

Low grade Mullerian adenosarcoma of pouch of Douglas recurring as bilateral ovarian high grade Mullerian adenosarcoma with rhabdomyosarcomatous overgrowth after 11 years

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Abstract

Mullerian adenosarcoma (MA) of ovary with sarcomatous (rhabdomyoblastic) overgrowth is an extremely rare malignant type of female genital tract neoplasm. These tumours are highly aggressive and presence of heterologous elements is associated with worse prognosis. A 44 year old female presented with lower abdominal pain and distension. She had history of removal of tumour from pouch of Douglas in 2006 for which she did not receive any additional treatment nor did she keep continuous follow up. Current preoperative radiological examination revealed bilateral ovarian masses. She underwent abdominal hysterectomy with bilateral oophorectomy. Microscopic examination revealed biphasic tumours exhibiting sarcomatous overgrowth with rhabdomyoblastic differentiation. Review of the previous biopsy revealed low grade Mullerian adenosarcoma without sarcomatous overgrowth. Hence the current tumour was considered recurrent. This report highlights the aggressive nature of MA even with low grade morphological features and emphasizes the importance of continuous follow up and additional treatment.

Keywords: Mullerian adenosarcoma, sarcomatous overgrowth, rhabdomyoblastic differentiation, extrauterine.

Introduction

Malignant mesenchymal neoplasms account for 1-3% of all female genital tract tumours and Mullerian Adenosarcoma (MA) constitute 8-10% of these malignancies.¹⁻³ MAs commonly arise in the uterus and presents as a polypoid mass. However, they can also involve extrauterine sites and ovary is the most common among these sites. Other extrauterine sites include pelvis, vagina, fallopian tube, peritoneum, intestine, liver, etc.¹⁻³

According to the classical description of Clement and

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Scully, MA is a mixed neoplasm comprising of malignant stromal and benign epithelial component.^{1,4,5} MA with sarcomatous overgrowth is defined as partial overgrowth of an otherwise typical adenosarcoma by pure high grade sarcoma occupying at least 25% of the tumour mass. Further classification of MA depends upon differentiation of mesenchymal elements; Homologous tumours are composed of nonspecific spindle shaped sarcomatous cells, whereas heterologous tumours are associated with myoid, chondroid and osteoid differentiation.^{2,3} Tumours with sarcomatous overgrowth have aggressive clinical course as compared to tumours without sarcomatous growth.²

Case Presentation

An abdominal hysterectomy and bilateral oophorectomy specimen was received at Histopathology Section, Department of Pathology and Laboratory Medicine, Aga Khan University Hospital, Karachi in April 2017. Patient was a 44 year old female who presented to the gynaecologist with complaint of lower abdominal pain. On clinical examination, a tender mass was palpable in the lower abdomen. Her preoperative ultrasound revealed a complex mass in right adnexa. MRI scan of pelvis showed bilateral ovarian masses. Right ovarian mass measured 8.5 x 8 cm with solid enhancing and cystic necrotic components. Left ovarian solid mass measured 5 x 4.5 cm. Uterus was bulky and contained multiple well defined hypo intense masses (Fibroids). There was no evidence of pelvic visceral, omental and peritoneal involvement. Pelvic lymphadenopathy was also not seen. Her serum CA-125 level was 50.9 u/ml. She underwent total abdominal hysterectomy with bilateral oophorectomy.

Gross examinations showed the uterus, cervix, fallopian tubes and multiple separate light brown, soft to firm, irregular pieces of tumour tissue. The largest of these tissue pieces measured 13 x 7 cm and the rest measured 11 x 9 cm in aggregate. On sectioning, cut surface was tan to light brown and exhibited areas of haemorrhage, necrosis and multiple cystic spaces. Uterus, cervix and fallopian tubes were grossly not involved by tumour. Myometrium also showed three fibroids.

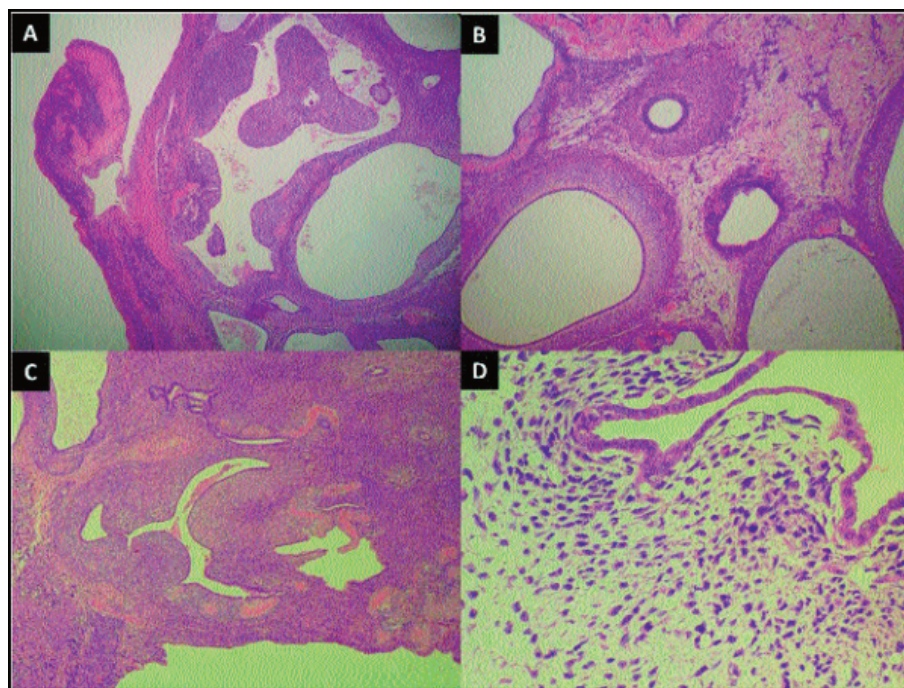


Figure-1: (A) Low power view of biphasic tumour exhibiting cystic spaces. Normal ovarian tissue is also appreciable on left side. (B) Medium power view showing condensation of stromal component around dilated glandular structures. (C) Medium power view showing compression of epithelial component by adjacent stromal component. (D) High power view showing benign low columnar epithelial lining surrounded by low grade sarcomatous component.

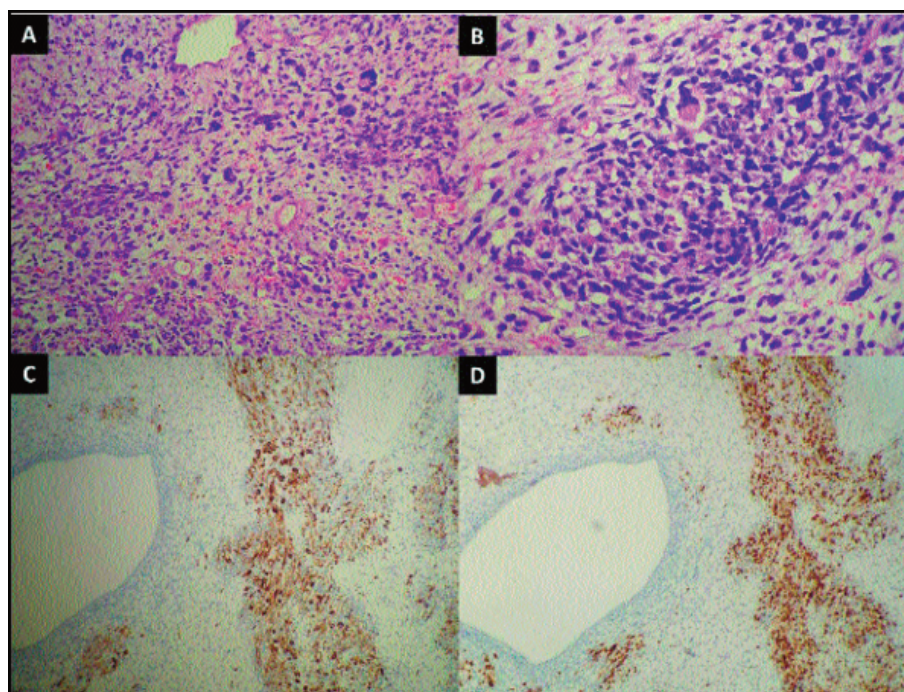


Figure-2: (A) Medium power view and (B) High power view of areas showing rhabdomyosarcomatous overgrowth. (C) Desmin and (D) Myogenin IHC stains demonstrating positive expression and confirming rhabdomyoblastic differentiation of tumour cells.

Microscopic examination of tumour tissue pieces revealed an extensively necrotic tumour. The viable areas showed a biphasic growth pattern comprising of predominant stromal component and scattered irregular, ectatic and compressed glands lined by bland looking columnar cells showing nuclear stratification. The stroma component showed marked hypercellularity with areas of necrosis and myxoid change. At some areas stromal cells appeared condensed around the glands (Figure 1A-D). Stromal cells were spindle to stellate in shape and exhibited prominent rhabdomyoblastic differentiation. Immunohistochemical (IHC) stains Desmin and myogenin also confirmed the rhabdomyoblastic nature of stromal cells (Figure 2A-D). The nuclei were highly pleomorphic and hyperchromatic. Frequent mitotic figures (approximately 22/10 HPF) were also appreciated. At foci, the background stroma showed hyalinized plaques resembling "collagen rosettes". Endometriosis and ovarian sex cord like elements were not found. Focally, normal ovarian stroma was also identified. Hence, the case was diagnosed as "Mullerian adenosarcoma with rhabdomyosarcomatous overgrowth".

Later the patient also revealed that she had undergone laparotomy and excision of a tumour in the pouch of Douglas in 2006. There was no evidence of disease in the ovaries, other pelvic organs and omentum at that time. The slides of the previous biopsy were reviewed which also revealed low grade adenosarcoma without any other lineage differentiation. Hence, we consider our case to be recurrence of the initial tumour. Since the patient belonged to a

remote rural area of the country, she neither kept continuous follow up nor received additional treatment at that time.

Patient was disease free 4 months after the removal of the recurrent tumour. Since the tumour had acquired high grade and sarcomatous overgrowth, patient was offered adjuvant radiotherapy which she refused due to financial reasons. She was then advised to keep close follow up with her gynaecologist and oncologist.

Discussion

The term "Mullerian adenosarcoma" was used first in 1974 by Clement and Scully for a distinctive uterine tumour characterized by a malignant, usually low grade, stromal component, and a generally benign, but occasionally atypical, glandular epithelial component.⁵ Since that time, similar cases have been reported from various places in the literature, most of which include a small number of patients.^{1,3,6-8} The largest series on MA included only 40 patients.²

MA can occur at any age including adolescence. Extrauterine MAs occur at younger age than their uterine counterparts as seen in our patient. Median age for uterine tumours is 71 years as compared to 53 years for extrauterine tumours. In vast majority (97.5%) of cases may tend to occur unilaterally.² In contrast, the ovaries were bilaterally involved in our case. The common presenting manifestations include abdominal pain, abdominal distention with palpable mass and irregular vaginal bleeding as also observed in our case.³ Some of these extrauterine tumours have been associated with and presumably arise from endometriosis. While others are not associated with endometriosis, they are thought to arise from surface epithelium, ovarian stroma, or peritoneal mesothelium as part of secondary Mullerian system.^{6,7}

Mullerian adenosarcoma of ovary is generally similar microscopically to uterine adenosarcoma except a few differences like sarcomatous overgrowth is seen in 30% of ovarian cases as compared to 8% in uterine adenosarcoma and SCLE (Sex cord like elements) were seen in 15% of ovarian cases as compared to 7% in their uterine counterparts.^{2,4}

Almost all endometrioid tumours of the ovary are carcinomas except for rare tumour types i.e. adenofibroma and MA. Adenofibroma resembles MA except that the stroma of adenofibroma lacks nuclear pleomorphism and mitotic activity found in adenosarcoma. The differential diagnosis in any

individual case depends on the morphologic features such as presence or absence of heterologous elements, sex cord like elements, and sarcomatous overgrowth. The differential diagnosis of MA with sarcomatous overgrowth also includes endometrial stromal sarcoma [ESS], immature teratoma, malignant mullerian mixed tumours (MMMT) and pure sarcomas when heterologous elements are present. ESS occurs in same age group as mullerian adenosarcoma and is usually unilateral. ESS resembles stromal component of adenosarcoma but lacks its glandular component. Thorough sampling should be done to search for epithelial component of MA as the prognosis of MA is worse than ESS. Immature teratoma can be excluded on the basis of age as these tumours most commonly occur in the first three decades of life and are almost nonexistent after menopause, and contain embryonal neuroectodermal elements and endodermal derivatives in almost all cases. In contrast to MA, malignant mullerian mixed tumours (MMMT) typically have a high grade mesenchymal component and an invasive carcinomatous component. The presence of typical adenosarcoma areas rule out the possibilities of pure sarcomas.^{1,2,7} Ovarian MAs have poor prognosis, higher recurrence and higher mortality rates than their more common uterine counterparts. Five year disease free survival is less than 25%.^{8,9} The main reason is probably related to the location of tumours with respect to the abdominal cavity and the lack of an anatomic barrier to spread. Another reason may also be the result of the larger size, higher stage, and higher frequency of rupture of the ovarian tumours. Surgery is the mainstay of treatment and additional chemotherapy and/or radiotherapy is administered in a proportion of patients.²

Conclusion

MAs of ovary are rare aggressive tumours which can present with recurrence after many years, even with low grade morphological features. Additional aggressive treatment modalities and close clinical follow up should be considered in all cases.

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Conflict of Interest: All authors declare that there is no conflict of interests.

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