Case Report

Extensively Metastasizing Leiomyosarcoma: A Diagnostic Challenge

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Abstract

Uterine leiomyosarcoma (ULMS) is a rare malignancy of the female genital tract and carries an extremely poor 5-year survival rate. It is known to metastasize early and to distant sites owing to a high propensity for hematogeneous spread. Lung, peritoneum, liver, and bone are relatively common sites of metastasis. Patient age, tumor size, FIGO stage, and grade of the tumor are important criteria for predicting metastasis. The incidence of ULMS is increasing, probably due to the use of improved imaging techniques and as a result of cancer patients' prolonged life expectancy. An early well thought diagnosis is only made possible if even in otherwise seemingly unsuspected cases, the histopathology slides are extensively screened and the treating clinician is alerted timely. We hereby report a case of an elderly female who underwent hysterectomy for resection of multiple fibroids in the uterus and later presented with distant metastasis to brain with the erosion of overlying skull bone, chest wall, and lungs. Microscopic features along with an extensive immunohistochemistry panel were used to ascertain tumor origin.

Keywords: *Hysterectomy, leiomyosarcoma, metastasis, pan cytokeratin, smooth muscle tumor, uterus*

Introduction

Uterine leiomyosarcomas (ULMS) are uncommon malignant smooth muscle tumors constituting for about 1% of all uterine malignancies.[1] ULMS have a high propensity for hematogeneous spread, most commonly to the lungs, followed by liver and peritoneal cavity.[2] Intracranial and soft tissue metastasis are extremely rare with only a handful of case reports available in literature.[2,3] An accurate early diagnosis of ULMS is essential as these patients have a dismal prognosis and a high recurrence (45%–75%) rate even when the disease is confined to the uterus.[4] Tirumani *et al*. studied the metastatic pattern of 113 ULMS and found 81.4% cases with distant metastases and 50% patients had local recurrence.[5] Radical hysterectomy followed by radiotherapy and chemotherapy is the mainstay of the current treatment protocol, but despite patient tailored and intensified therapy, the outcome is poor.[6] Fine needle aspiration (FNA) findings of metastatic ULMS have seldom been discussed at unusual sites.[7-9] We report a case of extensively metastasizing leiomyosarcoma that was under-diagnosed on hysterectomy.

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Case Report

A 60-year-old woman came with the complaints of easy fatigability, persistent dull aching headache for the past 3 months with intermittent episodes of aggravation. Headache was predominantly localized on the right side and throbbing in nature. She also had a nodular growth over the right forehead measuring about 2.5 cm × 2.5 cm for 3 months. It began as a small nodule of pea size and progressed to about 1 cm × 1 cm. Due to pain over the swelling, she went to a local practitioner and got it excised. However, the swelling recurred and grew to its present size over a period of 1½ months. There was no alteration in appetite, bowel, and bladder habits or weight loss. She had a history of total abdominal hysterectomy done for multiple uterine fibroids, 6 months back.

Local examination of forehead swelling showed a nodular surface with an overlying scar mark of previous excision [Figure 1a]. The swelling was fixed,

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nontender, and nonpulsatile on palpation. The patient also had a firm, fixed swelling over right chest wall measuring about 4 cm × 4 cm [Figure 1c]. There was no other palpable organomegaly. Her serum chemistry and blood investigations were within normal limits. Contrast-enhanced computed tomography (CECT) of head revealed a large heterogeneously enhancing mass of approximately 5 cm × 4 cm in the right frontal region. The lesion caused destruction of both outer and inner tables of frontal bone along with inward compression of the right frontal lobe [Figure 1b]. CECT chest and abdomen also revealed a heterogeneously enhancing mass lesion measuring 5.7 cm × 4.1 cm × 3.5 cm in superior and posterobasal segment of the right lower lobe with evidence of infiltration into right branch of inferior pulmonary vein. Multiple nodular opacities with few showing spiculations were seen in bilateral upper lobes [Figure 1d]. Also seen was a pleura-based soft tissue dense enhancing mass involving the right posterolateral chest wall with the destruction of right 10th rib [Figure 1e]. There was evidence of contiguous infiltration of the mass into overlying subcutaneous fat and right posterolateral chest wall.

Multiple FNAs were performed from forehead and lateral chest wall nodular masses. Smears prepared from both sites showed similar morphology. Pleomorphic tumor cells were seen predominantly in cohesive overlapping clusters with hyperchromatic oval to bizarre nuclei. At places, the cells were seen embedded in a pink matrix material. Features were those of a poorly differentiated malignant tumor. Immunocytochemistry could not be performed, as the patient did not consent for a repeat FNA. The patient was asked to retrieve paraffin blocks from previously resected forehead nodule. Reviewed histomorphology and serial sectioning revealed elongated fascicles of a cellular spindle tumor with cells displaying moderate anisokaryosis along with occasional bizarre nuclear form. Mitosis was evident along with foci of necrosis. Lymphovascular emboli were not identified [Figure 2a-d]. Overlying skin was free of tumor. A panel of immunohistochemical stains was put up for further characterization. Tumor cells were strongly positive for vimentin, muscle specific antigen (MSA), and smooth muscle actin (SMA) along with distinct perinuclear dot positivity for pan cytokeratin (pan-CK) [Figure 3a-d]. Cells were negative for desmin, S-100, and CD34. A final diagnosis of metastatic leiomyosarcoma was given. In an attempt to locate the primary and considering patients sequential history, her previous hysterectomy specimen was retrieved and extensively regrossed. Serial sections revealed leiomyoma with two 10 mm and 7 mm foci showing moderate nuclear atypia, stippled necrosis, and evident mitosis; consistent with leiomyosarcoma. Hence, a final impression of ULMS with metastasis to chest wall and forehead was made. The patient was started on a chemotherapeutic regimen comprising of three cycles of gemcitabine/docetaxel, followed by intensity modulated radiation therapy to abdomen. The patient became symptomatically better for a few weeks. However, a 6-month follow-up computed tomography scan chest, done posttherapy was suggestive of approximately 20% increase in size of mass in lower lobe and right chest wall; indicating progressive disease. The patient is now further planned for intensified chemotherapy regimen.

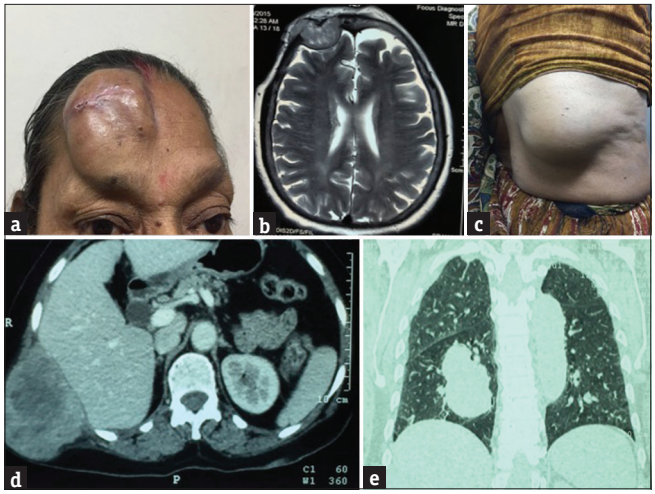

Figure 1: (a) Nodular forehead swelling with scar of the previous resection. (b) Magnetic resonance imaging brain-expansile lytic lesion involving the right frontal bone. (c) Firm, fixed, right chest wall swelling. (d) Contrast-enhanced computed tomography abdomen-pleura-based enhancing mass lesion involving chest wall, causing the destruction of the 10th rib. (e) Contrast-enhanced computed tomography chest: Heterogeneously enhancing mass in the right lower lobe of lung along with multinodular opacities with spiculations in bilateral upper lobes

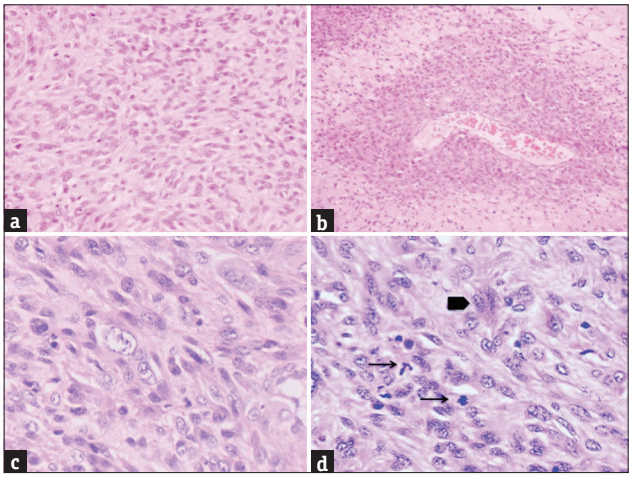

Figure 2: (a) Cellular spindle cell neoplasm (H and E, ×20). (b) Perivascular arrangement of tumor cells (H and E, ×20). (c) Tumor cells showing moderate pleomorphism (H and E, ×40). (d) Scattered multinucleate tumor cells (arrowhead) and mitotic figures (arrow) (H and E, ×40)

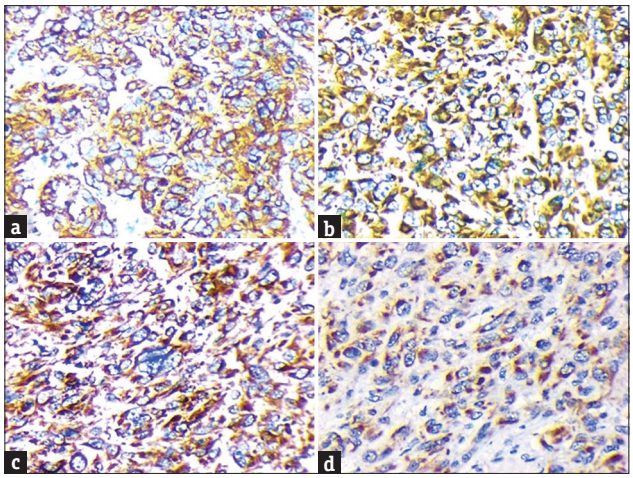

Figure 3: Immunohistochemistry for (a) Vimentin. (b) Muscle specific antigen. (c) Smooth muscle actin shows membranous positivity. (d) Pan cytokeratin shows perinuclear dot positivity

Discussion

Diagnosis and management of ULMS can be challenging as disease presentation and prognosis varies considerably from patient to patient. However, literature available for studying the same is scant, and most studies are retrospective probably due to disease rarity and dynamic nature.[5,6] Tirumani *et al*. and Bernstein-Molho *et al*. observed that diagnosis of ULMS often occurs in retrospect after surgical resection of a presumed benign uterine neoplasm, as was seen in our case.[5,10] Therefore, patients many a times do not undergo preoperative staging work up, leading to inadequate management.

A surgical pathologist has a crucial role in these situations. Extensive sampling, especially of unusual areas, is mandatory to elucidate the nature of the tumor. The final diagnosis of ULMS is based on the assessment of three major histologic features: increased mitotic activity (≥10/10 HPF), nuclear atypia, and tumor cell necrosis. However, it is prudent to point out differential diagnosis is difficult when a variant of leiomyosarcoma shows unusual morphological features or if morphology mimics other mesenchymal sarcomas encountered in the uterus such as endometrial stromal sarcoma, malignant melanoma, tumors with rhabdoid differentiation, and even poorly differentiated carcinomas.[11] Immunohistochemistry for vimentin, SMA, and MSA is characteristically positive in leiomyosarcomas, which further confirms tumor origin and diagnosis.[12] In addition, in the present case, an aberrant strong positivity of pan-CK was observed which is highly unusual for a sarcoma. CK positivity has been described in few reports as a "potentially serious diagnostic pitfall" in diagnosing a malignant spindle cell tumor.[13]

We describe a case of ULMS that metastasized to unusual locations and required multidisciplinary approach; clinical history, critical analysis of FNA slides and review of archival material and assay of histomorphology to arrive at a confirmatory diagnosis. The present case highlights the importance of close microscopic examination in an otherwise clinically unsuspected case.

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Conflicts of interest

There are no conflicts of interest.

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