RESEARCH PAPER

Clinicopathological Analysis of Ovarian Carcinosarcomas in a Cancer Hospital- A 13 Year Study

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ABSTRACT

Background: Ovarian carcinosarcoma (OCS), also referred to as malignant mixed Müllerian tumour, is a rare and highly aggressive ovarian malignancy characterized by the presence of both epithelial and mesenchymal components. It accounts for a small proportion of ovarian cancers and is often diagnosed at an advanced stage, resulting in poor clinical outcomes.

Objectives: The present study aimed to analyze the clinicopathological features, treatment modalities and outcomes of ovarian carcinosarcoma cases managed at a tertiary cancer hospital over a 13 year period.

Materials and Methods: This non-randomized retrospective and prospective study included 14 cases of ovarian carcinosarcoma diagnosed between January 2010 and April 2023. Clinical presentation, radiological findings, tumour marker levels, gross morphology, and histopathological features were reviewed from institutional records. Formalin-fixed paraffin-embedded tissue sections were evaluated using hematoxylin and eosin staining, and immunohistochemistry was performed in selected cases. Statistical analysis was carried out using SPSS version 16.0.

Results: The age of Patients ranged from 35 to 80 years, with a mean age of 55.7 years. Abdominal pain was the most common presenting symptom. Most tumors were unilateral, large, and exhibited solid or solid-cystic morphology with areas of haemorrhage and necrosis. Elevated CA-125 levels were observed in majority of cases. Histologically, all tumors demonstrarted biphasic morphology with both carcinomatous and sarcomatous components; heterologous elements were present in half of the cases. Many patients presented with advanced FIGO stages and ascites. Surgical cytoreduction followed by chemotherapy was the primary treatment approach, though recurrence and mortality rates remained high.

Conclusion: Ovarian Carcinosarcoma is a rare but extremely aggressive tumor with an unfavourable prognosis. Optimal surgical cytoreduction combined with chemotherapy remains the cornerstone of treatment; however, patient outcomes continue to be poor. Larger studies incorporating molecular and immunohistochemical analyses are required to better understand tumor biology and improve therapeutic strategies.

Keywords: Add keywords here.

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INTRODUCTION

Throughout the female reproductive tract, carcinosarcomas—also known as malignant mixed Müllerian tumors—are an uncommon and aggressive type of cancer.[1, 2] Only 1-4 percent of ovarian malignancies are caused by it, and it is primarily found in the uterus and ovaries.[3, 4] The two histologic component types of ovarian carcinosarcoma (OCS) are sarcomatous and carcinomatous. The sarcomatous component of ovarian cancer can be categorized as homologous or heterologous based on whether it is present in the uterus or ovaries, while the carcinomatous component can be clear cell, serous or squamous epithelium, or endometrioid cell. Patients with OCS are typically diagnosed between the ages of 50 and 70, and upon presentation, they typically have higher rates of advanced International Federation of Gynecology and Obstetrics (FIGO) stage [5]. The majority of OCS patients experience pelvic masses, lower abdominal pain, and abdominal distention, similar to epithelial ovarian malignancies (EOC). Nonetheless, compared to EOC patients with comparable FIGO stages, the prognosis for OCS patients is poorer.[1, 6] The FIGO stage and the patient's age are said to be associated with prognosis.[7–8] The current investigation was carried out to examine the clinicopathological examination of ovarian carcinosarcomas.

MATERIAL AND METHODS:

It was a non-randomized retrospective and prospective study on ovarian carcinosarcoma, diagnosed between January 2010 to April 2023. Their clinical data (age, site, clinical presentation and levels of tumor markers),

radiologic findings and gross appearance were obtained from the surgical histopathological record section of the institute. Formalin fixed paraffin embedded tissue sections stained with Hematoxylinand Eosin were retrieved and reviewed. Immunohistochemistry was performed in few cases.

Statistical analysis:
All analyses were performed using SPSS (SPSS Inc., Chicago, IL, USA) statistical software version 16.0.

RESULTS:
The women impacted by the current study ranged in age from 35 to 80 years old, with a mean age of 55.7 years. Overall, the 55–65 age range was observed to be the top.(Table 1) Abdominal pain was the most prevalent presentation (6 out of 42.8%) among patients with ovarian carcinosarcoma.(Table 2) The largest tumor was 25 cm in its maximum transverse dimension, while the smallest was only 6 cm in size.(Table 2) Nine instances (64.2%) out of the total patients had CA125 elevated(Table 2). In the current investigation, the maximum CA125 value was 1756 u/ml, observed in 1 (7%) patient. Six cycles of primary neoadjuvant chemotherapy (NACT) preceded surgery in 2 (14%) of the cases. Two (14%) of the 14 individuals underwent interval cytoreduction, which involved three rounds of post-operative chemotherapy and three rounds of NACT. Two instances (14%) received three rounds of NACT; nevertheless, no surgery was performed. Treatment was rejected in one case following a biopsy diagnosis. Three (22%) instances had no known history of chemotherapy. Only 6 (42.8%) of the 14 individuals received the cytoreduction surgical method, which is Two (14%) of these six individuals had interval cytoreduction following neoadjuvent treatment. Two instances (14%) had complete hysterectomy. Treatment was rejected in one case following a biopsy diagnosis. Regarding three cases, no information was available. Six patients (42.8%) out of the 14 cases had a highly ill-defined solid necrotic tumor. Solid cystic mass was the second most frequent gross characteristic, observed in 5 (35.7%) cases. For 3 cases (22%), gross findings were not provided. All of the tumors had a biphasic tumor with both sarcomatous and carcinomatous components, as revealed by microscopic analysis. A high grade serous carcinoma's epithelial component was seen in the majority of OCS. Of the fourteen instances, seven (or 50%) had heterologous elements, most often rh abdomyosarcoma to us component in three cases (or 22%) and chondroid component in two. Single cases were observed for osteosarcoma and squamoid components, respectively. Five of the seven remaining cases involved biopsies. The para-aortic, retroperitoneal, and pelvic lymph nodes in each of the five (35.7%) cases where cytoreduction was performed were all negative for tumor metastases. In two cases (14%), lymph node dissection was not performed. Treatment was rejected in one case following a biopsy diagnosis. For three cases (22%) no information was available. In the individuals whose complete medical histories and radiological results were available at the time of diagnosis, there was no evidence of distant metastases. There was no history of distant metastases available in biopsies or review cases. Since five of the 14 cases involved biopsies, the FIGO stage was unavailable. FIGO stages IIIA and IIB applied to five of the nine cases. Four of the cases are in FIGO stages IIA and IIB. Based on the clinical and histological results at the time of diagnosis, these staging systems were applied. Seven instances (about 50%) had ascitis. Six peritoneal fluid samples from these seven instances were positive for cancerous cells. There were three occurrences when ascites data was unavailable. In three cases (22%), recurrence was reported. Five patients had no follow-up, therefore recurrence could not be identified. The remaining 3 instances (28%) that required biopsies and reviews were treated at different hospitals. Four of the 14 cases resulted in death.

DISCUSSION
Approximately 1% of ovarian tumors are OCSs, an uncommon histological type of malignancy. Nearly 70% of OCS patients reportedly had advanced stages at diagnosis.[9] As our investigation revealed, the incidence of primary ovarian MMMT/OCS is incredibly uncommon and has a prolonged, aggressive clinical course. After menopause, at a median age of 60 to 70 years old, OCS of the female vaginal tract are frequently discovered. Over two thirds of OCS patients receive an advanced diagnosis.[10] Nevertheless, **Dasgupta** represented one patient who was forty years old.[11] **Menon et al.** demonstrated that, in line with our findings, the age range at which OCS was diagnosed was 33 to 70 years old, with a median age of 51.[12] OCS is characterized by nonspecific clinical characteristics that are linked to tumor location, size, and invasiveness. Early satiety, bloating, abdominal distention, pelvic and/or abdominal pain, and gastrointestinal issues are among the symptoms.[13] Of the cases in this investigation, three had stomach fullness as their predominant symptom and six exhibited clinical symptoms of abdominal discomfort. An unintentional case detection occurred. The nonspecific clinical symptoms of OCS are supported by this investigation. The non-specific tumor marker CA 125 is typically linked to malignant ovarian cancers. According to a study by **Menon et al.,** 9 out of the 12 patients of ovarian carcinosarcoma had elevated CA 125 values.[12] In individuals with OCS, the mean CA 125 level was 696.54 ±314.06 U/mL, according to **Dai et al.[**13] In nine of the fourteen instances in the current investigation, CA 125 was elevated. In one instance, however, it was within typical bounds. Numerous ovarian tumors present as substantial pelvic masses. Clinical research has indicated that a unilateral, big pelvic mass is more common in OCS patients. In a case study published by **Daimon et al**., the tumor's solid portion was hemorrhaging, and it had many locular, mixed cystic-solid masses with a diameter of 27 cm.[14] A substantial, well-circumscribed mass of OCS with a maximum transverse dimension of 18 cm was described by Uçaret al. A case of OCS with a mixed cystic-solid mass of 10 ×6.8 cm was presented by **Pankaj et al**.[15] In one example, solid and cystic elements were present in a

gigantic mass of 33 ×22 ×10 cm, as reported by **Vernadakis et al**.[16] The maximum transverse diameter in our sample, which spanned from 10 to 15 cm, was consistent with data indicating that the majority of masses were unilateral, cystic-solid masses.[14–17]

Ascites and peritoneal seeding are frequently seen in 67–100% of ovarian MMMT patients.[18] In the current investigation, ascitic fluid tested positive for malignant or atypical cells in 50% of the cases when a thorough clinical history was obtained. The clinical history pertaining to ascites was unavailable in the remaining cases. Usually, serous, endometrioid, or undifferentiated adenocarcinoma make up the epithelium. It may also be a clear cell adenocarcinoma or squamous cell carcinoma.[18] Sarcomatous elements can include mesenchymal tissue that is not native to the ovary-heterologous, such as chondrosarcoma, rhabdomyosarcoma, lipoma, osteosarcoma, or angiosarcoma, or it can include mesenchymal tissue that is normally present in the ovary-homologous tissue, such as endometrial stromal sarcoma, fibrosarcoma, and leiomyosarcoma.[18] It is debatable whether the ratio of the sarcomatous or malignant epithelial component, as well as homologous vs heterologous, has an impact on the disease course of OCS under a microscope. According to certain preliminary research, having heterologous sarcomatous components is linked to a dismal prognosis.[10] Tumors having a serous epithelial component and stromal predominance have a poorer prognosis, according to **Athavale et al**.[19] Five instances in our investigation exhibited the heterologous sarcomatous component. Since carcinosarcoma is such an uncommon tumor, there are currently no established treatment protocols for it. According to the literature, OCS are extremely aggressive tumors that develop quickly and have a dismal prognosis. A poor prognosis is attributed to advanced age at presentation, unsatisfactory surgical resection, and advanced stage. When OCS patients are first diagnosed, their disease is typically advanced, and around 75% of cases have widespread metastatic disease (stages III–IV) at the time of initial surgery.[17] Similar to epithelial ovarian cancer, chemotherapy and surgery are often used in OCS instances. Chemotherapy has been demonstrated to be an effective treatment with good responses following optional cytoreduction surgery.

CONCLUSION

Ovarian carcinosarcoma or MMMT represents an extremely aggressive form of ovarian cancer, with distinct clinical behaviour. The main treatment for ovarian OCS is surgery with subsequent chemotherapy. Surgical treatment is an important determinant of survival. These patients are poorly served by currently available treatment options, and new therapeutic strategies that have been hindered by a lack of research attention and the relative rarity of OCS are urgently required to improve patient outcomes. However, the risk of recurrence and mortality is high across all patient populations. Despite its aggressive behaviour, OCS has received relatively little research attention to date. A limited number of studies have characterized an appreciable number of OCS patients in detail. More studies are needed for further evaluation including molecular studies and immunohistochemistry.

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Table 1: Age distribution

Age (years)	No of cases	Percentage (%)
31 – 40	3	22
41 – 50	2	14
51 – 60	4	28
61 – 70	4	28
71 – 80	1	7
Total	14	100

Table 2: Clinical and histopathological features

Symptoms	**No of cases**	**Percentage (%)**
Abdominal pain	6	43
Abdominal fullness	4	28
Incidentally found	1	7
Data not available	3	22
Tumor size (in cm)		
6 – 8	3	22
8 – 10	3	22
10 – 12	2	14
12 – 15	2	14
> 15	2	14
Size not known	2	14
Specimen laterality		
Unilateral	8	58
Bilateral	4	28
Not known	2	14
Specimen		
Biopsy	5	36
Total hysterectomy	2	14
Cytoreduction	7	50
CA 125 levels		

Within normal limit	1	7
Increased	9	65
Data not available	4	28

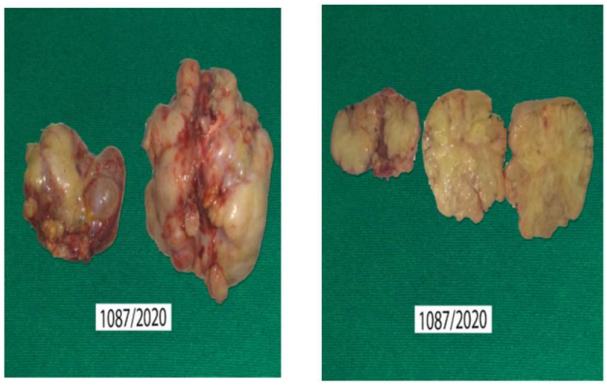

Fig. 1 (A & B)Specimen of ovarian carcinosarcoma showing solid cystic areas, the tumour was grey-white, fleshy with areas of haemorrhage and necrosis.

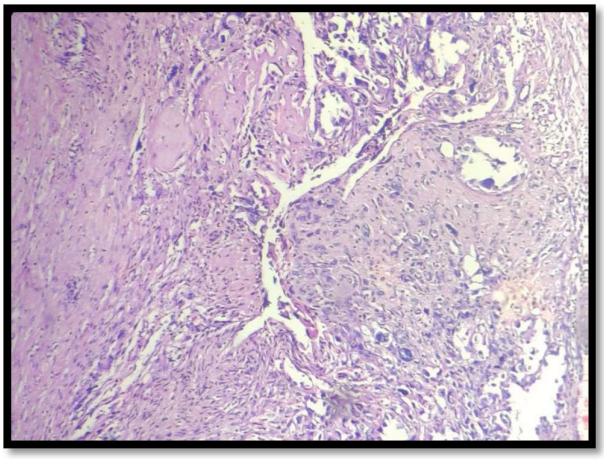

Fig: 2 Photomicrograph of OCS Showing both Malignant epithelial and mesenchymal components.

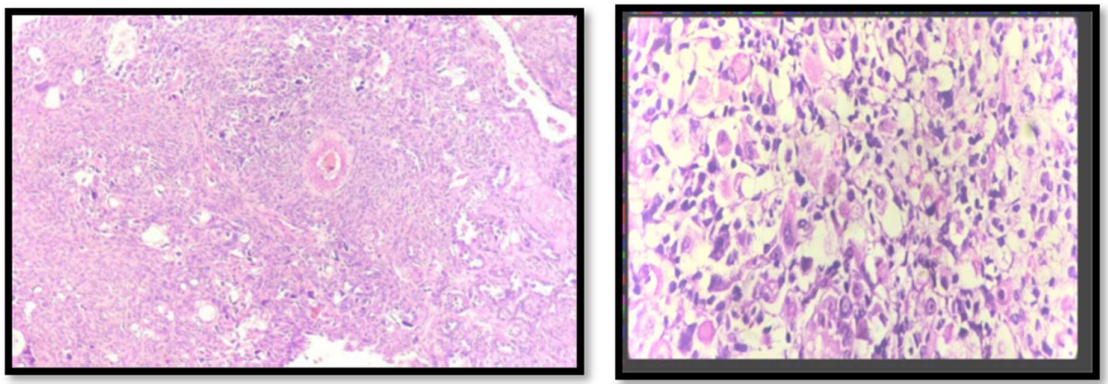

Fig 3(A&B) A: Photomicrograph showing component in a case of ovarian carcinosarcoma.
B: sPhotomicrograph showing rhabdomyomatous in a heterologous Sarcomatous component of OCS.