Case Report
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Post-Radiation Vaginal Angiosarcoma: A Case Report

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Abstract

Angiosarcoma, an uncommon sarcoma, comprises only 1% of all soft tissue sarcomas. In the female genital tract, fewer than 70 cases have been reported previously. Due to rarity, there is no consensus about their treatment, especially in female genital tract. Herein, a 56-year-old woman, who was a known case of human papillomavirus-associated endocervical mucinous adenocarcinoma, stage Ib2 was presented with vaginal bleeding. The patient underwent total abdominal hysterectomy, bilateral salpingo-oophorectomy, lymph node dissection and radiotherapy 15 years ago. Pelvic magnetic resonance imaging before and after contrast administration showed an area of mass-like thickening in the left side of vaginal cuff. A core needle biopsy was performed and demonstrated anastomosing vascular channels with atypical endothelial cell lining. 12 months after anterior pelvic exenteration, the patient remains in good condition with no evidence of recurrence or metastasis, and the ileal conduit is functioning well. Post-radiation vaginal angiosarcoma is a rare complication of female genital tract tumors that should be considered in differential diagnosis of late onset tumors in this region. Primary or adjuvant chemotherapy should be considered for treatment of these patients.

Keywords: Radiation, Angiosarcoma, Vagina, Case report

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Introduction

Angiosarcoma, an uncommon sarcoma, comprises only 1% of all soft tissue sarcomas.[1] The tumor originates from endothelial cells of lymphatic or blood vessels, and therefore can occur in any part of the body. Cutaneous angiosarcoma

in men and sun-exposed areas is the most common presentation.[2] Chest wall or axillary involvement following radiotherapy for breast cancer is another common presentation of this rare tumor.[3] In female genital tract, less than 70 cases have been reported previously, and it can occur post-radiation.[4, 5] The interval from the treatment of the primary malignancy to the diagnosis of post-radiation gynecologic angiosarcoma ranged from 6.5 to 21 years.[6]

By definition, angiosarcomas have a poor prognosis, a feature that correlates with their propensity for distant metastasis, local recurrence and high-grade nature.[7, 8] Due to rarity, there is no consensus about their treatment, especially in female genital tract. The current treatment options include: surgery, chemotherapy, and radiotherapy.[9] Herein, we present a rare case of vaginal cuff angiosarcoma after radiotherapy of uterine cervix adenocarcinoma. This case report adheres to the CARE guidelines.[10]

Case Presentation

A 5- year-old woman, a known case of human papillomavirus-associated endocervical mucinous adenocarcinoma, stage Ib2 was treated with total abdominal hysterectomy, bilateral salpingo-oophorectomy, lymph node dissection and radiotherapy 15 years ago. She was presented with vaginal bleeding.

Initial trans-vaginal ultrasound showed thickening and increased vascularity (color score 3) of the left side of the vaginal cuff with extension and adhesion to the vesicovaginal septum and the posterior bladder wall. Pelvic magnetic resonance imaging (MRI) before and after contrast administration showed an area of mass-like thickening in the left side of vaginal cuff with diameter about 36 × 30 mm in the most prominent part (Figure 1). This area showed significant progressive post contrast enhancement (Figure 1b) and had diffusion restriction on diffusion weighted imaging images (apparent diffusion coefficient value about 0.9) (Figure 2). These findings were suggestive for a local tumor lesion at the vaginal cuff. Extension of enhancement to the adjacent fat planes was seen with adhesion to the posterior bladder wall (Figure 1). The bladder wall showed diffuse thickening in other parts with mild enhancement in favor of background cystitis. At least partial muscular bladder wall invasion was suspected, however

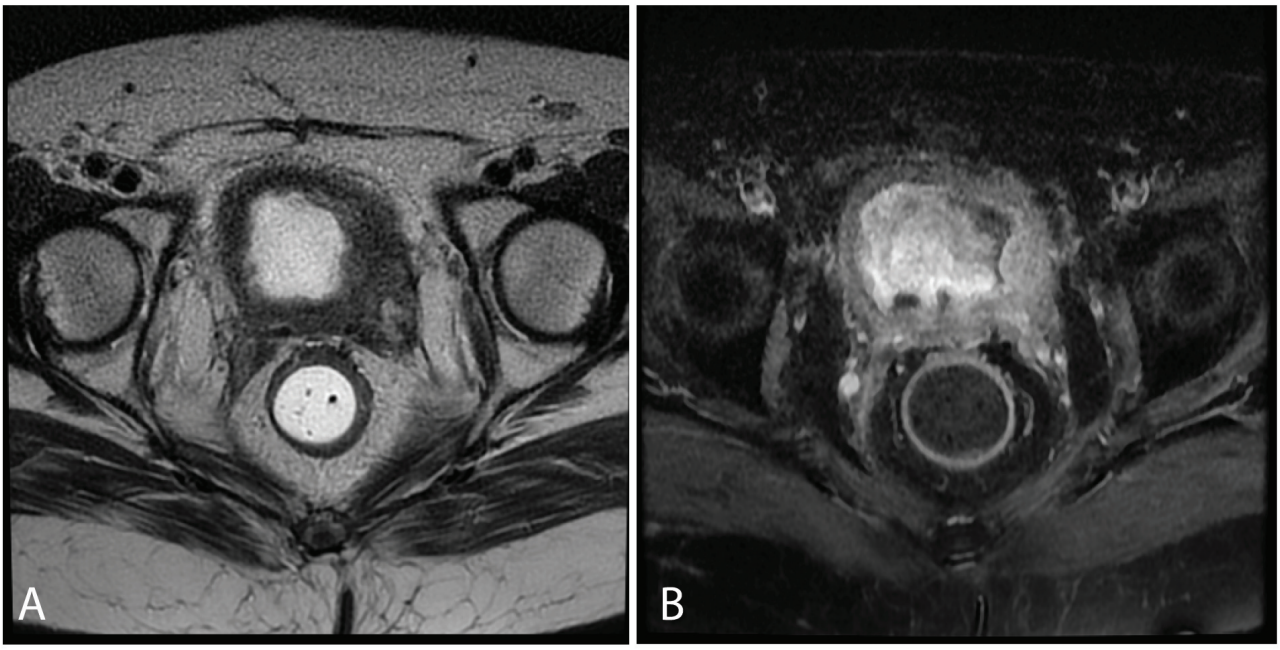

Figure 1. (A) Axial T2 weighted image shows diffuse bladder wall thickening. A mass like lesion is seen at the left posterolateral vaginal cuff, which cannot be separated from the adjacent bladder wall. There is no discernible fat plane between the cuff and the bladder, likely related to pelvic adhesions. (B) Post contrast T1 weighted fat suppressed image shows marked enhancement of the lesion.

there were limitations due to background cystitis and multiple pelvic post-radiation pelvic adhesions. No pelvic or para-aortic lymphadenopathy was seen.

A core needle biopsy was performed which demonstrated anastomosing vascular channels with atypical endothelial cell lining. The endothelial cells revealed positive reaction with CD31, CD34 and ERG on immunohistochemistry study (Figure 3).

On cystoscopy and colonoscopy, the urinary bladder and colonic mucosa were unremarkable. No distant metastasis was detected. The patient was discussed in a multidisciplinary team and became candidate for radical surgery and anterior pelvic exenteration. Despite extensive fibrosis and adhesions of radiotherapy as well as extension of tumoral involvement, the tumor was removed en-block including the bladder, while fortunately the rectum was saved. Urinary tract continuity was reconstructed using an ileal conduit and the patient was transferred to intensive care unit. The post-operative course was uneventful, and the patient was discharged on the seventh post-operation day. The final diagnosis was supportive of angiosarcoma with free margins. The patient was regularly followed every three months during the first year after surgery by clinical examination and imaging studies. 12 months after anterior pelvic exenteration, she remains in good general condition with no evidence of local recurrence or distant metastasis on pelvic MRI and chest computed tomography scans. The ileal conduit functioned well, and no significant post-operative complications such as infection, obstruction, or parastomal hernia were reported. The patient has returned to her routine activities under continuous oncologic surveillance.

Ethical approval

This study was conducted in accordance with the Declaration of Helsinki. The study protocol was reviewed and approved by the ethics committee of Tehran University of Medical Sciences (Imam Khomeini Hospital), Tehran, Iran (ethics code: IR.TUMS.IKHC.REC.1405.192). Written informed consent for publication of the clinical details and any images was obtained from the patient.

Discussion

Most cases of angiosarcoma are idiopathic. Only about 3% can occur as hereditary neoplasms

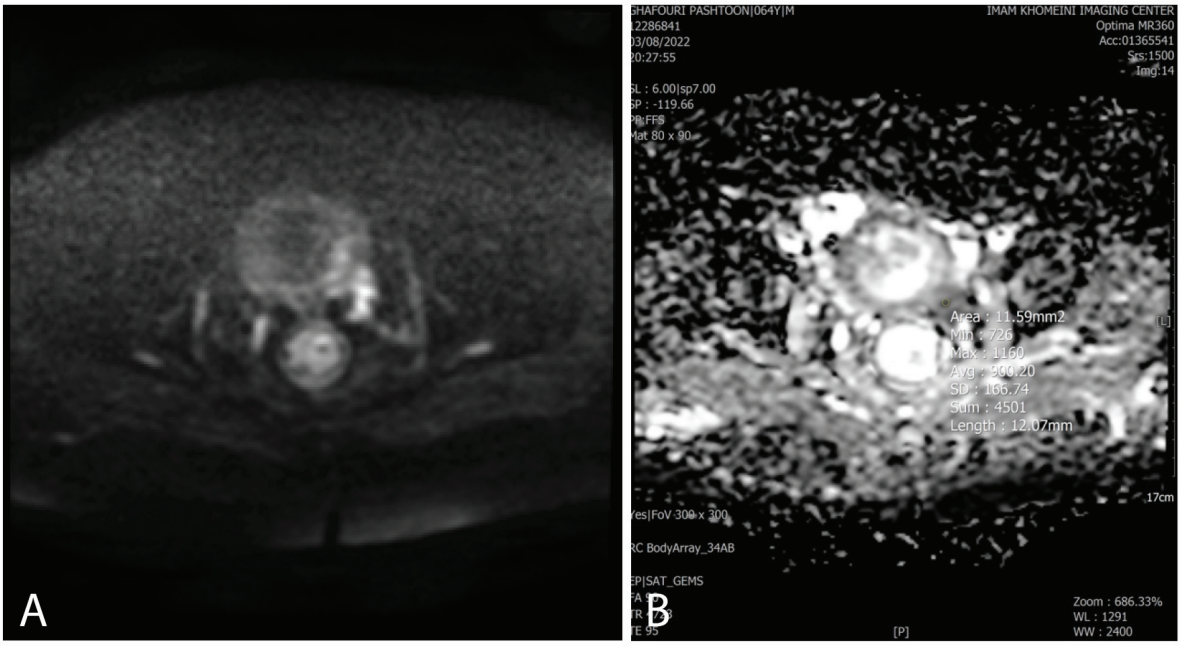

Figure 2. (A) The diffusion weighted MRI shows an area of diffusion restriction. (B) The corresponding ADC map demonstrates a low signal region at the same site, with an ADC value of approximately 0.9.
MRI: Magnetic resonance imaging; ADC: Apparent diffusion coefficient

in neurofibromatosis syndrome. Predisposing factors include: sun exposure, ionizing radiation, chemical toxins, foreign material and chronic lymphedema. Women with breast cancer who are treated with surgery and radiotherapy may develop angiosarcoma about 5-10 years later, either as the consequence of radiation or chronic lymphedema induced by surgery as well as fibrosis of radiotherapy.

For management of female genital tract cancers, brachytherapy or radiotherapy with or without surgery is widely used as the adjuvant treatment for patients with endometrial carcinoma (stage Ib or more), uterine cervix (stage Ib or more) and carcinoma of the vulva.[6] In patients who survive the primary cancer, there is a possibility of developing angiosarcoma over the long time. Less than 70 cases of primary female genital tract angiosarcoma have been reported in English literature, hitherto.[5] Most of them were in uterine corpus and ovary.[4, 5] Only a limited number of cases of uterine cervical and vaginal angiosarcoma have been reported in the literature.[6-8] All of the vaginal angiosarcomas were associated with radiotherapy for other gynecological malignancies. According to Cahan's criteria for radiotherapy-induced sarcom, when a tumor occurs in the field of previous radiation therapy after an interval of more than 5 years and the pathology is different from primary tumor, it could be called a radiation-induced sarcoma.

In our presented case, all the criteria are met and she can be considered as a radiation-induced angiosarcoma. Microscopically, the tumors are poorly demarcated and highly infiltrate the adjacent structures composed of anastomosing channels or sheets of endothelial cells with nuclear atypia, increased mitosis and foci of necrosis.[2] The morphologic features vary from well-differentiated tumors which are difficult to differentiate from benign vascular tumors, such as hemangioma or hemangioendotheliomas, to poorly-differentiated cancers or epithelioid subtypes. Differentiation from other sarcoma or even carcinomas may be challenging in these cases.

Immunohistochemically, the tumor cells are positive for endothelial markers, including CD31,

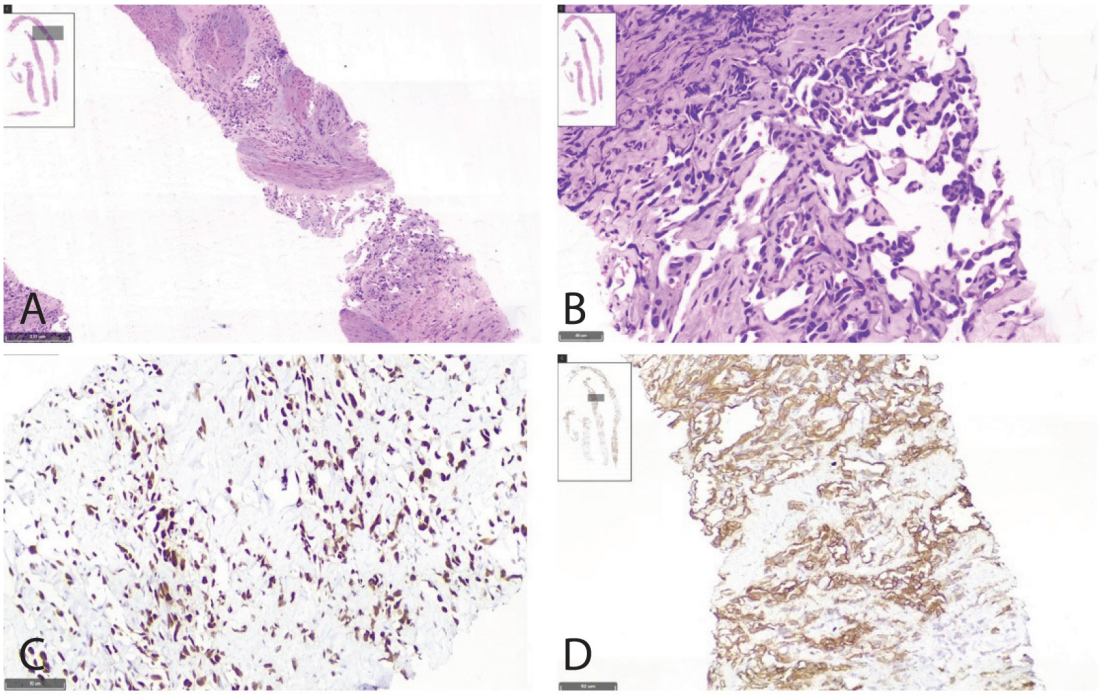

Figure 3. (A) Histopathologic examination of the tumor at ×4 magnification demonstrates a vascular neoplasm composed of anastomosing channels. (B) At ×10 magnification, the vascular spaces are lined by atypical endothelial cells. (C, D) Immunohistochemical (IHC) staining shows strong nuclear positivity for ERG (C) and positive membranous staining for CD31 (D) in the tumor cells.

CD34, ERG, Factor VIII and FLI1. Expression of Podoplanin (D2-40) is suggestive of lymphatic differentiation. Epithelioid subtypes express CK AE/AE3, EMA, and CD30.[9] Angiosarcoma is an aggressive tumor with a 5-year survival rate of 27%-35%. Radical surgery is the first treatment strategy. There is no evidence for improvement of survival rate after neoadjuvant chemotherapy in localized skin angiosarcomas. However, in female genital tract, adjuvant chemotherapy is recommended as it increases survival rates.[5-8]

Two cases of previously described vaginal angiosarcoma were treated only with radiotherapy. The other reported cases, chemotherapy with weekly paclitaxel or paclitaxel and cisplatin were conducted and obtained longer overall survival. Despite its rarity, and small number of reported cases, it seems that primary or adjuvant chemotherapy with paclitaxel in female genital tract angiosarcoma can be considered.[8, 9] The tumor was completely disappeared with 15 months free of the disease.

Conclusion

Post-radiation vaginal angiosarcoma is a rare complication of female genital tract tumors which should be considered in the differential diagnosis of late-onset tumors in this region. Primary or adjuvant chemotherapy is recommended to be considered for treatment of these patients.

Informed Consent

Written informed consent was obtained from the patient's legal guardian for publishing this case report and any accompanying images. A copy of the written consent is available upon the request of the Editor-in-Chief of the journal.

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Authors' Contribution

Fatemeh Nili was involved in the study concept and design, data collection, and drafting of the manuscript. Sara Parviz was responsible for radiologic interpretation and literature review. Amirmohsen Jalaeefar contributed to the surgical management of the patient and revision of the clinical description. Seyedeh Zahra Mousavi performed the pathologic and immunohistochemical evaluations and reviewed the manuscript for diagnostic accuracy. Mohammad Hossein Teymoori was responsible for the critical revision and editing of the manuscript for important intellectual content. Nastaran Tayebi supervised the study and approved the final version of the manuscript. All authors read and approved the final manuscript.

Conflicts of Interest

None declared.

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