

Case Report

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Elevation of Alpha-Fetoprotein in Sertoli-Leydig Cell Tumor: A Case Report

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ABSTRACT

Sertoli-Leydig cell tumors represent about 0.2 to 0.5% of all primary ovarian tumors. One of the main features of this type of tumor is the high production of androgens, which promotes hirsutism and virilization. This case reports a 28-year-old patient with severe abdominal pain whose physical examination showed a right adnexal mass, confirmed by pelvic US, without clinical evidence of virilization, who presented elevated alpha-fetoprotein (636 ng/mL), negative hCG- β and was negative to other tumor markers. Exploratory laparotomy was performed with right salpingo-oophorectomy. Histologically, it was identified a tumor with heterogeneous areas, retiform, tubular, microcystic, anastomosing cords and trabeculae with Leydig cells and areas of hepatoid differentiation. The tumor was positive for inhibin, cytokeratin AE1/AE3 and calretinin. One week after surgery, alpha-feto protein levels dropped to 150 ng/ml and to 0.89 ng/ml five months later. This is a case of Sertoli-Leydig cell tumor with elevated alpha fetoprotein no evidence of virilization and the histological pattern showing focal areas of hepatoid differentiation.

KEYWORDS: Sertoli-Leydig cell tumor; Alpha-fetoprotein; Hepatoid differentiation areas.

ABBREVIATIONS: CBC: Cell Blood Count; hCG- β : Chorionic-beta Gonadotropin; AST: Aspartate aminotransferase; ALT: Alanine aminotransferase; HCC: Hepatocellular carcinoma; FIGO: International Federation of Gynecology and Obstetrics.

INTRODUCTION

Sertoli-Leydig cell tumors are considered a rare disease, representing about 0.2 to 0.5% of all primary ovarian tumors.¹ They frequently occur in patients younger than 25 years-old. One of the main features of these tumors is the high production of steroid hormones (androgens), which promotes virilization, hirsutism, deepening voice, clitoromegaly, oligomenorrhea and temporary baldness in the patients.

Microscopically, it is characterized by a pattern similar to the stromal cell and sex cords tumors.² However, these tumors generally do not produce alpha-fetoprotein; as, until 1998, only 20 cases have been described.³ We report the case of a patient with Sertoli-Leydig cell tumor with a high production of alpha-feto protein without any clinical feature added.

CASE

A 28-year old patient presented with a history of abdominal pain. Physical examination

revealed a right adnexal mass, subsequently confirmed by pelvic ultrasound. At diagnosis, alpha-fetoprotein level was 636 ng/mL, the dehydrogenase level was 157 IU/L, the Chorionic-beta Gonadotropin (hCG-β) was 0.00 mIU/mL, the CA-125 antigen level was 12.20 IU/mL and CA-19.9 antigen was 0.80 IU/mL. The Cell Blood Count (CBC) revealed hemoglobin of 15.3 g/dL, 212,000 platelets/mcL, 7,400 leukocytes/mm³ and glucose level was 101 mg/dL. No features of virilization or hirsutism were detected. The patient underwent an exploratory laparotomy and a right salpingo-oophorectomy.

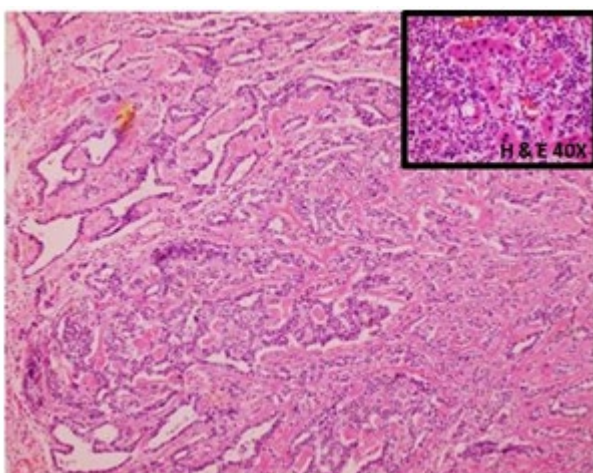
The tumor presented an irregular pattern of ovoid shape; measuring 13 cm long, with a gray-violet smooth outer surface, with congestive vessels. The cross-sectional surface was solid, cystic and whitish, with necrotic focal areas (Figure 1).



Macroscopic piece of ovoid shape, smooth, 13 cm in diameter at its major axis, purplish gray color. When cut, it is observed a white cystic solid surface with focal necrosis.

Figure 1: Right Ovary.

Histologically, it was a tumor with a heterogeneous pattern with retiform, tubular, and microcystic areas in cords and trabeculae, anastomosed with a few Leydig cells. Hepatoid areas of differentiation were focally identified (Figure 2).

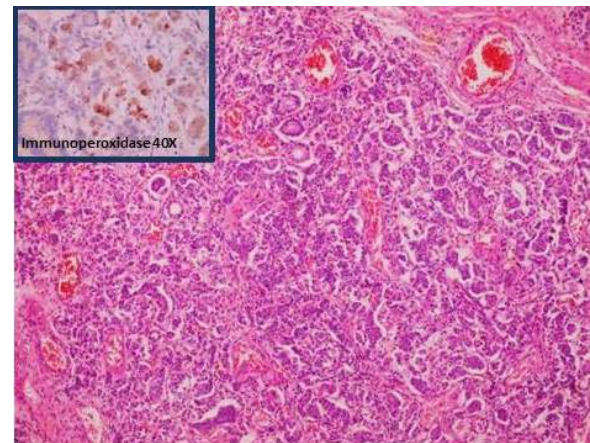


There is a retiform pattern on top and the tubular pattern with endometrioid areas. In the small square (H&E 40X) some areas with focal hepatoid differentiation can be identified.

Figure 2: Photomicrograph H&E 10X.

The immunohistochemistry staining was positive for inhibin, cytokeratin AE1/AE3 and calretinin. The epithelial membrane antigen was negative.

Microscopically, a composition of cells with scarce cytoplasm, large nuclei with granular chromatin and reinforcement of the membrane was described, and the cells were arranged in tubular structures of vesicular formation (Figure 3).



This photomicrograph with hematoxylin and eosin staining (10X) shows a tubular pattern on top and anastomosing cords with immature Sertoli cells. The small square with immunoperoxidase staining (40X) shows inhibin positive.

Figure 3: Photomicrograph H&E 10X.

One week after surgery, AFP dropped to 150 ng/ml, hCG-β levels continued at 0.0 mIU/mL, the Aspartate aminotransferase (AST) level was 19.0 IU/mL, the Alanine aminotransferase (ALT) level was 36.0 IU/L, and the lactic dehydrogenase level was 157.0 IU/L.

Finally, five months after surgery, measured level of alpha-fetoprotein was 0.89 ng/mL. The patient had been under surveillance for six months without evidence of recurrent disease.

DISCUSSION

We report the case of a patient with a Sertoli-Leydig cell tumor in the right ovary and its association with an overproduction of alpha-fetoprotein. A main characteristic in these patients is virilization, which has been found in about 70% of the previously reported cases. Sertoli-Leydig cells are classified as hormone (testosterone)-producing cells.⁴ In our case, the levels of steroid hormones were not asked because of the lack of clinical evidence of testosterone production by the neoplasm.

Twenty-five cases of patients with Sertoli-Leydig cell tumors with elevation of the alpha-fetoprotein levels have been described since 1980; six of these ones have been reported in post menopausal women.⁵ As expected, our 28-year old patient falls in the prevalent age range.

The reason why these tumors produce AFP is not clear, but it is suggested that the presence of hepatic tissue in the tu-

mor is responsible for its synthesis.⁶ Although the elevation of AFP has been associated with liver carcinoma, it is not specific to this condition, and its presence does not necessarily indicate malignancy.⁷ This statement is confirmed by Gard GB, et al. who suggest that AFP is secreted in an endocrine fashion and the cyst fluid is an ultra filtrate of blood rather than a pooled secretion from an exocrine tumor.³

Alpha-fetoprotein (AFP) is a member of a multigene family comprising genes encoding albumin, alpha-protein bound to albumin and vitamin.⁸ It is basically produced primarily by the fetal liver so it is considered a fetal specific glycoprotein. Normally, AFP levels decline rapidly after birth, reaching undetectable levels (less than 10 ng/mL) within several months after birth.⁹ Its biological role is unknown; however, because it is synthesized during the G1 and S phases of the cell cycle, it is thought to affect cell growth. AFP is able to bind other steroids and endogenous and exogenous substances such as fatty acids, bilirubin, and various pharmaceutical agents suggesting that it may play a role as conveyor.⁸

Histological examination revealed a moderately-differentiated Sertoli-Leydig cell tumor with areas containing a retiform pattern.¹ This type of pattern is characterized by the presence of tubular structures of Sertoli cells arranged in a dense or hyaline stroma-like the rete testis stroma. These structures build buds or polypoid structures with hyaline or edematous stroma, resulting in an aspect of a borderline serous tumor.¹⁰

Normal values of AFP in serum range from 0 to 0.89 ng/ml), five months after surgery AFP levels dropped to 0.89 ng/ml. These data confirm previous reports where the AFP has been used as a marker of malignancy in adults.¹¹ However, this is also an important marker of surgical prognosis because clinical studies have shown a close relationship between the level of serum AFP and Hepatocellular carcinoma (HCC) incidence, recurrence and metastasis. Accordingly serum AFP level has been used as the main index of prediction for HCC prognosis after laparotomy with higher preoperative AFP levels correlating with poorer prognosis.¹²

Considering initial surgery in ovarian cancer has the purpose to diagnose and stage disease and to provide therapeutic benefit with cytoreduction, in this case, a unilateral salpingo-oophorectomy was performed, the histology report showed an immunohistochemistry staining inhibin and vimentin positive and EMA negative. These was a predicted result because literature confirms that positive immunohistochemical staining for Sertoli-Leydig cell tumors are inhibin, calretinin, AE1/3CD 99 and vimentin, and negative markers are EMA and chromogranin.⁴

The clinical and pathological features of 207 ovarian Sertoli-Leydig cell tumors reviewed in 1985, Young, et al.¹³ found at operation that 97.5% of the tumors were Stage I, 1.5% were Stage II, and 1% were Stage III. Both ovaries were in-

cluded in 1.5% of the cases. In this case, the tumor extirpated in our patient was in Stage IA according to the International Federation of Gynecology and Obstetrics (FIGO) staging system, and due to her age (28 years old), the fertility-sparing surgery is the treatment of choice.¹⁴ These patients with early stage disease (stage I and II) have a very good prognosis with 5 year overall survival of 99% so they usually do not require any postoperative treatment. On the other hand, patients with stage IC disease or a higher stage, associated with poor prognostic factors, have a higher chance of relapse, and may benefit with neoadjuvant treatment.¹⁵

The incidence of malignancy in these tumors is 10-30% and recurrence occurs in a period of 46 months in average. The 10-year survival in Sertoli-Leydig cell tumors is near 90%¹⁶ but it depends on prognostic factors such as stage, intermediate and poor differentiation, presence or not of heterologous tissue, retiform structure, tumor spread beyond the ovary, etc., situations in which the patient may benefit from neoadjuvant chemotherapy, but the treatment must be according to each particular case.

The fact that the AFP is elevated does not rule out a sex cord tumor, although the probability is very low and the patient's age is necessary to diagnose a germ cell tumor as the first option. An accurate diagnosis is critical because treatment can be modified depending on the histological report, whether she requires adjuvant management or not.

In this case, the patient is in stage IA, accomplishes the criteria for surgical treatment so she has a favourable prognosis. However, her close surveillance and monitoring continues every 6 months.

Finally, due to Sertoli-Leydig tumors are a rare disease, and even less frequent when combined with a raised alpha-fetoprotein at diagnosis, it is important to consider AFP as a reliable tumor marker not only at diagnosis, but after surgery and during follow-up so it must be documented as a baseline level in all patients with Sertoli-Leydig cell tumors. Despite these tumors produce high quantities of steroid hormones (androgens), which promotes virilization, hirsutism, etc., in this case, no virilization signs were found, which suggests not all of these tumors are virilizing.

As most patients are young women in early stages, they can benefit from fertility-sparing surgery as the treatment of choice. An accurate histological diagnosis and staging is necessary before systematic treatment because subsequent treatment and prognosis will depend on it. Fortunately, prognosis with 5-year overall survival is very good in most healthy women in this range of age.

CONFLICTS OF INTEREST

The author(s) declare(s) that there is no conflict of interests regarding the publication of this paper.

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DISCLOSURES

In our setting, for these cases neither acknowledgments nor consent statements are included, because it is not required in our institution.

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