

Uterine Adenosarcoma with Sarcomatous Overgrowth and Rhabdoid Features: A Rare Case

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Abstract

Uterine adenosarcoma is usually a low-grade neoplasm with a mixed benign epithelial component and malignant stroma, commonly found in postmenopausal women. In the presence of sarcomatous overgrowth, it has been shown to have poor prognosis. Uterine adenosarcoma with sarcomatous overgrowth and rhabdoid features is extremely rare. We report here a case of a 28-year-old female who was found to have adenosarcoma with sarcomatous overgrowth with extensive rhabdoid features. The tumor had metastasized to the pelvis, omentum, iliac, and obturator lymph nodes. She was lost to follow-up for 10 months, after which she presented with recurrent tumor at the hysterectomy site. She was started on palliative chemoradiotherapy, on which she progressed but later experienced drug toxicity, became cachectic, and was unwilling to continue chemotherapy. There are a few cases of adenosarcoma with sarcomatous overgrowth reported in young women and only two cases with rhabdoid features. Based on this report, adenosarcoma with sarcomatous overgrowth and rhabdoid features appears to be an extremely aggressive tumor with poor prognosis.

Keywords: Adenosarcoma, neoplasm, rhabdoid tumor, sarcomatous overgrowth, uterine adenosarcoma, uterine sarcoma

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INTRODUCTION

Uterine adenosarcoma accounts for 0.6% of uterine sarcomas and most commonly involves the endometrium; other reported sites include the cervix, fallopian tube, ovary, and para-ovarian tissue.^[1] It is usually encountered in postmenopausal women, though the affected age range in the literature is 15-90 years.

Extrauterine adenosarcoma has been reported in younger women and is considered more aggressive than its uterine counterpart. About 33-50% of such cases have shown the presence of sarcomatous overgrowth,^[2] which imparts poor

prognosis with a high risk of recurrence.^[3] Heterologous elements, i.e., rhabdomyosarcoma and leiomyosarcoma, have also been identified in the sarcomatous overgrowth.^[4] Uterine adenosarcoma with sarcomatous overgrowth and rhabdoid features is extremely rare, with only two cases reported in the literature.^[5,6] We hereby report another case with a similar tumor morphology.

CASE REPORT

A 28-year-old newly married Asian woman, without any comorbidities, presented with vaginal bleeding since a few

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weeks. On imaging, there was a large polypoidal uterine mass with deep myometrial invasion and right adnexal involvement with possible lymph node metastasis. On examination, a polypoid lesion in the cervix was identified and a biopsy was obtained. Histologic examination of the biopsy revealed a malignant neoplasm with morphology suggestive of adenosarcoma with stromal overgrowth.

Hysterectomy with bilateral salpingo-oophorectomy, omentectomy, and lymphadenectomy was performed. Intraoperatively, a 6-cm pelvic mass separate from the uterus was also identified. It was resected along with right common iliac and obturator lymph nodes.

On gross examination, a tan, friable tumor was identified. The tumor rose from the fundus and extended into the cervix, and measured around 10 cm [Figure 1]. On

histopathological analysis, the uterine tumor was composed of polypoid masses surfaced by benign endometrial glandular epithelium [Figure 2]. The underlying stroma was markedly cellular and composed of small round cells with moderate amount of pale cytoplasm and round-to-ovoid vesicular nuclei, some of which contained prominent nucleoli [Figure 3]. Mitoses were frequent and areas of tumor necrosis were noted. In some areas, subepithelial condensation of the sarcomatous component was noted. Sheets of rhabdoid cells with abundant cytoplasm containing eosinophilic inclusions with a laminated architecture were found scattered throughout the stromal elements [Figure 4]. These inclusions were associated with eccentric displacement of the nuclei [Figure 5]. The rhabdoid inclusions in periodic acid-Schiff with diastase stain were negative. On immunohistochemistry, the tumor



Figure 1: Gross photograph of uterus with tan yellow necrotic mass arising in the fundus and infiltrating the cervix

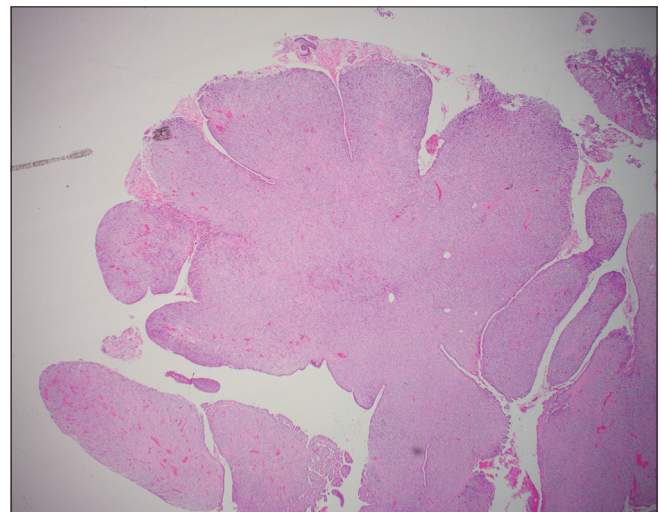


Figure 2: Low power view photomicrograph showing leaf like architecture with underlying cellular stroma

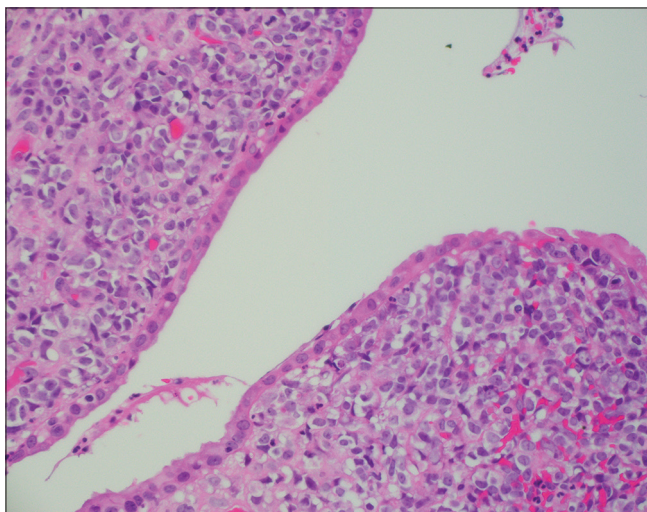


Figure 3: Photomicrograph showing benign endometrial lining with underlying cellular stroma

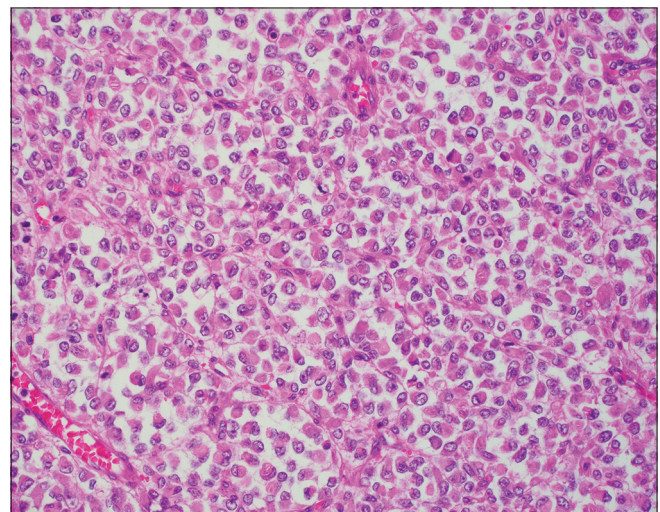


Figure 4: High power view showing sheets of plump round cells with rhabdoid features

was positive for vimentin, and integrase interactor-1 (INI-1) was retained within the nuclei [Figure 6]. It also showed strong focal staining for CD10 [Figure 7]. Myo-D1 was negative. The tumor extensively invaded the myometrium and the cervical stroma. The pelvic mass had a similar morphology.

The omentum showed multiple microscopic foci of metastatic sarcoma. Two right common iliac lymph nodes and one obturator lymph nodes also showed metastatic sarcoma. Both fallopian tubes and ovaries were unremarkable. The parametria and the serosa were not involved by the tumor. There was no lymphovascular or perineural invasion. The background endometrium was inactive. Pathological stage of pT3a pN1 and FIGO stage IIIc was assigned. Accordingly, palliative chemotherapy and pelvic radiation was suggested; however, the patient

refused any further therapy and returned to her home country.

She again presented 10 months later with lower abdominal pain, diarrhea, and a 15-kg weight loss. Repeat MRI pelvis revealed tumor recurrence at the site of hysterectomy along with peritoneal spread in the pelvis and lower part of the abdomen. The mass was compressing the rectum. PET-CT showed local recurrence with extensive abdominopelvic lymph nodal involvement and suspicion of liver metastasis [Figure 8]. She was started on palliative chemoradiotherapy: first on pegylated liposomal doxorubicin, and as clinical progression was noted in three cycles, she was shifted to doxorubicin and ifosfamide. However, she experienced features of drug toxicity such as continuous nausea and vomiting, became cachectic, and was unwilling to continue chemotherapy. The patient insisted on returning

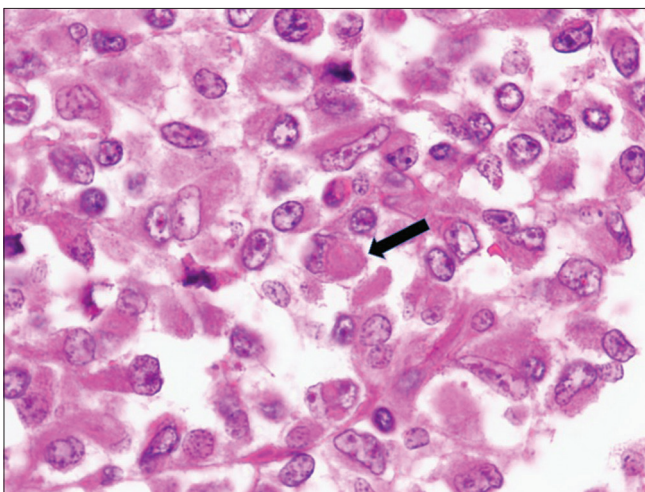


Figure 5: Hematoxylin and eosin-stained section under oil emersion lens (100x) showing plump atypical rhabdoid cells with large nuclei and abundant eosinophilic cytoplasm (indicated by black arrow)

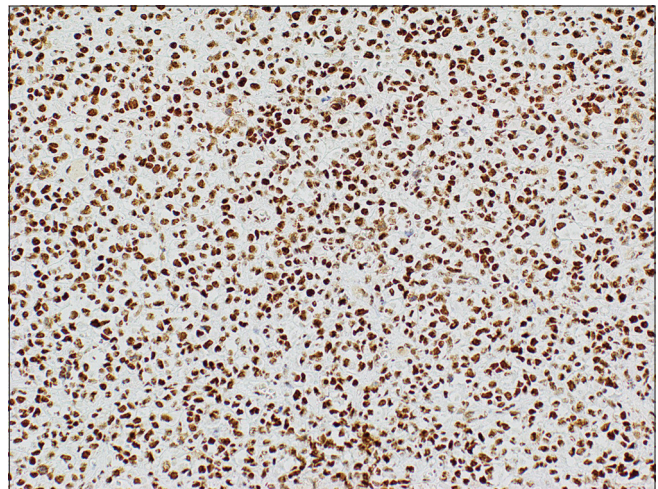


Figure 6: Immunohistochemistry for INI-1 shows intact nuclear expression

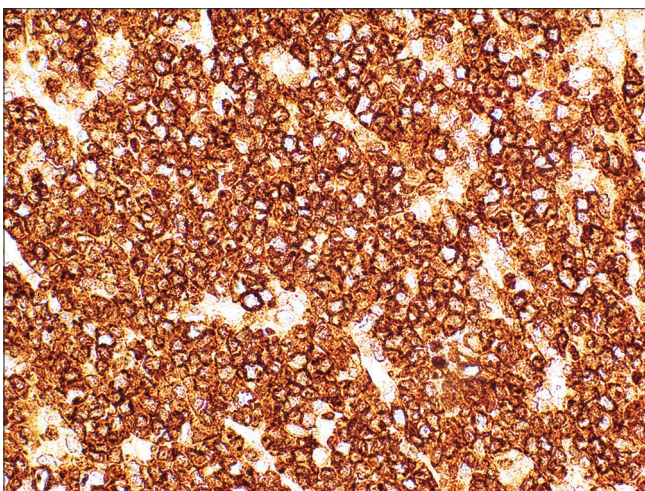


Figure 7: CD10 immunohistochemistry showed focal strong staining in the neoplastic cells

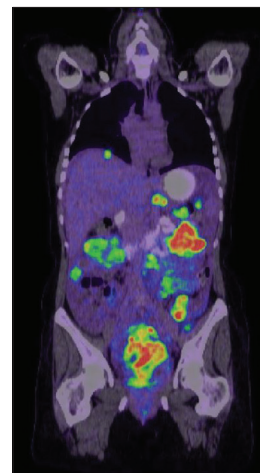


Figure 8: Positron emission tomography image showing extensive peritoneal involvement with suspicious liver metastasis

to her home country to be with her family, after which she was lost to follow-up.

DISCUSSION

Sarcomatous overgrowth was described in uterine adenosarcomas for the first time in 1989 by Clement.^[7] He reported 10 cases of uterine adenosarcoma overgrown by a pure sarcoma that accounted for 25-80% of the tumor. Adenosarcoma with sarcomatous overgrowth is defined as a tumor that contains >25% of the sarcomatous component and has a more aggressive clinical course than adenosarcoma. Sarcomatous components are usually homologous, but heterologous elements such as rhabdomyosarcoma, cartilage, and skeletal muscle tissue have also been reported. Ulker *et al.* have also reported ovarian sex cord-like differentiation.^[8]

The rhabdoid cell is a distinct cell type in tumors, showing a striking cytoskeletal inclusion composed of intermediate filaments that are visualized as an eosinophilic, eccentrically placed cell body usually displacing the atypical nucleus to one side. Rhabdoid tumors consistently show absence of nuclear reactivity for the chromatin-remodeling factor, SRF5/INI 1, although this is not required for recognition of rhabdoid component in other tumors.^[9] Malignant tumors containing variable amounts of rhabdoid cells commonly exhibit a more aggressive biology. Therefore, the identification of rhabdoid features is important.^[10,11]

Rhabdoid features in adenosarcoma have previously only been described twice in the literature. One was the case of a 52-year-old female with a history of invasive ductal carcinoma treated with surgery, paclitaxel, and radiation.^[5] The second case was published in Chinese language and does not provide any significant clinical or pathological information in the English abstract.^[6]

Adenosarcoma epithelial component stains positive for cytokeratin and negative for estrogen receptors (ER) and progesterone receptors (PR). The mesenchymal component bears a resemblance to stromal sarcoma and usually stains for CD10 and may also express WT 1, ER, PR, AR, SMA, and desmin. Staining is accentuated in periglandular areas. MyoD-1 and myogenin are positive in rhabdomyosarcomatous differentiation. CD 10, ER, and PR are often lost in sarcomatous overgrowth, which, in many cases, is positive for p53.^[1]

Next-generation sequencing has shown amplification of the E3 ubiquitin protein ligase (MDM2) and cyclin-dependent kinase 4 (CDK4) in 28% of the cases, and alterations in the

phosphatidylinositol-4,5-bisphosphate 3-kinase (PIK3CA/AKT/PTEN) pathway in 72%. TP53 mutations are not common in adenosarcoma but may be more common in the subset with the sarcomatous overgrowth.^[12]

The differential diagnosis of uterine adenosarcoma includes adenofibroma, which also presents in an analogous fashion clinically. It has similar biphasic appearance, but the stromal component appears bland and lacks peri glandular cuffing which is a characteristic feature in adenosarcoma. Adenosarcoma can focally resemble adenofibroma, and thus, adequate sampling is vital. Another differential is endometrial stromal sarcoma, which can infiltrate benign glands. However, there is lack of periglandular cuffing of stroma, phyllodes-like architecture. Moreover, the glands are only found at the periphery and not within the sarcoma. Uterine carcinosarcoma, like adenosarcoma, has a biphasic growth pattern. However, in carcinosarcoma, both epithelial and stromal component are malignant and usually of high grade.

SMARCA4-deficient uterine sarcoma is a recently described entity that closely mimics the large cell variant of the small cell carcinoma of the ovary morphologically, immunohistochemically, and carry the same genetic alteration.^[13] Unlike the undifferentiated endometrial sarcoma that can also have SMARCA4 mutation, the uterine sarcoma with rhabdoid features has a far worse prognosis, similar to other tumors with this mutation. SMARCA4 deficient uterine sarcomas have sheets of rhabdoid cells and can focally show leaf-like architecture infiltrating into adjacent benign glands. But these are CD10-negative, which differentiates them from uterine adenosarcoma with sarcomatous outgrowth. It is important to recognize it as this is a very aggressive entity.

Uterine adenosarcoma is usually managed with hysterectomy with bilateral salpingo-oophorectomy. The role of radiation, chemotherapy, and hormonal therapy cannot be properly evaluated because of limited data availability. In the absence of the sarcomatous component, the rate of recurrence is low. Studies have showed that the 2-year progression-free and overall survival rate for adenosarcoma patients with sarcomatous overgrowth was 20% compared to 100% for adenosarcoma without sarcomatous overgrowth, irrespective of the grade of the tumor.^[14,15]

Other poor prognostic features include high grade and presence of heterologous elements especially rhabdomyosarcoma. However, as stated above, there is very limited knowledge regarding cases with rhabdoid features. Lymph node metastasis is rare in uterine adenosarcoma;

however, when present, the tumor carries same prognosis as endometrial stromal sarcoma and leiomyosarcoma.^[16] Based on the clinical course in our patient, uterine adenosarcoma with sarcomatous overgrowth and rhabdoid features appears to have a poor prognosis.

CONCLUSION

The case of uterine adenosarcoma with sarcomatous overgrowth and rhabdoid features reported here had a very aggressive clinical course with extensive metastasis and rapid recurrence on chemotherapy.

Patient consent

Informed consent for publication could not be obtained as the patient was lost to follow-up. Requirement for patient consent for publication was waived by the institutional ethics committee, and Medical Research Center (MRC) of Hamad Medical Corporation, Qatar, granted permission for this case report to be published (Ref no.: MRC-04-20-1083; dated November 21, 2020). The authors and the MRC understand that the name and initials will not be published, and due efforts will be made to conceal the patient's identity, but anonymity cannot be guaranteed.

Peer review

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Conflicts of interest

There are no conflicts of interest.

REFERENCES

- Howitt BE, Carlson JW, Quade BJ. Adenosarcoma of the uterine corpus. In: WHO Classification of Tumours Female Genital Tract. 5th ed., Vol. 4). Lyon (France): International Agency for Research on Cancer; 2020. p. 305-6.
- Wang B, Yang HD, Shi XH, Li H. Advanced uterine adenosarcoma with sarcomatous overgrowth in a young woman: A case report. *Medicine (Baltimore)* 2019;98:e18119.
- Kaku T, Silverberg SG, Major FJ, Miller A, Fetter B, Brady MF. Adenosarcoma of the uterus: A Gynecologic Oncology Group clinicopathologic study of 31 cases. *Int J Gynecol Pathol* 1992;11:75-88.
- Gast MJ, Radkins LV, Jacobs AJ, Gersell D. Müllerian adenosarcoma of the cervix with heterologous elements: Diagnostic and therapeutic approach. *Gynecol Oncol* 1989;32:381-4.
- Carvalho F, Carvalho J, Motta E, Souen J. Müllerian adenosarcoma of the uterus with sarcomatous overgrowth following tamoxifen treatment for breast cancer. *Rev Hosp Clín* 2000;55:17-20.
- Wei WU, Jin-Lin HU, Xing-Hao NI. Adenosarcoma of the uterus with mesenchymal rhabdoid tumor differentiation: A case report and review of literature. *Chin J Clin Exp Pathol* 2005;21:688-91.
- Clement PB. Müllerian adenosarcomas of the uterus with sarcomatous overgrowth. A clinicopathological analysis of 10 cases. *Am J Surg Pathol* 1989;13:28-38.
- Ulker V, Yavuz E, Gedikbasi A, Numanoglu C, Sudolmus S, Gulkilik A. Uterine adenosarcoma with ovarian sex cord-like differentiation: A case report and review of the literature. *Taiwan J Obstet Gynecol* 2011;50:518-21.
- Al-Hussaini M, Hirschowitz L, McCluggage WG. Uterine neoplasms composed of rhabdoid cells do not exhibit loss of IN11 immunoreactivity and are not related to childhood malignant rhabdoid tumor. *Int J Gynecol Pathol* 2008;27:236-42.
- Brennan B, Stiller C, Bourdeaut F. Extracranial rhabdoid tumours: What we have learned so far and future directions. *Lancet Oncol* 2013;14:e329-36.
- Moussaly E, Atallah JP. A rare case of undifferentiated carcinoma of the colon with rhabdoid features: A case report and review of the literature. *Case Rep Oncol Med* 2015;2015:531348.
- Howitt BE, Sholl LM, Dal Cin P, Jia Y, Yuan L, MacConaill L, *et al.* Targeted genomic analysis of müllerian adenosarcoma. *J Pathol* 2015;235:37-49.
- Kolin DL, Dong F, Baltay M, Lindeman N, MacConaill L, Nucci MR, *et al.* SMARCA4-deficient undifferentiated uterine sarcoma (malignant rhabdoid tumor of the uterus): A clinicopathologic entity distinct from undifferentiated carcinoma. *Mod Pathol* 2018;31:1442-56.
- Tanner EJ, Toussaint T, Leitao MM Jr., Hensley ML, Soslow RA, Gardner GJ, *et al.* Management of uterine adenosarcomas with and without sarcomatous overgrowth. *Gynecol Oncol* 2013;129:140-4.
- Lee JC, Lu TP, Changou CA, Liang CW, Huang HN, Lauria A, *et al.* Genomewide copy number analysis of müllerian adenosarcoma identified chromosomal instability in the aggressive subgroup. *Mod Pathol* 2016;29:1070-82.
- Machida H, Nathenson MJ, Takiuchi T, Adams CL, Garcia-Sayre J, Matsuo K. Significance of lymph node metastasis on survival of women with uterine adenosarcoma. *Gynecol Oncol* 2017;144:524-30.