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Uterine leiomyosarcoma with skeletal muscle metastasis

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Summary

Background: Leiomyosarcoma of the uterus is a rare tumor; hence there is lack of evidence on the tumor behavior in terms of prognostic factor for recurrence and its metastatic pattern. Practitioners usually find difficulty in choosing the best management options in treating rare diseases. *Case Report:* A case of uterine leiomyosarcoma underwent staging laparoscopy and adjuvant chemotherapy. First recurrence was discovered as a single lung nodule after two years follow up, so the patient underwent a metastatectomy. Second recurrence was isolated right biceps muscle metastasis which was removed and followed by chemo-radiotherapy. Patient died one year following the second recurrence. *Conclusion:* There are no specific pathological findings or independent factors which can predict the metastatic pattern or the site of recurrence. Surgical resection appears to be the best option in management of leiomysarcoma metastasis if feasible. Evidence supports the roll of chemotherapy in non-operable recurrence.

Key words: Leiomyosarcoma; Metastasis; Recurrence site.

Introduction

Sarcoma of the uterus contribute 4.7 % to all of female cancers [1]. Three to eight percent of uterine cancer are sarcomas while leiomyosarcoma contribute only 1% [1]. The incidence varies depending on the age and ethnicity. In white women, the incidence peaks at the age of 50 years in 20 per 100,000 [1]. Overall, half of patients with disease confined to the pelvis at the time of diagnosis will develop metastasis within the first two years [2]. A different site of leiomyosarcoma metastases was observed and skin and soft tissues metastasis occurred in 15.3% in recent reviews [2]. However, in reviewing literature no article mentioned skeletal muscle uterine leiomyosarcoma metastasis.

Case Report

The patient is a 55-year old gravida 3, para 2, miscarriage 1 women. Four years ago she underwent total laparoscopic hysterectomy, bilateral salpingo-oophorectomy, and pelvic lymphadenectomy, based on vaginal ultrasound which reported posterior wall uterine fibroid with degenerative change 8×10 cm, and frozen section during operation which reported uterine leiomyosarcoma (the frozen section ordered by surgeon due to suspicious looking fibroid which was adherent to the left ovary). Postoperative histopathological examination revealed a diagnosis of high grade leiomyosarcoma Stage 1B. Thus the patient had whole body tumor survey which was negative and she received six cycles of chemotherapy with doxorubicin and ifosfamide over six months, followed by follow up CT-scan, and there was no evidence of residual tumor or recurrence. Two years later follow up CT-scan showed right lower lobe lung nodule, and this was confirmed by whole body tumor survey which gave the impression of lung nodule with probability of malignancy. As a result, a VATS right lower lobe resection was performed. Histopathology confirmed metastatic leiomyosarcoma with free margin resection and visceral pleural invasion.

One year ago the patient began to complain of painless mass in the right upper arm. On examination the mass was mobile and not tender. MRI showed a large intramuscular tumor within the right biceps with similar signals to muscles, internal septation, necrosis, and avid rim enhancement (no skin involvement) (Figure 1). Differential diagnosis included leiomysarcoma and peripheral nerve sheath tumor (no gross bony lesion in the right humorous. The mass was removed through vertical incision, and the pathology study confirm metastatic leiomyosarcoma 7×5×5 cm with an area of necrosis (Figure 2). The patient received chemotherapy doxetaxel and gemcitepine and radiotherapy. Twelve months later the patient died due disseminated lung recurrence.

Discussion

Leiomyosarcoma of the uterus is a rare cancer. As a result, there is not enough evidence on the metastatic pattern. However, as any mesenchymal tumor, the vascular route is

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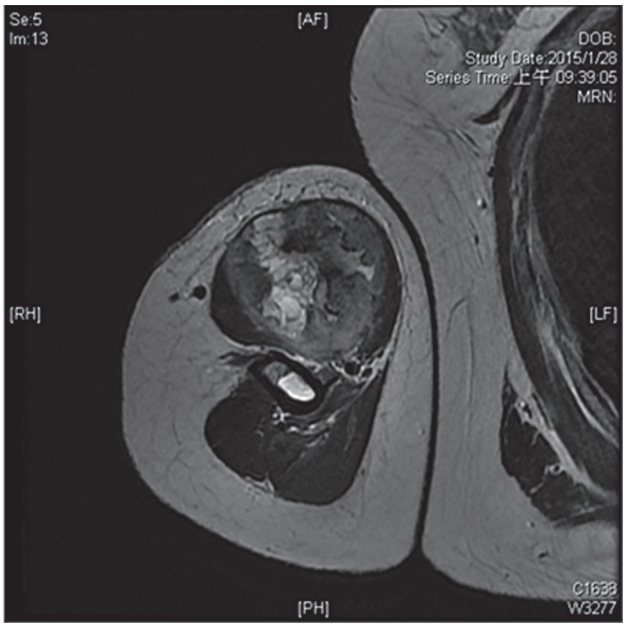

Figure 1. — MRI showing a large intramuscular tumor within the right biceps with similar signals to muscles, internal septation, necrosis, and avid rim enhancement (no skin involvement).

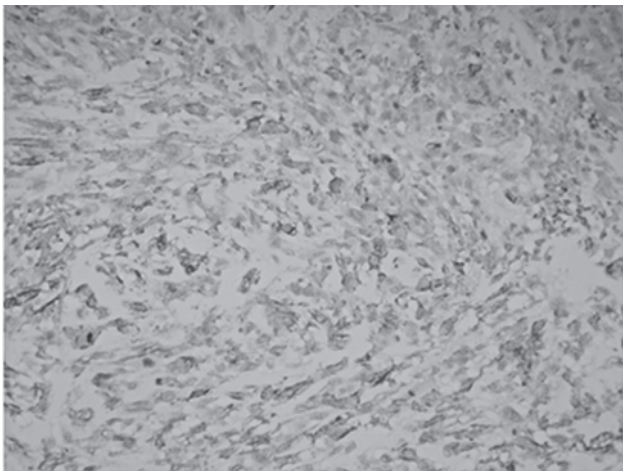

Figure 2. — Cells of the metastatic tumor are diffusely and weakly positive to SMA.

the preferred one for metastasis, where lung is the most frequent site of first metastasis, as shown by most studies [2]. In reviewing literature, there is no specific research on the immunohistochemical markers expression and the site of recurrence. One study confirmed that markers expression (such as desmin and smooth muscle actin) had better prognosis [3]. According to 2008 SEER analysis African-American patient showed the worst survival [4]. Nevertheless, there is no direct relation between race and metastatic disease prognosis [5]. The size of the primary tumor more than 11 cm and the presence of adhesion are ominously a prognostic factor [5].

Muscular metastasis from any primary solid is rare and the prevalence in autopsy and radiological series is between 0.03% to 5.6% and 1.2% to 1.8%, respectively [6]. The most common primary cancer for skeletal muscle metastasis is the lung [6], and this may give an explanation for muscular metastasis in this case as a second site after lung metastasis. It is important to mention that there is no specific radiological feature for muscular metastasis [6].

The mainstay treatment for disease which is confined to the pelvis is total abdominal hysterectomy and preferably bilateral salpingo-oophorectomy and pelvic lymphadenectomy, even if they are not macroscopically affected because the probability of the microscopic invasion varies up to 4% and 3%, respectively (although these figure may rationalize preservation of the ovaries in premenopausal women if the ovaries appear to be normal) [7]. Most studies available on the treatment of leiomyosarcoma prove that aggressive debulking and removal of metastasis if possible will improve survival [7]. The five-year survival for patients with pulmonary metastasis is between 25% to 53% according to a different study [7]. However, there is a lack of studies for other site mastectomy survival, possibly because other site metastasis is in fact a second site, and at this stage patients are usually unfit for surgery.

Based on meta-analysis of 14 study [8] and EORTC sarcoma group [9], there was no difference in overall survival whether the patient received adjuvant chemotherapy (doxorubicin and ifosfamide) after completely resected FIGO Stage 1 or 2 or not. However, there was difference between the meta-analysis and EORTC studies in terms of period to local and distant recurrence, where the first reported that there is a significant difference while the second reported that there was no significant difference. There is no proven benefit in giving radiotherapy for patients after complete resection of FIGO Stage 1 or 2 tumor in terms of free survival or overall survival [10]. Doxorubicin and ifosfamide are the first line management for recurrent uterine leiomyosarcoma for the previous 30 years. However, three prospective studies showed that combination of gemcitabine and docetaxel is at least as effective as doxorubicin and ifosfamide in terms of objective response rate, overall survival, and progression-free survival [11–13].

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References

[1] McMeekin D.S.: "Clinical gynecologic oncology". 8th ed. In: *Sarcoma of the uterus*. Philadelphia, PA: Elsevier Saunders, 2012, 175.

[2] Bartosch C., Afonso M., Pires-Luís A.S., Galaghar A., Guimarães M., Antunes L., Lopes JM.: "Distant Metastases in Uterine Leiomyosarcomas: The Wide Variety of Body Sites and Time Intervals to Metastatic Relapse". *Int J Gynecol Pathol.*, 2016 Mar 24. [Epub ahead of print]

[3] Demicco E.G., Boland G.M., Brewer Savannah K.J., Lusby K., Young E.D., Ingram D.Y., *et al.*: "Progressive loss of myogenic differentiation in leiomyosarcoma has prognostic value". *Histopathology*, 2015, *66*, 627.

[4] Kapp D.S., Shin J.Y., Chan J.K.: "Prognostic factors and survival in 1396 patients with uterine leiomyosarcomas: emphasis on impact of lymphadenectomy and oophorectomy". *Cancer*, 2008, *112*, 820.

[5] Lusby K., Savannah K.B., Demicco E.G., Zhang Y., Ghadimi M.P., Young E.D., *et al.*: "Uterine leiomyosarcoma management, outcome, and associated molecular biomarkers: a single institution's experience". *Ann. Surg. Oncol.*, 2013, *20*, 2364.

[6] Surov A., Köhler J., Wienke A., Gufler H., Bach A.G., Schramm D., *et al.*: "Muscle metastases: comparison of features in different primary tumours". *Cancer Imaging*, 2014, *14*, 21.

[7] Amant F., Lorusso D., Mustea A., Duffaud F., Pautier P.: "Management strategies in advanced uterine leiomyosarcoma: focus on trabectedin". Sarcoma, 2015, *2015*, 704124.

[8] Sarcoma Meta-analysis Collaboration (SMAC): "Adjuvant chemotherapy for localised resectable soft tissue sarcoma in adults. Sarcoma Meta-analysis Collaboration (SMAC)". *Cochrane Database Syst Rev.*, 2000, *4*, CD001419.

[9] Woll P.J., Reichardt P., Le Cesne A., Bonvalot S., Azzarelli A., Hoekstra H.J., *et al.*: "Adjuvant chemother- apy with doxorubicin, ifosfamide, and lenograstim for resected so -tissue sarcoma (EORTC 62931): a multicentre randomised controlled trial". *Lancet Oncol.*, 2012, *13*, 1045.

[10] Surov A., Hainz M., Holzhausen H.J., Arnold D., Katzer M., Schmidt J., *et al.*: "Skeletal muscle metastases: primary tumours, prevalence, and radiological features". *Eur. Radiol.*, 2010, *20*, 649.

[11] Hensley M.L., Blessing J.A., Mannel R., Rose P.G.: "Fixed-dose rate gemcitabine plus docetaxel as second-line therapy for metastatic uterine leiomyosarcoma: a Gynecologic Oncology Group phase II study". *Gynecol. Oncol.*, 2008, *109*, 323.

[12] Hensley M.L., Blessing J.A., Mannel R., Rose P.G.: "Fixed- dose rate gemcitabine plus docetaxel as rst-line therapy for metastatic uterine leiomyosarcoma: a Gynecologic Oncology Group phase II trial". *Gynecol. Oncol.*, 2008, *109*, 329.

[13] Hensley M.L., Maki R., Venkatraman E., Geller G., Lovegren M., Aghajanian C., *et al.*: "Gemcitabine and docetaxel in patients with unresectable leiomyosarcoma: results of a phase II trial". *J. Clin. Oncol.*, 2002, *20*, 2824.

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