Identification of a de novo mutation in the SRY gene in a 46,XY complete gonadal dysgenesis patient with gonadal neoplasia and review of tumor risk in 46,XY DSD patients

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- **Objective** To determine the mutation in the SRY gene in a 46,XY complete gonadal dysgenesis patient with bilateral gonadoblastoma and coexisting dysgerminoma. Evaluate the functional consequence of mutated SRY gene in the tumor risk of 46,XY DSD.
- **Methods and Materials** The proband was a 13-year-old girl who was admitted for examination due to undeveloped secondary sexual characteristics. She had no breast development, menarche, pubic hairs and axillary hairs. Blood samples from the family members were obtained for genetic testing and karyotyping. 99 patients with a diagnosis of 46,XY DSD from November 1990 to April 2018 to assess the histopathological type and tumor risk of 46,XY DSD patients with SRY gene mutations were summarized.
- **Results** A de novo mutation (c.36dupC/p.13AsnfsGln) in SRY gene in this patient was identified. Through analyzing the recordings of 99 investigated 46,XY DSD patients with SRY gene muations, a total of 25 46,XY DSD patients (including the patient reported here) with gonadal tumor and SRY gene mutations were identified. And 21 cases were diagnosed as 46,XY complete gonadal dysgenesis (CGD, or Sywer Syndrome) retrospectively, 3 cases had gonadal dysgenesis, and one had gonadal dysgenesis with testicular gonadal syndrome (TDS). The gonadal neoplasia in our patients included gonadoblastoma, dysgerminoma, yolk-sac tumor. All patients who had undergone bilateral gonadectomy as reported were summarized. The total incidence of tumor was 25.25% (25/99) and the malignant rate was 12.12% (12/99). In 25 cases with gonadal tumor, gonadoblastoma (20 cases) and dysgerminoma (12 cases) were considered the most prevalent. And 46,XY CGD patients carried a comparatively highest gonadal tumor risk(12.12%, 12/99), and most of them represented with dysgerminoma in those 46,XY CGD patients, while only one patient had yolk-sac tumor.
- **Conclusions** In summary, a de novo mutation in SRY gene (c.36dupC/p.13AsnfsGln) in a 46,XY complete gonadal dysgenesis female patient with bilateral gonadoblastoma and coexisting dysgerminoma was identified. Our results futher indicate that mutations in SRY gene can cause abnormal SRY proteins and increase the risk of gonadal neoplasia.

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