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Carcinosarcoma of the Uterus and the Ovary - A Comparative Study.

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ABSTRACT

Background: Carcinosarcoma or Malignant Mixed Mullerian tumors of the female genital tract are very rare neoplastic lesions of the postmenopausal women. Uterus is the commonest site involved. Ovarian carcinosarcoma is one third less common than uterine carcinosarcoma. As studies comparing ovarian and uterine carcinosarcoma were less prevalent in the literatures, an attempt was made to do the same in our study. **Methods:** From the reported gynaeco-pathological cases during May 2014- April 2016, carcinosarcomas of the female genital tract were retrieved. Apart from gross and microscopy of the carcinosarcoma of the uterus and ovary, literatures were analyzed to compare both based on its demography, histopathology, behaviour and survival.**Results:** Two cases, one each of ovarian and uterine carcinosarcoma were reported during our study period. Both gross and microscopy was similar in uterine and ovarian carcinosarcoma. Survival and prognostic factors were analyzed based on the literature.**Conclusion:** Though the histogenesis and morphology of the carcinosarcoma of both the sites were similar, the uterine carcinosarcoma was found to be more aggressive with poorer prognosis when compared with its ovarian counterpart.

Keywords: Female genital tract, Postmenopausal, Prognosis.

INTRODUCTION

Carcinosarcoma or Malignant Mixed Mullerian tumors of the female genital tract are very rare neoplastic lesions of the postmenopausal women. Among the female genital organs, uterus is the commonest site involved followed by vagina, cervix, ovary and it least commonly involves the fallopian tube[1, 2].

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It comprises about 2-5% of all uterine malignancies and with a high recurrence rate of about 40-60% [3]. Carcinosarcoma of the ovary constitutes around 1-4% of all the ovarian tumors[3].Ovarian carcinosarcoma has a median survival rate of 8-32 months and recurrence rates of 50-100% against 16-40 months survival rate and 40-60% recurrence rate for uterine carcinosarcoma [3, 4]. But when stage by stage disease were analyzed, uterine carcinosarcoma was found to be more aggressive than ovarian carcinosarcoma. The aim of our study is to evaluate both the tumors based on the demography, histopathology, treatment and prognosis.

MATERIALS AND METHODS

From the reported gynaeco-pathological cases during May 2014- April 2016, carcinosarcoma cases were retrieved.

Inclusion criteria

- Carcinosarcomas arising from the female genital tract were included.
- Only the primary carcinosarcoms arising from the female genital tract were included.

Exclusion criteria

- Carcinosarcoma of the other sites
- All other tumors of female genital tract.

Two cases of carcinosarcoma, one from the uterus and other from the ovary were reported during the period of May 2014- April 2016. Demography was taken from the records. They were analyzed based on both gross and microscopic features. Relevant literatures on both uterine and ovarian carcinosarcoma were reviewed and their differences in microscopic features and prognostic factors were analyzed.

RESULTS

Case 1:

A forty five year old female was operated on for an abdominal mass. She had no other complaints. Total abdominal hysterectomy and bilateral salpingo-oophorectomy was done and the specimen was sent to us for evaluation.

Gross: We had received uterus with the cervix and bilateral tubes and ovaries. Uterus with cervix measured 10x7x5cm. On cut surface a fleshy polypoidal mass was seen arising from the fundus and extending upto the cervix measuring 7x5x4cm [Figure 1]. Cervix, ovaries and tubes were uninvolved grossly.

Figure 1: Show Uterus and a fleshy polypoidal mass arising from the fundus and extending up to the cervix.

Microscopy: Multiple sections studied from the uterus showed a biphasic tumor composed of epithelial and sarcomatous components. The epithelial component was arranged in a glandular pattern. The cells were pleomorphic and vesicular and showed stratification. The sarcomatous component was arranged in fascicles exhibiting pleomorphism and mitosis. Chondroid areas were also noted [Figure 2]. Cervical cut end, ovaries, tubes and parametrium were free of tumor invasion. Nodes were not involved.

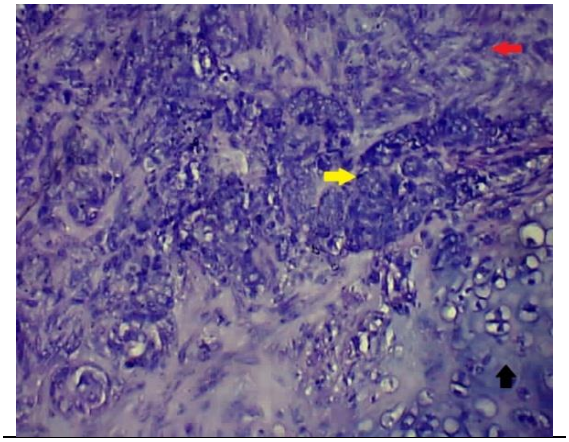

Figure 2: Shows malignant epithelial component [yellow arrow], sarcomatous component [red arrow] and Chondroid areas [black arrow][40x H&E].

Case 2:
A thirty six year old had abdominal mass and was diagnosed as having ovarian tumor and hence was operated on and the specimen was sent to us for examination.

Gross:
We received a total abdominal hysterectomy specimen with bilateral tubes, ovaries and parametrium. Uterus, cervix, both tubes, one side ovary and the parametrium were grossly normal. One ovary measured 13x8x6cm. The external surface of the ovary was nodular. On cut surface the tumor was fleshy, solid grey white with areas of haemorrhage replacing the entire ovary [Figure 3].

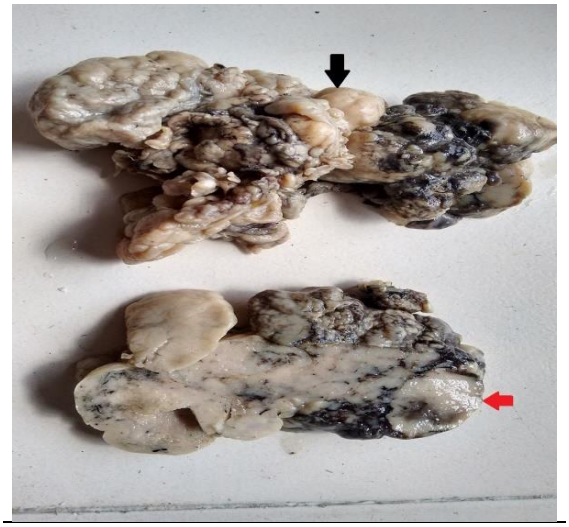

Figure 3: External surface of the ovary is nodular [black arrow]. Cut surface show a grey white fleshy tumor with areas of haemorrhage [red arrow].

Microscopy:
Sections studied from the ovary showed a biphasic tumor composed of epithelial and sarcomatous components. The epithelial component was arranged in a glandular pattern. The cells were pleomorphic and vesicular. The sarcomatous component was arranged in fascicles exhibiting pleomorphism and mitosis [Figure 4 & 5].

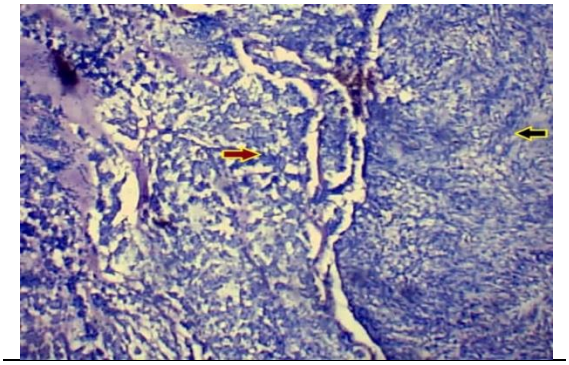

Figure 4: Shows juxtaposed epithelial component [brown arrow] and sarcomatous areas[black arrow][10xH&E].

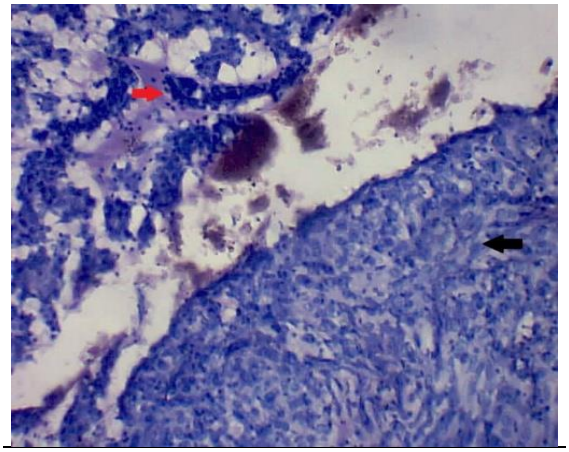

Figure 5: Shows both epithelial [red arrow] and sarcomatous component [black arrow][40x H&E].

DISCUSSION

As the name implies carcinosarcoma is a biphasic tumor composed of epithelial and mesenchymal components. They are very rare neoplasms. Carcinosarcomas of the uterus constitute around 5% of all uterine tumors[5]. Uterine carcinosarcoma is seen in post-menopausal women between the sixth and seventh decade with a median age of 62 years[6]. It is common among blacks[7]. Abnormal uterine bleeding is the most common presenting symptom[8]. Other symptoms include pelvic pain, palpable lower abdominal mass or features of metastasis. Risk factors that are involved in the development of carcinosarcoma of the uterus include nulliparity, advanced age, obesity, hypertension, exposure to exogenous estrogen, and long-term use of tamoxifen[9]. Oral contraceptives have a protective effect. Pelvic irradiation was also proposed as a predisposing factor. But Schaepmen Van Geuns EJ et al did not agree that pelvic irradiation was of prognostic significance[10]. The median survival ranged from 16 to 40 months for uterine carcinosarcoma[11].

Carcinosarcoma of the ovary constitutes 1-4% among all ovarian tumors[12]. Compared to uterine carcinosarcoma, ovarian carcinosarcomas are three times less prevalent[13]. Ovarian carcinosarcoma affects post-menopausal women, and the mean age of presentation is 65 years[14]. Palpable mass and ascites are the presenting symptoms. Irradiation is associated with the increase incidence of ovarian carcinosarcoma[13]. The median survival ranged from 8 to 32 months for ovarian carcinosarcoma[15]. In our study, both the females were premenopausal in contrast to others studies.

Histogenesis

Four theories were proposed regarding the histogenesis of carcinosarcoma[16]:

1. The collision theory
2. The combination theory
3. The conversion theory
4. The composition theory[17]

According to collision theory, carcinoma and sarcoma are two independent neoplasms. But in combination theory, both components are derived from a single stem cell that undergoes divergent differentiation. Conversion theory suggests sarcomatous elements are derived from the epithelial component during the tumour evolution. In composition theory, the sarcomatous component is considered as a pseudosarcomatous stromal reaction to the carcinoma. The clinical, histopathological, immunohistochemical, ultra structure, tissue culture, and molecular data suggest that a sarcomatous component originates from the carcinomatous component favouring combination and conversion theory.

Gross

Uterine carcinosarcomas are polyploid and fill the endometrial cavity and protrude through the cervical Os mimicking cervical carcinoma. On cut surface the tumor is soft to firm, with prominent areas of haemorrhage, necrosis and cystic degeneration [18]. Occasionally, bony or cartilaginous areas may be seen. Myometrial invasion is also noted.

Ovarian carcinosarcoma causes enlargement of the ovaries. On cut surface the tumor is soft and fleshy, with areas of haemorrhage and necrosis.

Histopathology

Both uterine and ovarian carcinosarcoma are composed of an admixture of malignant epithelial and mesenchymal components[19]. Serous carcinoma and high-grade endometrioid carcinoma are the most frequent carcinomatous components. Atypical carcinosarcomas with neuroendocrine or melanocytic differentiation are associated with aggressive behaviour[20]. The mesenchymal elements may be:

- Homologous -containing native cells including Stromal sarcoma, fibrosarcoma or leiomyosarcoma (2%) or
- Heterologous –containing rhabdomyosarcoma (18%), chondrosarcoma (10%), osteosarcoma (5%) or liposarcoma (1%)[21]
- Heterologous elements are a poor prognostic factor even in patients having stage-1 carcinosarcoma according to Ferguson SE et al [22]. There was no difference in survival between homologous and heterologous carcinosarcoma according to Muntz JE et al[23]. This topic is still controversial[24].

Spread

Unlike other sarcomas, carcinosarcoma spreads through the lymphatics and the metastatic lesions will show carcinomatous elements with or without a coexisting sarcomatous component. Solitary sarcomatous metastasis is uncommon[17]. Lung (49%), peritoneum (44%), pelvic node, para-aortic

lymph nodes (35%), adrenal gland, bone (19%), heart, pericardium (9%), and brain (7%) are the metastatic sites that are frequently involved[25].

Immunohistochemistry

Co-expression of the epithelial markers like Cytokeratin, CEA, EMA and mesenchymal antigens –Vimentin and Desmin are noted in both uterine and ovarian carcinosarcoma. Such co-expression of the antigens favours conversion hypothesis.

Differential diagnosis

The histopathological differential diagnosis of the uterine carcinosarcoma includes de-differentiated endometrial carcinoma and endometrioid adenocarcinoma. In de-differentiated endometrial carcinoma, both differentiated and un-differentiated components are seen. The differentiated component is usually of well-differentiated endometrioid type like those of carcinosarcoma but the undifferentiated component is composed of small, round cells of uniform size instead of pleomorphic spindle shaped cells seen in carcinosarcoma.

Endometrioid adenocarcinoma is another histopathological differential diagnosis for carcinosarcoma. These tumors are composed of low-grade endometrioid component with areas of squamous metaplasia and mitotically active spindle cell elements with no atypia. In contrast carcinosarcoma exhibits pleomorphism in both the epithelial and mesenchymal elements.

Treatment

Till date there is no consensus regarding optimal treatment of carcinosarcoma is reached due to the rarity of the tumor. In most of the centres, for stage I tumors, total hysterectomy, bilateral salpingo-oophorectomy, omentectomy, lymphadenectomy are performed. For other stages cyto-reduction followed by ifosfamide and platinum based chemotherapy are used[26].

Prognostic factors

- Surgical stage and, particularly, depth of myometrial invasion are the most important prognostic indicators in uterine carcinosarcoma.
- Serous and clear cell morphology in carcinosarcoma are associated with higher frequency of metastases, deep myometrial invasion, lymphatic or vascular space invasion, and cervical involvement[27].
- In short, age, stage, lymphadenectomy and radiation are the significant prognostic factors in uterine carcinosarcoma.
- Age, stage and lymphadenectomy are significant predictors in ovarian carcinosarcoma.

Comparative analysis

Although uterine and ovarian carcinosarcoma share the same histogenesis and pathogenesis there are few differences that are highlighted in the [Table 1].

Table 1: Comparative analysis between uterine carcinosarcoma and ovarian carcinosarcoma.

Parameters	Uterine carcinosarcoma	Ovarian carcinosarcoma
Median Age	62 years	65 years
Race	Africo-American	Caucasian
Regional metastasis	Common	-
Distal metastasis	-	Common
Survival	Worst	Comparatively better

CONCLUSION

When uterine carcinosarcoma was compared with ovarian carcinosarcoma, uterine tumors presented early because of the specific symptoms it produce, has a more aggressive course and has shorter survival when compared to its ovarian counterpart.

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