A rare case of follicular dendritic sarcoma of the vagina

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ABSTRACT

Follicular dendritic sarcoma of the vagina is an exceptionally rare malignancy. Here, we present a reproductive-aged female with no pertinent past medical history who initially presented with a protruding vaginal mass. Pathology from initial excision was consistent with follicular dendritic sarcoma of the vagina. This was ultimately treated with wide radical resection of the mass leading to iatrogenic vaginal stenosis.

1. Introduction

Vaginal cancer is uncommon and accounts for 1–2% of reproductive tract malignancies (Creasman, 2005). The most prevalent subtype, comprising 80% of total cases, is squamous cell carcinoma (Shah et al., 2009). Sarcomas of the vagina are exceptionally rare and make up 4% of all vaginal malignancies (Creasman, 2005). Dendritic follicular cell sarcoma (FDCS) is an intermediate-grade tumor typically found in lymph nodes within nodal germinal centers. In fewer than a third of cases, this tumor may arise extra-nodally (Chen and Gopal, 2017). Thirty-seven percent of cases present with only extranodal disease. The most common nodal involvement is seen in the neck and the most frequent site of extranodal disease is the liver. Half of patients have intraperitoneal disease at diagnosis which has been associated with a worse prognosis (Kaur et al., 2021).

Immunohistochemistry can help significantly in the identification of a spindle-cell neoplasm such as FDSC. At least one follicular dendritic cell marker needs to be positive for diagnosis which include CD21, CD 35, and CD 23. Additionally, vimentin positivity signifies a mesenchymal origin (Swerdlow et al., 2017). Molecular and cytogenic abnormalities in nFKB gene activation may play a role in the pathogenesis of FDCS. BRAF mutations are found in nearly a fifth of FDCS cases (Kaur et al., 2021).

FDSC tends to have an indolent course and is most likely to be diagnosed as an isolated lesion rather than metastatic disease. However, 40–50% of patients will experience local recurrence (Chen and Gopal, 2017). Poor prognostic factors include: tumor size of 6 cm or larger, intra-abdominal location, coagulative necrosis, 5 mitoses/10 high-power fields or more, and prominent nuclear atypia (Chen and Gopal, 2017).

2. Presentation

2.1. Initial presentation and management

A 38-year-old gravida 2 para 2–0–0–2 female with no significant past medical history initially presented to her gynecologist with a protruding vaginal mass. She was otherwise asymptomatic. The lesion was described as a 3–4 cm anterior vaginal mass 2 cm beyond hymenal ring that appeared cyst-like and described as fluid-filled on palpation initially thought to be a cyst. A transvaginal ultrasound (TVUS) revealed a 9.9 cm × 5.5 cm × 8.4 cm uterus with a simple left ovarian cystic mass measuring 8.5 cm × 8.0 cm × 6.3 cm and a 3.6 cm × 2.5 cm simple-appearing right sided ovarian cyst. No comment was made regarding a vaginal mass on the ultrasound report.

The patient underwent laparoscopic left salpingo-oophorectomy and vaginal wall mass excision by her gynecologist. The majority of the tumor was noted to be excised at that time with 1–2 cm left in situ. Pathology was consistent with ovarian cystadenoma and concern for possible follicular dendritic cell sarcoma of the vagina with positive deep and peripheral margins. Secondary review confirmed the diagnosis of follicular dendritic cell sarcoma.
2.2. Secondary assessment and management

The patient was referred for a second opinion to a gynecologic oncologist. At that time, her primary complaints were fatigue, nervousness, and night sweats. PET CT and MRI of the pelvis were performed to evaluate for metastatic disease and for preoperative planning. The PET CT showed no pathologic areas of hypermetabolic activity. MRI demonstrated a nabothian cyst as well as a 7.5 × 5.2 × 6.4 cm uterus with a 3.3 cm uterine fibroid. The vaginal vault and vaginal cuff appeared unremarkable without evidence of residual disease. Normal cystic follicles were identified on the right ovary.

2.3. Reoperation

She underwent radical partial vaginectomy, anterior repair, and cystoscopy. Intraoperative findings included a 3 × 5 cm mobile tumor of the anterior vagina extending from pubic symphysis to mid-vagina. A wide radical resection was performed of the anterior vaginal wall and included paravaginal tissue extending from 3 to 9 o’clock laterally from the posterior urethra extending proximally 2 cm from the cervix. She had an anterior repair due to the extent of the dissection which was logistically difficult due to the extent of the resection which was performed from a vaginal approach. She had a normal cystoscopy at the end of the procedure.

2.4. Pathology

Final pathology revealed residual FDSC 1.6–2.0 cm in greatest dimension with the epicenter in the subepithelial stroma of anterior vagina. Surgical margins were negative, but the lesion focally extended within 0.1 cm of the deep margin and 0.5 cm from the 12–6 o’clock and 6–12 o’clock margins. IHC showed lesional cells CD 21 diffusely positive in addition to CD 23 and CD35 positivity. Vimentin also stained diffusely positive. IHC controls EMA, D420, CD15, CD30, Cam 5.2, S100, desmin, CD34, p40, CK 5/6, sox 10 were negative. These controls helped to rule out a carcinoma, lymphoma, colorectal and pancreatic origin, neuro-ectoderm origin, leukemia, pulmonic origin, and breast origin. Slide descriptions included patchy nuclear atypia, giant cells, and benign lymphocytes. The tumor pattern was a combination of diffuse sheets of cells (Fig. 2) with areas of vague nodularity (Fig. 1). The tumor cells had indistinct cell borders with a subset of tumor cells demonstrating binucleation and multinucleation. Areas of tumor cells were infiltrated by populations of small, normal lymphocytes Fig. 3. The majority of the tumor demonstrated approximately 10–20% Ki-67 positivity, with focal areas demonstrating 30–40% Ki-67 positivity Fig. 4.

2.5. Complication

This patient developed vaginal stenosis postoperatively which was treated with nightly vaginal estrogen cream, pelvic PT, and vaginal dilation starting two months postoperatively. She has since obtained a regular vaginal width and has resumed intercourse.

3. Discussion

FDSC is a disease typically diagnosed in young adults, whereas vaginal cancer predominately impacts older women. In fact, half of the reported cases of vaginal cancer arise in women over 70 (Shah et al., 2009). FDSC of the vagina in a 78-year-old woman has been reported once in Cordova, Spain (Zaya et al., 2016). Our patient has a particularly unique presentation because a diagnosis of vaginal cancer at age 38 is already unusual, but is further exaggerated by the rarity of FDSC of the vagina.

Recurrence rates are reduced to less than 15% when a local tumor less than 5 cm is completely resected and thus radical local excision was chosen for her operative strategy. Because negative margins were achieved on secondary resection and the risk of distant metastasis is low, surveillance was recommended. The typical pattern of relapse is locoregional accounting for 50% of recurrences (Jain et al., 2017). The behavior of FDSC typically mirrors soft tissue sarcoma when found extranodally and is managed similarly(Kaur et al., 2021).

Pathologically, this is a rare tumor that must remain on the differential in order to properly diagnose. Morphologically, this tumor was very consistent with WHO classification. FDSC can form vague nodules,
diffuse sheets, storiform arrays, or whorls per WHO classification (Swerdlow et al., 2017). Regarding cell morphology, cells typically have indistinct borders and the nuclei are elongated or oval with finely dispersed chromatin and a distinct nucleoli. The mitotic rate of these tumors are usually 0–10 mitoses per 10 high-power field (HPF), however, pleomorphic tumors may have higher rates. To confirm the diagnosis, these tumors must be positive for one or more FDC markers CD 21, 35, and 23 (Swerdlow et al., 2017). The tumor in this case was positive for all FDC markers. Clusterin and vimentin are typically diffusely positive in these tumors as well, though not specific for FDSC (Chen and Gopal, 2017).

When diagnosing FDSC it is important to take into account possible comorbid conditions. One study showed that of 66 cases reviewed, 20% had underlying autoimmune disorders. FDCS is also associated with Castleman disease, a disease of abnormal lymph node growth, and nearly 14% had other malignancies diagnosed before or after their diagnosis of FDCS (Jain et al., 2017).

The evidence available regarding treatment approach are from retrospective and underpowered studies with widely varying stage at diagnosis and management strategy and including both nodal and extranodal cases (Soriano et al., 2007; Gounder et al., 2015). Due to the rarity of the condition, prospective data on management of FDCS is not

Fig. 2. 10x diffuse sheets of tumor with uninvolved epidermis.

Fig. 3. 100x Large tumor cells with indistinct borders and infiltrating small lymphocytes.
available. Treatment typically involves surgical resection and upfront gross total resection is associated with improved progressive free survival (PFS) and overall survival (OS). Consolidative radiotherapy has been shown to improve local control (Jain et al., 2017). A retrospective chart review from Memorial Sloan Kettering showed that neither adjuvant nor neoadjuvant chemo or radiation improved 5 yr overall survival, however due to the rarity of the tumor it is likely that the study is underpowered (Gounder et al., 2015). A retrospective analysis from MD Anderson indicated that the patients with the longest disease-free intervals underwent surgery, chemotherapy, and radiation, however, this represented 3/14 patients and overall survival was not compared (Soriano et al., 2007). For widespread disease, lymphoma-based treatment regimens are typically utilized and include cyclophosphamide, doxorubicin, vincristine, and prednisone (Jain et al., 2017). Further studies are needed to delineate an approach for management based on stage and nodal versus extranodal disease on presentation.

4. Conclusion

Here we present a unique case of a follicular dendritic cell sarcoma of the vagina in a young female. One must maintain a high index of suspicion regarding the diagnosis of dendritic follicular cell sarcoma as it is a rare tumor, especially when identified extra-nodally. Yet, this tumor is easily differentiated with immunohistochemistry after other possible diagnoses have been excluded. Increased awareness of this tumor may assist in the reduction of diagnostic errors.

Author contributions

JG conception, collected the data, coordinated case, manuscript writing, manuscript editing. NZ manuscript writing, manuscript editing. BW manuscript writing, manuscript editing. AM manuscript writing, manuscript editing. LB pathology review and manuscript editing. TT supervision and conception, manuscript writing, manuscript editing.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper. TT works with Intuitive in multiple capacities none of which are directly related to the content of this manuscript and none of which represent a conflict of interest.

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Fig. 4. 100x area of lower Ki-67 index (10–20%) adjacent to area of higher Ki-67 index (30–40%).