Journal Homepage: - www.journalijar.com

INTERNATIONAL JOURNAL OF ADVANCED RESEARCH (IJAR)

Article DOI: 10.21474/IJAR01/16379
DOI URL: http://dx.doi.org/10.21474/IJAR01/16379

RESEARCH ARTICLE

AN OVARIAN GRANULOSA CELL TUMOR IN A PATIENT WITH POLYCYSTIC OVARIAN SYNDROME: A CASE REPORT

A. Aouragh, H. Kamal, H. Taheri, H. Saadi and A. Mimouni
Department of Obstetrics and Gynecology, Mohammed VI University Hospital Center, Oujda, Morocco.

Manuscript Info

Manuscript History
Received: 31 December 2022
Final Accepted: 31 January 2023
Published: February 2023

Abstract

Granulosa cell tumors (GCTs) are the second most common ovarian sex cord stromal tumors after fibroma/thecomas, accounting for less than 2% of all ovarian malignancies. GCTs are most common in postmenopausal women between the ages of 50 and 55, are usually diagnosed early, and have a good prognosis. GCTs are typically characterized by hyperestrogenism and have an average size of 10 to 15 cm. A 39-year-old nulligravida with polycystic ovarian syndrome (PCOS) discovered a 50-mm mass in her right ovary on ultrasonography. Pathological examination revealed an adult-type granulosa cell tumor with necrosis and hemorrhage. The tissue was positive for inhibin-, Wilms' tumor-1, and CD56 but negative for cytokeratin 7. Finally, we performed a right salpingo-oophorectomy, an endometrial biopsy, a peritoneal biopsy, and a partial omentectomy. Pathology revealed an adult-type granulosa cell tumor. IA stood for International Federation of Gynecology and Obstetrics staging. The patient did not require any additional care. Surprisingly, her normal menstruation returned two weeks later, and she had a normal pregnancy and parturition. Following the surgery, There have been no complications and the patient is disease-free.

Introduction:-

Malignant neoplasms arising from granulosa cells in ovarian follicles account for approximately 10% of all ovarian sex cord stromal tumors. The majority of GCTs (95%) were adult type, with only 5% being juvenile type. The most common age in postmenopausal women is between the ages of 50 and 55. [1] The majority are confined to the ovary (stage I) and rarely spread to the lung or liver. Lymph node metastases are uncommon, with more than 95 percent confined to the ovaries.

They are typically encapsulated with smooth lobulated surfaces that are tan or yellow (depending on the degree of luteinization and lipid content), soft to firm (depending on the amount of fibromatous component), solid and cystic with straw-colored or mucoid fluid, and can have necrosis and hemorrhage. Tumors that are more luteinized are yellow/orange in color. [2] This study describes an unusual case of adult type granulosa cell tumor (AGCT) with amenorrhea, mild hirsutism, dienogest resistance, normal testosterone, normal estrogen, and high anti-Müllerian hormone (AMH) levels.

Corresponding Author:- A. Aouragh
Address:- Department of Obstetrics and Gynecology, Mohammed VI University Hospital Center, Oujda, Morocco.

Case presentation

A 39-year-old Moroccan nulliparous woman with an enlarging right ovarian mass. She didn't have any medical or surgical history. She had been diagnosed with polycystic ovarian syndrome (PCOS) ten years before and was using progestatif contraception due to irregular menstrual periods. She was diagnosed with a 50 mm latero uterine mass by chance. An ultrasound scan revealed a 47 37-mm round solid mass with a spongiform appearance and little vascularity in the right ovary. The endometrium was 3 mm thick, and the left ovary had a PCO pattern. (**FIGURE1)**

The levels of tumor markers such as alpha-fetoprotein, CA 19–9, CA 125, and carcinoembryonic antigen were not elevated. Hormonal tests were performed as follows: Estradiol levels were 43.9 pg/mL (reference range 27-433 pg/mL); luteinizing hormone (LH) was 25.2 mIU/mL, FSH was 5.11 mIU/mL, and testosterone was 0.26 ng/mL (0.084-0.481 ng/mL). The AMH level was 23.60 ng/mL, which is in the 90th to 100th percentile for people of the same age. Chest radiography revealed no noteworthy findings. As a result, a benign right ovarian endometrioma or dermoid cyst was diagnosed as the initial diagnosis. The mass did not rupture during the procedure, which was performedlaparoscopically on the patient's right ovarian cyst. The mass was brittle and yellow.

The findings of the ovarian tumor on frozen section analysis suggested that AGCT could be a possibility. A microscopic examination of the right ovarian mass revealed architectural patterns that were diffuse, solid, cordlike, and trabecularly admixed. Fine chromatin and round-to-oval nuclei with a single small nucleolus were found in the tumor cells. Some nuclei, dubbed "coffee-bean nuclei," had pale, round longitudinal grooves. Mitotic figures are uncommon. There was also fibromatousstroma present. Tumors were positive for inhibin-, Wilms' tumor (WT)-1, and CD56 but negative for CK7.

As a result, the findings backed up the final diagnosis of AGCT in the right ovary. We performed a right salpingo-oophorectomy, an endometrial biopsy, a peritoneal biopsy, and a partial omentectomy. 2 weeks after the initial procedure A microscopic examination revealed that there were no remaining AGCT cells.

An endometrial biopsy revealed no evidence of hyperplasia. Furthermore, the tumor was classified as stage IA by the Federation of Gynecology and Obstetrics. The patient did not require any additional care. Surprisingly, her normal menstruation returned two weeks later, and she had a normal pregnancy and parturition. Following the surgery,there have been no complications and the patient is disease-free.

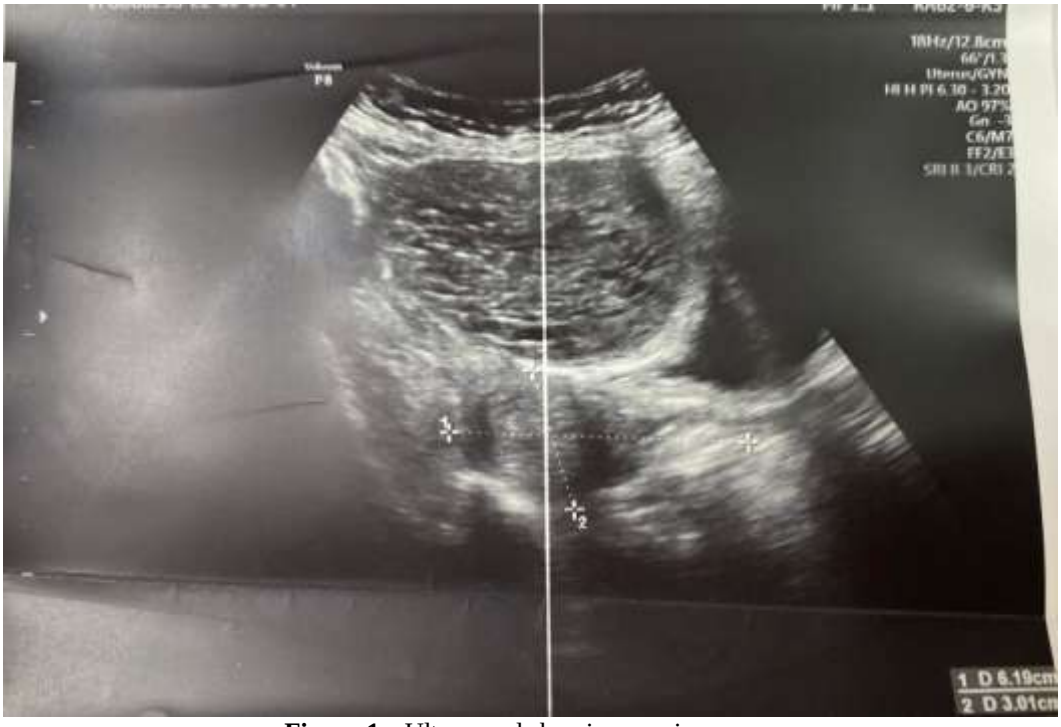

Figure 1:- Ultrasound showing ovarian mass.

Discussion:-

The granulosa cell layer of ovarian follicles produces GCTs. These cells normally proliferate in response to rising levels of circulating gonadotropins and decline in response to rising levels of circulating testosterone. The granulosa and theca cells are ovarian follicle cells that form the cellular stroma that surrounds the developing oocyte. Estradiol is normally produced by them. When the hypothalamus and anterior pituitary detect excess estradiol, it reduces the production of gonadotropin-releasing hormone, FSH, and LH. [3] Activin stimulates granulosa cells, which increases FSH binding and FSH-induced aromatization in follicles. This also improves the action of LH on theca cells in the ovary, which increases androgen synthesis.

AMH, as well as inhibins A and B, are produced by granulosa cells. Inhibin B is produced in response to FSH stimulation and provides feedback to the pituitary gland, causing it to produce less FSH. The tumor's excess estradiol frequently causes abnormal uterine bleeding, postmenopausal bleeding, and abdominal pain. [4] Excess estradiol from granulosa cell tumor (GCT) causes endometrial hyperplasia and an increased risk of breast cancer in women who still have a uterus. [5] GCTs are classified as AGCT or juvenile GCT (JGCT), based on not only the patient's typical age and distinguishing histologic features, but also on their natural history. However, both types of GCTs can occur at any age.

After reviewing the literature, we discovered that two-thirds of all AGCT cases occurred in postmenopausal women, with a peak incidence between the ages of 50 and 55, and that only 1% of AGCT cases occurred in prepubescent girls. JGCTs are most common in prepubescent girls and women aged 30 years, with more than half of the cases occurring in patients as young as 10 years. [6] Most GCTs are large multilocular solid masses with a large number of locules or solid tumors with heterogeneous echogenicity of the solid tissue on ultrasound examination. Hemorrhagic components are common, and color/power Doppler ultrasound examination has revealed increased vascularity. [7] The tumor's hyperestrogenic state frequently causes endometrial pathology, with bleeding problems as a common symptom.

Radiological findings include irregular, thick walls and septa, papillary projections, solid and echogenic foci, and papillary projections. [8,9] GCTs are distinguished histologically by Call-Exner bodies and coffee bean nuclei. Pathology revealed GCTs with macrofollicular and microfollicular patterns in the solid and cystic masses. The spongiform solid masses displayed prominent hemorrhagic necrosis and diffuse proliferation of granulosa cells with trabecular and microfollicular patterns. On histological examination, the classic features of AGCT include Call-Exner bodies and "Coffee-bean" nuclei, as well as a low mitotic rate. Call-Exner bodies are gland-like structures that resemble ovarian follicles. The nuclei of "coffee beans" are pale, round, and longitudinally grooved.

JGCTs, on the other hand, have only a few common findings. JGCTs have fewer Call-Exner bodies and gland-like structures that resemble ovarian follicles in size and shape. [10] JGCTs also have immature nuclei, atypia, and increased mitotic activity. Immunohistochemistry revealed that granulosa cells expressed inhibin-, WT-1, and CD56 consistently. Pathologists can always be confident in the diagnosis of GCT based on the combination of inhibin-, WT-1, and positive CD56. [11] In the preceding case, the ovarian tumor epithelial cells were also positive for inhibin-, WT-1, and CD56. The most important indicator of prognosis, recurrence, and treatment is surgical staging. [12] Surgery is the primary treatment for both primary and relapsed tumors, whereas chemotherapy is reserved for advanced or incurable tumors.

The only factor that is consistently associated with prognosis is tumor stage. However, one-third of patients typically relapse within 4 to 7 years of diagnosis, with 50% of these patients dying. AMH and inhibin B are the most accurate circulating biomarkers that correlate with disease status at the moment. Small series have reported low recurrence rates in Stage I (5.4 percent), increasing to 21.1 percent and 40% in Stages III and IV, respectively. [13,14] Adjuvant chemotherapy is typically given to patients with stage IC who have excrescences on the surface of the ovary or who are at a later stage of the disease. The primary treatment for early stage GCT tumors is unilateral salpingo-oophorectomy. [15] The most common presentation is stage I (confined to the ovary), and surgery is usually curative.

Lymphadenectomy, like other tumors of mesenchymal origin, has not been thought to play a role in the treatment of these patients. [16] According to a recent study, patients who were completely surgically staged fared significantly better. In cases of advanced disease, adjuvant therapies and traditional chemotherapies are used (stage IC or higher). [17] Uterine pathology is common in GCTs due to the tumor's overproduction of estradiol. The treatment of atypical

hyperplasia or endometrial carcinomas is followed by a total hysterectomy and resection of a unilateral adnexal tumor. Endocrine therapies were introduced as treatments primarily as second- or third-line therapies after one or more lines of chemotherapy failed.

Endocrine therapies were initially introduced with the rationale of interfering with hormone receptor signaling to achieve antitumor effects through a mechanism similar to that used in the treatment of hormone receptor-positive breast cancer. Tamoxifenis used at first, followed by progestins to modulate estrogen receptor function. Later, gonadotropin-releasing hormone agonists were added to the regimens to suppress ovarian function. [18,19] Aromatase inhibitors have recently become increasingly important in GCT management. GCTs are distinguished by late recurrences after resection, which can last up to 20 years, but with increasing aggressiveness. Early stage disease has a high five-year disease-free survival rate (approximately 90%). However, if a patient's disease recurs, the chances of death from the disease increase.

Metastases are most commonly found in the peritoneal cavity, but they can also spread to the lungs, liver, and spleen, as well as the bone and brain. Spread to regional lymph nodes is also uncommon, but may occur more frequently in advanced disease. [20] The goal of this study was to highlight the difficulty in detecting a rare small-sized GCT in a 31-year-old PCOS patient. This is significant because there have been few reports of AGCT in PCOS patients to date. If a woman with PCO develops a small ovarian mass at an unusually young age and is resistant to dienogest, GCT should be considered, even if similar symptoms exist.

Conclusion:-

If a female patient with PCOS and amenorrhea has a unilateral small solid mass, GCTs should be considered in the differential diagnosis. They are extremely uncommon malignant ovarian tumors that must be distinguished from other benign ovarian tumors, particularly endometriomas and dermoid cysts. Because the patient already had PCOS symptoms like mild hirsutism and amenorrhea, it was difficult for us to suspect a granulosa cell tumor. This case emphasizes the importance of physicians being aware of and suspicious of GCTs in similar cases, as well as being familiar with their characteristics when considering possible differential diagnoses.considered if a woman with PCO develops a small ovarian mass at an unusually young age and is resistant to dienogest.

References:-

1.Kdous M, Hachicha R, Gamoudi A.
Pseudo-puberté précoce isosexuelle révélant une tumeur de la granulosa juvénile chez une petite fille de six ans.
2.[02:32, 21/04/2022] Anass: S. Sekkate, M. Kairouani, B. Serji, H.M'Rabti I. El Ghissassi, H.Errihani, "'Les tumeurs de la granulosa de l'ovaire"', bulletindu cancer, Institut national d'oncologie, service d'oncologie médicale, Janvier 2014.
3.Elidrissi F, Ounejma S, Zeraidi N, Barhmi RS, Fadli A, Achour M et al.
TUMEUR DE GRANULOSA DE L'OVAIRE A PROPOS D'UN CAS.
Médecine du Maghreb 1999;76:21-7.
4.Boyce EA, Costaggini I, VitonisvA, Feltmate C, Muto M, Berkowitz R et al.
The epidemiology of ovarian granulosa cell tumors: A case-control study.
Gnecologic Oncology2009; 115:221-5.
5.Fox H, Agkawamlb K, Langlemyd A.
A CLINICOPATHOLOGIC STUDY OF 92 CASES OF GRANULOSA CELL TUMOR OF THE OVARY WITH SPECIAL REFERENCE TO THE FACTORS INFLUENCING
PROGNOSIS. Cancer 1975; 35: 231-41.
6.Bats A, Barranger E.
Mise au point sur les cancers de l'ovaire.
Journal de Gynécologie Obstétrique et Biologie de la Reproduction 2008; 37:64-8.
7.Unkila-kallio L,Titinen A , Walhstrom T et al. Reproductive features in women developing ovarian granulosa cell tumour at a fertile age. Hum Reprod 2000; 15:589-93.
8.Tavassoli FA, Mooney E, Gersell DJ, et al. Sex cord-stromal tumours. Nat ClinPractOncol 2003; 2:146-61
9.Stuart GCE, Dawson LM. Update on granulosa cell tumours of the ovary. CurrOpinObstetGynecol 2003;15: 33-7.
10.Miller BE, Barron BA, Wan JY, et al. Prognostic factors in adult granulose cell tumor of the ovary. Cancer 1997; 79: 1951-5.

11.Bjorkholm E , Pettersson F. Granulosa-cell and theca-cell tumors. The clinical picture and long-term outcome for the Radiumhemment series. Acta ObstetGynecolScand1980;59: 361-5
12.Ellouze S, Krichen-Makni S, Trabelsi K. Tumeur de la granulosa de l'ovaire : À propos de 16 cas. J GynecolObstetBiolReprod 2006; 35: 767-72.
13.krishnan A, Murdock C, Allard J, et al. Pseudo-isolated FSH deficiency caused by an inhibin B-secreting granulosa cell tumors: case report. Hum Reprod 2003; 18: 502- 5.
14.Kurithara S, Hirakawa T, Amada S et al. Inhibin-producing ovarian granulosa cell tumor as a cause of secondary amenorrhea: case report and review of the literature. J ObstetGynaecol Res 2004; 30:439-43
15. Nakashima N., Young R.H., Scully R.E. Androgenic granulosa cell tumors of the ovary. A clinico-pathologic analysis of 17 cases and review of the literature. Arch Pathol Lab Med 1984; 108: 786- 91.
16.Savage P, Constenla D, Fisher C, et al. Granulosa cell tumor of ovary: demographics, survival and the management of advanced disease. ClinOncol 1998; 10: 242-5.
17.Yousefi Z, Sharifi N, Sadatmand F, Shaid S.
Granulosa Cell - Stromal Tumors: An Immunohistochemical Study Including Comparison otCalretinin and Inhibin.Iranian Journal of Pathology 2009; 4: 172-6.
18.Schumer ST, Cannistra SA. Granulosa cell tumor of the ovary. J Clin Oncol2003; 21: 1180-9.
19.Bats A, Barranger E.
Mise au point sur les cancer de l'ovaire.
Journal de Gynécologie obstétrique et biologie de la reproduction 2008; 37 : 64-8.
20.Malmstrom H, Hogberg T, Risberg B, Simonsen E. Granulosa cell tumors of the ovary: prognostic factors and outcome. Gynecoloncol 1994; 52: 50-5.