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CASE REPORT

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Management of a pure uterine corpus rhabdomyosarcoma in a postmenopausal patient: A rare case report and review of the literature

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Key Clinical Message

Rhabdomyosarcoma of the female genital tract often involves the vagina and cervix. It usually occurs in infants and children. Such tumors are uncommon in the uterus, especially in adults. Treatment options are based on studies of younger individuals.

Abstract

Rhabdomyosarcoma (RMS) is a malignant mesenchymal neoplasm with a tendency to differentiate into skeletal muscle cells. RMS is an aggressive tumor that tends to develop in children and younger patients. A vast majority of genital tract RMSs occur in the vagina and cervix. Such tumors rarely occur in adults. Usually, these tumors either occur as a component of a biphasic uterine tumor (carcinosarcoma or adenosarcoma) or can be a pure heterologous tumor. Pure uterine RMSs are extremely rare in adult patients and difficult to diagnose. Accurate diagnosis of these tumors depends on precise histopathological evaluation. The present report describes a rare case of embryonal RMS of the uterus in a postmenopausal female and explores the most recent literature. The aim is to strengthen the existing literature and aid clinicians in the management of similar cases. A 64-year-old postmenopausal female presented with a history of abdominal pain associated with abdominal distension, per vaginal bleeding, and foul-smelling discharge for 6 months. A transabdominal ultrasound revealed a bulky uterus with a well-circumscribed heterogeneous lesion. Histopathology confirmed the diagnosis of high-grade embryonal RMS within the corpus region of the uterus. A total abdominal hysterectomy with bilateral salpingo-oophorectomy was performed, followed by adjuvant chemotherapy to prevent relapse of the disease. Six months after oncological care has passed, the patient remains symptoms-free without evidence of recurrence or metastasis.

KEYWORDS

management, postmenopausal, primary, pure, rhabdomyosarcoma, uterine corpus

1 | INTRODUCTION

Uterine sarcomas are extremely uncommon tumors.[1] This group of rare sarcomas is estimated to account for around 3% of all uterine tumors and 1% of female genital tract malignancies.[2] Uterine sarcomas develop from endometrial connective tissue, or the myometrium. Generally, sarcomas are clinically aggressive and have a poor prognosis compared to other uterine malignancies.[1] Leiomyosarcoma is the most prevalent malignancy arising in the myometrium. According to the World Health Organization, there are four different categories of sarcoma types that may arise in the endometrial connective tissue. These include endometrial stromal nodules, low-grade endometrial stromal sarcoma, high-grade endometrial stromal sarcoma, and undifferentiated uterine sarcoma.[1]

Rhabdomyosarcoma (RMS) is an aggressive tumor that most commonly affects children and young adults.[2] The vast majority of genital tract RMS develops in the vagina of newborns and adolescents. RMS of the uterine corpus is a highly malignant neoplasm comprised of rhabdomyoblasts in varying stages of development and often containing striated muscle fibers. Previously, this pure heterotopic tumor of the uterine corpus was classified as a separate entity. However, currently it is considered a variant of the so-called mixed mesodermal tumors of the uterus.[3] Uterine corpus RMS can arise as part of a biphasic uterine tumor (adenosarcoma or carcinosarcoma) or as a separate heterologous tumor.[4] Adult patients with pure uterine RMS are uncommon and difficult to diagnose. A precise histological assessment of these malignancies is required for an accurate diagnosis.[5,6] The management of such tumors requires a multimodal approach. Firstly, the tumor must be histologically sampled in order to confirm a diagnosis of RMS, and this involves an incisional or core biopsy.[6,7] Primary surgical resection of the tumor, followed by adjuvant chemotherapy, is the main treatment approach for the pediatric population.[8] Survival in adults with RMS is significantly decreased when compared with the pediatric population.[8,9] This may be due to a lack of an evidence-based treatment protocol to guide clinicians, primarily due to the rarity of adult RMS within the literature. Because of the rarity of pure uterine RMS, the diverse histopathologic types, the numerous theories concerning the histogenesis of the tumor described in the literature, and the convincing morphological characteristics found in our first case, we found it is worth reporting our case study.[10] Herein, we present a case of uterine corpus RMS in a 64-year-old postmenopausal patient. The pertinent literature is discussed.

2 | CASE HISTORY/ EXAMINATION

A 64-year-old female, nulliparous, presented to our facility with a 6-month history of lower abdominal pain associated with abdominal distension, per-vaginal bleeding, and foul-smelling per-vaginal discharge. She had no fever, change in bowel habit, or pain during urination. She had no significant past medical or surgical history. Her obstetric and gynecological history revealed no previous pregnancies, and she was 10 years post-menopause. She had no history of alcohol intake and was a nonsmoker. Currently, she is not married and lives with her relatives. On examination, a mass occupying her suprapubic area was noted, which was firm, globular, and approximately 12 × 7 cm in size on palpation. On a speculum examination, the cervix looked healthy.

3 | METHODS

On investigation, a Pap smear was negative for any intraepithelial neoplasm or malignancy. Laboratory workup results highlighted a hemoglobin level of 10.1 g/dL. Other basic laboratory parameters, including blood glucose, liver enzymes, and renal function tests, were within normal limits. Similarly, electrolytes, ECG, ECHO, and chest x-rays were all normal. Abdominal ultrasound showed a bulky uterus with well-circumscribed heterogeneous lesions with areas of fluid and calcification measuring 15.4 × 9 cm in size within her uterus. The working diagnosis of fibroid was entertained. Due to her postmenopausal status, it was decided to perform a total abdominal hysterectomy with bilateral salpingo-oophorectomy and pelvic lymph node dissection. Intra-operative visualization of the abdomen revealed a large uterus measuring 24 × 40 cm in size with multiple fibroid-like cystic lesions. Other abdominal organs appeared healthy. The uterine specimen (Figure 1) was submitted for histopathology evaluation.

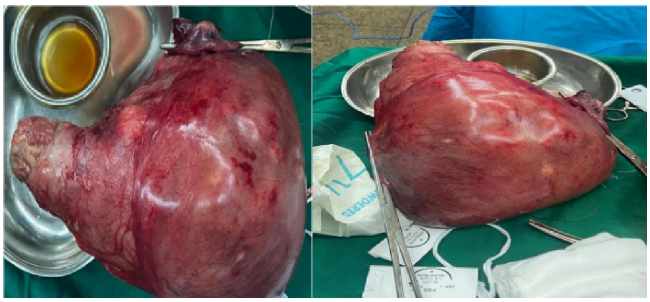

FIGURE 1 Uterine specimen with an unusual large size measuring 24 × 40 cm in size.

Her postoperative course was uneventful, and she was discharged 6 days after surgery.

Photomicroscopy revealed an infiltrative tumor consisting of a population of purely large primitive mesenchymal cells that show variable degrees of skeletal muscle differentiation. Areas of sheets of small, stellate, spindled, or round cells with scant or deeply eosinophilic cytoplasm and eccentric, small oval nuclei with a light chromatin pattern and inconspicuous nucleoli were noted. Occasionally, tumor cells that contained generous amounts of eosinophilic cytoplasm, a feature of rhabdomyoblastic differentiation (so-called strap cells), were appreciated (Figure 2). Neither epithelial nor other heterologous components were associated. The cervix, ovaries, and fallopian tubes were normal. Immunohistochemical testing demonstrated positive immunostaining with myogenin staining (Figure 3). The diagnosis of a high-grade pure RMS within the corpus of the uterus was considered. CT scans of the chest and abdomino-pelvis region excluded the presence of metastasis. A multi-disciplinary tumor board discussion recommended adjuvant chemotherapy to reduce the risk of recurrence.

4 | CONCLUSION AND RESULTS

To date, at least 6 months after oncological care has passed, the patient remains stable, symptoms-free, and without evidence of recurrence or metastasis.

5 | DISCUSSION

The present study describes a rare case of uterine RMS in a postmenopausal female. Given the rarity of the condition worldwide, and particularly in our setting in northern Tanzania, our initial clinical impression was uterine leiomyoma. However, following surgical intervention, we were able to definitively confirm the diagnosis of RMS on histopathology and thus, pursue adjuvant chemotherapy. In this report, we discuss the rarity of this particular condition, the literature surrounding similar reports, and the many challenges that arise in the management of adult RMS.

Given this patient's age and postmenopausal status, RMS is an incredibly uncommon tumor subtype. While RMS is the most common soft tissue sarcoma diagnosed in children, it occurs far less frequently in the elderly adult population. In fact, soft tissue sarcomas as a whole represent only 1% of adult malignancies, with only 2%–5% of this sub-population having a diagnosis of RMS.[11,12] The incidence of soft-tissue sarcomas in Tanzania is not well documented.[13] The most common sites for primary RMS tumors include the head, neck, extremities, and urogenital tract.[14] In children, around 35% of RMS occurs in the head and neck region, and around 25% occurs within the genitourinary tract, with the most frequent sites being the bladder, prostate, or vagina.[15] This data is less robust for the adult population, but RMS seems to preferentially occur in the trunk and extremities, with less than 20% of RMS cases occurring within the genitourinary organs.[15,16] Available literature from the United States suggests that within the genitourinary tract, adult RMS most commonly occurs within the cervix (53%), followed by the uterus (20%), vulva (13%), fallopian tube (7%), and ovaries (7%).[17]

While it is relatively common to diagnose uterine RMS as a heterologous part of a malignant mixed mullerian tumor (MMMT), a pure uterine RMS is far less frequently documented within the literature.[1,18] Therefore, an important factor in the diagnosis of a pure uterine

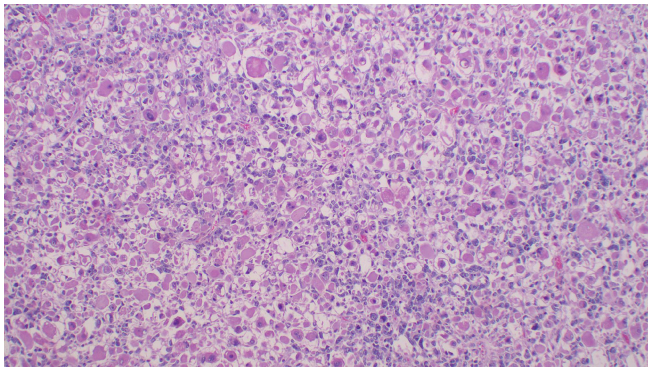

FIGURE 2 Histopathology of the uterine corpus rhabdomyosarcoma composed of large round or oval eosinophilic cells characteristic of rhabdomyoblasts. The cytoplasm of these cells contain granular material or deeply eosinophilic masses of stringy or fibrillary material concentrically arranged near or around the nucleus, H&E staining 200× original magnification.

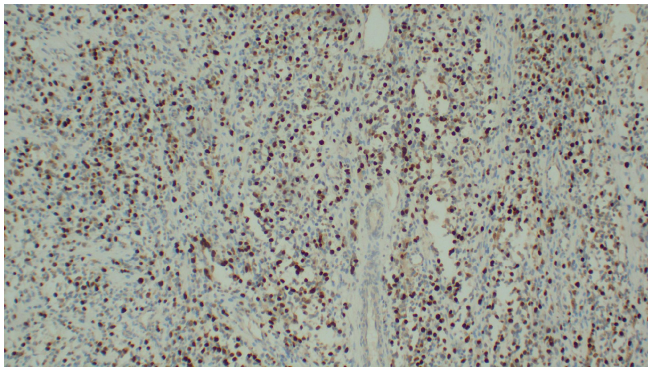

FIGURE 3 Immunohistochemistry staining of the tumor cells by myogenin antibody, the tumor cells demonstrate diffuse and strong intranuclear staining, IHC staining 100× original magnification.

RMS is the exclusion of a MMMT. This is achieved through extensive histological sampling of the tumor. This was particularly relevant in this case, as the tumor was relatively large. Pure RMS can be further classified based upon histological subtypes, and these subtypes often inform prognosis. The botryoid, spindle cell, well-differentiated, and embryonal subtypes are often associated with more favorable outcomes compared with pleomorphic and alveolar subtypes, often classed as unfavorable subtypes. As it was evidenced in the index case, within adult RMS of gynecological origin, the most common histological subtype was the embryonal subtype (73%), followed by the pleomorphic (13%) and alveolar (13%) subtypes.

Given the rarity of adult RMS, clear guidelines for management are lacking. A literature review by Li et al.[8] found only 28 cases of adult pleomorphic RMS within the English language literature between 1982 and 2020, focusing on treatment. They found that patients who received adjuvant chemotherapy experienced superior outcomes, including overall survival, compared with those who underwent surgery alone. These findings align with literature from a pediatric population as well, which suggests that patients with nonmetastatic RMS are best managed with local surgical resection in combination with adjuvant chemotherapy.[6] When examined individually, there are conflicting reports about the role of adjuvant chemotherapy in adult RMS. A study by Hawkins et al.[19] concluded that there was no survival benefit with adjuvant chemotherapy in adults with RMS, while Spreafico et al.[2] reported that adjuvant therapy improved outcomes among a sub-population with sufficient compliance to the full course of treatment.

Nevertheless, adults with RMS continue to have a poorer prognosis than the pediatric population, regardless of treatment. This may be attributed to various adverse factors, such as more aggressive histological subtypes and unfavorable anatomical sites of the primary tumor.[7,8] A delay in presentation to medical attention among adults may also result in more advanced staging of RMS and, subsequently, increased mortality. The success of the pediatric RMS treatment regime has been achieved through decades of international and multi-center clinical trials. The paucity of large multi-center trials of the management of adult RMS is extremely limited due to its rare incidence, making it difficult for clinicians to take an evidence-based approach to the management of adult RMS.[1]

Fortunately, we elected for surgical intervention in this patient given her very symptomatic presentation, her postmenopausal status, and the possibility of malignancy, despite our initial suspicion of uterine fibroids. As a result, we were able to diagnose this rare case of RMS via surgical pathology and, thus, determine the most appropriate treatment approach to optimize survival. Based on the available literature and extensive patient counseling, we elected to pursue adjuvant chemotherapy to extend survival and reduce recurrence risk. Fortunately, our particular medical center has both the medical and surgical infrastructure to comprehensively manage this patient with both surgery and chemotherapy, so our management did not vary from international standards despite being located in rural Tanzania. It should be noted that not all facilities in our setting have such capabilities, so diagnostic and treatment delays may contribute to worse outcomes.

To date, the number of uterine RMS cases reported in the English literature has been very small, and there has been no large series documented to the best of our knowledge. Therefore, it is critical to establish a genuine preoperative diagnosis, either by cytology or biopsy. The potential caveat for our case is the lack of essential information such as preoperative diagnostic tests, including MRI and cytopathology of the PV discharge, as well as access to molecular testing such as mutational analysis that are essential in identifying potential markers that may assist in diagnostic or therapeutic decisions in these tumors.[20] This is partly because of the limited availability of resources in our setting. Moreover, our report lacks photographs of the uterine specimen, highlighting the tumor macroscopically. The discrepancy between the preoperative clinical diagnosis and postoperative diagnosis observed in the index case implies that preoperative screening and the diagnosis were inadequate, which may have led to the patient's suboptimal treatment in some cases.

6 | CONCLUSION

This report describes a rare case of an embryonal RMS of the uterus in a postmenopausal patient. With our discussion of the most up-to-date literature, we hope this report will inform clinicians who may encounter similar cases in the near future. Numerous factors, including this patient's advanced age, location, and histological tumor type of RMS, make this a unique and difficult case for clinicians in terms of treatment. Pediatric RMS has a well-documented regime with expansive evidence reported within the literature showing the success of surgical resection of the primary tumor followed by adjuvant chemotherapy. The paucity of literature on uterine RMS in adults demonstrates

the importance of sharing similar cases in order to guide clinicians to achieve the best outcomes for patients.

AUTHOR CONTRIBUTIONS

John Lugata: Conceptualization; data curation; methodology; writing – original draft. **Caleigh Smith:** Conceptualization; data curation; writing – review and editing. **Onesmo Mrosso:** Data curation; methodology; writing – review and editing. **Doris Rwenyagila:** Data curation; methodology; writing – review and editing. **Baraka Shao:** Data curation; methodology; writing – review and editing. **Alex Mremi:** Conceptualization; investigation; methodology; supervision; writing – review and editing.

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All authors have declared that no competing interests exist.

DATA AVAILABILITY STATEMENT

There is no data generated from this study.

ETHICS STATEMENT

The patient provided written informed consent to allow for her de-identified medical information to be used in this publication. A waiver for ethical approval was obtained from the authors' institution review board committee.

CONSENT

Written informed consent for the publication of clinical details and images was obtained from the patient. A copy of the consent is available for review by the chief editor of this journal.

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