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Case report

Unusual indolent behavior of leiomyosarcoma of the vagina: Is observation a viable option?

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1. Introduction

Primary leiomyosarcoma (LMS) of the vagina is a rare disease with an overall poor prognosis (Berek and Hacker, 2010). Surgical resection of the tumor is currently the modality of choice for patients with localized disease (Khosla et al., 2014). There is no consensus on adjuvant therapy or management following surgery. Further, there is a paucity of data regarding conservative management options. Given the rarity of this tumor and controversy regarding treatment, we report a case of unanticipated indolent behavior of residual LMS after partial resection in a patient who received no adjuvant therapy for 24 months.

2. Case report

A 72-year-old woman initially presented to her gynecologist in June 2014 with vaginal and rectal bleeding. Her past medical and surgical history was remarkable for a remote history of hysterectomy for fibroids, congestive heart failure, atrial fibrillation and chronic renal insufficiency. Pelvic examination revealed a mass in the anterior vaginal wall. She was referred to a gynecologic oncologist for further evaluation and management. CT and MRI confirmed a 4 × 3.5 cm vaginal mass in close proximity to the ureter and bladder associated with right hydronephrosis (Fig. 1). The patient underwent placement of bilateral ureteral stents and transvaginal resection of the mass. Microscopic examination showed that the tumor was hypercellular and composed of sheets of spindle cells with marked atypia and > 10 mitotic figures per10 high power fields (Fig. 2A and B). Immunohistochemical studies showed that the neoplastic cells were positive for SMMS-1 and caldesmon (Fig. 2C and D) while negative for desmin, c-Kit and HMB-45. These results are in keeping with the diagnosis of LMS. In addition, the tumor was positive for estrogen receptor (ER) and progesterone receptor (PR). Postoperative positron emission tomography (PET) showed a residual 3 cm FDG-avid mass in the anterior vaginal wall near the surgical bed with concern for rectosigmoid involvement. The patient was taken to the OR for diagnostic laparoscopy with no evidence of peritoneal disease. Vaginal biopsy of the residual mass demonstrated fragments of fibrovascular connective tissue without malignant cells. Given the concern for residual disease, patient was offered anterior exenteration, adjuvant chemotherapy or radiation. However, the patient elected for surveillance. She underwent an MRI three months later which revealed stable disease with the vaginal wall mass measuring 3.9 × 2.3 × 2.9 cm. No new disease was identified. The patient was subsequently referred to our institution for a second opinion, 6 months after her initial presentation. Additional imaging was obtained which revealed the residual mass was stable in size (Fig. 3). Given her multiple co-morbidities in the setting of stable tumor size, lack of systemic symptoms and prolonged interval from initial surgical intervention, we recommended conservative management with surveillance. The patient was followed every 3 months with physical exam and MRI and remained without clinical evidence of progression until 24 months after her initial presentation. At 24 months, there was slight growth noted in the vaginal tumor, which was noted to be 5.2 × 4.6 cm. Given her positive hormonal receptor status and her continued medical comorbidities, she was started on letrozole monotherapy. Her tumor has remained stable for 6 months. She continues on this therapy with no adverse effects.

3. Discussion

We present a case of LMS of the anterior vaginal wall that was successfully managed conservatively for an extended period of time after partial resection.

Vaginal cancers are the least common gynecologic malignancy with estimated 4620 cases reported in 2016 (Siegel et al., 2016). Of those, sarcomas account for only 3.1% of vaginal neoplasms (Keller and Godoy, 2015). LMS are aggressive tumors that arise from the smooth muscle. They are typically characterized by prominent cellular atypia, abundant mitoses (≥ 10 per 10 high power fields) and areas of coagulative necrosis (Kumar et al., 2010). The average age at diagnosis is about 50 years, with a range extending from 21 to 86 years (Khosla et al., 2014). The presentation of primary vaginal LMS can vary, but the most common presentation is an asymptomatic vaginal mass (Khosla

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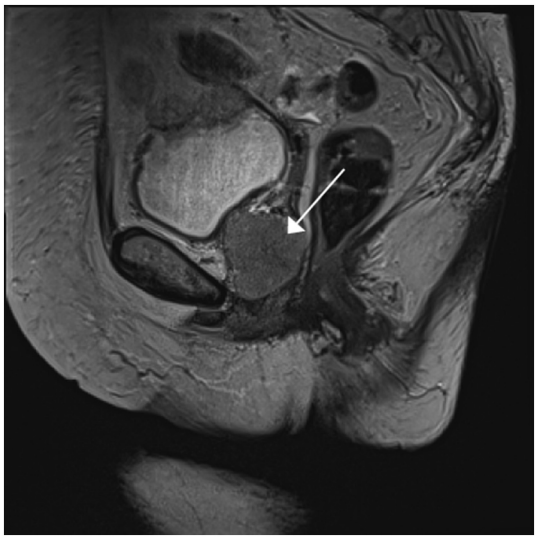

Fig. 1. Preoperative imaging showing sagittal view of a T2-weighted magnetic resonance image of the pelvis revealing vaginal mass.

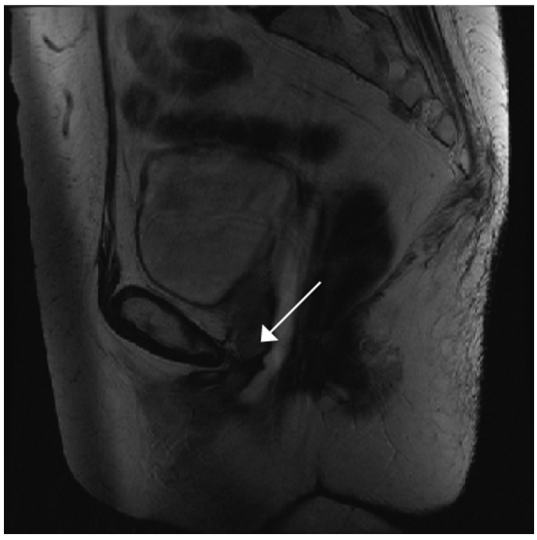

Fig. 3. Image showing sagittal view of a T2-weighted magnetic resonance image of the pelvis revealing residual vaginal mass after surgical resection.

et al., 2014). Other presentations include vaginal bleeding, vaginal discharge and discomfort (Keller and Godoy, 2015; Ciaravino et al., 2000; Curtin et al., 1995). Vaginal LMS tend to have a poor prognosis secondary to their hematogenous spread. There are limited data on the natural history of vaginal LMS, as most cases reported in the literature have been treated with adjuvant surgery, radiation, chemotherapy, or a combination of modalities (Khosla et al., 2014; Keller and Godoy, 2015; Ciaravino et al., 2000; Curtin et al., 1995; Morley et al., 1989; Suh and Park, 2008; Wang et al., 2015; Cooney et al., 2015).

LMS appear usually de novo with rare cases occurring as malignant transformation of a leiomyoma (Khosla et al., 2014; Cooney et al., 2015). Our patient had previously undergone a hysterectomy for fibroids years prior to her presentation of a vaginal mass. A biopsy obtained after initial resection of her LMS revealed only fibrovascular connective tissue. This suggests the potential for malignant transformation as the etiology of this patient's tumor. There has been one other case report describing the development of malignant transformation of a recurrent atypical leiomyoma, in which a patient was diagnosed with vaginal LMS occurring 22 months after the removal of a uterine smooth muscle tumor of uncertain malignant potential (STUMP) by robotically assisted total laparoscopic hysterectomy and bilateral salpingo-oophorectomy. The patient in this report underwent surgical resection of

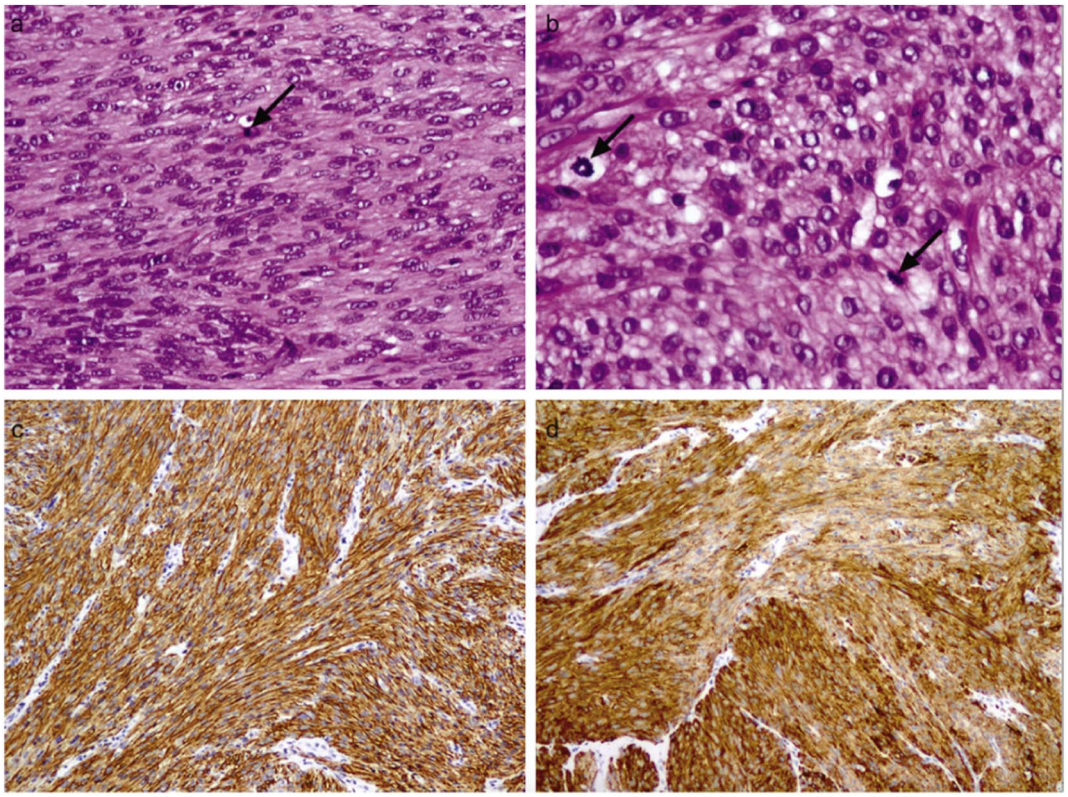

Fig. 2. Vaginal leiomyosarcoma. (A) Hypercellularity, spindle cells with marked cytologic atypia and mitosis (arrow). (B) Higher magnification demonstrating nuclear pleomorphism, irregular distribution of the chromatin and increased mitotic figures (arrows). (C) Tumor cells are positive for SMMS-1. (D) Tumor cells are positive for caldesmon.

the vaginal mass and then received 4 cycles of docetaxel and gemcitabine (Cooney et al., 2015).

Given the rarity of vaginal LMS, optimal management is controversial with wide variability in treatment options. The latter range from local surgical resection, pelvic exenteration, radiation therapy and chemotherapy or multimodality treatment with no clear consensus as presented in several case reports (Khosla et al., 2014; Keller and Godoy, 2015; Ciaravino et al., 2000; Curtin et al., 1995; Morley et al., 1989; Suh and Park, 2008; Wang et al., 2015; Cooney et al., 2015).

Ciaravino et al. performed the largest literature review to date which identified 66 cases of vaginal LMS of which 48 patients had follow up data. The 5-year survival rate for all stages was 43%. Surgical resection alone was associated with highest survival. Adjuvant radiotherapy and/or chemotherapy did not portend a survival benefit, although the analysis was underpowered to detect a difference (Ciaravino et al., 2000). Khosla et al. published an updated literature review noting that there were 77 cases of vaginal sarcoma (including LMS) in the English literature as of 2014. Again no consensus for adjuvant therapy was noted (Khosla et al., 2014). Although no level I evidence exists for vaginal LMS, there are data from a phase III randomized trial of stage I and II uterine sarcomas which demonstrated no survival benefit for adjuvant radiotherapy (Reed et al., 2008). The utilization of adjuvant chemotherapy is again extrapolated from data in uterine LMS with most studies utilizing gemcitabine with docetaxel (Hensley et al., 2009; Hensley et al., 2014). Given the rarity of vaginal LMS, it is reasonable to extrapolate data from uterine LMS to vaginal LMS and treat these disease sites similarly. Further, there was no difference in local recurrence for patients with LMS.

Hormonal therapy is a reasonable option for patients with ER/PR positive uterine LMS (Hensley et al., 2014; George et al., 2014). A phase 2 trial demonstrated letrozole to be an active agent in patients with unresectable uterine LMS with a 12-week PFS rate of 50% (George et al., 2014). Although there are limited data regarding the use of hormonal therapy in vaginal LMS, given the excellent side effect profile and benefit seen in uterine LMS it should be considerate a feasible strategy for patients with high surgical risk or in patients for whom the toxicities of treatment may outweigh the benefits. In this case, we waited until evidence of progression prior to initiating hormonal therapy given the long interval between her initial surgery and presentation to our institution, however it would have been reasonable to consider initiation of hormonal therapy earlier.

In conclusion, the optimal management of vaginal LMS is unknown. Published case reports tend to favor aggressive intervention with multimodality treatment although the natural history of this disease is unknown. We report on an unanticipated indolent behavior of vaginal LMS with initial observation followed by hormonal therapy. This conservative approach may be a viable option for select patients.

Informed consent

Informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the consent is available for review by the Editor-in-Chief of this journal upon request.

Conflicts of interest statement

The authors have no conflicts of interest to declare.

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