






A case of late diagnosis and management of 46 XY complete gonadal dysgenesis in adulthood

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Key words: 46 XY complete gonadal dysgenesis; prophylactic gonadectomy; germ cell tumor; difference of sex development

Ginekologia Polska 2021; 92, 5: 396–397

We present a case of 23-year-old woman with primary amenorrhea on hormonal replacement therapy referred for the first time to the Department of Gynecological Endocrinology. Her medical history revealed hypergonadotropic hypogonadism. On her physical examination she had tall stature, female phenotype and external genitalia, Tanner stage IV breast and pubic hair development. Vagina and normal uterus were confirmed on the gynecological exam. Pelvic ultrasound and MRI revealed remnant follicular structure (< 1 cm) localized in the right ovarian fossa, whereas there were no visible structures in the left ovarian fossa. The 46 XY karyotype was confirmed, however, molecular diagnosis was not available at the time of surgery. After she was diagnosed with 46 XY complete gonadal dysgenesis (historically named Swyer syndrome), the multidisciplinary team gathered.

Patients with differences of sex development (DSD, also known as disorders of sex development) are at risk of gonadal tumor development. The individual risk assessment is based on genetic analysis, clinical phenotyping, and biochemical analysis [1, 2]. Given the patient's age, female phenotype and gender identity, as well as no gonadal function proved on biochemical analysis, the decision for urgent removal of dysgenetic gonads was made. Due to oncological gynecologist qualification, the patient was referred to a bilateral laparoscopic adnexectomy.

During a laparoscopy ovoid shaped gonadal tissue and what seemed to be obstructed Fallopian tube were identified on the right side and streaked gonadal tissue with Fallopian tube on the left side. The uterus and rest of the pelvic cavity showed no abnormalities (Fig. 1). Histopathology of right gonad revealed dominant rete ovarii texture, hilus ovarii with presence of Leydig cells and the microcyst 0.4 cm in ovarian stroma, whereas the left side contained only connective tissue strands (Fig. 2). There was no evidence of invasive germ cell tumor. Hormonal replacement therapy has been reintroduced and patient has been well on follow-up since.

Gonadal dysgenesis is defined as an incomplete formation of the gonads, and it is caused by a disturbed process of germ cells migration into the gonadal ridge. The prevalence of females with 46 XY complete gonadal dysgenesis is estimated on 1.5 per 100,000 live born females [3]. Because of the lack of hormonal (AMH, testosterone) activity of dysgenetic gonads, affected individuals have female phenotype and Mullerian structures [4].

DSD patients have increased risk for gonadal germ cell cancer only in case of presence of the Y chromosome, particularly GBY (gonadoblastoma on the Y chromosome) region with TSPY (testis-specific protein Y) gene [5]. The risk is modulated by patient's age, location and differentiation of the gonads. It is believed to be greater in abdominal than in inguinal or scrotal gonads. Impaired differentiation relates to germ cells being blocked in an embryonic stage of development. Germ cell cancer originates from either germ cell neoplasia in situ (testicular environment) or gonadoblastoma (ovarian-like environment) [5]. Gonadoblastoma, being a preinvasive lesion in dysgenetic gonads, may differentiate into malignant tumors: dysgerminoma or less frequently into teratoma, embryonal carcinoma, yolk sac tumor, and choriocarcinoma [6].

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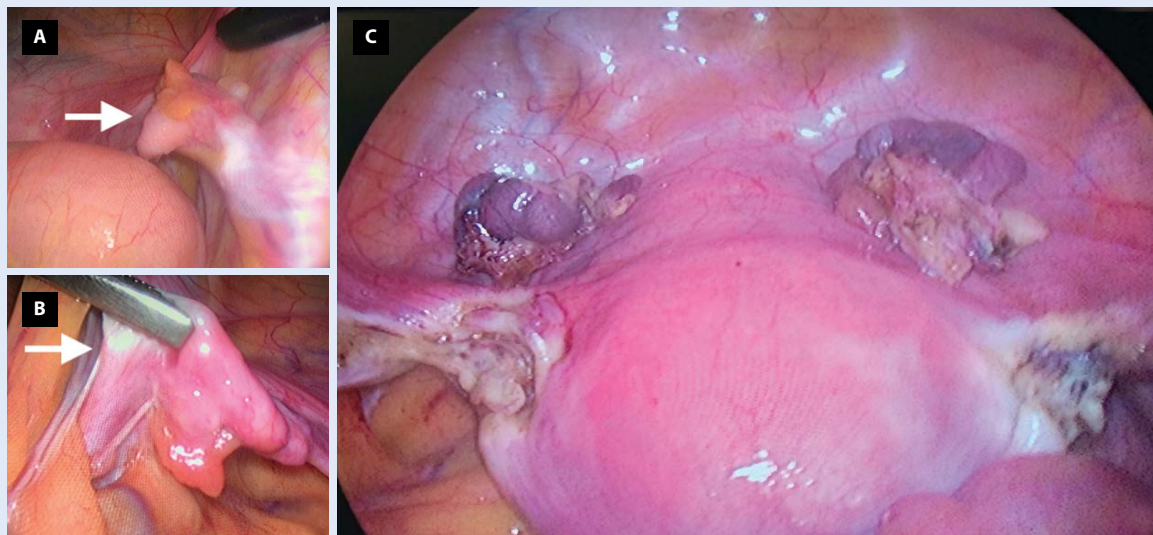


Figure 1. Laparoscopic findings. A — remnant ovoid shape gonadal tissue (marked with arrow) and obstructed distal opening of the Fallopian tube on the right side; B — Streaked gonadal tissue (grasped, marked with arrow) and Fallopian tube on the left side; C — After bilateral adnexectomy - uterus and the rest of pelvic cavity showed no abnormalities

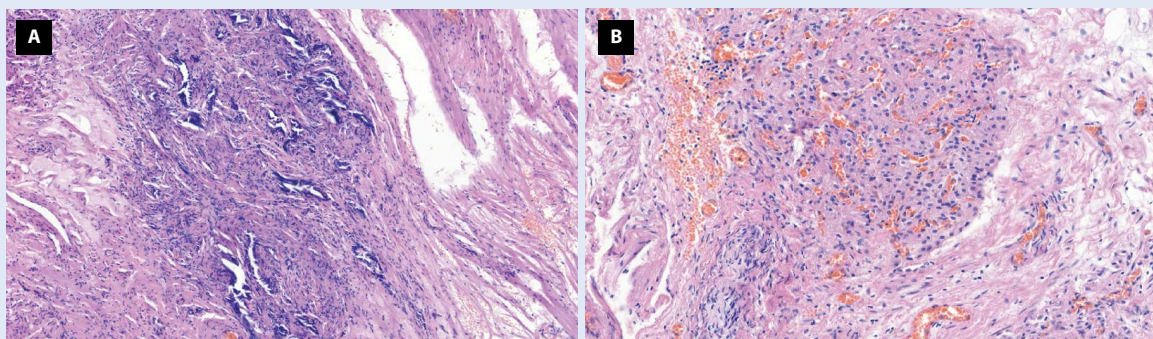


Figure 2. Postoperative histologic examination. A — The structure of rete ovarii in right gonad, hematoxylin and eosin (HE) staining, 10x; B — Leydig cells in the hilum of ovary, right gonad, HE, 20x

Lifetime risk of germ cell tumors in 46 XY DSD individuals varies according to exact diagnosis, however, in patients with complete gonadal dysgenesis is considered the highest and estimated on 12–40% [6, 7]. They are frequently found at a very young age, even in the first year of life [8, 9]. Therefore, in girls with 46 XY complete gonadal dysgenesis, female phenotype and no signs of virilization, early prophylactic gonadectomy before puberty is recommended [8].

Conflict of interests

The authors declare that they have no conflict of interests.

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