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Case Report

Unveiling ovarian carcinosarcoma: a rare case report

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ABSTRACT

Ovarian carcinosarcoma (OCS), also known as malignant mixed Müllerian tumor, is a rare and highly aggressive neoplasm, accounting for only 1-4% of all ovarian cancers. Characterised by both high-grade epithelial and mesenchymal components, it typically presents at an advanced stage, contributing to poor prognosis and low survival rates. A 36-year-old multiparous woman presented with progressive abdominal distention, pain, and gastrointestinal complaints. Her CA-125 levels were elevated (834 U/ml) and contrast-enhanced computed tomography (CT) findings revealed a large abdominopelvic mass. Histopathological examination confirmed OCS, with immunohistochemistry (IHC) showing positivity for pan-cytokeratin (PanCK) and S100, and negativity for WT1 on trucut biopsy. The patient received neoadjuvant chemotherapy with paclitaxel and carboplatin, followed by interval debulking surgery and adjuvant chemotherapy. Despite limited data on OCS, the case highlights the importance of cytoreductive surgery, optimal chemotherapy regimens, and emerging molecular-targeted therapies such as poly(ADP-ribose) polymerase (PARP) inhibitors and bevacizumab. Further research, including OCS-specific trials, is necessary to refine treatment approaches.

Keywords: Ovarian carcinosarcoma, Malignant mixed Müllerian tumor, Biphasic malignancy, Cytoreductive surgery, Paclitaxel, Carboplatin

INTRODUCTION

Ovarian carcinosarcoma (OCS), also known as malignant mixed Müllerian tumor, is a rare and highly aggressive type of ovarian cancer that accounts for only 1-4% of all ovarian cancer cases. It consists of both carcinomatous (epithelial) and sarcomatous (mesenchymal) malignant cell populations, which were once believed to represent separate tumors. However, molecular studies have revealed that these two components share a common clonal origin. OCS differs significantly from uterine carcinosarcoma (UCS), despite similar histology, with distinct clinical behaviors and molecular profiles.[1] Ovarian cancer incidence increases with age, with OCS typically diagnosed between ages 60 and 70. Risk factors include an aging population, nulliparity, and BRCA gene mutations.

OCS typically presents at an advanced stage and has a poor prognosis, with most patients experiencing recurrence within a year after initial treatment. The tumor's biphasic nature includes high-grade carcinomatous elements, which can resemble any ovarian carcinoma type (e.g., high-grade serous, endometrioid, clear cell), and sarcomatous components, which may exhibit homologous or heterologous differentiation. Common heterologous elements include chondrosarcoma and rhabdomyosarcoma, while rare cases may display angiosarcoma, osteosarcoma, or liposarcoma differentiation.[2]

Early detection is rare, with over two-thirds diagnosed at advanced stages, leading to poor 5-year survival rates of 20-40%. Standard treatment involves cytoreductive

surgery and platinum-based chemotherapy, but relapse occurs in 80% of cases within 12 to 18 months. Molecular targeted therapies show promise for specific patient groups due to the genomic diversity of ovarian cancer.[3] Advanced International Federation of Gynecology and Obstetrics (FIGO) stage and older age at diagnosis are associated with worse outcomes, and optimal cytoreductive surgery is crucial for survival. Here we present one such rare case of a young lady presented with ovarian carcinosarcoma.

CASE REPORT

A 36-year-old multiparous woman (P4L4) presented with a two-month history of progressive abdominal distention, accompanied by intermittent dull aching pain of insidious onset. She also reported anorexia and constipation. Her medical history included tubal ligation 10 years prior and a diagnosis of premature ovarian insufficiency, following evaluation for secondary amenorrhea five years ago. There were no significant findings in her personal or family medical history.

On examination, she appeared pale, although other general findings were unremarkable. Abdominal examination revealed soft distention with a palpable hard mass, demonstrating restricted mobility and irregular margins, corresponding to approximately 16 weeks gestation. Speculum examination showed a small cervix with a healthy vaginal mucosa. Bimanual pelvic examination revealed a fixed hard mass occupying the entire pouch of Douglas, with an irregular surface, and the uterus was indistinct from the mass. Rectal examination confirmed free rectal mucosa.

Laboratory tests revealed anemia, with a hemoglobin level of 7.2 g/dl. Tumor marker analysis showed elevated CA-125 (834 U/ml) and lactate dehydrogenase (LDH) (335 U/l), while CA 19-9, carcinoembryonic antigen (CEA), beta-hCG, and alpha-fetoprotein were within normal limits.

Contrast-enhanced computed tomography (CECT) of the abdomen and pelvis revealed a large, ill-defined heterogeneous mass measuring 10.5×9.5×8.8 cm, with a solid component and extensive necrotic areas. The mass involved abdominopelvic structures, including the uterus, and infiltrated the serosal surfaces of the small and large bowel loops. Both ovaries were not separately visualized. Moderate to gross ascites was present, with multiple enhancing nodular densities along the parietal peritoneum. Diffuse mesenteric thickening and edema were noted, along with bilateral enlarged obturator and iliac lymph nodes. The uterus appeared bulky with a fibroid.

Ascitic fluid cytology was negative for malignant cells. A tru-cut biopsy of the pelvic mass confirmed ovarian carcinosarcoma, with immunohistochemistry (IHC) positive for pan-cytokeratin (PanCK) and S100, and negative for WT1 (Figures 1 and 2).

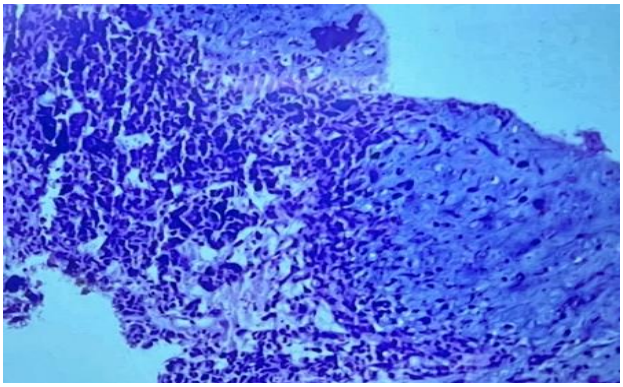

Figure 1: Histopathology showing carcinosarcoma with chondroid and epithelial components.

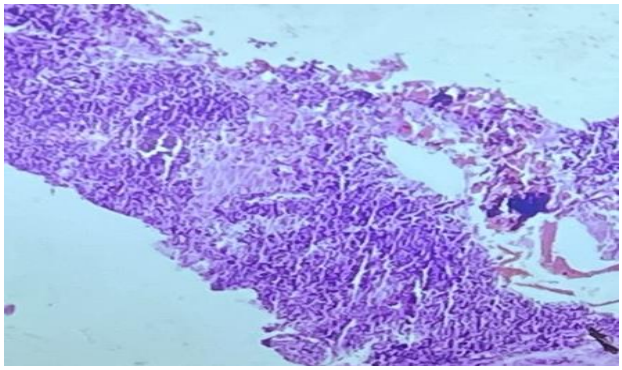

Figure 2: Histopathology showing carcinosarcoma with epithelial components.

Following a multidisciplinary tumor board discussion, neoadjuvant chemotherapy with paclitaxel and carboplatin was initiated. After three cycles, the patient exhibited a partial response, and interval debulking surgery (IDS) was performed, achieving R1 resection with final histopathology report suggestive of carcinosarcoma ovary. She completed three additional cycles of adjuvant chemotherapy along with bevacizumab, though paclitaxel was substituted with docetaxel for the final two cycles due to a mild hypersensitivity reaction. The patient has been under surveillance and remained in remission for six months.

DISCUSSION

OCS is a rare and aggressive biphasic malignancy characterized by high-grade epithelial and mesenchymal components. Similarly, in our case both the components were present. Despite its aggressive nature, research on OCS is limited, and the prognosis remains poor, with a median overall survival of 12.7 months.[4] The pathogenesis of OCS is not fully understood, but three primary theories exist including the collision theory, which suggests that epithelial and sarcoma components originate from different stem cells; the combination theory, which posits that both components arise from pluripotent stem cells; and the conversion theory, which suggests the sarcoma component evolves from the epithelial component.[5]

The majority of cases present with high-grade serous (HGS) epithelial components, while approximately 20% involve endometrioid carcinomas. OCS metastases are predominantly carcinomatous.[6] Interestingly, the presence of histological features such as heterologous elements do not appear to predict prognosis, underscoring the need for more effective treatment strategies.[4] Overexpression of proteins like p53 and WT1 has been linked to significantly reduced survival, while elevated CA 125 levels, though frequently observed, are not strong indicators of survival outcomes. OCS typically responds less effectively to platinum-based chemotherapy compared to high-grade serous ovarian cancer, which highlights the necessity for more targeted treatment options.[7]

Molecular profiling and the development of targeted therapies, such as poly ADP ribose polymerase (PARP) inhibitors and bevacizumab, show promise, although data remains scarce. To improve treatment outcomes, international collaboration and OCS-specific clinical trials are crucial.[6]

OCS is difficult to diagnose in its early stages due to the lack of symptoms, and when it does present, the symptoms are often non-specific and gastrointestinal. A definitive diagnosis is usually made after surgery through histopathological examination and IHC. Key IHC markers, such as CK, P53, P40, S100, and MyoD1, help identify biphasic tumor components while imaging modalities like ultrasound and MRI provide additional diagnostic information.[5] Similarly, in our case, the IHC showed panCK and S100 were positive.

Optimal cytoreductive surgery remains the cornerstone of OCS treatment, with better outcomes observed when minimal residual disease (≤1 cm) is left post-surgery.[8]

Chemotherapy is typically recommended, especially in early-stage patients, but there is no consensus on the best regimen. Paclitaxel and carboplatin are frequently used, with ifosfamide-based combinations showing some efficacy. Although platinum-based chemotherapy improves overall survival, response rates remain low, particularly in advanced stages. Radiotherapy may help in local control but has limited impact on overall survival.[8]

Emerging targeted therapies, such as those directed at HER2/neu, PD-L1, EpCAM, and Trop-2, offer hope for addressing residual or drug-resistant OCS, though further research is needed to validate their efficacy.[5]

CONCLUSION

Ovarian carcinosarcoma is a rare and highly aggressive malignancy with poor prognosis, requiring early detection and optimized treatment strategies. Emerging molecular profiling and targeted therapies may improve outcomes, but further research and clinical trials are needed to establish more effective treatments.

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