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Case Report

Carcinosarcoma of Uterus (Malignant Mixed Mullerian Tumor) with Squamous Differentiation - A Case Report

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ABSTRACT

Carcinosarcoma of uterus is aggressive mixed malignant tumor proposed to have mullerian duct origin. It is a rare gynecological tumor accounting for 1.5 - 3% of malignant uterine tumors. Tumor is composed of both mesenchymal and epithelial components. Carcinosarcoma is classified into two types depending upon the sarcomatous components. It is termed as "homologous" when sarcomatous components are fibrosarcoma or leiomyosarcoma and "heterologous" when the non-native sarcomatous components like osteosarcoma, chondrosarcoma and rhabdomyosarcoma etc are present. We present a case of carcinosarcoma of uterus in 56 years women presenting with irregular bleeding.

Key words: Carcinosarcoma, Uterus, Mullerian duct

INTRODUCTION

Carcinosarcoma of uterus is highly aggressive tumor composed of both mesenchymal and epithelial elements. [(1)] It is highly aggressive tumor with poor prognosis. [(2)] It is more common in postmenopausal women with increased risk in black women. Though the exact etiological factors are not yet known but exposure to radiation is considered to be possible etiological factor. Various theories have been proposed regarding histogenesis. Most widely accepted theory is conversion theory which proposes that carcinomatous component is driving force and sarcomatous component arises from carcinomatous component. [(3)] Patients present with postmenopausal vaginal bleeding. Management of carcinosarcoma of uterus requires combined modality approach including surgery, chemotherapy and radiotherapy.

CASE REPORT

A 56-year-old woman came to the Narayana Hospital for evaluation of post menopausal bleeding since 3 months. Her blood examination revealed anemia with haemoglobin about 8g%. On abdominal ultrasonography hypoechoic mass was noted at the fundus measuring 5X4cms. Clinically it was diagnosed as submucosal leiomyoma at the fundus. Endometrial biopsy was histopathologically diagnosed as adenocarcinoma. Later total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed.

Uterus with cervix was measuring 7X5X4cms. Both ovaries were measuring 3X2X1cm each. Cut surface of the uterus showed gray-white area at the fundus measuring 5X4cms (Figure 1). Microscopically sections from the lesion showed tumor cells arranged in glandular pattern and solid sheets (Figure 2). Many foci show squamous differentiation of tumor

cells (Figure 3). Interstitial stroma shows pleomorphic spindle shaped cells having oval elongated nuclei with prominent nucleoli (Figure 4). Areas of necrosis were present. Tumor cells were seen infiltrating the myometrium. Due to the above features histopathological diagnosis of Carcinosarcoma – homologous type was considered.

Figure 1 – Hysterectomy specimen with gray white tumor area at the fundus

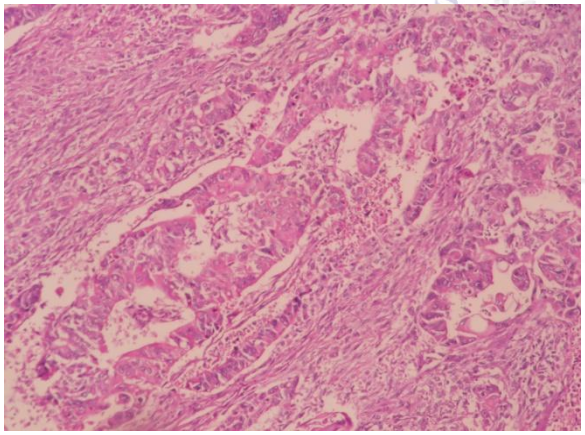

Figure 2- Microphotograph showing adenocarcinomatous epithelial component and pleomorphic spindle cells (H&E, X100)

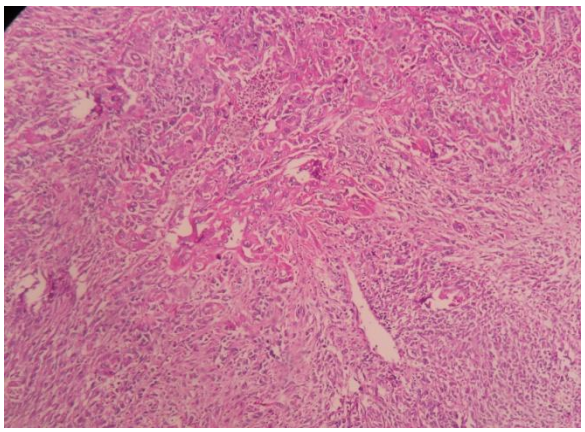

Figure 3 – Microphotograph showing carcinomatous cells with squamous differentiation (H&E, X100)

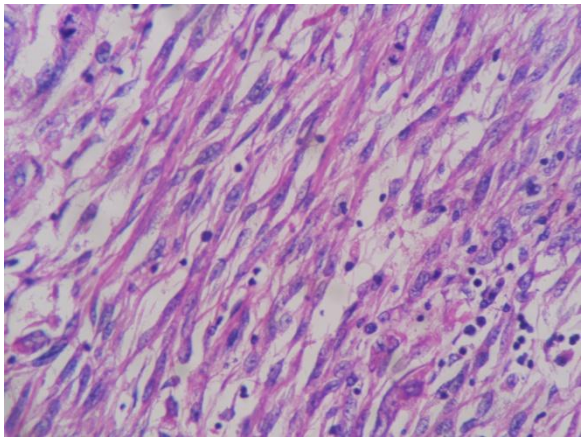

Figure 4- Microphotograph showing sarcomatous component with pleomorphic spindle shaped cells (H&E, X400)

DISCUSSION

Carcinosarcoma is rare uterine malignancy having origin from mullerian duct. Its incidence is about 1.5 –3% of uterine malignancies. Incidence of this tumor increases at the age of 50 years and is maximum at the age of 75 years and there after it plateaus. [(4)] The incidence of tumor is twice common in black than white.

Exposure to radiation is common associated etiologic factor. Other associated risk factor for the development of carcinosarcoma are exogenous estrogen, exposure to tamoxifen and obesity. Nulliparity is also suggested to be risk factor. [(5)] The primitive paramesonephric duct (mullerian duct) gives rise to the uterine elements like endometrial glands, stroma and smooth muscle cells. Hence the uterine tumors containing both epithelial and mesenchymal components are termed as "Mixed mullerian tumors". These tumors can be divided into homologous or heterologous subtypes depending upon the characteristic mesenchymal component. This classification has no prognostic significance. [(6)]

Four theories have been proposed regarding the origin of carcinosarcoma. First theory was "collision theory" which proposed that both mesenchymal and epithelial components have arisen independently and then collided giving the impression of mixed tumor. Second theory was "combination theory" which proposed that both mesenchymal and epithelial

components are derived from single stem cell which has undergone diverge differentiation during the evolution of the tumors. Third theory was "composition theory" which proposed that carcinosarcoma is an endometrial carcinoma with reactive atypical stroma. This theory was excluded as the sarcomatous component was not reactive but malignant. Fourth theory was "conversion theory" which proposes that sarcomatoid component is derived from carcinoma during evolution. This theory was accepted as most not all the tumors are of monoclonal origin and carcinomatous component is driving force. [(7)]

Grossly the tumor presents as polypoid or sessile bulky mass. In some instances it fills the entire uterine cavity or may protrude into and fill the vaginal vault. Cut surface is soft and may show areas of necrosis and hemorrhage. Tumor can be hard to firm if there are cartilages or osseous component. In our case the tumor was seen as firm gray white lesion at fundus of the uterus. Microscopically tumor has both mesenchymal and epithelial elements. The carcinomatous component is formed by endometrial carcinoma which can be serous, mucinous, clear cell type. Rarely squamous cell or undifferentiated carcinomas can occur. The mesenchymal component may be homologous or heterologous. Homologous component of sarcoma may be endometrial stromal sarcoma or fibrosarcoma. Heterologous component of sarcoma may be chondrosarcoma, rhabdomyosarcoma or osteosarcoma or liposarcoma. Most commonly found is high grade sarcoma without differentiation. In our case epithelial component was made by pleomorphic cells showing focal squamous differentiation and mesenchymal component by the sarcomatous cells without differentiation.

Studies have shown that carcinosarcoma of uterus metastasizes to lymphnodes, fallopian tubes, ovaries omentum and rarely to bowels, parametrium, liver and tonsils. In all the extrauterine metastatic sites epithelial component of the tumor was found. [(8)]

These tumors have worse prognosis when compared to high grade adenocarcinoma. CA 125 is an independent prognostic factor. Preoperative elevation of this tumor marker suggests that there is deep myometrial invasion or extra uterine disease. [(9)] Some studies have shown that hormonal receptors like estrogen and progesterone also has some prognostic significance. Receptor positivity in tumor is associated with favorable clinical outcome. [(10)] Few studies have shown that prognosis of these tumors depend upon the degree of differentiation and type of epithelial component of carcinosarcoma.

Standard mode of treatment is surgery which includes hysterectomy with bilateral salpingo-oophorectomy, along with lymph node dissection. Adjuvant chemotherapy and radiotherapy is also required depending upon the stage of disease. Chemotherapy is useful in advanced stage of disease and with metastasis but has no role in early stage. Vaginal brachytherapy or pelvic irradiation may be useful even in the early stage of the disease. Chances of local recurrences are reduced by adjuvant radiotherapy. [(11)]

CONCLUSION

Carcinosarcoma is a rare biphasic uterine malignancy consisting of both epithelial and mesenchymal components. Most of the tumors are monoclonal in origin regarding the tumor to be metaplastic carcinoma. Ultrasonography features are not specific for carcinosarcoma. These tumors have aggressive clinical course and poor prognosis. Surgical resection is treatment of choice with chemotherapy and adjuvant radiotherapy which reduces the chances of recurrences.

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