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Ewing Sarcoma of the Uterine Cervix: A Case Report and Literature Review

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ABSTRACT

Ewing sarcoma is a highly aggressive malignant small round-cell tumor that typically arises in bone and is rare in the female genital tract. Primary involvement of the uterine cervix is exceptionally uncommon, with fewer than 30 cases reported in the literature. We report the case of a 37-year-old woman who presented with heavy menstrual bleeding and was found to have a large cervical mass. She underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy, and histopathological examination with immunohistochemistry supported a diagnosis of extraosseous Ewing sarcoma of the cervix. Initial staging demonstrated no distant metastasis, and she received prolonged multimodal therapy. Despite complete surgical resection and systemic chemotherapy, the patient developed early locoregional recurrence followed by distant hepatic metastases. This case highlights the aggressive clinical behavior of cervical Ewing sarcoma and underscores the diagnostic and therapeutic challenges associated with this rare malignancy.

Highlights:

1. Primary Ewing sarcoma of the uterine cervix is an exceptionally rare malignancy.
2. Large tumor size may predict aggressive behavior despite multimodal therapy.
3. Immunohistochemistry plays a critical role in diagnosing cervical round-cell tumors.
4. Early recurrence and distant metastasis can occur even after complete surgical resection.
5. Multidisciplinary management remains essential in the absence of standardized guidelines.

Introduction

Ewing sarcoma (ES) is a highly aggressive malignant small round-cell tumor that typically arises in bone and affects children and young adults. It belongs to the Ewing sarcoma family of tumors (ESFT), which also includes primitive neuroectodermal tumor (PNET), and is defined by chromosomal translocations, most commonly t(11;22) (q24;q12), resulting in the EWSR1–FLI1 fusion oncogene [1]. Osseous sites such as the long bones, pelvis, and chest wall are most frequently involved, whereas extraosseous presentations are uncommon. Primary involvement of the female genital tract is exceptionally rare, with the uterine cervix representing one of the least frequent sites [2]. To the best of our knowledge, fewer than 30 cases of primary cervical Ewing sarcoma have been documented in the literature [2].

Clinical presentation is variable but most often includes abnormal vaginal bleeding, pelvic pain, or detection of a cervical mass [3]. Diagnostic challenges arise because the clinical and histopathological features can overlap with other small round-cell malignancies of the cervix, such as small cell carcinoma and endometrial stromal sarcoma [3,4]. Owing to the rarity of the disease, there is a lack of standardized treatment guidelines. Management is generally extrapolated from protocols for osseous and extraosseous Ewing sarcoma, which typically involves multimodal therapy with surgery, systemic chemotherapy, and radiotherapy. Prognosis, however, remains variable [5].

Given its rarity and diagnostic complexity, reporting additional cases is

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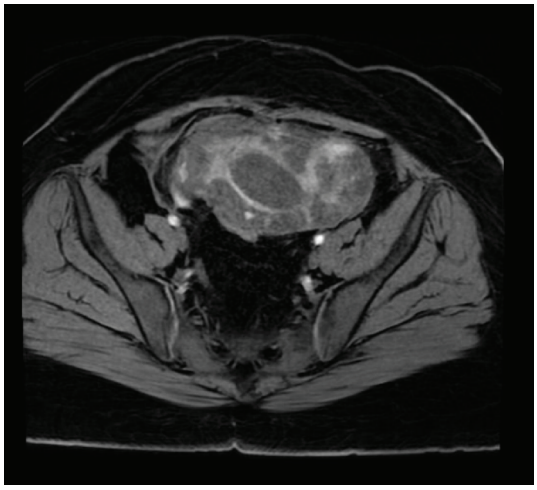

Figure 1: Axial pelvic magnetic resonance image demonstrating a large heterogeneous anterior pelvic mass, predominantly left-sided. It abuts the sigmoid colon without evidence of invasion and exerts mass effect on the urinary bladder with preservation of intervening fat planes.

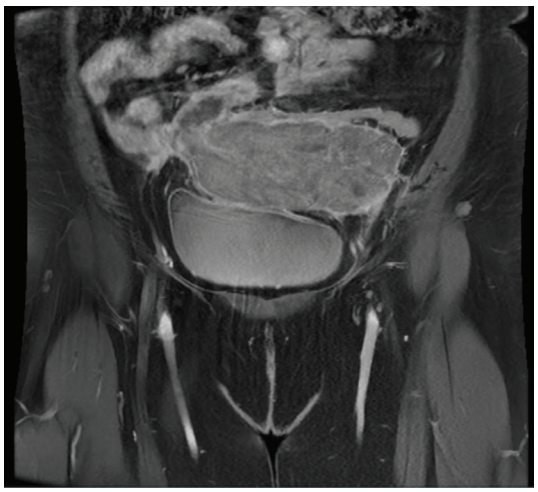

Figure 2: Coronal pelvic magnetic resonance image showing the same heterogeneous pelvic mass measuring approximately 12.4 × 6.8 × 6.1 cm (craniocaudal × transverse × anteroposterior dimensions). The lesion demonstrates heterogeneous enhancement and causes anterior displacement of the urinary bladder without direct infiltration. No pelvic lymphadenopathy or ascites is identified.

essential to enhance clinical understanding and to inform management strategies for this unusual tumor. This case highlights the aggressive clinical course of cervical Ewing sarcoma, characterized by early recurrence and rapid systemic dissemination despite complete surgical resection and prolonged multimodal therapy.

Case Presentation

A 37-year-old multiparous woman with a known history of type 2 diabetes mellitus presented in early 2023 with complaints of heavy menstrual bleeding (HMB). Evaluation revealed a cervical mass. On September 29, 2023, she underwent total abdominal hysterectomy with bilateral salpingo-oophorectomy (TAH+BSO) at a tertiary care center. Histopathological examination of the resected specimen showed a malignant round cell tumor involving all four quadrants of the cervix, measuring 7.0 × 6.5 × 3.5 cm. Immunohistochemistry (IHC) was positive for CD99, FLI-1, cyclin D1, and NKX2.2, with a high Ki-67 index, consistent with extraosseous Ewing sarcoma of the cervix. Surgical margins were negative, and no lympho-vascular or perineural invasion was identified.

Initial staging with CT chest and whole-body PET-CT (October 2023) revealed no evidence of distant metastasis. The patient was started on systemic chemotherapy with the VAC/IE regimen (vincristine, doxorubicin, cyclophosphamide alternating with ifosfamide and etoposide), completing 17 cycles by February 2025.

In March 2025, she developed pelvic discomfort. MRI of the pelvis demonstrated a multiloculated lesion in the left hemi-pelvis with multiple cystic areas and a suspicious soft tissue mass involving the sigmoid colon. CT imaging confirmed a hypodense enhancing lesion in the adnexal region, suggestive of recurrence. A CT-guided pelvic biopsy confirmed recurrent Ewing sarcoma. IHC remained positive for CD99, FLI-1, and cyclin D1, with a persistently high Ki-67 index.

She was restarted on systemic chemotherapy with gemcitabine and docetaxel in April 2025. Owing to persistent disease and mass effect, she underwent surgical exploration on July 7, 2025. Intraoperatively, a 12 × 10 cm pelvic mass was found, adherent to the bladder, left pelvic sidewall, and multiple small bowel loops. A partial cystectomy (approximately 40% of the bladder) and Hartmann's procedure were performed, along with bilateral ureteric preimplantation. Frozen section analysis of bladder margins was negative for tumor. Estimated blood loss was 1500 mL, requiring transfusion support.

By September 2025, restaging CT performed for radiation planning demonstrated multiple hepatic lesions. Ultrasound-guided biopsy of one of the lesions confirmed metastatic Ewing sarcoma.

Discussion

Ewing sarcoma (ES) is the second most frequent bone malignancy in children and young adults, accounting for around 2% of pediatric cancers. Peak incidence is at 15 years of age [6]. It has a predilection for the proximal long bones, pelvis, and ribs [2]. Disease manifesting outside the bone is described as extra osseous Ewing sarcoma (EES), which occurs in about 20% of the cases and most commonly involves the retro peritoneum, kidney, pancreas, esophagus, ileum, thyroid, breast, bladder, vagina, and spinal cord [2,6]. While the pathogenesis of EES is unclear, neural crest cell migration to the peripheral soft tissues during embryogenesis could potentially explain it [7].

Uterine cervical ES is exceptionally rare [3]. Overall, cervical sarcomas constitute less than 1% of cervical malignancies [8], and ES accounts for approximately 0.08% of tumors of the female genital tract [3]. In majority cases, cervical ES has been reported in younger women under 45 years of age [3]. Symptoms more commonly include irregular vaginal bleeding, lower abdominal pain, and malodorous vaginal discharge [2–4] and less commonly, increased uterine size, prolapsing pelvic mass, vaginal stenosis, painful micturition, and increased urinary frequency [3,9]. Tumors usually measure 3-10 cm [2,3]. Interestingly, cervical ES may mimic more common cervical malignancies such as small-cell carcinoma (SCC), leading to misdiagnosis [3,5,10]. However, SCC most frequently presents in older women and tends to be smaller in size compared to cervical ES [5].

On histological examination, ES appears as small round cells with hyperchromatic nuclei, arranged in sheets or aggregates, sometimes with spindle or epithelioid variants that complicate diagnosis [3,4]. Concurrently, immunohistochemistry aids in diagnosis: CD99 is highly sensitive, while FLI-1 has better specificity [5]. Thus, molecular techniques such as fluorescence in situ hybridization (FISH) and reverse transcription-polymerase chain reaction (RT-PCR) remain the gold standard, with combined use offering the highest diagnostic accuracy [11]. The most common type of fusion gene is the EWSR1-FLI1, which accounts for 85-90% of the cases; less common fusion genes include EWSR1-ERG, EWSR1-ETV1, EWSR1-E1AF, and EWSR1-FEV [6]. Simultaneously, imaging such as ultrasound (US), computed tomography (CT), magnetic resonance imaging (MRI) can be used; one article commented that these tumors exhibit strong fludeoxyglucose uptake, which is why positron emission tomography (PET) scan can be a viable option [10]. A combination of these diagnostics is vital for differentiating cervical ES from SCC who have similar morphology and immunoreactivity for neuroendocrine markers (e.g., chromogranin, synaptophysin) [3].

In terms of management, cervical ES is similar to osseous ES, with multimodal therapy combining surgery, chemotherapy, and radiotherapy [12]. A study reviewing 28 cases showed that the majority underwent radical hysterectomy with bilateral salpingo-oophorectomy and lymphadenectomy, followed by chemotherapy in 86% of cases [2]. The most frequently used regimens include VAC (vincristine, doxorubicin, cyclophosphamide) and alternating VAC/IE (ifosfamide, etoposide), consistent with bone ES protocols [13,14]. Tumor size and metastasis at diagnosis are key prognostic factors: in the same review of 28 patients, every fatality within 6 months was associated with a tumor size of greater than 7 cm or systemic disease [2]. Another article reported a patient who had metastatic cervical and thoracic spinal disease and despite decompression and excision, the patient died within 3 months [15]. The clinical course observed in our patient mirrors these previously reported poor prognostic features, including large tumor size and early recurrence, reinforcing the aggressive biological behavior of cervical Ewing sarcoma.

Despite aggressive treatment, there is no set prognosis; some patients have survived over 3 years when tumors were <5 cm and detected early, but many others have experienced rapid recurrence or metastasis within months [3]. This variability highlights the absence of standardized guidelines and the urgent need for multidisciplinary management. Experimental therapies targeting EWS-FLI1–mediated transcriptional pathways, such as LSD1 inhibitors and RNA helicase A disruptors, are under investigation, but their role in cervical ES remains undefined [6].

Conclusion:

Primary Ewing sarcoma of the uterine cervix is an exceptionally rare and aggressive malignancy. This case demonstrates that early recurrence and rapid systemic dissemination may occur despite complete surgical resection and prolonged multimodal therapy. Awareness of this entity, careful histopathological evaluation with immunohistochemistry, and close multidisciplinary follow-up are essential to optimize outcomes in affected patients.

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Author Contributions

- **Muhammad Ahmed Zaman:** Data collection, drafting of discussion.
- **Shaikh Saif Ur Rehman**: Literature review, manuscript drafting.
- **Asma Ali Depar:** Case management, preparation of figures.
- **Iqra Muhammad Aslam**: Data collection, literature review
- **Rozilla Sadia Khan**: Supervision, critical revision.

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