Case report

Primary uterine osteosarcoma arising in a leiomyoma with rapid local recurrence: A case report

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ABSTRACT

Background: Extraskeletal osteosarcoma is an extremely rare malignant neoplasm. Literature regarding primary osteosarcoma of the uterus is confined to only a small number of case reports.

Case: A 57-year-old female with a history of uterine fibroids presented to the emergency department with abdominal pain. Imaging was notable for an enlarged uterus with a 15 cm calcified fibroid extending along the posterior uterus. The patient underwent a laparotomy for total hysterectomy and bilateral salpingo-oophorectomy. Pathological evaluation of the specimen yielded mesenchymal proliferation with osteoid formation and tumor cells with densely eosinophilic cytoplasm resembling osteoblasts with a final diagnosis of primary uterine osteosarcoma. Multidisciplinary tumor board recommended against adjuvant treatment, given the lack of evidence for improved outcomes for early-stage uterine sarcomas. The patient was followed up with surveillance visits every three months, entailing physical examination and computed tomography (CT) scans. Unfortunately, she had locoregional oligometastatic recurrence of her disease at 1-year follow up.

Conclusion: Primary uterine osteosarcoma is an extremely rare and aggressive neoplasm with limited understanding regarding optimal treatment options.

1. Introduction

Extraskeletal osteosarcoma (ESOS) is a malignant mesenchymal neoplasm that produces osteoid, bone, or chondroid material without demonstrable attachments to bone or periosteum (Choi et al., 2014). This rare tumor can be diagnosed in the trunk, thigh, upper extremities, and retroperitoneum. ESOS represents approximately 2% to 5% of osteosarcomas and less than 1% of all soft-tissue sarcomas (Allan and Solle, 1971). Uterine sarcomas are uncommon, accounting for 1–2% of all uterine neoplasms. Pure heterologous osteosarcomas are a rare type of uterine sarcoma with documentation of disease limited to less than 20 case reports (Lin et al., 2002).

In the published literature composed of small number of case reports, the mean age of diagnosis of primary uterine osteosarcoma was 64 years of age (range 41 to 82) (Hardisson et al., 2001). Table 1 depicts a summary of prior published case reports. The main presenting symptoms included abnormal vaginal bleeding; abdominal pain/fullness caused by a large abdominal mass (Tsuchioka et al., 2016). Prognosis was noted to be poor for patients diagnosed with ESOS with five-year survival rate reported as low as 28%. There is a high risk for recurrence and a dismal survival rate (Jensen et al., 1998; May; Nystrom et al., 2013). There is limited data regarding adjuvant therapy after surgical management. In this case report, we present a 57-year-old female who presented with primary uterine osteosarcoma arising in a leiomyoma with rapid locoregional recurrence 1 year after initial diagnosis.

2. Case

A 57-year-old female with a history of uterine fibroids presented to the emergency department with abdominal pain. Her past medical history was unremarkable. The patient reported intense infraumbilical abdominal pain, abdominal distention, urinary frequency, and incomplete bladder emptying. Her physical exam was notable for large uterus measuring approximately 18 weeks with fullness palpated in the posterior cul-de-sac. Upon admission, she was found to have acute kidney injury with creatinine of 2.04 mg/dL (normal value 0.7 to 1.3 mg/dL). Other laboratory findings including serum electrolytes and hepatic functions were within normal limits. CT of the abdomen and pelvis noted a 15 cm heterogeneous pelvic mass with peripheral coarse...
calciﬁcation, inseparable from the posterior uterine wall and bilateral mild hydroureteronephrosis secondary to mass effect on the distal ureters. A pelvic magnetic resonance imaging (MRI) was notable for an enlarged uterus measuring approximately 19 × 12 × 14 cm with a complex proteinaceous and calcified lesion measuring 15 × 10 × 12 cm extending between the posterior uterine fundus to the lower uterine segment (Fig. 1). No malignant cells were seen on cervical cytology obtained during hospitalization. An attempt was made to perform an endometrial biopsy, however given the position of the cervix, this was not feasible and safe. After discussing the alternatives, the patient agreed to proceed with a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Intraoperative ﬁndings included an enlarged ﬁbroid uterus measuring approximately 24 weeks with a large calcified mass measuring 10 × 10 cm, adherent to posterior uterine wall and anterior to the rectosigmoid colon. The remainder of the abdominal survey did not yield any signiﬁcant ﬁndings suggestive of malignancy.

Final pathological evaluation of the hysterectomy specimen yielded a weight of 701 g and intermediate-grade primary uterine osteosarcoma, measuring 7 × 4 cm arising in a leiomyoma with degenerative changes. The specimen was noted to have dusty red brown, edematous tissue. Microscopically, low magniﬁcation showed mesenchymal proliferation with osteoid formation, with tumor cells having densely eosinophilic cytoplasm resembling osteoblasts. There was signiﬁcant cytological atypia and the associated leiomyoma consisted of proliferated smooth muscle cells without cytological atypia. There was a moderately pleomorphic sarcomatous component, forming thin trabeculae of bone extending between the posterior uterine fundus to the lower uterine segment (Fig. 1). No malignant cells were seen on cervical cytology, however given the position of the cervix, this was not feasible and safe. After discussing the alternatives, the patient agreed to proceed with a total abdominal hysterectomy and bilateral salpingo-oophorectomy. Intraoperative ﬁndings included an enlarged ﬁbroid uterus measuring approximately 24 weeks with a large calcified mass measuring 10 × 10 cm, adherent to posterior uterine wall and anterior to the rectosigmoid colon. The remainder of the abdominal survey did not yield any signiﬁcant ﬁndings suggestive of malignancy. An intraoperative frozen specimen pathological evaluation revealed acute inﬂammation. The patient had an uncomplicated post-operative course and was discharged home on postoperative day 3. Her acute kidney injury was resolved after the surgery, once the compression on the distal ureters was relieved with removal of the hysterectomy specimen.

Table 1
Previous primary uterine osteosarcoma cases.

| Author          | Year | Patient age | Presenting symptoms | Surgery                     | Radiation | Chemotherapy | Recurrence or Metastasis | Outcome          |
|-----------------|------|-------------|----------------------|----------------------------|-----------|--------------|--------------------------|-----------------|
| Sier and Lyman et al. | 1936 | 53          | Abdominal Pain       | Hysterectomy + BSO         | –         | –            | None                     | Deceased after 2 months |
| Shefery et al.   | 1956 | 67          | Vaginal Bleeding     | TAH + BSO                  | –         | –            | N/A                      | N/A              |
| Carleton et al.  | 1961 | 82          | N/A                  | TAH + BSO                  | –         | –            | Lung metastasis           | Decreased after 8 months |
| Karpas et al.    | 1964 | 62          | Vaginal bleeding     | TAH + BSO                  | –         | –            | N/A                      | N/A              |
| Piscioli et al.  | 1985 | 56          | Vaginal bleeding     | TAH + BSO                  | +         | –            | Lung metastasis           | Decreased         |
| Crum et al.      | 1990 | 41          | Vaginal bleeding     | TAH + BSO                  | +         | Doxorubicin/ CPA/ Dacarbazine | None                      | Deceased after 4 months |
| De Young et al.  | 1992 | 63          | Vaginal bleeding     | TAH + BSO                  | –         | –            | None                     | Deceased after 20 days   |
| Emoto et al.     | 1994 | 67          | Abdominal Pain       | TAH + BSO                  | –         | –            | Local recurrence          | Deceased after 4 months |
| Hardisson et al. | 2001 | 41          | Vaginal bleeding     | TAH + BSO                  | –         | Adriamycin/ ifosamide    | Local recurrence          | Alive after 8 months |
| Kostopoulou et al. | 2002 | 56          | Abdominal Pain       | TAH + BSO, colon resection | –         | CDDP/ epirubicin | Local recurrence          | Deceased after 6 months |
| Wang et al.      | 2011 | 53          | Vaginal bleeding     | RH + OMT                   | –         | CDDP/ epirubicin | None                     | No evidence of disease after 5 months |
| Kefeli et al.    | 2012 | 53          | Vaginal bleeding     | TAH + BSO                  | –         | –            | N/A                      | N/A              |
| Powell et al.    | 2014 | 60          | Vaginal bleeding     | TAH + BSO                  | –         | –            | Lung metastasis           | Decreased after 7 months |
| Abraham et al.   | 2014 | 47          | Vaginal bleeding     | TAH + BSO                  | –         | Doxorubicin/ ifosamide   | Heart and lung metastasis | Deceased after 6 months |
| Kitawaki et al.  | 2016 | 57          | Abdominal Pain       | TAH + BSO                  | –         | Doxetaxel/ gemcitabine  | Lung metastasis and local recurrence | Alive after 13 months |
| Current Case     | 2021 | 57          | Abdominal Pain       | TAH + BSO                  | –         | Doxorubicin/ ifosamide   | Local recurrence          | Alive after 15 months |

TAH, Total abdominal hysterectomy; RH, radical hysterectomy; BSO, Bilateral salpingo-oophorectomy; OMT, omentectomy; CPA, cyclophosphamide; CDDP, cisplatin.

3. Discussion

Extraskeletal osteosarcoma, also known as soft tissue osteosarcoma, is a rare malignant neoplasm that produces osteoid, bone, or chondroid material but lacks bone or periosteum involvement. It is an extremely aggressive tumor with a poor prognosis. The exact etiology of ESOS is still unknown but several associated prognostic factors have been proposed, such as the history of trauma, local radiation therapy, and changes in soft tissue lesions and malignant ﬁbrous tissue disease (Liao...
This case report presents a patient with initially confined uterine osteosarcoma and rapid recurrence of disease one year after diagnosis. In this particular case, histological evaluation yielded an absence of an epithelial component, no evidence of osteosarcoma origin in bone, and had presence of neoplastic osteoid. Immunohistochemical staining for smooth muscle cell markers was negative, indicating the absence of leiomyosarcoma components. Given all of these elements, the neoplasm reported fulfills the diagnosis of primary uterine osteosarcoma. As our patient’s osteosarcoma was uterine-confined after primary surgical resection, management was extrapolated from studies of leiomyosarcoma where observation is the standard of care (Byar et al., 2022). A systemic review addressing the effect of adjuvant chemotherapy or radiation on localized ESOS also found no difference in 5-year disease free survival rate between surgery and adjuvant chemotherapy versus surgery alone groups (Tsukamoto et al., 2022). After the patient’s locoregional recurrence was managed surgically, she was initiated on

Fig. 1. Findings of magnetic resonance imaging. A complex proteinaceous and calcified lesion is visible.

Fig. 2. A-D. Histological Features of the Uterine Osteosarcoma. Low magnification shows mesenchymal proliferation with osteoid formation (A, HE, 20 x). The tumor cells have densely eosinophilic cytoplasm resembling osteoblasts (B, HE, 100 x) and show significant cytological atypia (C, HE, 200x). The associated leiomyoma consists of proliferation of smooth muscle cells without cytological atypia (D, HE, 100x).
systemic chemotherapy. There is no clear consensus about the optimal chemotherapy regimen for patients with ESOS. For advanced or metastatic leiomyosarcoma cases, the use of gemcitabine plus docetaxel, doxorubicin (with or without ifosfamide), single-agent gemcitabine, ifosfamide, trabectedin, pazopanib, and dacarbazine are recommended (NCCN, 2020). The standard of care for high grade bone sarcomas includes a multi-agent regimen with a combination of doxorubicin, cisplatin +/- methotrexate or ifosfamide (Ferrari et al., 2018). There are some case reports suggesting the use of gemcitabine-docetaxol as a potential regimen for long term progression free survival (Strippoli et al., 2015). For our current case report, treatment options were deduced from previous studies of bone and soft tissue sarcomas. The patient is currently on her second cycle of chemotherapy and tolerating treatment well.

In summary, we present a 57-year-old female with a rare diagnosis of primary uterine osteosarcoma. Most notably in this case was the rapid and aggressive locoregional recurrence, approximately 1 year after initial diagnosis. This case adds to the growing but still sparse literature surrounding this rare tumor. There are limited data regarding systemic treatment options. Therefore, until more effective systemic treatment options are developed, surgical resection remains the primary treatment in the up-front and recurrence settings.

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

CRediT authorship contribution statement

Merima Ruhotina: Conceptualization, Writing – original draft. Joanna Kukla: Investigation, Writing – original draft. Annemieke Wilcox: Investigation, Writing – review & editing. Colleen Murphy: Investigation. Gulden Menderes: Conceptualization, Writing – review & editing, Supervision.

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.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.gore.2022.101102.

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Fig. 3. Operative specimen of recurrent mass. Specimen included 15 cm mass in the right pericolic gutter involving the ascending colon from cecum to the hepatic flexure. Mass is encircled.
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M. Ruhotina et al.