

Malignant Mixed Mullerian Tumor of Uterine Corpus: A Rare Case Report.

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Abstract: Carcinosarcomas which is also known as Malignant Mixed Mullerian tumor are rare high grade neoplasms. It accounts to about 2-5% of the tumors arising from the body of uterus. Generally occurring in the postmenopausal women with more incidence in the blacks as compared to the whites. Carcinosarcomas consists of endometrial adenocarcinomas co-existing with a malignant mesenchymal component. We present a case of 62 years old postmenopausal women presenting in the gynae OPD with complains of abdominal pain and postmenopausal bleeding since 2 months. On P/V examination the cervix was displaced high up. USG showed a heterogenous mass filling the endometrial cavity. She was investigated thoroughly. She had no other associated comorbidities. Total abdominal hysterectomy along with bilateral salpingo-oophorectomy was performed on her along with Bilateral pelvic and para-aortic nodes removal. We received the specimen in our pathology department. Histopathological examination revealed a case of Malignant mixed mullerian tumor.

Keywords: Carcinosarcomas, mullerian, heterologous, endometrial, postmenopausal, malignant, glandular etc.

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I. Introduction

WHO defines Malignant Mixed Mullerian tumors as a basic tumor composed of high grade carcinomatous and sarcomatous component. They are rare, high grade neoplasms which accounts to 2-5% of tumors arising from the body of the uterus [1]. They occur in the postmenopausal women with incidence more in blacks as compared to whites. They are alternatively also called as *carcinosarcomas* or *metaplastic carcinoma*. [2]. It is a biphasic neoplasm where the sarcomatous component is made up of endometrial stroma which can either be of smooth muscle type (which is known as the homologous) or other sarcomatous components like cartilage or bone (they are known as the heterologous component) [1]. The other component is the carcinomatous component.

II. Case Report

We present a case of 62 years old female who presented in Gynaecological Opd with complains of abdominal pain with postmenopausal bleeding since two months. On pelvic examination the cervix was high up. USG showed a heterogenous mass filling the endometrial cavity. She was thoroughly investigated. She had no other associated comorbidities like diabetes or hypertension. All her routine blood reports were within the normal limit. Total abdominal hysterectomy with bilateral salpingo-oophorectomy was done on her along with bilateral pelvic and para-aortic lymph node dissection. Histopathological Examination of the specimen was done.

GROSS EXAMINATION: We received the tissue specimen of uterus, cervix and bilateral adnexa along with pelvic and para aortic lymph nodes in a separate jar. The uterus was already cut open anteriorly measuring 8cm*6cm*2cm. A friable mass was seen occupying the endometrial cavity which was greyish in colour. Some areas of hemorrhage and necrosis was also seen. Endometrial myometrial junction was not well defined. Cervix measured 4cm*3m*2cm with no significant gross pathology. Bilateral adnexa received also did not show any significant gross pathology. The lymph nodes received were also entirely submitted for histopathological examination.

ON MICROSCOPIC EXAMINATION: the sections from the endometrial mass showed admixture of epithelial and mesenchymal components. The epithelial component had cells arranged in the glandular pattern with round to

oval pleomorphic vesicular nuclei, prominent nucleoli and moderate amount of cytoplasm. The mesenchymal component comprised of the spindle shaped cells arranged in a diffuse pattern. The individual cells were elongated with large prominent pleomorphic nuclei, indistinct nucleoli, irregular nuclear membrane and scant cytoplasm. Numerous mitotic figures along with bizarre pleomorphic tumor cells were also seen. Few giant cells along with areas of haemorrhage and necrosis were also seen. Cervix showed evidence of chronic cervicitis otherwise they were uninvolved. Bilateral adnexas showed no significant pathology and the lymph node examined showed reactive changes. We also did the immunohistochemical staining using markers cytokeratin and p53. Cytokeratin was diffusely positive in the epithelial component and focally in the spindle cell component. P53 nuclear stain was taken up diffusely in the stromal component.

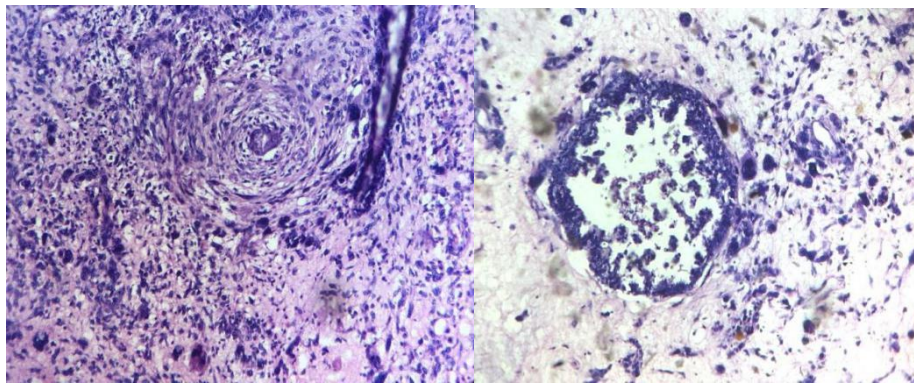


Fig 2

Fig 3

Figure 2: malignant mesenchymal component i.e atypical spindle cells along with few giant cells.

Figure 3: malignant epithelial component i.e an endometrial gland with individual cells showing nuclear pleomorphism and atypia.

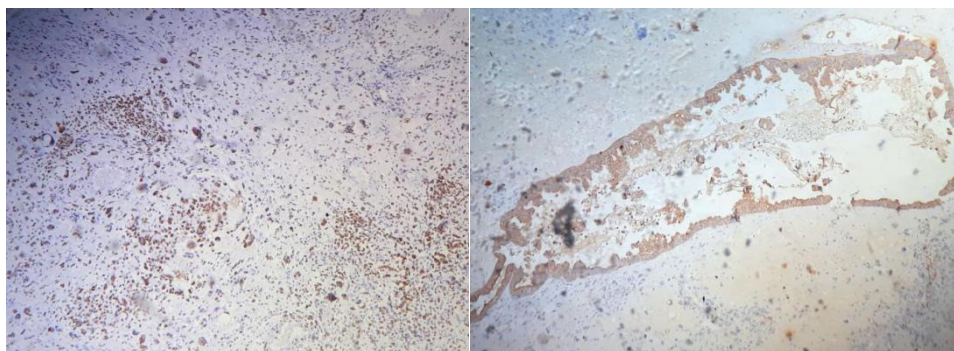


Fig 4

Fig 5

Figure 4: positive Tp53 nuclear stain taken up by the tumorous mesenchymal component.

III. Discussion

Malignant Mixed Mullerian tumors were first reported by Gerhardt in 1989 and was confirmed by Meyer on doing the histopathological examination of the slides [3].

They occur in the 5th decade of life. The lowest age of incidence of 15-17 years has also been recorded[4]. They mostly occur in the corpus of uterus but it may also involve the cervix, ovary, fallopian tube and vagina. In the uterus the posterior wall is most frequently involved[5]. Carcinosarcomas consists of endometrial adenocarcinomas co existing with a malignant mesenchymal component[6].

The latter may include endometrial stroma, smooth muscle (leiomyosarcoma), skeletal muscle (rhabdomyosarcoma), cartilage (chondrosarcoma) and even osteoid (osteosarcoma)[6]. They share the genetic changes of epithelial tumors that have secondarily developed a metaplastic stromal component, a concept supported by the fact that the stromal cells often stain positively with epithelial cell markers[6].

The predisposing factors are nulliparity, Diabetes mellitus, Obesity, chronic estrogen stimulation and history of previous pelvic irradiation. They classically present as a triad of pain, severe bleeding and passing necrotic tissue per vaginally[1]. In less than 5% they are associated with tamoxifen therapy or unopposed estrogen usage. Pelvic irradiating exposure risk requires a long time of about 10 -20 years for the tumor

development[7].From the above mentioned predisposing factors we can conclude that they have same risk factors for its development like that of endometrial carcinomas. Genetic profiling suggests that they have clonal origin and similar molecular profile to high grade endometrial cancer with Tp53 mutations being the most common alterations[7].The degree of differentiation of the mesenchymal component does not influence prognosis and metastasis. They are usually composed of epithelial component rather than mesenchymal tissue, implying that the sarcomatous differentiation is a marker of aggressiveness rather than being a more aggressive component[5].

A study has suggested various theories for its histogenesis which includes [4]:

- A) Collision theory : Here the carcinomatous and sarcomatous component are independent of each other.
- B) The second theory proposes that both these component arise from a single stem cell which shows a divergent differentiation.
- C) Conversion theory: It suggests that the sarcomatous component arises from the carcinomatous component during evolution.Mecluggage suggested that the spindle cell component is pseudosarcomatous stromal reaction. Mostly epithelial components are adenocarcinomas, but they may also be of clear cell type , mucinous, papillary, serous. Mesodermal component are mostly undifferentiated sarcoma among which the rhabdomyosarcoma is the heterologous type [6].

IV. Prognosis And Predictive Factors

The prognosis of these MMMTs are poor and they have similar pattern of spread like that of high grade endometrial carcinomas.A high proportion of patients with apparently clinically stage I have evidence of extra uterine spread at the time of diagnosis.Metastatic spread typically occurs to pelvic and para-aortic Lymph nodes, sometimes with distant hematogenous metastasis to lungs, brain and bones. However most patients die as a consequence of local pelvic/abdominal recurrence.The risk of advanced stage and metastasis is closely related to the depth of myometrial invasion.The serous and clear cell carcinomatous elements are associated with a higher frequency of other adverse prognostic factor in stage I patients;the presence of a rhabdomyosarcoma component has the worst prognosis.

Recurrence is seen over half of the patients after surgical or adjuvant therapy[4],5 years survival is seen in 21% cases and 70-90% deaths are seen within18 months of diagnosis[4]. The most important prognostic factor at the time of diagnosis as some of the authors postulate is the presence of heterologous component[4].

V. Conclusion

MMMTs are rare tumors occurring in elderly postmenopausal women of 5th to 6th decade if life.A high index of suspicion must be kept for diagnosis of these tumors in women presenting with postmenopausal bleeding along with gross appearance of areas of haemorrhage and necrosis.Careful examination of tissue must be done for the presence of the heterologous component as it indicates poor prognosis. Carcinosarcomas are needed to be distinguished from adenosarcomas which will not have malignant epithelial component.

As these are highly aggressive neoplasms they have worser prognosis than higher grades and more unfavourable histotypes of Endometrial adenocarcinomas.

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