Metastatic leiomyosarcoma presenting as bilateral, multifocal breast masses

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SUMMARY

Here we describe a case of metastatic leiomyosarcoma presenting as bilateral, multifocal breast masses. This case represents the convergence of three rare entities: leiomyosarcoma of unknown primary origin, metastases to the breast and bilateral, multicentric breast disease.

BACKGROUND

This case is an unusual type of cancer mimicking breast masses, a common oncological occurrence. This case highlights the importance of the breast itself as a site of metastasis, and sometimes equivocal nature of imaging in delineating a tumour's primary site.

CASE PRESENTATION

A 46-year-old woman presented with bilateral, painless breast masses noted on self-examination. The masses were present for 6 months and were stable in size. She reported a recent 10-pound weight loss. She also reported heavier and shorter menstrual cycles. She denied abdominal or pelvic pain, or change in urinary frequency. Her medical history is significant for right-sided glomus jugulare tumour, which was treated with γ -knife radiotherapy. Her family history is significant for breast and uterine cancer in her maternal aunt at age 41.

Breast examination revealed firm masses in the left breast at the 6 and 12 o'clock positions and mobile masses in the right breast at the 9 and 12 o'clock positions. There was no cervical, supraclavicular or axillary adenopathy on either side. Her gynaecological examination was normal.

INVESTIGATIONS

Bilateral diagnostic mammogram revealed two masses in the left breast. The first was an irregular and spiculated mass, measuring 2.0 cm $\times$ 1.2 cm $\times$ 1.8 cm; and the second an ovoid and microlobulated mass, measuring 1.3 cm $\times$ 2.2 cm $\times$ 2.4 cm. Several simple cysts were observed in both breasts. Real-time ultrasound showed two masses in the right breast. The first was an irregular, lobulated, hypoechoic mass, measuring 1.4 cm $\times$ 1.5 cm $\times$ 1.6 cm; and the second an ovoid, lobulated, hypoechoic mass, measuring 1.4 cm $\times$ 1.4 cm $\times$ 1.4 cm.

Ultrasound-guided core-needle biopsies were performed on the left breast at 6 o'clock (figure 1) and 12 o'clock, and the right breast at 9 and 12 o'clock. The microscopic features were similar for all areas biopsied. Pathological analysis revealed spindle cell proliferation with significant cytological atypia (figure 2), which were noted to be infiltrating the normal mammary adipose tissue (figure 2, inset). The mitotic count was low to moderate and 2–3 per 10 high-

power fields on average. Smooth muscle markers desmin, SMA, calponin and HHF-35 were diffusely and strongly positive in the tumour cells. Vimentin, AE1/AE3, p63, S-100, HMB-45, estrogen receptor (ER) and progesterone receptor (PR) immunostains did not show any reactivity. These findings are compatible with a low-grade leiomyosarcoma.

Subsequent metastatic workup followed, including CT scans of the chest, abdomen and pelvis, and MRI of the brain and pelvis. CT scan revealed several low-attenuation hepatic lesions, the largest of which measured 3.5 cm. Biopsy of this lesion revealed leiomyosarcoma. Also observed were numerous pulmonary nodules and a left renal mass. MRI of the brain revealed findings consistent with previous glomus jugulare tumour. Positron emission tomography (PET)/CT whole-body scanning revealed FDG-avid areas in the right lung, liver and skeleton. Also observed was an avid subserosal area of the uterus (figure 3), measuring 11 mm, consistent with fibroids. Cervical biopsy and Pap smear revealed benign tissue.

OUTCOME AND FOLLOW-UP

Given the rarity and extent of her tumour, there is a paucity of treatment options. This patient wished to undergo active surveillance, in the absence of progression of symptoms. If she would become symptomatic, it was decided to consider her tumour as a primary uterine leiomyosarcoma, as hormone therapy could be utilised in the case of new ER/PR positivity. In this framework, oophorectomy and hysterectomy or pharmacological suppression of the ovaries would be warranted to decrease oestrogen supplementation, as she is premenopausal. However, since she had metastatic disease, the utility of surgery is questionable. Thus, it was agreed that ER/PR status would be re-obtained upon progression of symptoms, and that, if it were positive, she would undergo ovarian suppression with a gonadotropin-releasing hormone agonist and would consider aromatase inhibitor treatment for palliation.¹ During this time of active surveillance, the patient died.

DISCUSSION

Here, we describe a case of metastatic leiomyosarcoma presenting as bilateral, multifocal breast masses. Metastases to the breast are uncommon, accounting for 2–3% of all breast tumours.^{2–3} The majority (~87%) of these metastases arise from the contralateral breast.³ The most common extramammary primary tumour is malignant melanoma. Approximately 8% of breast metastases represent sarcoma.⁴

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Figure 1 Ultrasound of the left breast shows an echogenic mass (arrow).

Leiomyosarcomas are a rare subset of soft tissue sarcomas. The most common primary site for leiomyosarcoma is the retroperitoneum, which accounts for 50% of all cases.⁵ Retroperitoneal leiomyosarcoma usually arises from the inferior vena cava or one of its branches. In this case, there were no retroperitoneal-avid areas on PET scan, making this an unlikely primary site.

Another possible primary site for leiomyosarcoma is the uterus. Uterine leiomyosarcoma usually presents with vaginal bleeding and/or pelvic and abdominal pain.⁶ This patient did not present with any abdominal or gynaecological symptoms. Primary uterine leiomyosarcomas are usually large (>10 cm).⁷ Tumour size is a major prognostic indicator in uterine leiomyosarcoma,⁸ so even if the small area seen on CT in this patient were to represent a primary site, such a grossly metastatic presentation would not be expected.

Primary breast sarcomas are rare, accounting for approximately 1% of all breast cancers. Primary leiomyosarcoma of the breast is an extremely rare subtype, and only 45 cases have been reported in the literature, none of which presented with metastases.⁹ Nearly half of the tumours are in or near the nipple-areola complex, but any quadrant may be affected.¹⁰ The presence of multicentric, bilateral lesions, as seen in this case, is

Figure 2 Breast biopsy shows proliferation of spindle cells (background) with atypical cells infiltrating the normal mammary adipose tissue (inset).

Figure 3 There was an FDG-avid area in the uterus measuring 11 mm.

highly suggestive of an extramammary metastasis rather than a primary breast tumour. Case reports of primary leiomyosarcoma of the lung,¹¹ liver¹² and bone¹³ have been reported but these are even more rare and usually present with more organ-focal symptoms. Thus, based on the presentation, imaging and histology, this patient presented with a breast metastasis from a leiomyosarcoma of unknown primary origin.

This patient's prognosis was poor. Retrospective studies of patients with surgically resected primary retroperitoneal¹⁴ and soft tissue¹⁵ leiomyosarcoma demonstrate 5-year survival rates of ~20% and ~50% of patients, respectively. Since this patient presented with gross metastases, it was likely that her survival rate would be worse. While a 2007 meta-analysis showed a role for doxorubicin-based adjuvant chemotherapy in resectable leiomyosarcoma,¹⁶ no clinical trials have assessed the role of chemotherapy for metastatic leiomyosarcoma, likely because of its rare presentation.

Learning points

- ▶ Metastases to the breast are rare, and the majority of them arise from the contralateral breast.
- ▶ The most common site for leiomyosarcoma is the retroperitoneum. Five-year survival rates for leiomyosarcoma are 20–50% depending on the primary site.
- ▶ Primary breast sarcomas are extremely rare; the presence of multicentric disease is suggestive of metastases to the breast.

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Competing interests None.

Patient consent Obtained.

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