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Bilateral gonadoblastoma in a 17-year-old patient with 46XY pure gonadal dysgenesis (Swyer syndrome)

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Summary

Gonadoblastomas are benign tumors composed of germ cells and sex cords derivatives resembling immature granulosa and Sertoli cells. They occur almost entirely in patients with gonadal dysgenesis and in those carrying the Y chromosome. The authors present a case of a 17-year-old patient admitted because of primary amenorrhea and delayed puberty diagnosed, and operated because of bilateral gonadoblastoma.

Key words: Gonadoblastoma; Gonadal dysgenesis; Swyer syndrome.

Introduction

46 XY pure gonadal dysgenesis (Swyer Syndrome) is a rare disorder of sexual differentiation described by Swyer in 1955. It arises from an abnormality in testicular differentiation and is thought to be due to a deletion or mutation involving the sex determining region of the Y chromosome [1]. The incidence of Swyer syndrome is 1: 100,000 [2]. It is usually characterized by a female phenotype with normal female external genitalia, a hypoplastic to normal uterus, streak gonads, and primary amenorrhea [3]. Patients with 46 XY pure gonadal dysgenesis are at a higher risk of developing malignant germ-cell tumors in intra-abdominal gonads.

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Case Report

A 17-year-old patient with an unremarkable medical history was admitted to the present department because of primary amenorrhea and delayed puberty. Physical examination revealed a normal body mass index (21.9 kg/m^2), Tanner scale: Th1, P5, A3, normal labia and clitoris, and no signs of virilisation. Transvaginal ultrasound showed a small uterus: 2.5 cm in length, linear endometrium, and small solid gonads with no focal abnormalities. Analytical tests revealed a high serum levels of gonadotrophins (follicle stimulating hormone (FSH): 62.01 mIU/ml, luteinizing hormone (LH): 26.97 mIU/ml), and low serum level of 17β-estradiol: 8 pg/ml. All other hormonal test (prolactin, testosterone, sex hormone binding globulin, dehydroepiandrosterone sulfate, tyreothropin (TSH) and thyroxin) and tumors markers [β –human chorionic gonadotropin (β-hCG), alphafetoprotein (AFP), lactate dehydrogenase (LDH), and carcinoembryonic antigen (CEA)]were within the normal ranges. Cytogenetic evaluation reveled 46 XY karyotype. Molecular analysis excluded abnormalities in coding and flanking regions of SRY gene.

Patient was diagnosed with 46 XY pure gonadal dysgenesis and laparoscopic bilateral salpingo-oophorectomy was decided. During surgery bilateral salpingo-oophorectomy was performed.

The pathologic diagnosis was a bilateral gonadoblastoma of the

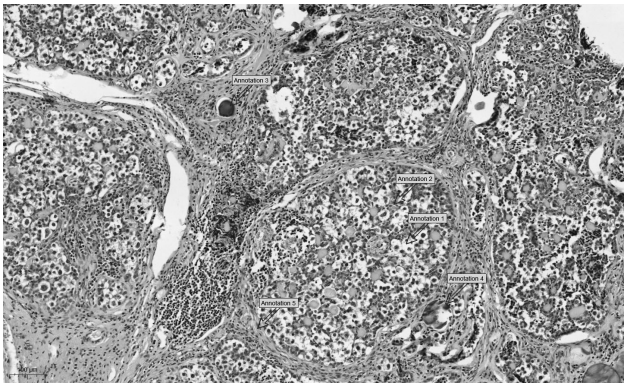

Figure 1. — Pathologic image with characteristic features of gonadoblastoma. In the center, a nest composed of germ cells with a clear cytoplasm (1) and sex cord type cells (2), and surrounded by fibrous stroma (5). Visible calcifications (3, 4).

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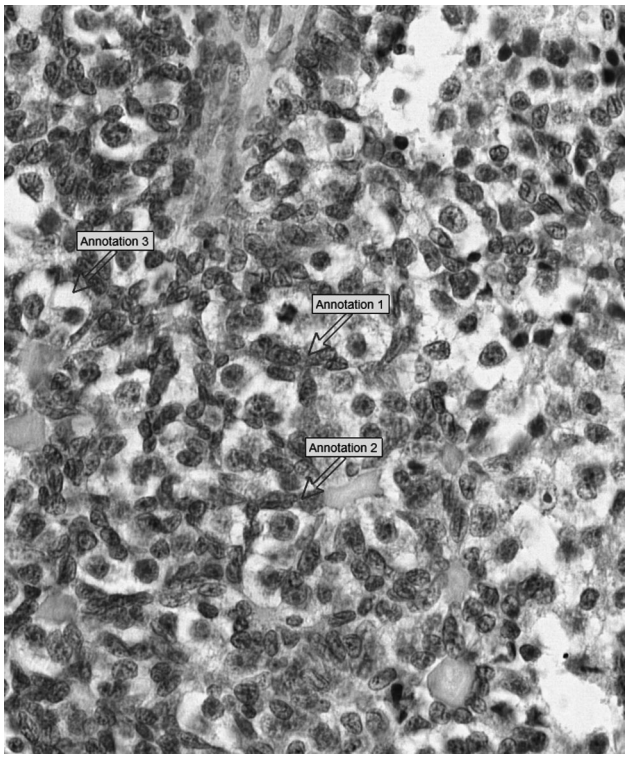

Figure 2a. — Sex cord type cells positive for α-inhibin (1, 2) and germ cells negative for α-inhibin (3).

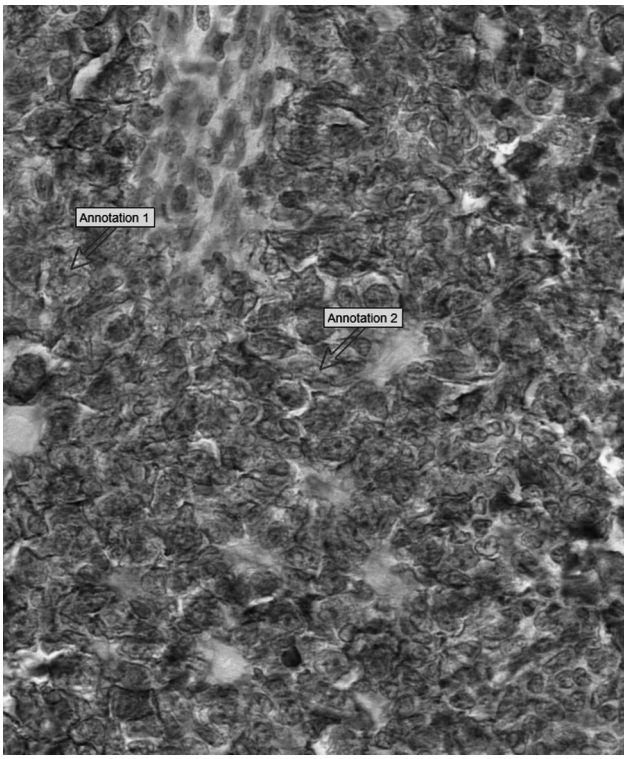

Figure 2b. — Germ cells positive for CD117 (c-KIT) (1) and sex cord type cells negative for CD117 (c-KIT) (2).

ovary measuring 330×10×10 mm in the right ovary and 10×10×5 mm in the left ovary. Both tumors had typical gonadoblastoma structure of rounded nests separated by fibrous stroma. The nests were composed of sex cord type cells forming acini that encircled primitive germ cells. In the acini hyalinization and calcifications occurred. No malignant elements were reported (Figures 1 and 2). Postoperatively the patient presented with no complications. Sequential estrogen-progestin therapy was proposed. The patient was then followed up within one month. At which time she reported the occurrence of menstruation. Transvaginal ultrasound showed no abnormalities in regards to the uterus and lower abdomen.

Discussion

Patients with 46XY pure gonadal dysgenesis have increased risk of malignancies. This risk is estimated to be approximately 30% [6-8]. The most frequent neoplasia related to gonadal dysgenesis are gonadoblastoma and dysgerminoma.

Gonadoblastomas arise from persisting undifferentiated gonadal tissue within the dysgenetic gonad. This tissue is similar in appearance to that found in the embryonic gonad prior to the expression of SRY gene and contains germ cells scattered in stroma and pre-Sertoli-granulosa cells [9]. Gonadoblastoma is a form of neoplasm that almost exclusively develops in dysgenetic gonads, and it can occur at a young age. The youngest case reported in the literature was in a nine-month old infant [10]. Gonadoblastomas are benign tumours with no metastatic potential; however, they can be precursors to germ cell malignancies, such as dysgerminomas, which is the most commonly associated malignancy, or teratomas, embryonal carcinomas, choriocarcinomas, and endodermal sinus tumours [11, 12].

Because of the oncological risk 46XY, pure gonadal dysgenesis requires prophylactic bilateral gonadectomy. Bilateral gonadectomy should be performed as soon as diagnosis is made [13].

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