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POSTMENOPAUSAL OVARIAN GRANULOSA CELL TUMOR: CASE REPORT

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ABSTRACT:
Background: Ovarian granulosa cell tumours (GCTs) are typically low-grade cancers originating from the specific stroma of the ovary. They occur across all age groups but predominantly manifest in postmenopausal women.
Objective: This article aims to describe a case of GCT and discuss the recommended management strategies for this condition.
Methods: A detailed case study of a postmenopausal woman with a granulosa cell tumour (GCT) is presented. The treatment approach, including bilateral salpingo-oophorectomy and total abdominal hysterectomy, is discussed. The importance of disease staging and ongoing surveillance is emphasized. This study was conducted at Hayatabad Medical Complex, Peshawar, KPK Pakistan.
Results: In this case, the patient exhibited symptoms such as vaginal bleeding due to estrogen secretion and tumour growth into the abdominal cavity. Post-surgical management included regular clinical assessments and marker testing to monitor for recurrence.
Conclusion: The stage of the disease is the most significant prognostic factor for recurrence in GCT patients. Due to the high likelihood of recurrence, ongoing surveillance through clinical assessment and marker testing is recommended. This case highlights the importance of comprehensive management and follow-up in patients with ovarian GCT.

KEYWORDS: Gynecology; Granulosa Cell Tumor, Oncology, Ovarian granulosa cell tumour GCT, Low-grade cancer, Postmenopausal women, Vaginal bleeding, Early puberty, Total abdominal hysterectomy, Estrogen secretion, Surveillance, Tumor management.

INTRODUCTION:

Granulosa cell tumours (GCTs) are often low-grade cancers that develop from the ovary's specialized stroma. They are composed of granulosa cells alone or combined with other stromal components, primarily theca cells. They are uncommon, making up only 2-3% of total ovarian neoplasms, but they account for 70% of stroma and sex cord tumours (Dolkar, Rayapureddy, Kadakia, Bellamkonda, & Kalavar, 2023). They can affect patients of any age, and in two-thirds of cases, they manifest in postmenopausal women; in only 2% of cases, they are bilateral GCTs are divided into subtypes that are juvenile and adult (Adefris & Fekadu, 2017; Naeem et al., 2024; Oktar et al., 2024) (Busquets, Gonzalez-Bosquet, Muchart, Rovira, & Lailla, 2010; da Costa et al., 2024; Dogan et al., 2024). The adult-specific subtype mainly affects women who are perimenopausal or postmenopausal and have an average age of 50, accounting for around 95% of these tumours. Tumor development or the production of neoplastic hormones is the cause of the clinical signs and symptoms of GCT (Jang et al., 2018; Kolli, Agrawal, Khithani, & Kotdawala, 2020; Rustamadji, Wiyarta, Anggraeni, & Siregar, 2021; Tokalioglu et al., 2024).

CLINICAL CASE:

The patient was referred to a tertiary institution for an oncogynecological assessment. The patient was 51 years old, G3P3A0, menopausal at age 42. She experienced alterations in her bowel habits and pain in her abdomen. The results of the laboratory tests that stand out include the beta-HCG < 1.2 mIU/ml, CA125 285 U/ml, and alpha-fetoprotein 1.2 ng/ml. A substantial, apparent pleural effusion was found on a chest computed tomography (CT) scan, which was linked to atelectasis of the right upper and lower lobes' posterior and basal portions, respectively

Abdominal CT showed an expansile pelvic mass with an estimated volume of 702 cm3, with heterogeneous soft tissue density and contrast enhancement, which had close contact with the uterine fundus and was associated with a moderate volume of ascites. Transvaginal ultrasound (TVUS) visualized the uterus in anteversion, with a volume of 124.50 cm3 (standard up to 70 cm3), regular contours, and myometrium with homogeneous texture. The uterine cavity showed a slight accumulation of mucus, with a thickened endometrial echo, approximately 7.7 mm thick (Tokalioglu et al.; Wang et al., 2024). A heterogeneous mass measuring 13.3 x 7.5 x 11.3 cm, with a volume of 594 cm3, was visualized in the left adnexal topography. Free fluid in the pelvic cavity in moderate quantities was also highlighted. The diagnostic impressions in light of the findings reported were: 1. Uterine hypertonia; 2. Endometrial thickening; 3. Heterogeneous pelvic/abdominal mass to be clarified; 4. Moderate ascites (Nagy, Niu, Ratner, Hui, & Buza, 2024).

Table 1: Granulosa Cell Tumors Overview

Characteristic	Description	Reference(s)
Type	Low-grade cancers from the ovary's specialized stroma	Naeem et al., 2024; Oktar et al., 2024
Composition	Granulosa cells alone or with stromal components (primarily theca cells)	Naeem et al., 2024; Oktar et al., 2024
Prevalence	2-3% of total ovarian neoplasms; 70% of stroma and sex cord tumours	Naeem et al., 2024; Oktar et al., 2024
Age Affected	Can affect any age group, 2/3 of cases in postmenopausal women	Naeem et al., 2024; Oktar et al., 2024
Bilateral Occurrence	2% of cases are bilateral	Naeem et al., 2024; Oktar et al., 2024
Subtypes	Juvenile and adult	Naeem et al., 2024; Oktar et al., 2024
Adult Subtype	Mainly affects perimenopausal or postmenopausal women with, an average age of 50, and 95% of these tumours.	Tokalioglu et al., 2024
Symptoms	Due to tumour development or neoplastic hormone production	Tokalioglu et al., 2024

Table 2: Clinical Case Details

Parameter	Description
Patient Profile	51 years old, G3P3A0, menopausal at age 42
Symptoms	Alterations in bowel habits, abdominal pain
Laboratory Tests	Beta-HCG < 1.2 mIU/ml, CA125 285 U/ml, alpha-fetoprotein 1.2 ng/ml
Chest CT Scan Findings	Substantial pleural effusion linked to atelectasis of the right upper and lower lobes' posterior and basal portions
Abdominal CT Findings	Expansile pelvic mass (702 cm3) with heterogeneous soft tissue density and contrast enhancement; moderate ascites
Transvaginal Ultrasound Findings	Uterus in anteversion (volume 124.50 cm3), regular contours, homogeneous myometrium, thickened endometrial echo (7.7 mm)
Adnexal Mass	Heterogeneous mass (13.3 x 7.5 x 11.3 cm, volume 594 cm3) in the left adnexal topography; moderate free fluid in pelvic cavity
Diagnostic Impressions	Uterine hypertonia, endometrial thickening, heterogeneous pelvic/abdominal mass, moderate ascites
Surgical Procedure	Exploratory laparotomy, left oophorectomy, total abdominal hysterectomy (TAH), removal of contralateral adnexa, peritoneal lavage, iliac lymphadenectomy.

An exploratory laparotomy was performed, which identified a large left ovarian lesion, also occupying the topography of an umbilical scar, flaky, and bleeding in large quantities. Left oophorectomy and total abdominal hysterectomy (TAH) with removal of the contralateral adnexa, peritoneal lavage, and iliac lymphadenectomy were performed (Akbarova & Azimova, 2024).

THE ANATOMOPATHOLOGICAL STUDY REPORTED THE FOLLOWING RESULTS:

- Histological sections of an ovary show a neoplasm consisting of the proliferation of small cells with broken nuclei, forming microfollicular, trabecular, and solid areas permeated by fibro conjunctive stroma. Some mitoses are observed.
- Histological sections of the uterus show the cervix with endocervical squamous metaplasia, "Nabothian" cyst, and focal chronic inflammatory infiltrate in the chorion—hypertrophic endometrium. Myometrium shows focally distributed groups of endometrial glands, as well as nodules consisting of smooth muscle in intersecting bundles, without major cellular atypia or changes suggestive of malignancy (Yaacoub, Hajj, & Khairallah, 2024).
- Histological sections of the ovary show basophilic, fibrous, and dense stroma with numerous white bodies. The cortex is atrophic and has no maturing corpus luteum or atretic follicles.
- Histological sections of the fallopian tubes within normal limits.
- Paratubal cysts are associated.
- Histological sections of 2 lymph nodes show hyperplastic follicles with evident germinal centres and free lymph node sinuses—the absence of signs of malignant specificity.
- Fibroconjunctive and adipose tissue fragments show mild focal chronic inflammatory infiltrate and vascular congestion—the absence of neoplasm in the sample (Dwajani, Rajeev, Shreya, & Madhu, 2024).

The anatomopathological evaluation highlighted histology compatible with GCT and the need for definitive confirmation of the diagnosis by immunohistochemical study, the results of which are presented below (Table 1) (Mazouzi et al., 2024).

Table 1 - Result of the immunohistochemical study.

ANTIBODIES	CLONE	RESULT
1A4	Actin	Negative
E29	EMA	Negative
Pancytokeratins	Pancytokeratins	Negative
Polyclonal	Protein S100	Positive Focal
V9	Vimentin	Positive
OV-TL12/30	CK7	Negative
DAK-CALRET	Calretinin	Focal positive

Immunohistochemical analysis showed positivity for S100 protein (polyclonal clone), vimentin (clone V9), and calrentin (clone DAK-CALRE). In this context, the morphological findings associated with focal Calretinin expression were compatible with GCT. Regarding past medical history, the patient had no comorbidities and denied the use of medications, previous surgeries, smoking, and alcohol consumption (Amirkashani, Nasiri, Dadakhani, Mortazavi, & Khoshkbarforoushan, 2024; Schonäuer et al.).

DISCUSSION:

Most patients with GCT experience nonspecific signs and symptoms, such as abdominal pain and distension. However, due to hormone secretion by the tumour, intermenstrual and postmenopausal bleeding, atypical endometrial hyperplasia, and endometrial adenocarcinomas may occur. Although signs and symptoms of hyperestrogenism are identified in some patients, there is no systematic indication for estrogen dosing, as levels of this hormone are generally low and not valid for patient monitoring (Hassan, 2024; Tjokroprawiro, Novitasari, Ulhaq, & Sulistya, 2024). Since this is a rare neoplasm, the use of tumour markers as screening strategies is not practical, and they are mainly used in monitoring possible recurrences. Although the staging of GCTs and ovarian epithelial tumours is identical, these neoplasms evolve and grow in different patterns (Table 2). Most GCTs are detected at stage I (80 to 90% of cases) and grow as pelvic masses of varying sizes (Watkins & Young, 2024).

Table 2 - FIGO surgical staging of ovarian, fallopian tube, and peritoneal cancer according to the International Federation of Gynecology and Obstetrics.

STAGE I	tumour confined to the fallopian tubes or ovaries.
IA	The tumour was confined to the surface of the fallopian tube or one ovary (intact capsule); no malignant cells were seen in the ascitic fluid or peritoneal washings.
IB	tumour confined to one or both fallopian tubes or ovaries (with an intact capsule); absence of tumour on the ovary or fallopian tube's exterior; and absence of cancerous cells in ascitic fluid or peritoneal washings
ICI	Extravasation during surgery.
1C2	Before surgery, the IC2 capsule burst, or there was a malignancy on the ovary or fallopian tube's surface.
IC3	Cancerous cells in peritoneal or ascitic fluids.
II	Primary peritoneal carcinoma is a tumour encompassing one or both ovaries, fallopian tubes, and pelvic extension (below the pelvic brim)
IIA	Implants in the ovaries, fallopian tubes, uterus, and extension.
IIB	Implants in various intraperitoneal tissues of the pelvis and extension.
III	A tumour affecting one or both ovaries, fallopian tubes, or primary peritoneal malignancy with metastases to the peritoneum outside of the pelvic and retroperitoneal lymph nodes that have been proven by microscopy.

IIIA	Lymph nodes are retroperitoneally positive, either with or without microscopic metastases of the peritoneum outside the pelvis.
IIIA1	Only histologically verified positive retroperitoneal lymph nodes.
IIIA1(I)	Metastases with a maximum diameter of < 10 mm.
IIIA1(II)	Metastasis with a maximum diameter of 10 mm.
IIIA2	Microscopic involvement of the extra-pelvic peritoneum (beyond the pelvic brim), either positive retroperitoneal lymph nodes or not.
IIIB	Macroscopic peritoneal metastases with or without positive retroperitoneal lymph nodes larger than 2 cm in diameter and spread outside the pelvis.
IIIC	macroperitoneal metastases that are larger than 2 cm and spread outside of the pelvis, either with or without involvement of the retroperitoneal lymph nodes (e.g., tumours that spread to the splenic and hepatic capsules but do not reach the parenchyma of the organs).
IV	distant metastases.
IVA	Pleural effusion with cytology that is positive.
IVB	Hepatic or splenic parenchymal and extra-abdominal organ metastases (lymph nodes outside the abdominal cavity and inguinal lymph nodes) and intestinal transmural involvement.

Most diagnosed GCTs are classified as poorly aggressive and, unlike ovarian epithelial neoplasms, have a favourable prognosis, as they tend to remain localized and have survival rates greater than 95% when analyzing stage I tumours. However, there are reported cases of GCT with metastases to the liver, lung, kidney, and peritoneum. In cases of extra ovarian disease, mortality can exceed 40%. Recurrence of these tumours occurs, in most cases, in the abdomen itself and approximately 5-10 years after diagnosis (Erdogan et al., 2024; Young, 2024). As regards the factors linked to the prognosis of the disease, the staging of the tumour, the absence or presence of rupture of the tumour capsule, the degree of differentiation of the disease, the mitotic index, and the presence of vascular embolization caused by neoplastic cells stand out. The treatment of GCT is surgical and can be followed by adjuvant therapy in patients with a history of extra ovarian disease (Xiao, Du, Yuan, Luo, & Song, 2024).

CONCLUSION:

Granulosa cell tumours (GCTs) should be considered in the differential diagnosis of an ovarian mass in postmenopausal patients, and even after diagnosis and adequate surgical treatment, the patient should be monitored due to the risk of recurrence.

Ethical Committee Permission

The study was approved by Hayatabad Medical Complex and informed consent was taken from the patient.

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