Skeletal Radiology (2020) 49:815–818
https://doi.org/10.1007/s00256-020-03373-4

CASE REPORT

# Angiosarcoma arising in massive localized lymphedema

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Received: 10 November 2019 / Revised: 30 December 2019 / Accepted: 2 January 2020 / Published online: 16 January 2020


**Abstract**
We report a case of a 70-year-old woman with a BMI of 58 who developed cellulitis refractory to treatment, within an area of massive localized lymphedema. Biopsy showed angiosarcoma. MRI showed multiple lobulated, low T1, high T2 masses within a background of prominent soft tissue septal stranding, dilated lymphatic channels, and skin thickening. CT also showed the mass well, within the background lymphedema. Massive localized lymphedema is increasing in prevalence due to the worsening obesity epidemic. Radiologists should be aware that the presence of a nodule within an area of massive localized lymphedema is suspicious for sarcoma.

**Keywords** Angiosarcoma · Lymphedema · Massive localized lymphedema · Stewart–Treves syndrome · Adiposis dolorosa

## Introduction

Stewart–Treves syndrome is a rare malignant phenomenon in which angiosarcomas arise within the background of chronic lymphedema. This association was first recognized and most often seen in the setting of treated breast cancer [1–3]. Although most cases are seen in the upper arm after axillary node dissection, any area with chronic lymphedema is at risk of malignant change to sarcoma, perhaps due to the localized immunosuppression induced by the lymphedema [4]. In a recent case series of five patients presenting over a 25-year period, Shon et al. described the clinical and histologic findings of Stewart–Treves syndrome in the setting of the relatively newly described disorder, massive localized lymphedema (MLL) [5]. MLL is a disorder of localized lymphedema forming a pedunculated mass, most commonly in the upper medial thigh of obese, postmenopausal females [6–9]. Four cases of angiosarcomas arising in the presence of severe obesity, without the classification of MLL, but presumed to be secondary to lymphatic dysfunction have also been reported [5, 10–12]. An increasing number of reports of MLL, and increasing variety in locations of the entity, may reflect increasing rates of morbid obesity [13–15]. In the original case series of angiosarcoma arising from MLL, patients presented with signs highly concerning for malignancy, such as dramatic weight loss. Imaging findings have not been previously reported. Here, we will present the MRI, CT, and pathology findings of a case of angiosarcoma arising in the background of MLL, in a patient who did not have any systemic signs of malignancy. This case is being presented to show the imaging findings of angiosarcoma superimposed on MLL. Given the rising prevalence of MLL, radiologists should be aware of the possibility of sarcomatous degeneration in MLL. Nodules are not a feature of MLL, and therefore the presence of a nodule within a region of MLL should raise concern for sarcoma. It is hoped that increased awareness may lead to the detection of future cases before they reach the large size seen in the case we report.

## Case report

Our study was HIPAA-compliant and IRB-approved. The patient is a 70-year-old obese female (BMI 58) with a past medical history of chronic cellulitis, chronic bilateral lower extremity lymphedema, chronic obstructive pulmonary disease, diabetes mellitus type 2, hypothyroidism, hypertension, and hyperlipidemia. She had a 2-year history of a growing mass in her inner thigh. A week before presentation, she reported that she developed an ulcer in this region and her upper thigh became erythematous, tender, and produced significant amounts of malodorous, serosanguinous discharge. She presented to an outside facility in sepsis, presumed secondary to cellulitis. Cultures from her cellulitis grew *Serratia*

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*marcescens* and appropriate antibiotics were started. Several days later, due to depth of the wound, the lack of improvement after treatment with antibiotics and debridement, and her history of increasing size of the thigh, the decision was made to perform an open incisional biopsy deep to the area of ulceration. Biopsy revealed a neoplasm consistent with high-grade angiosarcoma (Fig. 1). At this point, she was transferred to our facility for further surgical oncologic care.

An MRI without contrast of the right thigh was performed on arrival. Intravenous contrast was not given because of the patient's difficulty in lying flat for MRI. MRI (Fig. 2) showed a large, pedunculated fatty mass, characteristic of MLL, arising at the inner thigh. The skin was markedly thickened, and thick fascial bands were seen radiating centrally from the skin. A lobulated mass within this area measured 11 cm and showed low T1, high T2 signal intensity. Other smaller, satellite masses were present within the area of MLL, and there was an additional mass which lay beyond the area of lymphedema, consistent with local metastasis. Right inguinal enlarged lymph nodes were seen and were concerning for nodal metastasis. CT scan revealed hyperdense tumor underlying a large skin ulceration, in a background of edematous fat (Fig. 3). CT scan of the chest, abdomen, and pelvis showed no evidence of metastatic disease. Due to the poor health of the patient, the oncology teams felt chemotherapy was not an option, and the patient was not a good candidate for invasive surgery; treatment therefore was palliative local radiation and comfort care. The patient returned home and was lost to follow-up.

## Discussion

MLL is a rare disorder first described in 1998 by Farshid and Weiss [16]. They published 14 cases of large, benign masses simulating well-differentiated liposarcomas in a portion of their morbidly obese patients. The average BMI of the patients in their study was 59.6 kg/m$^2$, and so it was suggested that obesity and associated complications such as metabolic syndrome are the most significant risk factors for developing MLL. Other proposed risk factors include hypothyroidism, weight loss secondary to bariatric surgery, inguinal hernia repairs, and hemiparesis [17, 18]. The lesions tend to be pendulous masses located on the proximal and medial portions of limbs, with a particular predilection for the upper, medial thigh [13, 16]. Since the initial description, several other case studies have reported MLL in other locations including the

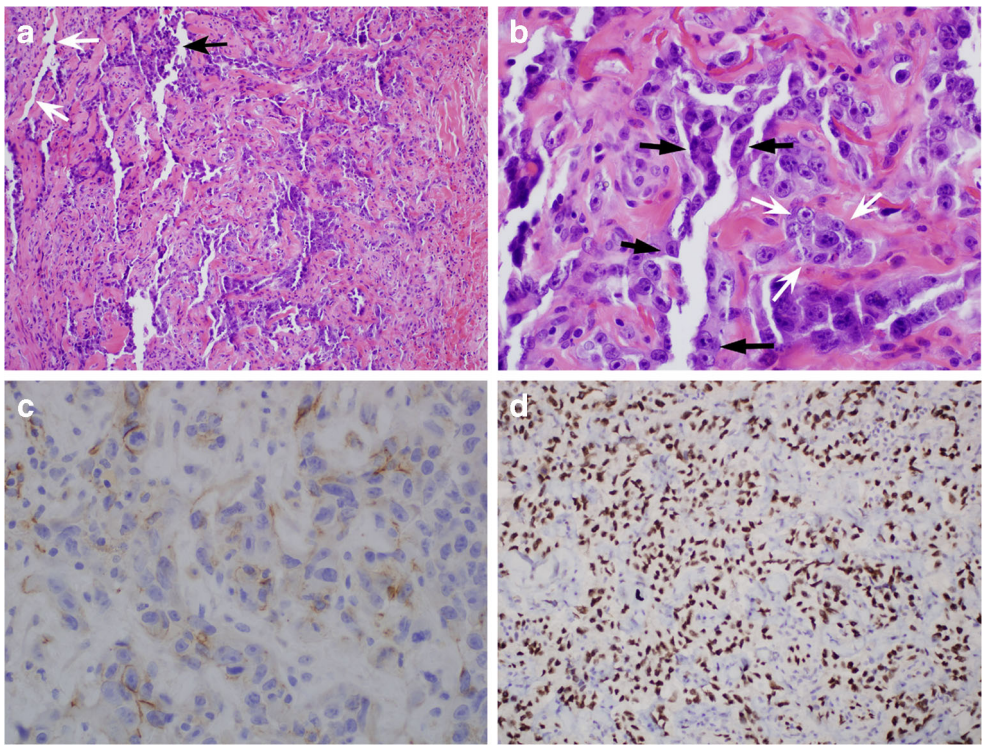


**Fig. 1** Biopsy of thigh mass. A The angiosarcoma was characterized by slit-like and anastomosing spaces (white arrows) lined by atypical endothelial cells (black arrow) reactive for both CD 31 and CD 34. (H&E × 100). B Higher power shows the plump, atypical polygonal cells lining the vascular channels. Black arrows point to the cells lining a channel seen in profile; white arrows show them nearly filling a vascular channel seen in cross section. The polygonal cells have large, vesicular nuclei with large nucleoli. C The cytoplasm of the cells lining the slit-like and anastomosing spaces are reactive for CD-31 (immunoperoxidase, × 400). They were also positive for CD-34. Both of these are markers for endothelial cells and are usually positive in angiosarcoma. D The tumor cell nuclei show strong positive staining with ERG, a stain for endothelial cells. (Immunoperoxidase, × 200)

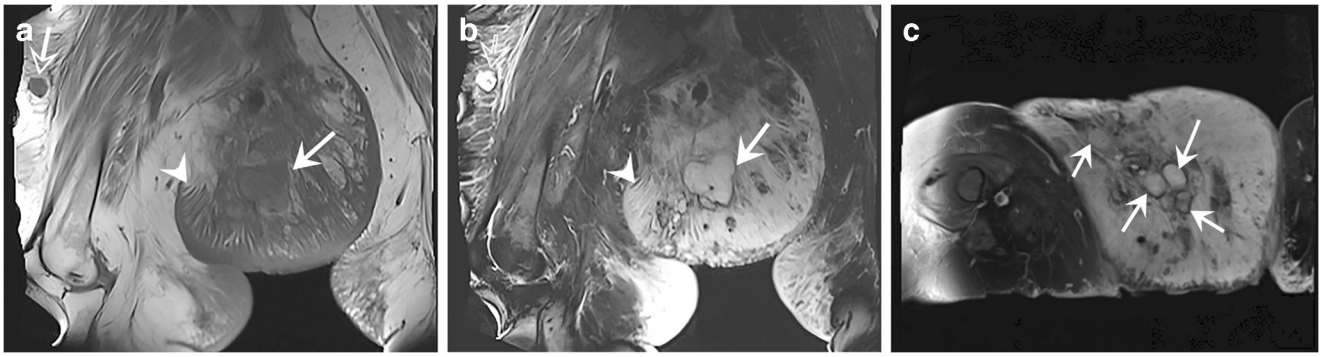


**Fig. 2** MRI. (A) coronal T1 weighted (B) coronal T2 weighted MR of the right medial thigh shows pendulous enlargement of the thigh due to MLL. The dermis is severely thickened, which may be related to the lymphedema or cellulitis. Thickened fibrous septae (arrowhead) are seen. Some of the tubular structures probably represent dilated lymphatics. There is a large dominant low T1, high T2 signal nodule in the central area of abnormality (arrow), with several adjacent small satellite lesions. Another nodule is present in the anterior thigh (open arrow), distant from the region of MLL, most likely local metastasis. Additional less severe, lymphedema changes are presented caudal to the main region of concern and in the contralateral thigh. C Axial T2 weighted, fat-suppressed image of right thigh shows the many tumor nodules (some marked with white arrows) arising from background MLL. The vertical band of increased signal at lateral aspect of right thigh reflects loss of fat suppression due to large field of view. The subcutaneous fat is nearly completely replaced by fluid; this pattern is more confluent than is commonly seen in cases of cellulitis

popliteal fossa, penis, inguinoscrotal area, vulva, mons pubis, retroperitoneum, and the lower abdominal wall [13, 17–23]. Grossly, the lesions are edematous-appearing fatty masses with epidermal thickening and "peau d'orange" changes. Patients may present with recurrent cellulitis [5–9, 13, 24]. Microscopically, dermal expansion and fibrosis are present with fibrous bands interwoven into the surrounding fatty tissue creating coarse, discrete nodules of adipose tissue [5, 13]. MR appearance reflects the microscopic findings of dermal fibrosis, lymphangiectasia, and septations of adipose tissue separated by fibrous bands [7]. The areas of lymphedema show only mild enhancement after administration of gadolinium contrast. It is important to note that soft tissue nodules are not a feature of MLL either at pathologic examination or on imaging studies. The presence of nodules should alert the radiologist to the likelihood of neoplasm.

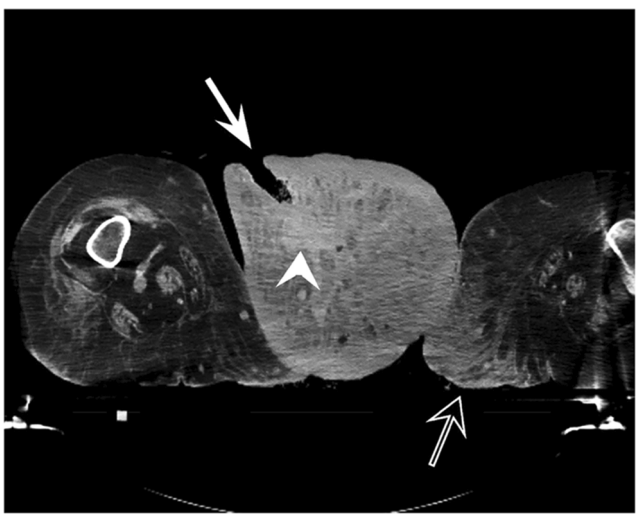

**Fig. 3** Axial CT soft tissue window shows deep ulceration (arrow) extending to one of the hyperdense tumor nodules (arrowhead). The ulcer appears to arise superficial to the tumor and probably is due to the infection. Less severe lymphedema is evident in the contralateral thigh (open arrow)

Despite the growing number of reports and awareness of MLL, the disease may be underreported [6, 16]. MLL may be mistaken for simple lymphedema, well-differentiated liposarcoma, or adiposis dolorosa (Dercum's disease) due to multiple shared features. On histologic examination, MLL and well-differentiated liposarcoma both show nodules of mature fat septated by fibrous bands, but lymphedema is not a finding of well-differentiated liposarcoma, and MLL lacks the nuclear atypia and lipoblasts seen in well-differentiated liposarcoma [8]. Adiposis dolorosa occurs in the same clinical setting and location as MLL and has a similar appearance but is characterized by painful lipomas as well as lymphedema. It may be considered as a variant manifestation of MLL [25, 26]. A suggested differentiating factor is increased prevalence of cellulitis and thickened epidermis in MLL compared to adiposis dolorosa, but either diagnosis may be argued for any individual case [6, 24].

MLL is not characterized by lymphadenopathy or by any focal mass. The presence of a mass in an area of MLL should be considered as likely to represent angiosarcoma. The imaging findings of angiosarcoma are not specific, however, and there could be other, coincidental tumors within an area of MLL.

To date, there are only five reported cases of angiosarcomas arising from MLL, four cases from chronic lymphedema, none arising from adiposis dolorosa, and an unknown number misdiagnosed as well-differentiated liposarcoma [5, 10–12]. The majority of the angiosarcomas reported grew as multiple satellite papules within the tumor of MLL, similar to the pattern of growth seen in our patient. It was characterized by anastomosing spaces lined by endothelial cells which stained

positive for CD 31 and CD 34. CD 31 (cluster of differentiation 31) is a marker of endothelial cells, platelets, and monocytes. Similarly, CD 34 is found in hematopoietic cells and in the endothelial cells of blood vessels but not lymphatic vessels. D2 40 is a marker for lymphatic vessels; that was not employed because of the positivity of CD 31 and CD34. A point that remains unclear in the literature is the length of time between initial presentation of MLL and the discovery of angiosarcoma. In our patient, we have a 2-year timeline of overt growth of the MLL before diagnosis of high-grade stage III angiosarcoma was made, suggesting malignant change in MLL may occur in a matter of months rather than years. It is disturbing that all reported cases of angiosarcoma in this setting have been stage III or IV. Because the true prevalence and rate of malignant change are not known, any patient with an enlarging area of MLL should perhaps be screened for sarcomas with MRI or ultrasound. The presence of a nodule should initiate a biopsy.

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