Pure Sertoli cell tumor. A case report and review of the literature

A. Zizi-Sermpetzoglou[1], N. Petrakopoulou[1], N. Tepelenis[1], V. Savvaidou[1], K. Manoloudaki[1], M. Katsoulis[2]

[1]Pathology Department of Tzaneion General Hospital of Pireaus
[2]Department of Gynecology of Tzaneion General Hospital of Pireaus, Pireaus (Greece)

Summary

Pure Sertoli cell tumor (SCT) is a rare sex cord tumor and a subtype of Sertoli-Leydig cell tumors according to the WHO Classification. They lack a Leydig cell component and do not contain the immature neoplastic stroma found in the neoplasms of the Sertoli-Leydig cell category. The age of the patients ranges between two and 79 years. Sertoli cell tumors occur in women of reproductive age but a few can also occur in children. The most common clinical presentation when occurring in children is isosexual pseudoprecocity. Women of reproductive age and postmenopausal women frequently present with abdominal pain, swelling and menstrual abnormalities. Occasionally SCTs occur in patients who have Peutz-Jeghers syndrome. The tumors are hormone functional in 40-60% of cases. They are often estrogenic, occasionally also androgenic or rarely both. Grossly they are usually yellow to brownish, solid or with several cystic areas. Microscopically they show always almost a tubular growth pattern, but they may also have other growth patterns which can be extensive, making the correct diagnosis difficult. These histologic patterns may result in SCTs mimicking other ovarian tumors. The immunohistochemical panel which usually includes EMA, inhibin, chromogranine, CD99 and calretinin is often helpful in establishing the diagnosis. Most SCTs are Stage I, unilateral, cytologically bland, and clinically benign, but occasional examples are high stage. About 11% of Stage I tumors have worrisome histologic features that may portend an adverse outcome.

Key words: Ovary; Sertoli cell tumor; Pure Sertoli cell tumor; Immunohistochemistry.

Introduction

Pure Sertoli cell tumors are rare sex-cord tumors as designated by the World Health Organization (WHO) [1]. They may be found in patients of any age, with an average age of 30 years. These tumors commonly produce hyperestrinism [2], but they may also be associated with virilization or rarely with a progestational decidual reaction [1, 2]. When these tumors occur in children, isosexual pseudoprecosity is the main clinical symptom. When occurring in reproductive age the main clinical manifestations are menometrorrhagia, amenorrhea, hirsutism, breast atrophy, clitoral hypertrophy and hoarsenes [1-4]. They are all unilateral, usually solid and yellow in color. The diameter of these tumors ranges from 0.8 to 3 cm with the majority being in the range of 4-12 cm. The microscopic patterns of SCT can be extremely variable. Several major categories have been described which may coexist in the same tumor [3, 5]: 1) Well differentiated, which is composed of tubules lined by Sertoli-like cells; 2) Intermediate in which the Sertoli-like cells are arranged in outlines of immature tubules, cords and aggregates; 3) Poorly differentiated which is composed of sheets of spindle shaped cells arranged in a sarcomatoid pattern; and 4) Retiform in which the typical elements of SCT coexist with formations resembling the rete of the ovary or testis. The prognosis of SCTs is usually good and correlates with the stage and degree of differentiation of the tumor. We present a case of rare sex-cord tumor of the ovary with the typical macroscopic and microscopic features of a pure Sertoli-cell tumor and a relevant review of the published literature.

Case Report

A 47-year-old, para 3, gravida 2 woman with a history of hypertension and hypothyroidism under medication, presented to our hospital with a 2-week history of intermittent pain localized in the right lower quadrant of the abdomen and secondary amenorrhea for the last five months. She had also noted hypertrichosis, localized mainly in the androgen-effected areas of the skin, such as upper lips, cheeks, abdomen and lumbus, enlargement of the clitoris and central type of obesity. Her menarche was at the age of 12 years and she normally had menses for five days in a 30-35 day cycle. Laboratory tests by repeated counting did not show increased levels of hormones such as free testosterone, delta$_4$-androstenedione and DHEAS. CA125 level was normal but the level of 17(OH)-progesterone was high. Ultrasound sonography of the ovaries revealed a mass in the right ovary. Subsequently the patient underwent total abdominal hysterectomy and bilateral salpingo-oophorectomy. The tumor had a tan to yellow cut-surface and a lobular appearance. The tumor measured 8 x 7 x 5 cm. At microscopic examination the tumor was characterized by tubules with lumens lined by well differentiated columnar cells (Figure 1). The tubules were separated by hyalinized collagenous tissue (Figure 2). In addition to the predominantly round tubules, cells were also arranged in cords with oval to round bland nuclei. No Leydig cells or other types of neoplastic cells were seen in this tumor in spite of extensive sampling and cutting of the specimen. The endometrium was weekly proliferative and the glands were

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Fig. 1

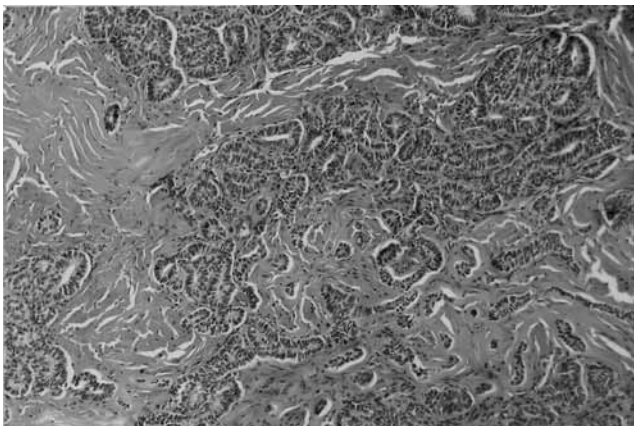

Fig. 2

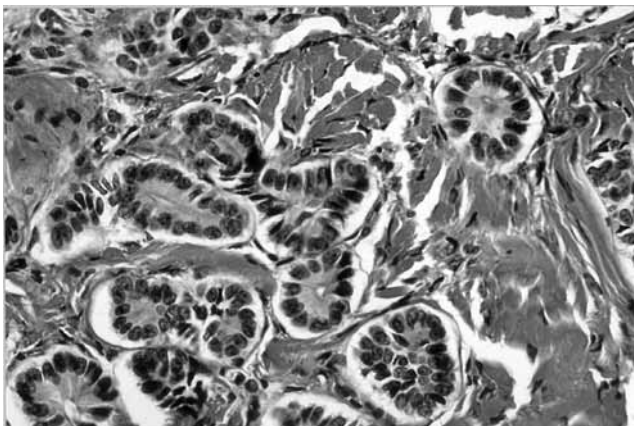

Fig. 3

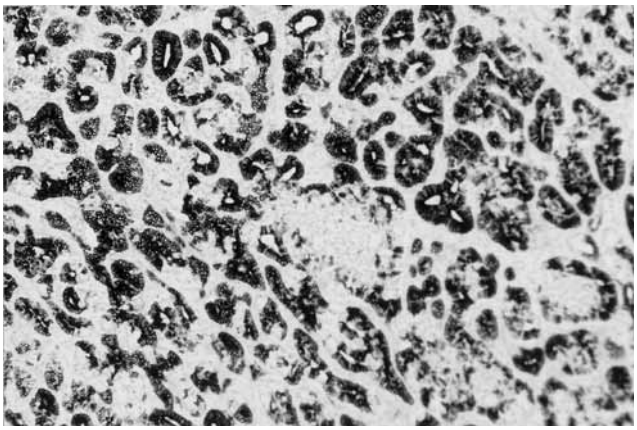

Fig. 4

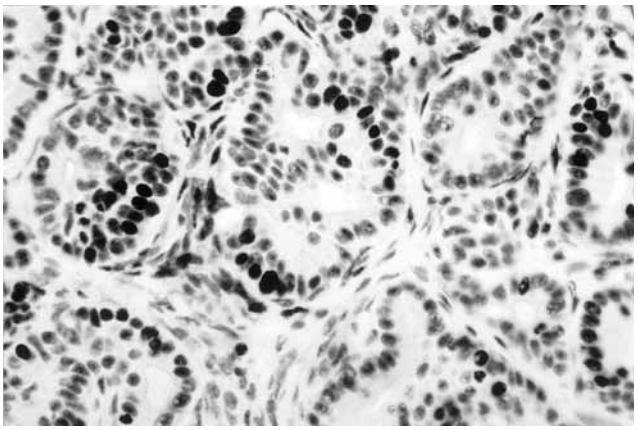

Figure 1. — Sertoli cell tumor H&E x100. Tubules with lumens lined by well differentiated columnar cells.
Figure 2. — Sertoli cell tumor H&E x400. The tubules of the tumor are separated by hyalinized collagenous tissue.
Figure 3. — The neoplastic cells show marked positivity for a-inhibin.
Figure 4. — The nuclei of the neoplastic cells are positive for progesterone.

lined by weekly proliferative endometrium. There was no mitotic activity. A few Nabothi cysts were present in the cervix. At immunohistochemical examination the neoplastic cells showed marked reactivity for low and high molecular weight cytokeratins, a-inhibin (Figure 3), CD99 and calretinin. Progesterone was expressed in 90% of the nuclei of the neoplastic cells (Figure 4). There was negativity for vimentin, CEA, CA125, CA19-9, TTF1, synaptophysine and chromogranine and estrogen. The diagnosis of a "pure Sertoli-cell tumor" was finally established. Our patient was free of disease 20 months after surgery.

Discussion

Sertoli cell tumors make up about 4% of Sertoli-Leydig cell tumors according to the WHO Classification [1]. The term Sertoli cell tumor was used by Morris and Scully [6]. Pure Sertoli cell tumors of the ovary are quite rare neoplasms. They typically occur in women of reproductive age but a few can also occur in children [7, 8]. When occurring in women in reproductive age or in postmenopausal women the patients usually present with abdominal pain or swelling and menstrual abnormalities [8, 9]. Sometimes the tumor can also be an incidental finding [10, 11] in a routine gynecologic examination. When occurring in children isosexual pseudoprecosity is the main clinical symptom [7, 8]. Patients with SCT may have elevated levels of serum estrogen, progesterone and luteinizing hormone [12, 13]. Estrogen production may result in menstrual abnormalities or postmenopausal bleeding and endometrial hyperplasia, depending on the menopausal status of the patient [14]. Progesterone production results in decidualization of the endometrium or peritoneum [15]. Testosterone production results in amenorrhea or virilization [11]. The secretion of androgen suggests the possible presence of unsampled Leydig cells. Occasionally SCTs present in patients with Peutz-Jeghers syndrome [7, 8], which is characterized by mucocutaneous pigmentation, hamartomatous polyps and occasionally carcinomas of the gastrointestinal tract, adenoma malignum of the uterine cervix and sex-cord tumors of the ovaries. SCT may rarely cause hypertension due to renin production [10, 11]. Grossly SCTs are unilateral and the two ovaries are involved with equal frequency. They are well circumscribed, solid neoplasms with a smooth and lobulated external surface and a yellowish sectioned surface. Areas of hemorrhage and or cystic degeneration may be seen in larger tumors. The most common microscopic pattern shows a tubular

growth pattern. The tubules can be round or elongated, hollow or solid or a combination of these features. The tubules are lined by columnar to cuboidal cells with moderate to abundant amounts of pale to eosinophilic cytoplasm. The nuclei are typically oval or spherical with a small nucleolus. Mitotic figures are usually scanty (< 1 per 10HPF) [11, 12].

The microscopic pattern of SCT can be variable: 1) Well differentiated which is composed of tubules lined by Sertoli-like cells; 2) Intermediate in which the Sertoli like cells are arranged in outlines of immature tubules, cords and aggregates; 3) Poorly differentiated which is composed of sheets of spindle shaped cells arranged in sarcomatoid pattern; and 4) Retiform in which the typical elements of SCT coexist with formations resembling the rete of the ovary or testis [13]. Heterologus elements such as mucinous glands, bone, skeletal muscle and cartilage may be present in some tumors [3, 11, 14]. Immunohistochemical staining of SCT shows reactivity for low molecular weight keratins, a-inhibin [16], vimentin, S100 and SMA. Recently the markers calretinin CD99, NSE and MART-1 have also been added to the immunohistochemical panel [17]. The tumor is typically negative for the epithelial membrane antigen, placental alkaline phosphatase. The differential diagnosis of SCT includes mucinous tumors, low-grade endometrioid carcinoma [19], carcinosarcoma, tubular Krukenberg tumor, tubular carcinoid [20] and ovarian tumors of probable Wolffian [20] origin and dysgerminoma [11, 22]. The most important differential diagnosis is endometrioid carcinoma of the ovary. It is well known that endometrioid carcinoma of the ovary may have a Sertoli-like appearance which even allows the use of the term "sertoliform endometrioid carcinoma" [11]. The oxyphilic variant of SCT can rarely cause any problems in the differential diagnosis with other oxyphilic [23] tumors. In these cases clinical information may be helpful because this variant of SCT may be associated with Peutz-Jeghers syndrome. The most important predictors of biological behavior are the stage and degree of differentiation of the tumor. Patients with Stage I tumor have been reported to have a 95% five-year survival, while some series report a 100% mortality rate in patients with tumors in Stage III or higher. The complete cure consists of hysterectomy and bilateral salpingo-oophorectomy in women who have children. In women who want to bear a child the surgeons apply usually unilateral salpingo-ophorectomy [24]. In conclusion we have presented a rare sex cord tumor of the ovary with the typical microscopic features of a pure SCT. Postoperatively the signs of hyperandrogenemia subsided and the patient improved clinically.

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Address reprint requests to:
A. ZIZI-SERMPETZOGLOU, M.D.
P.O. Box 3143
Alikos
19400 Ag. Marina, Koropi
Athens (Greece)
e-mail: adserbet@yahoo.gr