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A SINGLE CENTRE CASE SERIES STUDY OF CLINICO-PATHOLOGICAL SPECTRUM OF PRIMARY OVARIAN MALIGNANT MIXED MULLERIAN TUMOURS

Pathology

Dr. Dhanesh Kumar MBBS ,MD (Pathology), Department of Pathology, JawaharLal Nehru Medical College , Bhagalpur812001, India.

ABSTRACT

Aims and Objectives: To study the clinical and pathological characteristics of primary ovarian malignant mixed mullerian tumor (OMMMT) and assess the prognostic factors associated with treatment outcome and survival.

Materials and methods: The pathology database was searched for primary ovarian carcinosarcoma diagnosed or managed at our institute from period of february 2014 to June 2019. The histological sections were reviewed, with emphasis on type and grade of epithelial and sarcomatous component. The medical records were retrospectively analyzed for clinical details and follow up.

Results: A total of 35 cases of primary ovarian carcinosarcoma were identified. The median age at diagnosis was 49 years. Sixteen patients had advanced stage (stage III and IV) at presentation. Cytoreductive surgery was done in 17 cases, and 9 had received upfront chemotherapy. Histologically, 12 cases had epithelial predominance (> 50% epithelial component) and 13 had sarcoma predominance. The most frequent epithelial component was endometroid type, and most common sarcoma component was rhabdomyosarcomatous. Hyaline droplets within sarcomatous stroma were seen prominently in 16 cases. Three cases showed germ cell or yolk sac-like areas. Twenty cases had follow up with a median of 14 months (4-45 months). The recurrence-free survival in advanced stage and sarcoma predominant was 9.5 months in comparison to 13 months in early stage and epithelial predominant OMMMT.

Conclusion: Primary ovarian carcinosarcoma is a rare biphasic malignancy with variable proportions of epithelial and spindle elements. Presence of hyaline droplets within spindle sarcoma in a biopsy from ovarian mass should alert the pathologists regarding MMMT. Advanced stage, suboptimal cytoreduction, and sarcoma predominant tumors are likely to have a worse outcome in ovarian MMMT.

KEYWORDS

Malignant ,Mixed, mullerian, ovary, primary

INTRODUCTION

Ovarian carcinosarcomas, also known as malignant mixed mesodermal tumors or malignant mixed mullerian tumors (OMMMT), are exceedingly rare and comprise 1–3% of ovarian malignancies. These tumors are defined histologically by the admixture of malignant epithelial and stroma elements. They are sub-classified as "heterologous" or "homologous" based on the presence or absence of a stromal component containing mesenchymal tissue not normally found at the primary tumor site.Recent studies propose a monoclonal theory of histogenesis of ovarian carcinosarcomas, and these may be best regarded as metaplastic epithelial carcinomas. These tumors follow an aggressive clinical course, and survival is significantly reduced when compared to that in epithelial ovarian cancers.Clinico-pathologic case series on this malignancy indicate that advanced stage and suboptimal cytoreductive surgery to be the most significant poor prognostic factors. Presence of heterologous elements that was previously believed to carry prognostic importance does not appear to be significant. Recently, presence of stromal predominance and serous epithelial component in advanced cases have been suggested to have a worse outcome.In the current study, we retrospectively analyzed the data concerning the clinical and pathological characteristics, management and follow up of patients of ovarian carcinosarcoma.

MATERIALS AND METHODS

The pathology database was searched for primary ovarian carcinosarcoma diagnosed and/or managed at our institute from period of february 2014 to June 2019.The histological sections were reviewed, with emphasis on type and grade of epithelial and stromal components and their relative percentages of distribution in the tumor sections.

RESULTS

Patient demographics

A total of 35 cases of primary ovarian carcinosarcoma were identified. The age at time of diagnosis varied from 29 to 81 years with a median age of 49 years. Majority of patients presented with increasing abdominal girth and or pain with abdominal discomfort. Radiologically, a complex solid- cystic mass was demonstrable in most patients.Seven cases were for pathology consultation only with limited clinical and treatment details, and follow up details were not available in them. Four cases had no follow up after surgery.

Pathological features

The most common epithelial component was endometrioid adenocarcinoma (12 cases) followed by serous adenocarcinoma (9 cases). Admixture of 2 or more epithelial components was seen in 12 cases. Heterologous sarcomatous elements were seen more commonly (59%) compared to homologous elements (41%) (16 cases vs. 11 cases). The most common heterologous element was rhabdomyosarcomatous, seen in 9 cases. Majority of the cases had admixture of more than one sarcomatous component with rhabdomyosarcoma and endometrial stromal sarcoma being the commonest combination. Interestingly, the stromal sarcoma component had undifferentiated appearance in most of the cases. Epithelial predominant tumors (> 50% to < 95% epithelial component) were seen in 10 cases. Out of these 10 cases, 8 presented in advanced stage (III or IV). Sarcoma- predominant tumors (> 50% to < 95% sarcomatous component)were seen in 11 cases with 8 of these being advanced at presentation. Equal epithelial and sarcomatous components were seen in 6 cases. droplets/globules were seen in 16 cases, frequently in areas of undifferentiated sarcoma or foci of rhabdomyosarcoma.The droplets were seen both intra- and extracellularly. In some cases, these droplets were abundant and seen in small group and clusters..Three cases were labeled as teratoidcarcinosarcoma that had foci morphologically resembling germ cell tumors, including embryonal, yolk sac and immature teratomatous areas in the form of neuroepithelium with rosette- like pattern. These patients had all presented as stage III disease . A peculiar basement membrane thickening around epithelial islands was seen in 1 case.

DISCUSSION

Carcinosarcoma of the female genital tract is known as) mixed mullerian (mesodermal)malignant tumors, are biphasic tumors comprised of varying proportion of both malignant epithelial and mesenchymal (stromal) components. Current evidence implicates metaplastic transformation of epithelial component, which initiates tumorigenesis and gives rise to sarcomatous component.] They most commonly are identified in the uterine corpus. Primary ovarian MMMT are uncommon and account for about 1-3% of all ovarian malignancies. Boucher et al., in their series of 15 cases found equal representation of the epithelial endometrioid (4 cases) and serous (4 cases) component types. The mesenchymal component was largely heterologous, of which 5 were of chondromatous and 5 of rhabdomyoblastic differentiation.[8] However, Kunkel et al. in a recent series had an overwhelming

erous carcinoma component in 57% of their cases with a predominance of heterologous cartilaginous component in 36%.In comparison, we found endometrioid carcinoma and heterologous rhabdomyosarcoma in the present series.Hyaline globules, as seen in 16 of our cases, may been seen in OMMMT and may be reactive to alpha-1-antitrypsin. If seen in a small biopsy sample, this morphological finding may aid in

pre-operative diagnosis of OMMMT. The presence of peculiar basement membrane thickening seen in one of cases of OMMMT has not been previously reported, although stromal hyalinization and deposition of basement membrane material has been seen in clear cell ovarian carcinomas. We surmise that this morphological alteration in basement membrane may be biologically related to the phenomenon of epithelial-mesenchymal transition, which plausibly underlies the pathogenesis of these tumors.Malignant germ cell tumor and neuroectodermal elements resembling immature teratoma have been rarely seen in combination with OMMMT. In conclusion, we have described the pathological features of a series of primary ovarian carcinosarcoma, a rare biphasic malignancy with variable proportions of epithelial and spindle elements, seen at our institute. Majority of the patients present in advanced stage of disease. Presence of hyaline globules within spindle arcoma in a small biopsy from an ovarian/pelvic mass should alert the pathologists regarding MMMT.

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