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Clear Cell Ovarian Tumor (CCOT): 03 Cases Report And Literature Review

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Abstract
Ovarian tumors represent a diverse group of neoplasms with varying clinical presentations, histological features, and therapeutic challenges. This article presents three clinical cases of ovarian masses, each with distinct characteristics, to highlight the diagnostic and management complexities in this field. Case 1 features a 40-year-old patient with an ovarian mass diagnosed through imaging and confirmed by histological examination. Case 2 discusses a 65-year-old patient presenting with chronic pelvic pain and a large pelvic mass, with surgical and pathological findings consistent with peritoneal carcinoma. Case 3 describes a 50-year-old postmenopausal patient with an abdominal mass, later diagnosed with a tubulopapillary carcinoma after surgical resection and histopathological analysis.
In all cases, imaging modalities such as ultrasound, CT scans, and CA 125 measurements played a pivotal role in guiding diagnosis and treatment planning. Surgical management, including adnexectomy and total hysterectomy, along with peritoneal biopsies, were essential in obtaining definitive diagnoses. Histopathological examination revealed varying tumor architectures, including tubulopapillary and solid-cystic structures, with specific cellular characteristics indicative of malignancy.
Adjuvant chemotherapy and lymphadenectomy were considered based on staging and tumor spread, underscoring the importance of multimodal approaches in the management of ovarian malignancies. The article also discusses the therapeutic challenges, particularly in cases with poor response to standard chemotherapy and the potential role of emerging targeted therapies.
These cases underscore the importance of early diagnosis, precise surgical intervention, and personalized treatment strategies to improve patient outcomes in ovarian cancer. Continued research into molecular markers and novel therapies is essential for optimizing management in the face of these heterogeneous and often aggressive tumors.

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I. Introduction:

Clear cell ovarian carcinoma (CCOC) is a rare epithelial tumor, accounting for approximately 5–10% of ovarian cancers. It is distinguished from other histological subtypes by unique clinical, molecular, and therapeutic characteristics. Associated with endometriosis in nearly 50% of cases, it primarily affects perimenopausal women and often presents with non-specific symptoms such as pelvic pain, adnexal masses, or ascites(1).

Histopathologically, CCOC is characterized by the presence of glycogen-rich clear cells and the expression of specific markers, particularly **HNF-1β**. At the molecular level, recurrent mutations in **ARID1A** and **PIK3CA** are frequently observed, opening new therapeutic perspectives. Unlike high-grade serous carcinomas, CCOC exhibits relative resistance to platinum-based chemotherapy, making its treatment more challenging and its prognosis often poorer in advanced disease stages.

Given these specificities, a better understanding of the mechanisms involved in CCOC tumorigenesis is essential for developing appropriate diagnostic and therapeutic strategies. This article aims to provide an overview of the clinical, histopathological, and molecular characteristics of this entity while exploring current and future therapeutic approaches.

II. Patients And Case Reports

Case Report 1

This is a 40-year-old patient with no significant medical history who presented with an increase in abdominal volume. Clinical examination revealed a firm latero-uterine mass.

Pelvic ultrasound showed an enlarged right ovary. Pelvic CT scan identified a 15 cm right latero-uterine mass with solid and cystic components, suggesting an ovarian origin.

Surgical exploration revealed a 10 cm right ovarian mass with no signs of peritoneal carcinomatosis. A right adnexectomy, total hysterectomy, and peritoneal biopsy were performed. Histological examination confirmed the diagnosis.

Case Report 2

A 65-year-old postmenopausal patient with no significant medical history presented with chronic pelvic pain. Clinical examination revealed an enlarged uterus with a firm latero-uterine mass.

Pelvic ultrasound showed a large myomatous uterus with an enlarged right ovary. Pelvic CT scan identified two latero-uterine masses with solid and cystic components, most likely of ovarian origin, along with a myomatous uterus and peritoneal carcinoma. CA 125 levels were elevated at 400 UI/ml.

Surgical exploration revealed two irregular ovarian masses measuring 12 cm and 7 cm on the right and left sides, respectively. A bilateral adnexectomy, total hysterectomy, and peritoneal biopsy were performed.

Histopathological Findings: The tumor displayed a carcinomatous structure composed of solid masses, tubules, and cystic formations. Tumor cells varied in size and had irregular nuclei with abundant chromatin, which appeared either clear or eosinophilic. Some nuclei were apically projected, creating a "hobnail" appearance. Peritoneal involvement was also observed.

Case Report 3

A 50-year-old postmenopausal, single patient with no significant medical history presented with a sensation of heaviness and an increase in abdominal volume. Clinical examination revealed a firm latero-uterine mass palpable up to the umbilicus, with no signs of abdominal effusion.

Pelvic ultrasound showed a normal-sized uterus and a solid-cystic abdominopelvic mass extending to the epigastrium, measuring 19 cm in its largest axis, with areas of Doppler signal and no peritoneal effusion. The right adnexa was not visualized.

Pelvic CT scan revealed a large solid-cystic pelvic mass, measuring **12.5 × 12.8 × 15 cm**, located medially, above the bladder, and suspected to be malignant. Its anatomical relationships were as follows:

- **Anteriorly:** In contact with the abdominal wall, with focal loss of the fat separation plane.
- **Posteriorly:** In contact with the external iliac vessels bilaterally, with loss of the fat separation plane.
- **Superiorly:** Displacing the pelvic small bowel loops and the cecum, with loss of the fat separation plane. A thin layer of pelvic fluid was also noted.

Surgical Exploration Surgical exploration revealed a **right latero-uterine mass measuring 15 × 15 cm**, without exophytic growths or atypical vascularization. The left adnexa appeared normal. There was minimal ascites, no evidence of peritoneal carcinomatosis, and the omentum appeared normal. **CA 125 level was 34 UI/ml**. A right adnexectomy, total hysterectomy, and peritoneal biopsy were performed.

Histopathological Findings The tumor exhibited a **tubulopapillary architecture** with a fibrous and edematous stroma. The tumor cells were cuboidal or columnar, with **atypical central nuclei, prominent nucleoli, and a characteristic hobnail appearance**. The cytoplasm was eosinophilic, and multiple mitotic figures were observed.

The patient subsequently underwent a **second surgery** for **pelvic and para-aortic lymphadenectomy**, with the following results:

- **Right pelvic lymph nodes:** 13/13 negative
- **Left pelvic lymph nodes:** 11/11 negative
- **Para-aortic lymph nodes:** 5/5 negative

She then received **chemotherapy** as part of her treatment plan.

III. Discussion

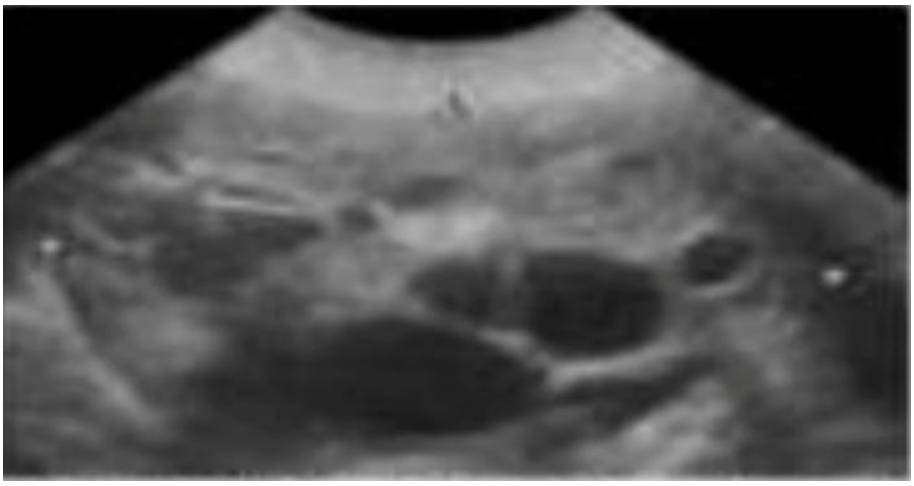
Ovarian tumors, particularly those of epithelial origin, present a significant diagnostic and therapeutic challenge due to their often non-specific clinical presentation and variable prognosis. Among these, clear cell ovarian tumors (CCOT)and serous cystadenocarcinomas are the most frequently encountered, but other rare subtypes, such as tubulopapillary carcinoma and solid-cystic masses, can also pose difficulties in diagnosis and management. The three clinical cases discussed in this article highlight the diversity in presentation, diagnostic workup, and treatment strategies for ovarian masses.

Clinical Presentation and Diagnosis

Ovarian masses are typically diagnosed during imaging studies performed for unrelated abdominal complaints or routine examinations. In the presented cases, the patients' symptoms varied from abdominal

distention and pelvic heaviness to chronic pain, which are often non-specific. This highlights the importance of a thorough clinical evaluation and imaging workup, as early symptoms can be subtle and misinterpreted.(3)

Pelvic ultrasound and CT scans are crucial diagnostic tools for evaluating ovarian masses. As seen in the cases presented, imaging studies often reveal solid-cystic masses with heterogeneous characteristics that suggest malignancy. The use of Doppler ultrasound, as well as the measurement of tumor markers such as CA 125, is essential for assessing the potential malignancy of the mass. In our cases, elevated CA 125 levels and imaging characteristics raised suspicion of ovarian cancer, guiding surgical management and further investigation.(2,5,6)



Surgical Exploration and Histopathological Findings

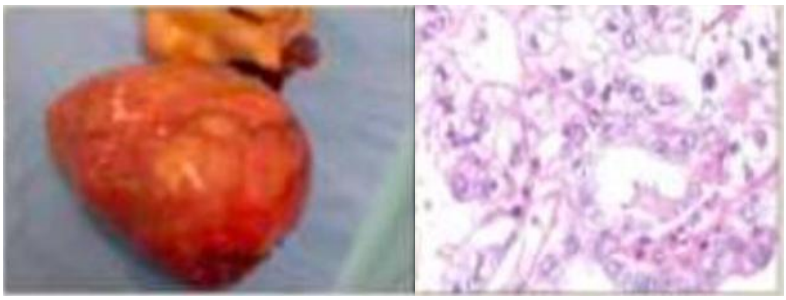
The surgical exploration of ovarian tumors aims to achieve both diagnostic clarity and therapeutic intervention. In these cases, total hysterectomy and bilateral adnexectomy were performed, with peritoneal biopsies to rule out peritoneal carcinomatosis. Histopathological examination confirmed the malignancy in all cases, revealing varied tumor architectures including tubulopapillary structures with hobnail cells in one case, a classic finding in clear cell carcinoma and related subtypes(3).

Macroscopic appearance: The lesion is solid, beige-yellow in color, and associated with a unilocular or multilocular cystic component. The contents of the cyst can be serous, mucinous, or hemorrhagic (3).

Microscopy:

Tumor cells are organized into four distinct architectural patterns, which may be predominant to varying extents. These patterns are, in decreasing order of frequency: papillary, tubulocystic, solid, and reticular, resembling the micro-vesicular architecture of the yolk sac tumor.

The importance of obtaining adequate tissue for histological analysis cannot be overstated. Distinguishing between benign, borderline, and malignant tumors based on cellular and stromal features is crucial in formulating an appropriate management plan. Tumor characteristics such as mitotic activity, cytoplasmic eosinophilia, and cellular pleomorphismcan offer important clues to the malignancy grade and prognosis.



Treatment and Prognosis

The treatment of ovarian tumors generally involves a combination of surgery and, when necessary, chemotherapy. The role of chemotherapy in ovarian cancer is well established, particularly in patients with advanced-stage disease or positive surgical margins(4). However, as seen in these cases, the response to

chemotherapy can be variable depending on the histological subtype and the molecular characteristics of the tumor(4).

In clear cell ovarian tumors, the response to platinum-based chemotherapy is often suboptimal, and there may be a need for alternative or adjunctive treatments. Emerging targeted therapies, such as PI3K/AKT/mTOR inhibitors and PARP **inhibitors, show** promise in improving outcomes for patients with resistant forms of ovarian cancer. The use of lymphadenectomy in staging and treatment has also become an integral part of management, particularly when assessing the extent of metastasis.

The Role of Lymphadenectomy and Chemotherapy

In our third case, the patient underwent a comprehensive pelvic and para-aortic lymphadenectomy following the initial surgery. Lymph node involvement remains one of the most important prognostic factors in ovarian cancer. The negative lymph node findings in this case are a favorable prognostic sign, suggesting that the tumor had not spread beyond the pelvic region. Chemotherapy was subsequently administered, highlighting the continued importance of adjuvant treatment in preventing recurrence and managing microscopic disease.

The management of peritoneal carcinomatosis remains challenging. Although early-stage disease may be amenable to surgery alone, patients with peritoneal involvement often require multimodal treatment approaches, including aggressive cytoreductive surgery and chemotherapy.

Targeted therapies and immunotherapy may eventually improve outcomes, but much remains to be learned in this area.

IV. Conclusion

Ovarian tumors, particularly when presenting with complex imaging characteristics and elevated tumor markers, require careful evaluation and management. While surgery remains the cornerstone of treatment, the use of chemotherapy and newer targeted therapies is essential, especially in the case of advanced or resistant disease. Early diagnosis, appropriate staging, and comprehensive surgical intervention are crucial in improving patient outcomes. Continued research into molecular markers and novel therapies will hopefully improve prognosis, particularly for those with high-risk, difficult-to-treat tumors like clear cell carcinoma

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