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Epidemiology and Pathology of Granulosa Cell Tumors: Insights from Nine Ovarian Tumor Cases

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ABSTRACT

Granulosa cell tumors are malignant neoplasms that arise from the sexual cords and ovarian stroma. This study reviews the characteristics of 9 cases of granulosa cell tumors, with findings drawn from the existing literature. Among the cases, eight patients had adult-type granulosa tumors, while one patient had the juvenile form. The age of the patients ranged from 29 to 75 years, with a predominance of postmenopausal women (77.77%). The most common presenting symptoms were abdominal-pelvic pain (77.77%) and abdominal-pelvic masses (55.55%), followed by endocrine symptoms such as metrorrhagia (22.22%), and dysuria in one patient. Histologically, most cases showed typical microscopic features, including a diffuse tumor proliferation pattern with nuclear grooves present in all cases and Call-Exner bodies observed in two-thirds of cases. Surgical resection is the primary treatment approach, with the extent of surgery guided by the tumor stage and the patient's overall health status. Although adjuvant chemotherapy and/or radiation may be used in certain cases, the optimal treatment strategy remains unclear due to the rarity of these tumors and the absence of large-scale clinical studies.

Keywords: Ovary, Granulosa tumor, Epidemiological profile, Anatomopathological study

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Introduction

Granulosa tumors of the ovary are uncommon malignant neoplasms that fall under the category of stromal and sex cord tumors [1]. These tumors are characterized by a typically slow progression, a high likelihood of being localized at diagnosis, and a tendency for delayed recurrence [2].

Originating from the sex cord-stromal cells of the ovary, granulosa tumors are classified into two main types: adult and juvenile. Adult granulosa tumors are more frequently encountered and generally present as a unilateral mass with a relatively low risk of malignancy. On the other hand, juvenile granulosa tumors, though rare, are more aggressive and often manifest as precocious puberty in younger girls [3].

The disease course of ovarian granulosa tumors is often prolonged, with many cases showing recurrence even after periods of apparent remission. This slow progression is typically attributed to the presence of well-differentiated tumor cells with minimal mitotic activity and a low proliferative index [1].

Treatment primarily involves surgical removal of the tumor, with the approach depending on the disease stage and the patient's overall condition. Although adjuvant therapies such as chemotherapy or radiation may be utilized in certain circumstances, the optimal management strategy for ovarian granulosa tumors remains uncertain, mainly due to the rarity of the condition and the limited number of comprehensive clinical trials [4].

This study examines the characteristics of 9 cases of granulosa cell tumors, with findings drawn from the existing literature.

Materials and Methods

A retrospective study was conducted over 10 years, from January 2010 to December 2019, at the Pathological Anatomy Department of CHU Mohammed VI. We reviewed 9 cases of ovarian granulosa tumors to examine both the epidemiological and anatomical-pathological features of these tumors.

Results and Discussion

Out of the 9 patients, 8 were diagnosed with adult-type granulosa tumors, while only 1 had a juvenile form. The patients were aged between 29 and 75 years, with a significant proportion being postmenopausal (77.77%).
The most common initial symptoms were abdominal-pelvic pain (77.77%) and the presence of abdominal-pelvic masses (55.55%), followed by endocrine signs, such as metrorrhagia (22.22%), and a case of dysuria in one patient.
All the tumors were unilateral, with an average size of 18 cm. Macroscopic analysis revealed that the majority of the tumors had a solid-cystic appearance (75%), with hemorrhagic changes being observed in 87.5% of the cases.
Histological examination showed a characteristic diffuse architecture with the presence of nuclear grooves in all the cases. Two-thirds of the cases also exhibited Call-Exner bodies. Most patients had a mitotic index of fewer than 10 mitoses per 10 high-power fields (77.77%).
Immunohistochemical tests were conducted on 3 patients, with the most strongly expressed marker being inhibin (100%), followed by calretinin (66.66%) and vimentin (33.33%).
The estimated incidence of ovarian granulosa tumors is approximately 1.3 cases per 100,000 people annually. These tumors can occur at any age but are most commonly seen in women around the age of 53. The adult form of these tumors tends to have a solid and multicystic appearance and is often encapsulated. The microfollicular subtype is the most common in adult tumors. Immunohistochemical analysis revealed strong expression of vimentin (100%), CD 99, and AML (92%), with inhibin being the most prominently expressed marker **(Figure 1)**.

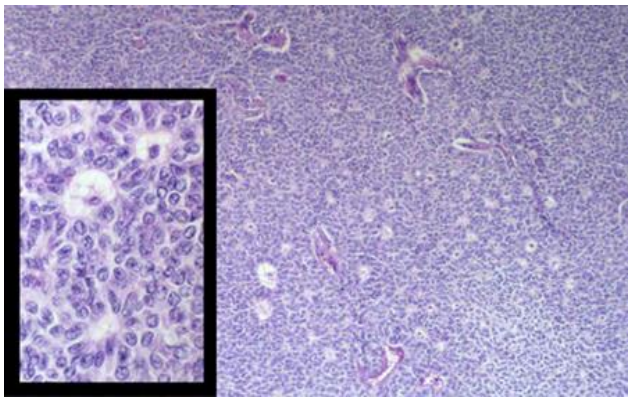

Figure 1. Microfollicular architecture (at x100 magnification), we note in the insert (at x400 magnification), the Call-Exner bodies and the characteristic nuclear grooves

Ovarian granulosa cell tumors are a rare category of tumors originating from the sex cord-stromal cells of the ovary. These tumors are classified into two main types: adult and juvenile. The adult form is more common and tends to develop as unilateral ovarian masses with low malignancy, whereas the juvenile form, though rare, is known to be more aggressive and typically presents with precocious puberty in young girls [5-7].
While these tumors can develop at any age, the adult form is most commonly diagnosed in women aged 40 to 70 years, with a peak occurrence around 53 years. In contrast, juvenile granulosa tumors are seen in prepubertal girls or young women under the age of 30 years.
Granulosa tumors usually progress slowly, with a tendency for late recurrence. This slow course is often linked to the well-differentiated tumor cells that exhibit minimal mitotic activity and a low proliferative rate [8-11].

Clinical presentation

The clinical symptoms of ovarian granulosa tumors are diverse, including abdominal pain (30-50%), bloating due to mass effect, and hormonal symptoms like menstrual irregularities, intermenstrual bleeding, postmenopausal bleeding, or amenorrhea (41%). These tumors generally exhibit a benign course, although recurrence after long intervals is common.

Tumor features

Granulosa tumors usually present with solid, multicystic masses that are often encapsulated. Macroscopically, the tumors appear yellowish or grayish, with hemorrhagic areas and necrotic zones. The tumors typically measure around 12 cm in diameter but can range anywhere from 1 to 30 cm. Most cases are unilateral.

Histologically, adult granulosa tumors are classified into five subtypes, with microfollicular being the most prevalent. This subtype is marked by "Call-Exner" bodies, which are eosinophilic fluid-filled spaces, and "coffee bean"-shaped nuclei. Other subtypes include macrofollicular, trabecular, insular, and solid tubular forms. In contrast, juvenile granulosa tumors tend to show lobulated architecture, fewer "Call-Exner" bodies, and more pronounced luteinization.

Immunohistochemistry

Immunohistochemical testing reveals that granulosa tumor cells predominantly express vimentin (100%), CD 99, and smooth muscle actin (92%). Inhibin is the most strongly expressed marker, while other markers include AE1 AE3 (present in one-third of cases), S100 (in one-third of cases), and desmin (65%). Calretinin, though positive in some cases, is less specific than inhibin.

Management and prognosis

These tumors generally exhibit a slow-growing nature and are frequently diagnosed at localized stages, but they are known for delayed recurrences. Surgical resection remains the primary treatment approach for both initial management and recurrence. However, the roles of chemotherapy, radiation therapy, and hormonal treatments remain unclear, as the rarity of the disease makes it difficult to establish standardized treatment protocols.

Conclusion

While surgery is the mainstay treatment for both the initial diagnosis and subsequent recurrences of ovarian granulosa tumors, the role of chemotherapy, radiotherapy, and hormonal therapy in managing these tumors requires further investigation.

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Ethics Statement: None

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