

Undifferentiated endometrial sarcoma of the cervix: a case report

P.-S. Huang^{1,6,7}, C.-T. Yue², W.-Y. Kao³, J.-M. Hwang⁴, H.-W. Kuo⁵, S.-C. Huang¹

¹Department of Obstetrics and Gynecology, ²Department of Pathology, ³Department of Hematology and Oncology,

⁴Department of Radiation Oncology, ⁵Department of Diagnostic Radiology, Taipei Tzu Chi Hospital, Buddhist Tzu Chi Medical Foundation, Taipei

⁶Department of Obstetrics and Gynecology, College of Medicine, Taipei Medical University, Taipei

⁷Department of Obstetrics and Gynecology, Taipei Medical University Hospital, Taipei (Taiwan)

Summary

Undifferentiated endometrial sarcoma is an aggressive sarcoma. The authors report a case of such a large tumor arising from the cervix in a 53-year-old multiparous woman presenting with urinary retention and vaginal bleeding. Ultrasound and Doppler imaging revealed a large mass about 13.3×7.6 cm in the cervix. MRI revealed a large polypoid heterogeneous hyperintensity tumor (12.2×8.2 cm) in the cervix with vaginal lumen protrusion and urinary bladder compression. Total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed. The pathology revealed FIGO Stage IIb. Adjuvant radiotherapy and chemotherapy with doxorubicin were given. The patient tolerated the treatment well, and so far she has no evidence of recurrence.

Key words: Undifferentiated endometrial sarcoma; Vaginal bleeding; Hysterectomy.

Introduction

After leiomyosarcoma, endometrial stromal sarcoma (ESS) is the second most common primary uterine sarcoma. [1] The 2003 World Health Organization (WHO) Classification recommended that the term ESS be reserved only for low-grade tumors that have a genuine resemblance to endometrial stroma. [2] Thus, tumors previously classified as high-grade ESS should now be designated “undifferentiated endometrial sarcoma (UES)”. In contrast to the generally indolent behavior of ESS, UESs behave aggressively, and patients have a poor prognosis [3, 4].

ESS in the cervix [5], vagina or extragenital organs [6] is much rarer, and frequently associated with stromal endometriosis [7]. Recently, the authors encountered a very rare case of undifferentiated endometrial sarcoma (UES) arising from the uterine cervix with unusual clinical and pathologic finding.

Case Report

The patient, 53-years-old, G4P2A2, had intermittent vaginal bleeding and urine frequency since April 2017. She had difficult urination in these three months, and came to visit a urologist first. Cystoscopy revealed external compression of bladder only, and a Foley catheter was inserted for urine drainage. On August 1, she was referred to the gynecologic OPD for further examination. Physical examination revealed mild fever (38.8°C), BP 137/79 mmHg, heart rate 118/minute and respiratory rate 18/minutes. Pelvic examination revealed a large mass in the cervix. Cervical biopsy was performed which showed granulation tissue with marked acute and chronic inflammation masking the structures. Immunohistochemical stains: CK (-), vimentin

(+), chromogranin (-), synaptophysin (-), and Ki-67 10% (+). Review of history, she had regular annual Pap smear, which revealed no malignancy. She was admitted on August 1, 2017 for further workup and treatment. Lab data showed CRP 7.14 mg/ml, FDP dimer 984.55 ng/ml, CA125 39.8 IU/ml, SCC 1.7 ng/ml, CEA 1.13 ng/ml, and creatinine 0.6 mg/dl. Chest X-ray was normal. MRI on August 3, 2017 (Figures 1 and 2) revealed a large polypoid heterogeneous hyperintensity tumor (12.2×8.2



Figure 1. — MRI T2-weighted image of a large polypoid heterogeneous hyperintensity tumor in the uterine cervix with vaginal lumen protrusion and urinary bladder compression, free of endometrium.

Revised manuscript accepted for publication March 29, 2018

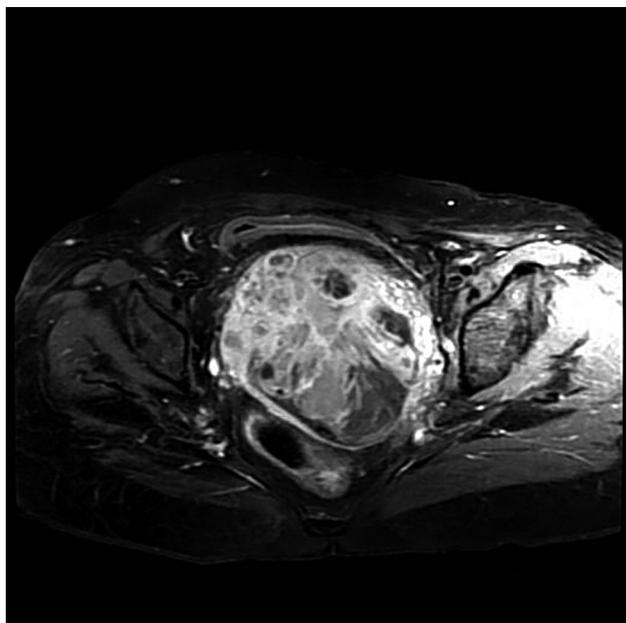


Figure 2. — Contrast-enhanced T1 image contrast-enhanced MRI showing obvious heterogeneous enhancement of the tumor.

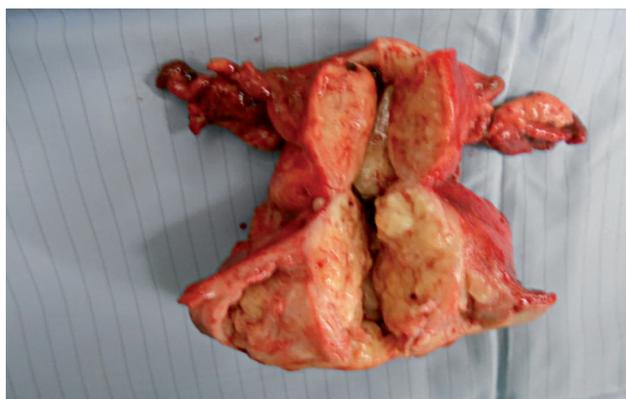


Figure 3. — Extirpated uterus showing a tumor arising from the cervix.

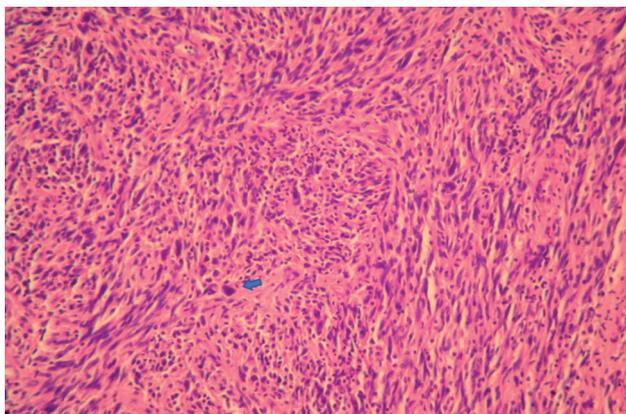


Figure 4. — H & E stain, $\times 100$, the tumor shows short spindle nuclei with occasional nuclear pleomorphism (arrow).

cm) in the cervix with vaginal lumen protrusion and urinary bladder compression.

On August 7, 2017, diagnostic conization was performed but massive hemorrhage occurred. Therefore, an emergency total abdominal hysterectomy and bilateral salpingo-oophorectomy were performed (Figure 3). Frozen section pathology showed spindle cell tumor with nuclear atypia, and malignancy could not be excluded. August 10, 2017, the paraffin block showed undifferentiated endometrial sarcoma of the cervix (Figure 4), with tumor invasion to cervical stroma, but endometrium, myometrium, and bilateral adnexa were free of tumor invasion. The tumor was positive for CD10, cyclin D1, vimentin, negative for SMA, calponin, h-caldesmon, and cytokeratin. Cervical undifferentiated endometrial sarcoma with no lesion in the endometrial cavity considered to be derived from endometriosis focus. FIGO Stage was IIb.

After surgery, she recovered very well, and she could void urine without difficulty. She received adjuvant chemotherapy with doxorubicin and external beam radiation therapy (EBRT) between August 2017 and October 2017. She was immobilized by vacuum cushion with CT simulation of 3.75 mm slice. Clinical target volume (CTV) included the primary cervical tumor bed, peripheral, and pelvic lymphatic area. Planning target volume (PTV) was 0.3 cm expansion from CTV. The EBRT technique was intensity modulated radiation therapy (IMRT). Seven-field IMRT under image guided with 15-MV photon was used to deliver a total tumor dose of 45 Gy/25 fractions of the pelvic, and 66.6 Gy/37 fractions of the cervical tumor bed area, with conventional fractionation (1.8 Gy per day, five days per week). There were no complaints of acute or delayed toxicity except for grade 1 and poor appetite during chemotherapy and radiotherapy.

Discussion

UES is staged in the same way as uterine leiomyosarcoma; staging is performed using the modified FIGO system [8]. UES is an aggressive rare malignancy with no treatment consensus. Standard management of UES comprises total hysterectomy and bilateral salpingo-oophorectomy; however, the benefit of regional lymphadenectomy is unclear [9]. Beyond surgery, the effect of adjuvant treatment on UES (pelvic radiotherapy and/or chemotherapy) remains poorly understood and deserves further investigation. Increasing tumor size was significantly associated with a decrease in survival (five-year survival [OS] 61%, 54%, 37% for size < 5 cm, 5-10 cm, > 10 cm). On multivariable analysis, only tumor size and stage significantly predicted survival [10].

In the present patient, tumor size was 12.2 \times 8.2 cm, and FIGO Stage IIb. No coexistence of superficial endometriosis or infiltrating adenomyosis of the cervix was noted. Though frequency of superficial endometriosis of the cervix ranged from 1.7% [11] to 2.4% [12], ESS is rarely found in the cervix [13].

ESS tumors may be asymptomatic or could present as postmenopausal or atypical premenopausal bleeding [14-15], and rarely present with mass effect causing urinary and bowel obstructive symptoms. The present case

showed atypical premenopausal bleeding and urinary obstruction symptoms at presentation.

Sonography usually demonstrates the endometrial mass. Sonographic findings alone cannot definitively diagnose uterine sarcomas [16]. However, few studies have described patterns on transvaginal sonography like diffuse myometrial thickening, central cavity mass, mural mass, and polypoidal mass protruding into the endometrial cavity from the myometrium. They may have partially nodular, smooth or ill-defined margins with heterogeneous, hypoechoic and septate cystic echotexture [17]. Color Doppler may show central or peripheral vascularity and low resistivity index (RI) values [18]. Our case demonstrates one huge cervical mass extend to vaginal lumen with Doppler showed low RI due to increased tumoral vascularity.

MRI is a more useful investigation tool for suspecting the malignancy and for staging. MRI of ESS commonly shows polypoidal endometrial mass, heterogeneously isointense on T1-weighted, and hyperintense on T2-weighted images. Low grade ESS shows variable presentation, from a polypoidal mass to an intramural lesion mimicking leiomyoma, extensive necrosis and peripheral hypointense rim on T2-weighted images. [19] UES may present as heterogeneous signal intensity voluminous polypoidal mass with more frequent myometrial involvement [20], UES frequently have hemorrhage, necrosis, and vascular and lymphatic invasion. Increased signal intensity of the lesion on diffusion weighted imaging (DWI) and low apparent diffusion coefficient (ADC) values indicate malignancy [9]. Vascular, lymphatic, and peritoneal metastases are known to occur in ESS [21]. The present case had hemorrhage and necrosis.

Review of available literature, the ten-year-survival is 65-76% in ESS and OS in UES is poor [3]. Surgery and adjuvant hormonal therapy are the essential elements in the treatment of ESS [22]. Hysterectomy along with bilateral salpingo-oophorectomy is the standard surgical treatment. ESS is usually managed by cytoreductive surgery and hormonal treatment which include progestins and aromatase inhibitors as maintenance therapy. However, for UES, cytotoxic agents like doxorubicin and ifosfamide or gemcitabine, with docetaxel and doxorubicin, have been used prior to surgery for tumor shrinkage [21]. To date, external pelvic irradiation has been widely used as adjuvant treatment for uterine sarcoma, an approach reported to decrease local recurrence [23]. UES poor prognosis was mainly related to the presence of extrapelvic sites of recurrence with lung and peritoneum. In the present case, the patient underwent hysterectomy with bilateral salpingo-oophorectomy. She then received adjuvant chemotherapy with doxorubicin and EBRT.

References

- [1] D'Angelo E., Prat J.: "Uterine sarcomas: a review". *Gynecol. Oncol.*, 2010, 116, 131.
- [2] Hendrickson M.R., Tavassoli F.A., Kempson R.L., et al.: "Mesenchymal tumours and related lesions. In: Tavassoli FA, Devilee P, (eds). *World Health Organization Classification of Tumours. Pathology and Genetics of Tumours of the Breast and Female Genital Organs*. Lyon: IARC Press, 2003, 233.
- [3] Chew I., Oliva E.: "Endometrial stromal sarcomas. A review of potential prognostic factors". *Adv. Anat. Pathol.*, 2010, 17, 113.
- [4] Tanner E.J., Garg K., Leitao M.M. Jr., Soslow R.A., Hensley M.L.: "High grade undifferentiated uterine sarcoma: surgery, treatment, and survival outcomes". *Gynecol. Oncol.*, 2012, 127, 27.
- [5] Abell M.R., Ramirez J.A.: "Sarcomas and carcinomas of the uterine cervix". *Cancer*, 1973, 31, 1176.
- [6] Chang K.I., Crabtree G.S., Lim-Tan S.K., Kempson R.L., Hendrickson M.R.: "Primary extrauterine endometrial stromal neoplasms: a clinicopathologic study of 20 cases and a review of the literature". *Int. J. Gynecol. Pathol.*, 1993, 12, 282.
- [7] Clement P.B., Young R.H., Scully R.E.: "Stromal endometriosis of the uterine cervix. A variant of endometriosis that may simulate sarcoma". *Am. J. Surg. Pathol.*, 1990, 14, 449.
- [8] Prat J.: "FIGO staging for uterine sarcoma". *Int. J. Gynecol. Obstet.*, 2009, 104, 177.
- [9] Gadducci A., Cosio S., Romanini A., Genazzani A.R.: "The management of patients with uterine sarcoma: a debated clinical challenge". *Crit. Rev. Oncol. Hematol.*, 2008, 65, 129.
- [10] Orr B.C., Lin J.F., Edwards R.P., Kelley J.L. III, Olawaiye A.B., Comerci J.T., et al.: "Undifferentiated endometrial sarcoma: Does adjuvant treatment impact outcomes of stage I disease?" *Gynecol. Oncol.*, 2016, 141, 120.
- [11] Williams G.A., Richardson A.C.: "Endometriosis of the cervix. Classification and analysis of 17 cases". *Am. J. Obstet. Gynecol.*, 1961, 81, 111.
- [12] Veigo-Ferreira M.M., Leiman G., Dunber F., Margolius K.A.: "Cervical endometriosis facilitated diagnosis by fine needle aspiration cytologic testing". *Am. J. Obstet. Gynecol.*, 1987, 157, 849.
- [13] Chen X., Hamel-Bena D., Galic V.L., Liu-Jarin X., Ko Y.C.K., Herzog T., et al.: "Infiltrating adenomyosis of the cervix with features of a low-grade stromal sarcoma: a case report and a literature review". *Int. J. Gynecol. Pathol.*, 2014, 33, 253.
- [14] Puliyaath G., Nair M.K.: "Endometrial stromal sarcoma: A review of the literature". *Indian J. Med. Paediatr. Oncol.*, 2012, 33, 1.
- [15] Shah S.H., Jagannathan J.P., Krajewski K., O'Regan K.N., George S., Ramaiya N.H.: "Uterine sarcomas: then and now". *Am. J. Roentgenol.*, 2012, 199, 213.
- [16] Toprak U., Paşaoğlu E., Karademir M.A., Gülbay M.: "Sonographic, CT, and MRI findings of endometrial stromal sarcoma located in the myometrium and associated with peritoneal inclusion cyst". *Am. J. Roentgenol.*, 2004, 182, 1531.
- [17] Kim J.A., Lee M.S., Choi J.S.: "Sonographic findings of uterine endometrial stromal sarcoma". *Korean J. Radiol.*, 2006, 7, 281.
- [18] Tepper R., Altaras M., Goldberger S., Zalel Y., Cordoba M., Beyth Y.: "Color Doppler ultrasonographic findings in low and high grade endometrial stromal sarcomas". *J. Ultrasound Med.*, 1994, 13, 817.
- [19] Rha S.E., Byun J.Y., Jung S.E., Lee S.L., Cho S.M., Hwang S.S., et al.: "CT and MRI of Uterine Sarcomas and Their Mimickers". *Am. J. Roentgenol.*, 2003, 181, 1369.
- [20] Nucci M.R., Harburger D., Koontz J., Dal Cin P., Sklar J.: "Molecular analysis of the JAZF1-JJAZ1 gene fusion by RT-PCR and fluorescence in situ hybridization in endometrial stromal neoplasms". *Am. J. Surg. Pathol.*, 2007, 31, 65.
- [21] Lange S.S., Novetsky A.P., Powell M.A.: "Recent advances in the treatment of sarcomas in gynecology". *Discov. Med.*, 2014, 18, 133.
- [22] Amant F., De Knijf A., Van Calster B., Leunen K., Neven P., Berteloot P., et al.: "Clinical study investigating the role of lymphadenectomy, surgical castration and adjuvant hormonal treatment in endometrial stromal sarcoma". *Br. J. Cancer*, 2007, 97, 1194.

- [23] Reed N.S., Mangimni C., Malmstrom H., Scarfone G., Poveda A., Pecorelli S., *et al.*: "Phase III randomized study to evaluate the role of adjuvant pelvic radiotherapy in the treatment of uterine sarcoma stage I and IIL an European Organization for Research and Treatment of Cancer Gynaecological Cancer Group Study (protocol 55874)". *Eur J. Cancer*, 2008, 44, 808.

Corresponding Author:
SU-CHENG HUANG
Department of Obstetrics and Gynecology
Taipei Tzu Chi Hospital,
Buddhist Tzu Chi Medical Foundation
No.289, Jianguo Rd., Xindian District
New Taipei City 231 (Taiwan)
e-mail: schuang@tzuchi.com.tw