Gonadoblastoma and Papillary Tubal Hyperplasia in Ovotesticular Syndrome

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Background

Ovotesticular disorder of sexual development (DSD), formerly known as *true hermaphroditism*, is a rare form of DSD in which both testicular and ovarian tissues are present in the same individual either in a single gonad (ovotestis) or in opposite gonads with a testis and an ovary on each side. The diagnosis of ovotesticular DSD is based solely on the presence of ovarian and testicular tissue in the gonad and not on the characteristics of the internal and external genitalia, even if ambiguous.

Objective and Hypotheses

To discuss rare cases of ovotesticular DSD and one of the novel findings of these cases. Papillary tubal hyperplasia may be predictive of gonadal malignancy in ovotesticular disease.

Method & Subjects

Case 1 is the first child of unrelated parents and was referred on the third day after birth due to ambigious genitalia. Upon physical examination, the patient had ambiguous genital including a phallus with a length of 2.3 cm, bifid labioscrotal folds, incomplete labioscrotal fusion, ventral opening of the urethra, chordea, and non-palpable gonads. Case 2 was a 15-year-old female presented with lack of pubertal development and primary amenorrhea. Physical examination revealed short stature (-2.1 SDS), Tanner stage I breast development, normal female external genitalia phenotype.

Results

Hormonal investigations of case 1 excluded congenital adrenal hyperplasia, leydig hypoplasia, 5a-reductase deficiency and androgen insensitivity syndrome. Chromosomal analysis and fluorescence in situ hybridisation (FISH) of SRY revealed a SRY-positive 46,XX. Laparoscopic examination of case 1 revealed Mullerian remnants. Histopathological examination of bilateral gonadal biopsies showed ovotestes. Karyotype analysis and FISH of SRY of case 2 showed an SRY (+) 46,XY karyotype. Laparoscopic examination of case 2 revealed rudimentary Müllerian structures. Histopathological examination of bilateral gonadal biopsies showed ovotestes, gonadoblastoma and papillary tubal hyperplasia.

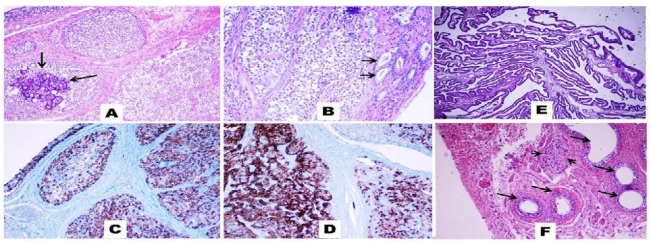

Figure 1: Histological examination of gonadoblastoma with superimposed dysgerminoma in the left gonad (A-D) and streak right gonad (E, F). (A) A focus calcification (arrows) lies in a dysgerminoma nest and tumour nests were encapsulated by immature granulose/Sertoli cells (middle upper) and were progressing to gonadoblastoma (H&E × 200). (B) Sertoli cells (arrows) and dysgerminoma nests progressing to gonadoblastoma (H&E × 400). Immunohistochemically, dysgerminoma cells showed reactivity with placental alkaline phosphatase (PLAP) (PLAP × 400) (C) and c-kit (CD117) (CD117 × 400) (D). (E) The right streak gonad showed polypoid and *papillary hyperplasia* of the *tubular* epithelium. Multiple small papillae floating in the tubal lumen (H&E × 200). (F) Leydig cell remnants (arrowheads) and epididymis (arrows) (H&E × 200).

Conclusion

Laparoscopic examination and gonadal biopsy for histopathological diagnosis remain the cornerstones for a diagnosis of ovotesticular DSD. Moreover, SRY positivity in a 46,XX patient, a 46,XY karyotype, an intra-abdominal gonad, and the age of patient at the time of diagnosis are predictive risk factors for the development of gonadoblastoma and/or dysgerminoma in ovotesticular DSD.