CASE REPORT

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Coexistence of Ovarian Mucinous Cystadenoma and Gynandroblastoma: A Very Rare Case Report

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ABSTRACT Gynandroblastoma (GA) is a very rare subgroup of ovarian sex cord-stromal tumors. GA contains both granulosa and Sertoli-Leydig cell differentiation in varying proportions. A 31-year-old female patient applied to our hospital with a history of lower abdominal pain. Ultrasound examination revealed a 95 mm multilobulated cyst in the left ovary. The patient underwent laparotomy, and left ovarian cystectomy was performed. Microscopic examination revealed mucinous cystic neoplasia consisting of multiple cystic structures covered with non-proliferative mucinous epithelium. Besides, a well-structured tubule formation consisting of granulosa cell tumor component and Sertoli cells were observed. These findings suggest that mucinous cystic neoplasm and GA coexist in this case. This finding was unprecedented in the literature.

Keywords: Ovarian gynandroblastoma; sex cord-gonadal; stromal tumors

Gynandroblastoma (GA) is a very rare subgroup of ovarian sex cord-stromal tumors.[1] Robert Meyer first described the GA in 1930, and after this, the English literature reported only 28 cases.[2] Although the pathogenesis of GA remains undiscovered, it is presumed that this tumor develops from a single progenitor cell that can differentiate into both male and female components.[3] Morphologically, GA contains both granulosa and Sertoli-Leydig cell differentiation in varying proportion.[4] These granulosa cells generally show the characteristics of adult-type granulosa cells.[1] However, in extraordinarily rare cases, the granulose cell component of GA consists of juvenile type granulosa cells.[5] The presence of an epithelial tumor component in gynandroblastoma has not been reported to date. Heterologous mucinous epithelium may rarely be seen in adult-type granulosa cell tumors (GCT).[6] However, the co-occurrence of mucinous neoplasm with GCT is an unexpected condition. To the best of our knowledge, this is the only case in the literature in which gynandroblastoma and mucinous cystic neoplasm coexist.

CASE REPORT

An informed consent form was obtained from the patient. A 31-year-old female patient admitted to Emergency Department of Diyarbakır Gazi Yaşargil Training and Research Hospital with complaints of lower abdominal pain. Ultrasound examination revealed a 95 mm multilobulated cyst in the left ovary. The right ovary and uterus were normal. Endometrial thickness was 6 mm. Pelvic doppler ultrasound examination revealed a 118x96x80 mm cystic mass with multiple contours and septations in the left ovary. Ovarian torsion could not be ruled out. Her age of menarche was 15 years. She had no family records of genetic syndromes and no other underlying disorders. She had irregular menstrual bleeding and

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virilization that had continued for the last year. There were no abnormal results in hemogram and biochemical tests. CA 125 value was found to be 48.2 U/mL while other serum tumor markers, CA 15-3, Ca 19-9, and CEA were within the normal range. The patient underwent laparotomy, and left ovarian cystectomy was performed. We detected a stage 1 tumor, and there was no extra-ovarian involvement with it. Macroscopic examination revealed a 12x9x8 cm, well-circumscribed, multicystic mass with serous-mucinous fluid drainage. The wall thickness was measured as 2 mm at the thickest location of the cyst. No solid component was detected. Microscopic examination revealed mucinous cystic neoplasia consisting of multiple cystic structures covered with non-proliferative mucinous epithelium (Figure 1-6). Some of these cysts were crowded back to back and millimeter in size, while others were enlarged. Also, a well-structured tubule formation consisting of granulosa cell tumor

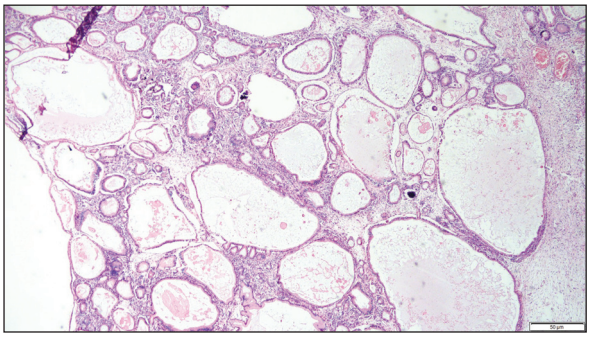

FIGURE 1: Single layer of columnar cells with abundant intracellular mucin and small basilar nuclei with multipl cysts. There is no stratification, hyperchromasia, or mitotic activity (H&E x100).

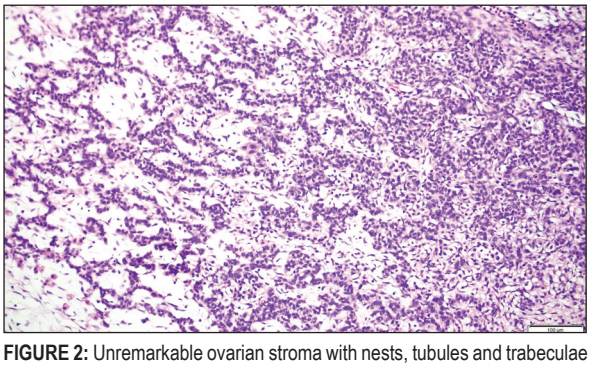

FIGURE 2: Unremarkable ovarian stroma with nests, tubules and trabeculae composed of polygonal cells with moderate pale vacuolated cytoplasm, no atypia and no mitotic figures; focal solid and microfollicular growth patterns with rare Call-Exner like structures, with cells having only scant cytoplasm and occasional cells with angulated nuclei and rare grooves (H&E x200).

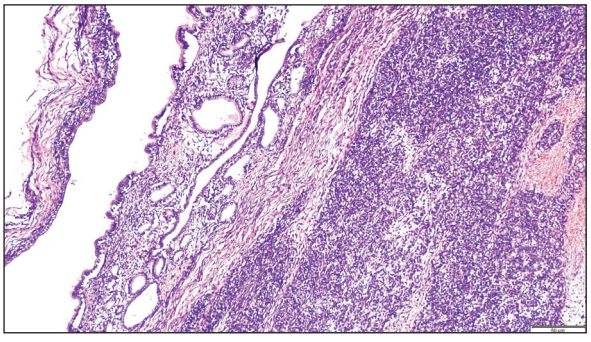

FIGURE 3: On the right side sex cord stromal tumor with equal numbers of granulosa-theca cells and Sertoli-Leydig cells and mucinous component on the left side (H&E x100).

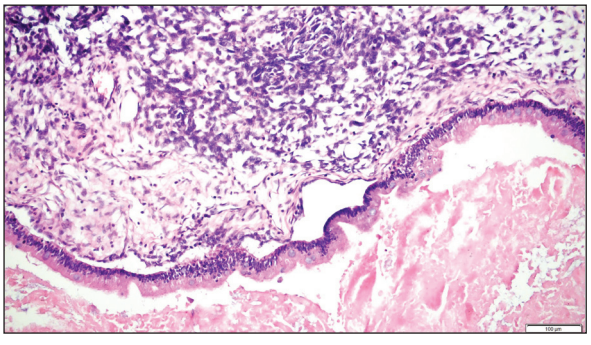

FIGURE 4: Cyst epithelium with mucinous epithelium and mucinous secretion and sex cord stromal component within stroma (H&E x200).

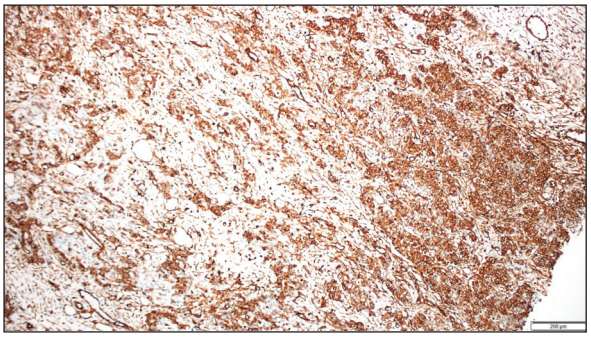

FIGURE 5: Positive staining of sex cord stromal cells by immunohistochemical staining of Calretinin (x100).

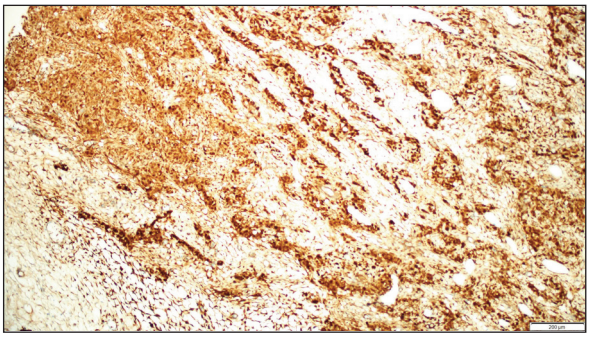

FIGURE 6: Positive staining of granulosa-theca cells by immunohistochemical staining of Vimentin (x100).

component (some of which show trabecular alignment or small tumor islands) and Sertoli cells were observed. Sertoli-Leydig cell tumor components, including ambiguous Leydig cells in the fibrous band-like stroma, were also observed. In the presence of these morphological findings, the patient was diagnosed as gynandroblastoma and mucinous cystadenoma.

DISCUSSION

GA is a very rare subtype of ovarian sex cord-stromal tumors. The majority of these tumors occur in young patients. GA consists of a compound of two histological components: GCT and Sertoli-Leydig cell tumor (SLT) differentiation. Since it is hormonally active, estrogenic and androgenic symptoms are often seen in these patients.[7] Virilization is common in patients with GA.[8] Peripheral conversion of testosterone to estrogen can cause endometrial proliferation or hyperplasia.[8] This can cause abnormal uterine bleeding. In this case, there were irregular menstrual bleeding and virilization symptoms that persisted for about one year. But the patient had no history of infertility. However, preoperative FSH, LH, testosterone, and androstenedione levels were not measured. Therefore, it should be kept in mind that a detailed preoperative hormonal evaluation may be beneficial in ovarian masses.

Serum tumor marker values are generally normal in GA. In contrast, serum alpha-fetoprotein levels were high in GA with juvenile granulosa cell component, which was correlated with the proportion of Leydig cells.[4] In this case, serum CA-125 levels were high. This can be explained by the presence of a mucinous component in this case.

Although GA is seen in a wide age range (15-65), the average age is 31 years. GA is usually unilateral and is seen as pink-yellow-brown nodules divided by fibrous septa.[9] It can be solid or partly cystic. Solid areas are white, tan, or yellow. GA is available in a wide range of sizes from 1 cm to 20 cm in diameter.[4] Our case was 31 years old, and the macroscopic appearance of this mass was consistent with the aforementioned features.

For the diagnosis of GA, the minor tumor component (both granulosa cells in an SLT and Sertoli-Leydig cells in a GCT) should be seen in at least 10% of the tumor and easily recognizable.[5] Sometimes, researchers can focally observe well-differentiated Sertoli-Leydig cells in GCT's and vice versa. Hence, adequate tumor sampling is crucial for a precise diagnosis.[2] In this case, the granulosa cell component constituted 30% of the tumor, the Sertoli-Leydig cell component constituted 30% of the tumor, and the mucinous component constituted 40% of the tumor.

GA's consist of granulosa cell regions containing Call-Exner bodies, Sertoli cells forming hollow tubules and Leydig cell regions containing Reinke crystalloids.[10] There are several immunohistochemical markers used in the differential diagnosis. Still, these markers are not specific to GA, and researchers use these markers to diagnose all types of ovarian sex-cord stromal tumors. Some of the immunohistochemical stains for markers that have known variable specificity for sex cord-stromal tumors are calretinin, inhibin, steroidogenic factor 1 (SF-1), CD99, MART-1/melan-A, and WT1. MART-1/melan-A marker is specific for SLT and steroid cell tumors.[11] Recently, the cell cycle regulatory protein 14-3-3 sigma is a diagnostic marker for GCT and steroid cell tumors.[12] In this patient, in the immunohistochemical study, both GCT and SLT components were positive for calretinin and vimentin. Besides, microscopic examination of the hematoxylin-eosin (H&E) stained preparation revealed mucinous cystic neoplasia consisting of multiple cystic structures covered with non-proliferative mucinous epithelium. These findings suggest that mucinous cystic neoplasm and GA coexist in this case. This was unprecedented in the literature before.

Since GA is a very rare tumor, it may be difficult to predict this tumor's biological behavior in a patient. The majority of previously reported GA have been clinically evaluated as stage 1 and showed benign behavior.[7] In general, this neoplasia with low potential for malignant behaviour has been recognized to be well differentiated. Clinicians treat the majority of the patients with stage 1 GA by surgical resection successfully and follow up without adjuvant therapy. Although the risk of recurrence is reported to be negligible, molecular and immunohistochemical

analyses demonstrated recurrence in one patient at 10th year after the initial diagnosis.[7] In the same case, primary and recurrent tumors presented minor genetic instability in the 17q12.2 gene locus. Some authors believe that these patients should be followed as GCT, while others may be followed as SCT.[7] Due to the small number of patients in the literature, and insufficient studies on long-term follow-up, the care and clinical follow-up of GA patients should be performed with caution. The published recurrent case also highlights the importance of long-term follow-up. In our case, the clinical follow-up was ongoing, and no recurrence was detected in postoperative 24-month period. The presence of mucinous cystadenoma with GA makes the follow-up more critical. Because the association of GA with mucinous cystadenoma or any epithelial tumor has not been reported in the literature.

In conclusion, GA should be kept in mind in the differential diagnosis of ovarian mass, and patients should be questioned and examined carefully for androgenic and/or estrogenic symptoms. To the best of our knowledge, GA, a very rare ovarian neoplasia, has not been reported in the literature associated with mucinous cystadenoma or any epithelial tumor. It reveals that there are many more secrets about this tumor. Also, a long-term clinical follow-up of patients with GA should be kept in mind.

Source of Finance

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Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

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