Pleomorphic liposarcoma of the male breast: lessons from a rare malignancy during COVID-19 pandemic

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SUMMARY

A 52-year-old man presented with a recurrent right side breast lump. He had undergone excision of a lump on the right breast followed by adjuvant chemoradiotherapy 1 year ago for a diagnosis of pleomorphic liposarcoma. Imaging revealed a 47×36 mm lesion on the right side of the chest wall involving the pectoralis muscle. The patient underwent right radical mastectomy. Histology of the specimen showed an undifferentiated pleomorphic sarcoma infiltrating into the underlying skeletal muscle. Therefore, he was planned for chemoradiotherapy. But due to lockdown during the COVID-19 pandemic, he was lost to follow-up and later presented with malignant pleural effusion. This case emphasises the impact of COVID-19 pandemic over such rare malignancies.

BACKGROUND

Sarcomas of the breast are rare, and account for 0.06% of all breast malignancies.[1] Liposarcomas being the second most common type and constitute only 5% of all breast sarcomas.[2] Sarcomas in men are rare, aggressive and are associated with high recurrence; furthermore, there is no established treatment protocol. The global health issue related to COVID-19 has led to delayed presentation, upstaging of the disease and poor prognosis due to delay in further treatment.[3] We present a case stuck in similar circumstances that led to loss of follow-up and delay in initiation of adjuvant treatment, leading to systemic recurrence.

CASE PRESENTATION

A 52-year-old man presented to our outpatient department with a lump in his right breast for 5 months. The lump increased in size over 5 months and was not associated with pain or nipple discharge. There was no history suggestive of metastasis and no family history of breast cancer. Biopsy of the lump showed fibrocollagenous tissue with no evidence of malignancy. The patient underwent excision of the lump, which on histopathology revealed pleomorphic liposarcoma. The patient received ifosfamide and epirubicin-based adjuvant chemoradiotherapy.

Seven months after the initial surgery, the patient reported a lump in right breast for 1 month. The lump increased in size gradually and was associated with pain at local site. Examination revealed a hard lump measuring 5×4 cm in the upper half of the right breast, extending to the retroareolar region (figure 1). Scar from previous surgery was present over the lump. The lump had restricted mobility over the chest wall. The nipple, areola and overlying skin were not involved. The contralateral breast examination was unremarkable. There was no clinically palpable axillary and supraclavicular lymph nodes.

INVESTIGATIONS

Biopsy of the lump yielded focal chronic inflammation with few foamy macrophages. In view of high suspicion of recurrence, contrast-enhanced CT of thorax and positron emission tomography and CT (PET-CT) were performed to stage the tumour and assess resectability. The contrast-enhanced CT thorax showed an ill-defined, lobulated, heterogeneously enhancing lesion measuring 47×36×31 mm on the right-sided chest wall involving the pectoralis muscle and abutting the third rib with no underlying bone erosion (figure 2). On PET-CT, there was no evidence of distal metastasis (figure 3). Based on the imaging, tumour was T2N0M0, with stage of IB (American Joint Committee on Cancer, eighth edition).

A multidisciplinary team concluded the necessity of repeat biopsy followed by surgical excision. As the patient opted for surgical excision in view of his history with likely possibility of recurrence, he was counselled for radical mastectomy and adjuvant chemoradiotherapy.

TREATMENT

Right-sided radical mastectomy was performed to obtain a clear margin from all the margins (figure 4). The histology of the operative specimen showed undifferentiated pleomorphic sarcoma infiltrating into the skeletal muscle with all the resected margins free of tumour (figure 5). Immunohistochemistry was negative for all the lineage-specific markers. There was no involvement of lymph nodes from the axillary tail.

OUTCOME AND FOLLOW-UP

In the postoperative period, the surgical wound was healthy and healed satisfactorily. The patient was discussed in multidisciplinary team and plan for adjuvant chemoradiotherapy and follow-up once in 3 months. However, due to COVID-19 lockdown, the patient did not turn up for follow-up and adjuvant therapy. Six months later, the patient presented to the casualty with shortness of breath. The chest radiograph and contrast-enhanced CT chest revealed massive pleural effusion with lung nodules in the lung parenchyma suggestive of

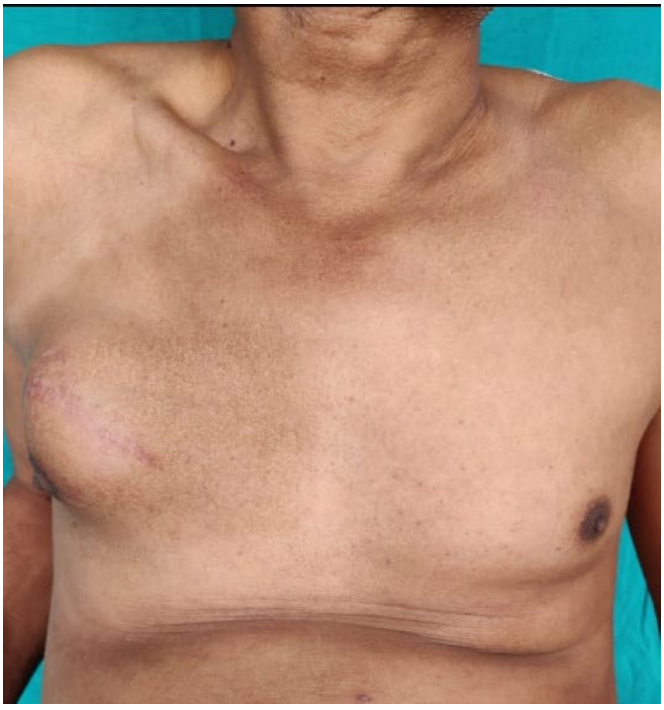

Figure 1 Clinical image of recurrent lump in the right breast extending to the retroareolar region with scar mark overlying the lump (solid arrow).

systemic metastasis (figure 6). The patient was managed by chest drain placement and is currently on palliative care.

DISCUSSION

Breast cancer in men is uncommon and constitutes less than 1% of all breast cancers. Among all breast malignancies, breast sarcomas account for 0.06% and breast liposarcomas for 0.003%.[1 2] Liposarcoma of the breast may arise from pre-existing benign lesions, like lipoma[1], fibroadenoma and phyllodes tumour.[2 4 5] Studies have shown significant association of breast sarcoma with ipsilateral breast radiation.[6] However, our patient had not received radiotherapy in the past.

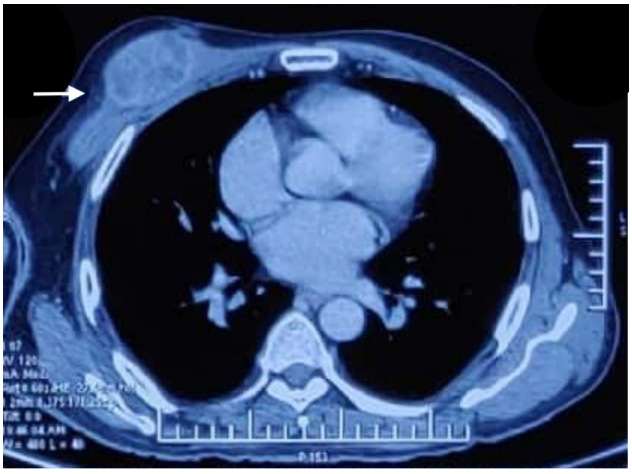

Figure 2 Contrast-enhanced axial CT of thorax showing the tumour (solid arrow) involving the pectoralis muscle but not involving the ribs/intercoastal muscles.

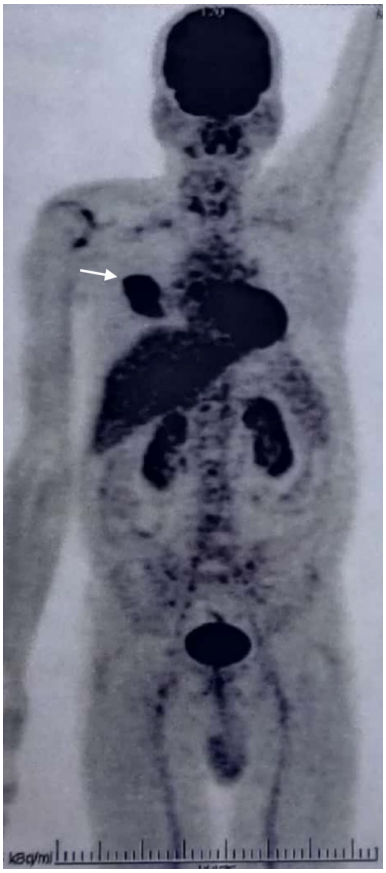

Figure 3 Positron emission tomography scan showing fluorodeoxyglucose-avid lesion (solid arrow) in right chest wall with no evidence of distal metastasis.

Based on histology, liposarcomas are classified into four subclasses: most common are atypical lipomatous tumour, followed by myxoid, pleomorphic and dedifferentiated liposarcomas.[2 4] Liposarcomas are prevalent in the fourth to seventh decades of life, typically present as soft, slowly growing painful unilateral masses.[5]

On imaging, liposarcoma have several specific features. On ultrasound, they appear as a homogeneous or heterogeneous echogenic mass. On mammography, they can appear as very dense and well-circumscribed lesions. CT scan features hazy amorphous densities representing spindle formation, thick streaks of entrapped muscle fibres, and thin streaks of fibrous tissue and solid masses with low densities representing fat. T2-weighted MRI shows heterogeneous enhancement with thickened or nodular septa.[2 7]

On histology, typical lipoblasts with irregular, hyperchromatic nuclei and well-defined intracytoplasmic vacuoles are pathognomonic for liposarcoma. Genetic aberrations like MDM2 amplification and TP53 alterations have been detected in pleomorphic liposarcoma.[8] The level of differentiation can be assessed by desmin, vimentin, smooth muscle antigen, Cytokeratin (CK), leucocyte common antigen, CD34, HMB-45, smooth muscle actin (SMA), epithelial membrane antigen and S-100 protein.[6 7] In our case, the tumour was negative for CD99, SMA, desmin, CD34, S-100, MDM2 and STAT6, which suggests undifferentiated pleomorphic liposarcoma.

There is no standard treatment protocol for mammary liposarcoma. However, excised margin and tumour size

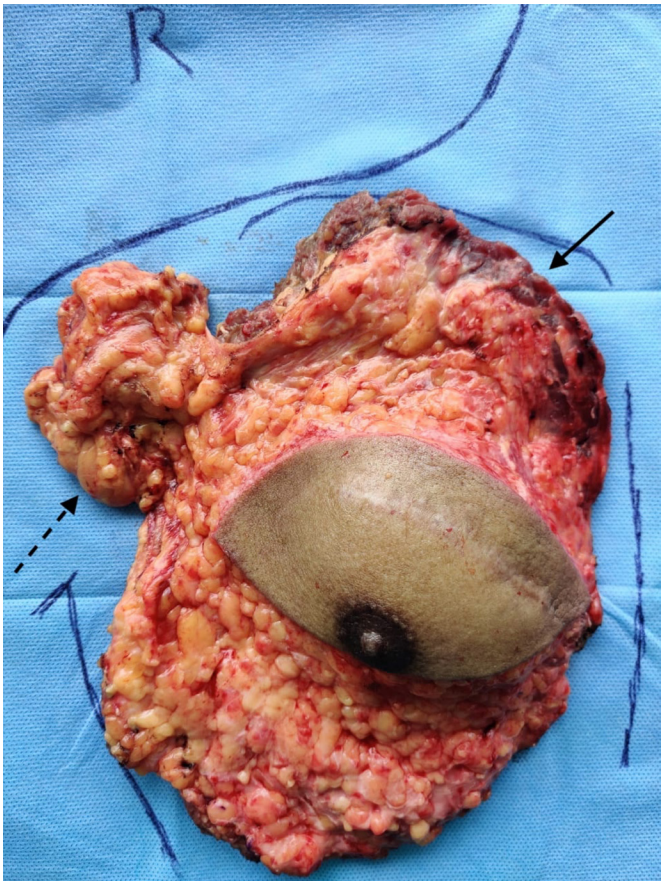

Figure 4 Gross specimen of right radical mastectomy with overlying scar, underlying muscle (solid arrow) and axillary tissue (broken arrow).

are important factors that determine local recurrence and distant metastasis.[9] Wide local excision with clear margin is the preferred technique.[10] However, due to involvement of pectoralis muscle in our patient, radical mastectomy was performed to obtain clear margins.

According to the recommendation by the ESMO–EURACAN (European Society for Medical Oncology–European Reference Network for rare adult solid cancers) clinical practice guidelines, postoperative radiation therapy should be administered at a dose of 50–60 Gy with fractions of 1.8–2 Gy, possibly with boosts up to 66–68 Gy, depending on tumour presentation and quality of surgery.[10]

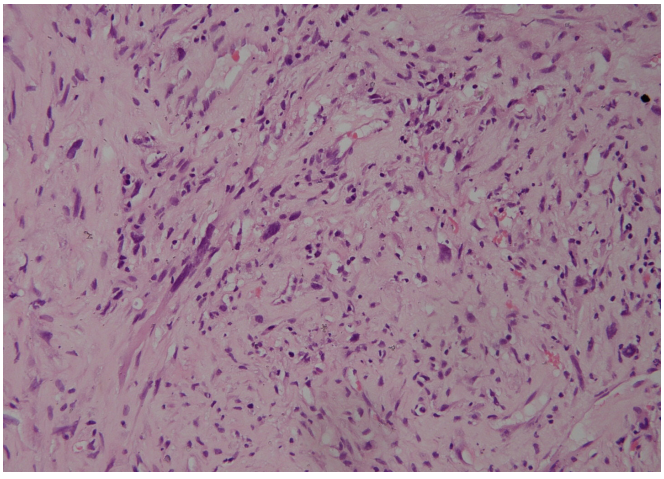

Figure 5 Photomicrograph showing malignant spindle cells exhibiting moderate to marked nuclear pleomorphism, elongated nuclei with coarse chromatin, brisk mitotic activity and moderate to abundant cytoplasm.

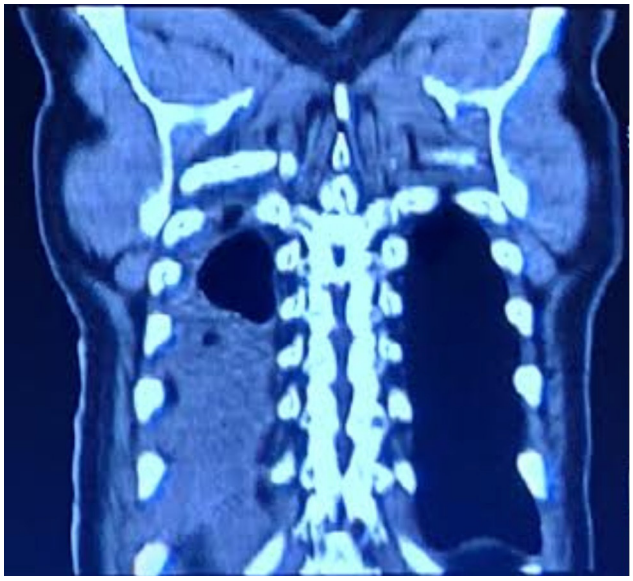

Figure 6 Non-contrast coronal images of CT thorax showing massive right pleural effusion with underlying partial lung collapse and multiple nodules in the right lung.

Long-term follow-up is needed because of the risk of local recurrence or delayed dedifferentiation.[11] Here, the patient is followed every 3–4 months in the first 2–3 years, then two times a year up to the fifth year, and once a year thereafter.[7]

The COVID-19 pandemic has affected every aspect of cancer care. As a result, there is delay in treatment or loss of follow-up. Studies from pandemic-affected areas show diminution in breast surgery clinic activities[12] and a lack of breast cancer patient care in diagnostic and surgical procedures as well as delay in adjuvant therapy.[3] This adversely affects the prognosis of aggressive malignancies like pleomorphic liposarcoma here, and has resulted in upstaging of the tumour and poor prognosis.

Recommendations from international groups for breast cancer management during this pandemic suggest a tiered approach to categorise patients into different priorities for receiving active cancer therapy during the pandemic.[9] Curigliano *et al* suggested a surgical priority-based triage as categorising breast cancer patients into four categories: urgent priority: surgery within 2 weeks; high priority: surgery within 4 weeks: medium priority: surgery within 8 weeks: and low priority: surgery after 8 weeks.[10] These recommendations can help in better allocation of resources and expedite the treatment processes.

Use of technology by virtual multidisciplinary cancer team meetings should be done to discuss individual treatment plans and logistics. Patients with high-risk rapidly proliferating tumours should be considered for radiotherapy and shortening of treatment duration by hypofractionation have shown promising results.[11 13] They also help in better allocation of resources and shorten the treatment course.[14] The risks of infection should be weighed against potential hazards of cancer progression and recurrence of breast cancer from the delay in treatment.[9]

Learning points

- Pleomorphic liposarcoma is a challenging tumour in terms of treatment due to its aggressive local invasion and high risk of recurrence.
- Multidisciplinary team approach needed to improve survival.
- Recurrence is common in pleomorphic sarcoma of the breast; therefore, the patient needs to undergo stringent follow-up and surveillance for early detection of recurrence and treatment.
- There is need for better and more streamlined follow-up protocols in the setting of COVID-19 pandemic to ensure better outcomes in such rare and aggressive malignancies.

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