

Discussion

Ovotesticular disorder of sexual differentiation formerly known as true hermaphroditism (TH) is the rarest form of intersexuality and the term is applied to an individual who has both well-developed ovarian and testicular tissues[6] .It accounts for less than ten percent of intersex patients.[7]. Krob et al examined the histopathological structures of the gonads in 283ovotesticular DSD cases and found that the most common gonad type was ovotestis (44.4%), followed by ovary (21%) and testis (12.5%).[5]

Ovotestes are usually compartmentalized, with connective tissue separating the ovarian components from the testicular components. However, on rare occasions, an intermixture of these elements may occur.Testicular tissue in OT-DSD is defined by the presence of immature seminiferous tubules lined by immature sertoli cells and primitive germ cells, and ovarian tissue is defined by the presence of numerous primordial and/or maturing follicles within the ovarian stroma.[6]

Various types of chromosomal abnormalities have been described in OT-DSD with ovotestis such as 46, XX; 46, XY; 46, XX/46, XY, 45, X/46, XY.[5] This diagnostic nomenclature is applied regardless of the peripheral karyotype. 45XO/XY is a very rare genotype as reported in the present case to be associated with ovotestis .The clinical phenotype associated with 45, X/46,XY mosaicism is broad, ranging from women, with or without Turner syndrome stigmata, to apparently normal males, with intervening variable ambiguous phenotypes[8]. Gonad histology associated with 45, X/46,XY mosaicism is also variable with partial, complete, mixed, or asymmetric gonadal dysgenesis showing streak gonads.[9]

In patients with ovotesticular DSD,the rate of occurrence of neoplasia is estimated at 2.6% [4] However some studies estimate that the risk of germ cell tumor development in OT-DSD ranges from 4% among those with the 46,XX karyotype to up to 10% in those with 46,XY and 46,XX/XY chimerism .[10] The removal of the opposite gonad from the assigned gender and a biopsy of remaining gonadal tissue for histological evaluation may be appropriate.[6]

Ovotesticular disorder also needs to be differentiated from mixed gonadal dysgenesis (MGD) with which it may show histological and genotypic overlapping.MGD has varying degree of histological presentations such as streak testis,streak ovaries but unlike OT-DSD maturing primordial follicles are not identified in gonads of MGD [6]. Also various structural and systemic anomalies which need early medical attention are seen in patients of MGD unlike OT-DSD. MGD carries a high risk of tumor development at 12% and possibly at more than 30% if gonadectomy had not been performed. In patients with mosaic karyotype

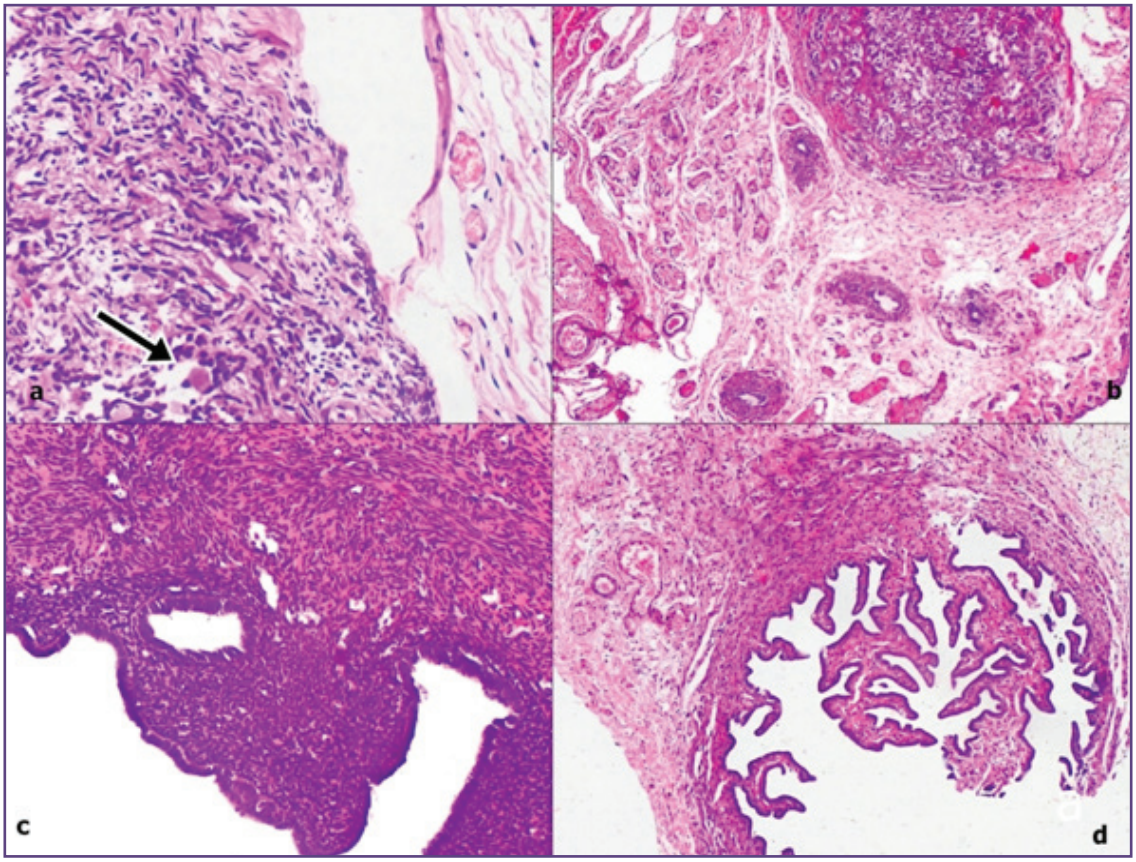

Fig. 1. (a). Ovarian tissue identified in the gonad revealed characteristic ovarian stroma and the presence of scattered primordial follicles (H&E ×40). (b). Numerous solid seminiferous tubules filled with immature sertoli cells and a few primitive germ cells along with rudimentary epididymis (H&E ×20). (c). Endometrium and myometrium from the uterine part of gonad (H&E ×20). (d). Fallopian tube (H&E ×40).

the prevalence ranges between 15 and 40%. [4] Bilateral gonadectomy is recommended in all individuals with MGD containing Y-chromosome material.[11] In the present case no such abnormalities were present supporting the histological diagnosis OT-DSD.

Conclusion

The most common genotype associated with ovotesticular DSD is 46,XX . 45,XO/46XY mosaic karyotype is rarely seen with it. This case highlights the importance of histological finding in ovotesticular disorder of sexual development as clinical features, cytogenetic results, hormonal profiles do not appear to be useful in a differentiating it from mixed gonadal dysgenesis.

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Competing Interests

None

Refrences

1. Sperling MA, editor. Pediatric endocrinology, 3rd ed.Philadelphia: WB Saunders; 2008:138.
2. Hughes IA, Houk C, Ahmed SF, Lee PA; Lawson Wilkins Pediatric Endocrine Society/European Society for Paediatric Endocrinology Consensus Group. Consensus statement on management of intersex disorders. J Pediatr Urol .2006;2:148 – 62.
3. Bhansali A, Mahadevan S, Singh R, Rao KL et al. True hermaphroditism: clinical profile and management of six patients from North India. J Obstet Gynaecol . 2006;26:348–50.
4. Pleskacova J, Hersmus R, Oosterhuis JW, Setyawati BA,*et al.* Tumor risk in disorders of sex development. Sex Dev. 2010;4:259–69.

5. Krob G, Braun A, Kuhnle U. True hermaphroditism: geographical distribution, clinical findings, chromosomes and gonadal histology. Eur J Pediatr .1994;153:2– 10.
6. K.-R. Kim et al.Hermaphroditism and Gonadal Dysgenesis.Mod Pathol. 2002;15:1013-9.
7. Damiani D, Fellous M, McElreavey K, Barbaux S et al. True hermaphroditism: clinical aspects and molecular studies in 16 cases. Eur J Endocrinol. 1997;136(2):201-4.
8. Moussaif NE, Haddad NE, Iraqi N, Gaouzi A. 45,X/46,XY mosaicisme: report of five cases and clinical review. Annales d'Endocrinologie. 2011 ;72: 239–243.
9. Ocal M. Berberoglu Z. Siklar et al. The clinical and genetic heterogeneity of mixed gonadal dysgenesis: does "disorders of sexual development (DSD)" classification based on new Chicago consensus cover all sex chromosome DSD? Eur J Pediatric .2012;171:1497–1502.
10. Wettasinghe K, Sirisena N, Andraweera P, Jayasekara R et al. A Case Series of Five Sri Lankan Patients with Ovotesticular Disorder of Sex Development. Clin Pediatr Endocrinol. 2012 ; 21(4): 69–73.
11. Hughes IA, Houk C, Ahmed SF, Lee PA. Consensus statement on management of intersex disorders. Arch Dis Child .2006;91: 554–63.