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UTERINE ADENOSARCOMA WITH SARCOMATOUS OVERGROWTH:A RARE CASE WITH UNUSUAL PRESENTATION AND BRIEF REVIEW OF LITERATURE

Pathology

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ABSTRACT

Uterine adenosarcoma with sarcomatous overgrowth is an aggressive variant of adenosarcoma, which is extremely rare. Out of these uterine sarcomas, adenosarcomas are very rare biphasic tumors constituting around 8% of these tumors. Overall incidence of adenosarcomas is 0.2% of all uterine malignancies which indicates its rarity. If the sarcomatous part occupies >25% of the tumor volume, it is referred to as sarcomatous overgrowth. This is a case report of 60 years old female who presented with complaints of bleeding per vagina and passage of clots for 8 days. She underwent total abdominal hysterectomy with bilateral salpingo oophorectomy. Histopathological examination of small polypoidal mass revealed Adenosarcoma with Sarcomatous overgrowth without myometrial invasion. Because of the rarity and aggressiveness of the tumor, Pathologists and clinicians should be well with this entity so as to get early diagnosis and proper treatment. Also, it is important to assess the presence of poor prognostic factors like myometrial invasion. The present case is very rare to have abnormal gross presentation and lack of myometrial invasion. These tumors are usually of large size and it is very unusual to find small polypoidal mass on presentation.

KEYWORDS

MASO, HETEROLOGOUS, SARCOMATOUS OVERGROWTH

INTRODUCTION

Uterine sarcomas are rare tumors constituting less than 4% of all uterine malignancies. Out of these uterine sarcomas, adenosarcomas are very rare biphasic tumors constituting around 8% of these tumors. Overall incidence of adenosarcomas is 0.2% of all uterine malignancies which indicates its rarity.[1] If the sarcomatous part occupies >25% of the tumor volume, it is referred to as sarcomatous overgrowth. Other mixed epithelial and mesenchymal tumors are Adenomyoma, Adenofibroma and Carcinosarcoma. Adenosarcoma with sarcomatous overgrowth (ASSO) was first described by Clement et al. in 1974.[2] Herein, we are reporting a rare case of uterine ASSO along with brief review of literature.

CASE REPORT

A 60 years old multiparous postmenopausal female presented at Gynaecology outdoor department with complaints of bleeding per vagina for 8 days, along with passage of blood clots. Per vaginal examination revealed polyp of 3x4cm at external os, along with tenderness. Patients' routine haematological and biochemical investigations were within normal limits except anemia. PAP smear was reported as Negative for intraepithelial lesion or malignancy (NILM). Endometrial biopsy was done but was inconclusive. On radiological examination, ultrasonography abdomen revealed a bulky uterus measuring 91x75x56mm with highly thickened endometrium (45.5mm). MRI examination revealed a large well-defined abnormal signal intensity polypoidal mass in endometrium suggestive of endometrial polyp (Figure 1).

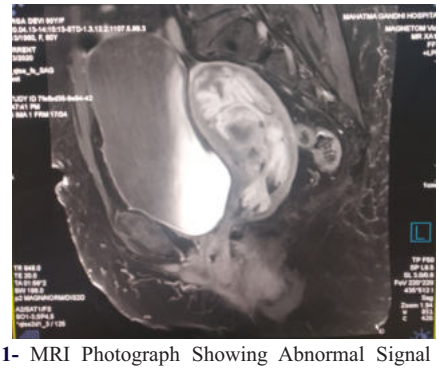

Figure 1- MRI Photograph Showing Abnormal Signal Intensity Polypoidal Mass In Endometrium

Patient was then planned for surgery. Hence, total abdominal hysterectomy with bilateral salpingo oophorectomy was done and the surgical specimen was sent for histopathological examination in the department of surgical pathology. Gross examination of the specimen showed a small polypoidal growth at the level of junction measuring 3.5x3x2cm (Figure 2).

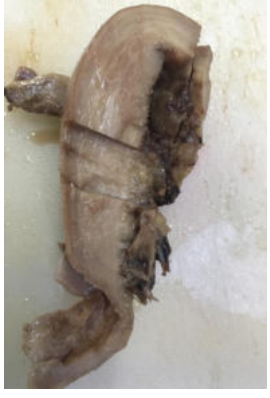

Figure 2- Gross Photograph Showing Small Polypoidal Growth At The Level Of Junction

Cut section was variegated showing haemorrhage, necrosis and calcification.

On histopathological examination, the polypoidal mass showed highly cellular stroma forming polypoidal fronds comprising of sheets of highly atypical, round to oval to spindled cells arranged in nests (Figure 3).

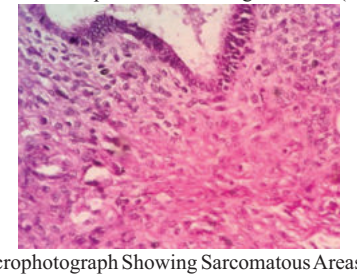

Figure 3- Microphotograph Showing Sarcomatous Areas, H/E 400X

Extensive areas of haemorrhage and focal necrosis were identified. Cells had vesicular chromatin and prominent nucleoli. High mitotic activity with atypical mitotic figures identified. Also seen heterologous differentiation into cartilage (Figure 4)

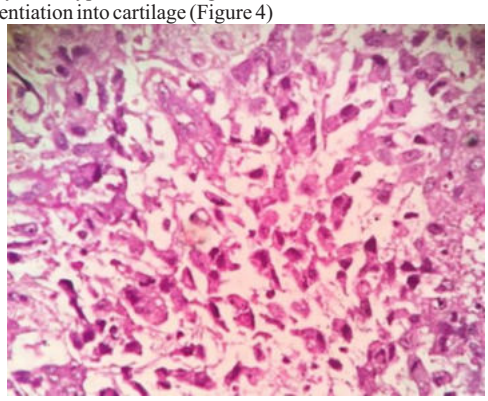

Figure 4- Microphotograph Showing Heterologous Differentiation Into Cartilage, H/E 400X along with osteoid deposition (Figure 5).

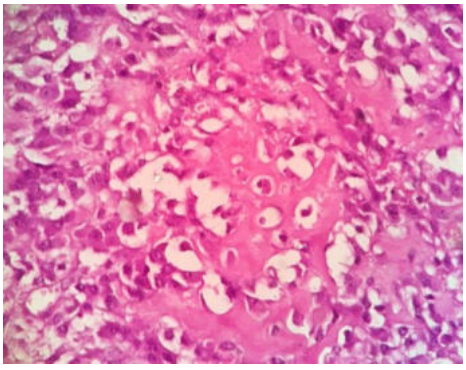

Figure 5- Microphotograph showing heterologous differentiation into osteoid, H/E 400X

The areas were devoid of glandular differentiation. Rest of the stroma show mild nuclear atypia with low mitotic activity.

The endometrial glands in the tumor tissue showed apocrine changes with presence of squamous metaplasia in some areas. No foci of lymphovascular invasion identified. Despite examining multiple sections, no myometrial invasion by tumor cells identified which was a very rare pathological finding for these aggressive tumors. Hence final histopathological diagnosis was made as Adenosarcoma with sarcomatous overgrowth (>25%). Postoperative period of the patient was uneventful. The tumor was confined to body of uterus. Patient was then lost to follow up.

DISCUSSION

Adenosarcoma is a mixed epithelial and mesenchymal tumor in which the epithelial component is benign or atypical and stromal component is predominantly of low-grade malignant potential. Whenever at least 25% of the tumor contains a high grade sarcomatous component, it is classified as "Adenosarcoma with sarcomatous overgrowth". The present case showed >25% high grade sarcomatous area in the mesenchymal component. They are usually associated with aggressive clinical course,recurrence,metastasis and fatal outcome.

Majority of adenosarcomas, including the present case, occur in postmenopausal women.[2,7] Risk factors associated are previous pelvic radiotherapy, long term unopposed estrogenic therapy, in particular tamoxifen therapy and long-term contraceptive pills.[3] The present case did not reveal correlation with any of the above risk factors.

Usually gross presentation of MASO is of large polypoidal mass in the uterus but in the present case, a small polypoidal growth was identified. Microscopically, Adenosarcoma is composed of benign appearing epithelium and malignant stroma. Malignant stroma demonstrates a broad leaflike architecture compressing benign epithelium. Peri glandular cuffing of stromal cells condensing under the epithelium is characteristic. The epithelial or glandular component is usually endometrioid and demonstrates metaplasia and show mild to moderate atypia.[4]
Vigorous and recent literature review showed that sarcomatous stroma containing heterologous elements is seen in only 22% of cases.[2] In present case, heterologous differentiation into cartilage along with osteoid deposition was seen. The unfavourable prognostic factors included high mitotic index, deep myometrial invasion, lymphovascular invasion and heterologous rhabdomyoblastic differentiation.[5] The present case showed high mitotic activity,necrosis and heterologous differentiation as poor prognostic factors. Clement published a clinicopathological analysis of 10 cases of Mullerian adenosarcoma in which myometrial invasion was noted in majority of the patients.[2,8] In the present case, myometrial invasion and lymphovascular invasion was not identified which is a very rare finding for these tumors.

Mullerian adenosarcoma with sarcomatous overgrowth are sometimes difficult to distinguish from embryonal rhabdomyosarcomas and carcinosarcomas.[4,5] In Carcinosarcomas, glandular element appears malignant along with sarcomatous component. ER, PR and CD10 receptors are expressed in low grade sarcomatous component in adenosarcoma with sarcomatous overgrowth while their expression is insignificantly decreased in sarcomatous overgrowth component. In Embryonal Rhabdomyosarcoma hormonal receptors are completely absent. Other important differentials include Endometrial stromal sarcoma and Leiomyosarcoma. In Endometrial stromal sarcoma tumour cells are monomorphic with presence of delicate vasculature with whorling of tumor cells around them. CD10 is of no special help as it is positive in both. In Leiomyosarcoma, the typical fascicular architecture and reactivity of SMA and Caldesmon is of utmost help to distinguish it from MASO.

Table 1-Summary Of MASO Cases Published In English Literature

Author	Year	Number of cases	Site	Myometrial Invasion	Lymphovascular invasion	Heterologous component	Treatment
Hallak et al[6]	1992	Single	Endometrium	Present	Absent	Present	TAH, BSO with lymph node sampling
Krivak et al[9]	2001	11					TAH with BSO and tumor debulking
Farhat et al[8]	2007	Single	Body of uterus	Present	Present	Present	Patient died before adjuvant therapy could be given
Singh et al[7]	2010	Single	Posterior wall of uterine corpus	-	-	Present	-
Podduturi et al[5]	2016	Single	Cervix	Absent	Absent	Present	Chemotherapy followed by radical hysterectomy, BSO and Bilateral pelvic lymph node dissection
Wang et al[3]	2019	Single	Posterior uterine wall	Present	Absent	Present	Exploratory laparotomy followed by chemotherapy
Mohapatra D et al[1]	2019	Single	Cervix	Present	Absent	Present	Hysterectomy followed by pelvic radiotherapy and chemotherapy
Present study	2020	Single	Uterocervical junction	Absent	Absent	Present	TAH with BSO

In view of highly malignant potential of Mullerian adenosarcoma with sarcomatous overgrowth, these patients should be managed aggressively.[6] Surgery should include total abdominal hysterectomy, bilateral salpingo oophorectomy, omentectomy and consideration should be given to lymph node sampling. Chemotherapy or radiotherapy should be considered postoperatively. There is no standardized chemotherapy, hormonal therapy or radiotherapy but standard chemotherapy regimens such as doxorubicin, ifosfamide, or gemcitabine/ docetaxel, and newer drugs such as trabectedin, are of some importance in adenosarcoma with sarcomatous overgrowth.[4] In

50% of cases of MASO, MYBL1 amplification and ATRX mutation are identified. In the literature, few cases have been published related to MASO. Krivak et al in 2002, published a largest review related to 37 cases of MASO upto 2001.[9]

CONCLUSION

Because of the rarity and aggressiveness of the tumor, Pathologists and clinicians should be well with this entity so as to get early diagnosis and proper treatment. Also, it is important to assess the presence of poor prognostic factors like myometrial invasion. The present case is very rare to have abnormal gross presentation and lack of myometrial invasion. These tumors are usually of large size and it is very usual to find small polypoidal mass as present.

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