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Juvenile Ovarian Granulosa Cell Tumor - A Case Report

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Abstract: The granulosa cell tumor is an unusual ovarian tumor, even more so in pediatric age. The literature indicates that the prevalence and the incidence is more higher in patients after the fifth decade of the life with a frequency of 3.4 % of all ovarian malignancies, since most of them correspond to the benign pathologies. The tumor produces symptoms derived from the secretion of the estradiol. The granulosa cell tumor has been described as better prognosis, less aggressive than other ovarian neoplasms and the natural history was longer. Surgery is the main diagnostic, staging and therapeutic approach. The adjuvant chemotherapy is recommended only in the early stages with risk factors or in the advanced stages, as it can improve disease-free and relapse-free survival rates, such as radiation therapy. So far, the most commonly used regimens are bleomycin, etoposide, and cisplatin, with a high reaction rate. Whenever possible, surgical rescue is proposed.

Key words: cancer; cells; granulosa; tumor; pediatrics

1. Introduction

Granulosa cell tumor (GCT) is a rare tumor, which is characterized by the ability to secrete sex steroid such as estrogen [1]. Its manifestations are similar to other ovarian cancers, but it is necessary to specify its serum markers, biological behavior, prognostic factors, and treatment methods.

In view of the unusual incidence rate of this tumor in pediatrics, and considering that granulosa cell tumors are more common in the fifth decade of life, it refers to adult granulosa cell subtypes, and the incidence rate of young granulosa cell tumors occurs in patients under 30 years of age [2]. We present the clinical evolution and treatment of an infant diagnosed with ovarian GCT and the knowledge of this rare tumor has been updated.

2. Clinical Case

This is a 5-month-old female infant from the State of Apure, with onset of current disease in June 2015 when she began to present distension, diffuse abdominal pain and liquid evacuations, for which she was taken to a local health center, where infectious pathology was ruled out. However, due to persistent increase in abdominal perimeter and palpation of a solid mass in the hypogastrium and left iliac fossa, an abdominal ultrasound and abdominal computed axial tomography (CT) with double contrast were performed, reporting severe ascites and left abdominal space-occupying lesion. Therefore, a diagnosis of left ovarian tumor was proposed (Figure 1, 2).

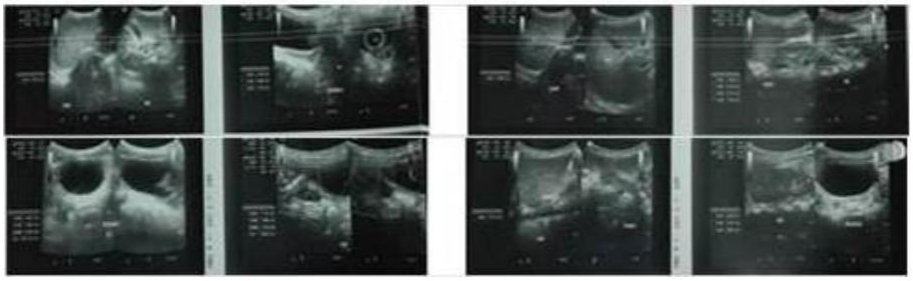

Figure 1. There is evidence of left ovarian space-occupying lesion, with moderate ascites.

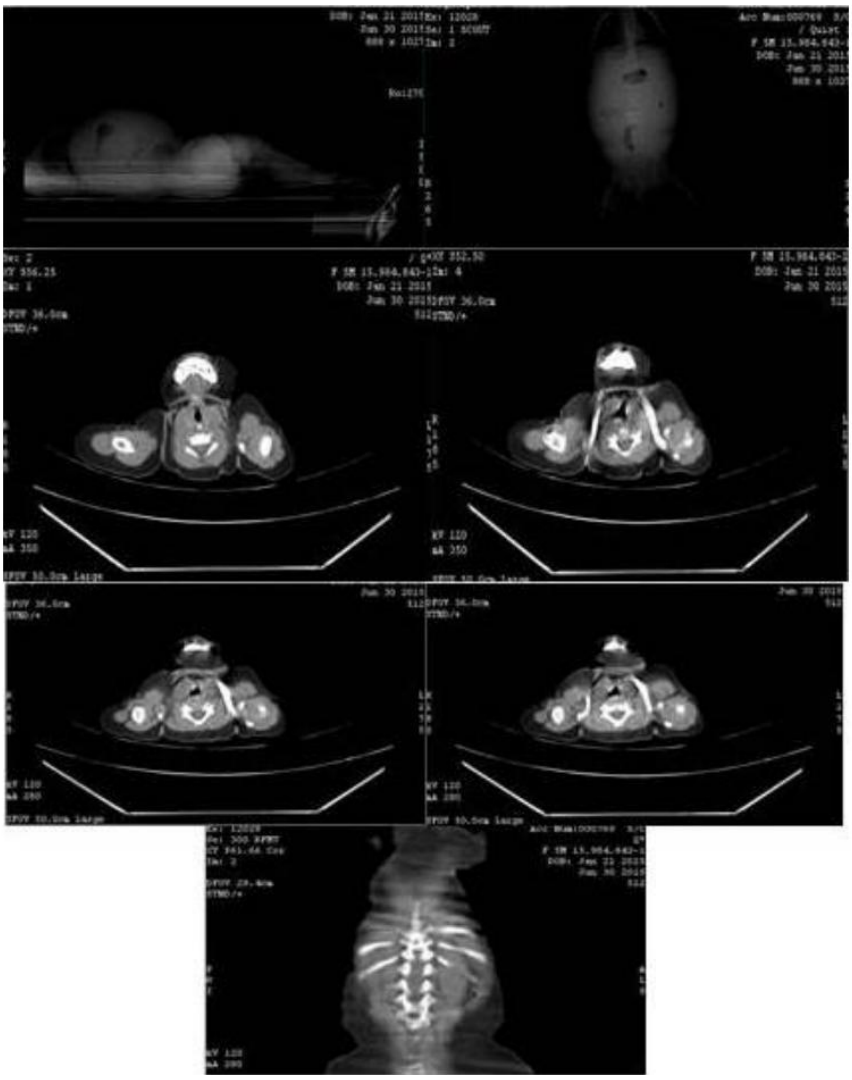

Figure 2. CT axial scan image showing tumors in the pelvic cavity.

An exploratory open surgery was performed on July 3, 2015, during which a large amount of bloody fluid was found in the abdominal cavity, the size of the left ovarian tumor was about 10 cm × 5.5 cm, the appearance was plagioid with secretion of bloody contents, and the uterus was enlarged compared to her age. A sample was obtained and ascitic fluid cytochemistry was performed, which reported transudate. An anatomical pathology study was performed, which reported left ovarian tumor and small cell carcinoma of the ovary; in view of such findings, she was transferred to the Military Hospital "Dr. Carlos Arvelo" (Caracas, Venezuela) for study and follow-up.

Given the evidence of age-related abnormal tumors in children, a review of cell blocks and immunohistochemistry is required, and the results are as follows: the immunohistochemistry results are consistent with granulosa cell tumors in the microcapsule area. The diagnosis was confirmed by a second cell block and immunohistochemical examination, which also reported a high mitotic index of 7-8 atypical mitoses per 40x fields (Figure 5). A gamma spectrum was reported within the normal range, as well as hormone profiles including α fetoprotein (AFP), estradiol, progesterone, free testosterone, and total testosterone, all of which were within the normal range, because this tumor behaves like a reproductive tumor.

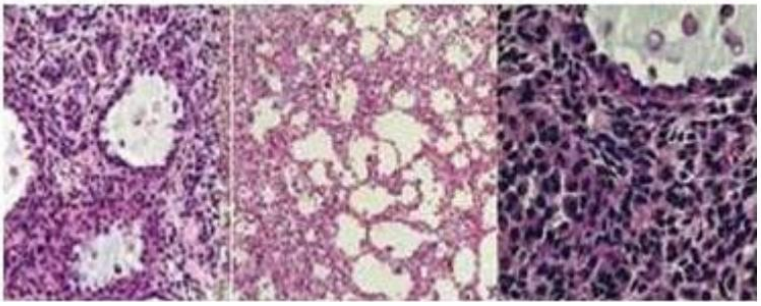

Figure 5. Histologic sections of GCT showing medium-sized cells with scant eosinophilic cytoplasm, prominent nucleoli and coffee bean clefts.

The patient received systemic chemotherapy based on bleomycin (0.5 mg/kg/dose), etoposide (3 mg/kg/dose), and cisplatin (0.7 mg/k/dose).

The patient received 6 cycles of protocolized chemotherapies every 21 days, showing satisfactory clinical evolution and level of α fetoprotein and hormonal profile without evidence of recurrence to date. She is currently being followed up by the pediatric oncology service.

3. Discussion

GCT constitutes 2 - 5% of all ovarian carcinomas, and the juvenile subtype constitutes a minimal percentage. These neoplasms, as their name indicates, derive from the granulosa cells that form part of the ovarian stroma and are responsible for the production of estradiol. The literature describes two subtypes: adult and juvenile, with different clinical and histopathological findings [2, 3]. Juvenile GCT involves only 5% of all GCT and affects prepubertal girls and women under 30 years of old who may show precocious pseudo-puberty; in up to 10% of cases it is associated with abdominal pain accompanied by pelvic mass. 80% of these patients are prepubertal girls, with an increased incidence in those with Ollier's disease (multiple enchondromatosis) or Maffucci's syndrome (dyschondroplasia). An increased prevalence has also been observed in patients undergoing infertility treatments. It can even appear during pregnancy, being diagnosed incidentally, with a behavior similar to that of non-pregnant women, but with a higher risk of complications [2, 3, 4, 5]. Although the youth subtype may appear more undifferentiated, its prognosis is more favorable due to early diagnosis; unlike adult subtypes, insidious clinics in adult subtypes often delay their suspicion, thereby delaying their diagnosis and showing a greater trend of recurrence [1, 2]. It presents with menstrual irregularity, menorrhagia or amenorrhea and rarely infertility, precocious pseudo-puberty in pre-menarchal and hirsutism and virilization data in cases with Sertoli and Leydig cell component. Abomino-pelvic pain is caused by distension secondary to the ovarian mass, sometimes as a result of ovarian sprain [2, 4]. Because of its highly vascularized particularity, GCT sometimes appears with intra-tumoral hemorrhagic rupture simulating an ectopic pregnancy [2]. The initial step for diagnosis is physical examination, which may be normal or show evidence of a palpable pelvic or abdominal mass and ultrasound study which may reveal an echogenic, cystic or septated mass in the ovary.

The main method of treatment and staging is surgery. In cases of adult GCT and postmenopausal women, the adjustment of surgery and ovarian tumors is similar [1]. In adolescent subtypes and women who wish to preserve fertility, once distant diseases are ruled out and endometrial biopsy is performed to exclude involvement, conservative measures such as unilateral salpingectomy can be attempted [6, 7].

Macroscopically, there is evidence of a yellowish cystic mass which is histologically constituted by granulosa cells alone or in combination with other stromal cells of the sexual cords and diffuse growth pattern in macro-follicles (Figure 3, 4). They present round or oval morphology with abundant cytoplasm and without the typical "coffee bean" nucleus (with a cleft across it) of the adult GCT (Figure 5); neither do Call-Exner bodies appear [2, 8, 9]. These peculiarities are useful for the differential diagnosis of juvenile and adult GCT (Figure 5) and ovarian undifferentiated carcinomas, sometimes very difficult [2].

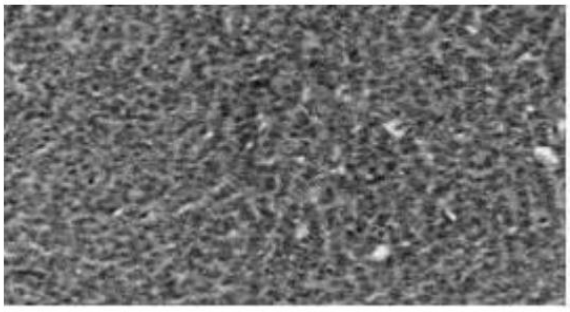

Figure 3. Granulosa tumor (HE 200 x). Diffuse pattern.

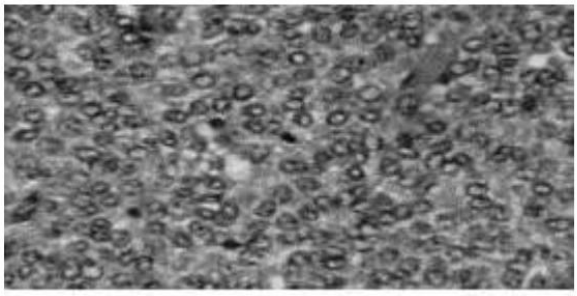

Figure 4. Granulosa tumor (HE 400 x). Detail of the previous one in which cells of uniform size are observed, with eosinophilic cytoplasm and round nuclei with scarce pleomorphism. A figure of mitosis in the center.

Conflicts of Interest

The author declares no conflicts of interest regarding the publication of this paper.

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