Cutaneous Lymphomas

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12.1 Introduction

Superficial soft-tissue tumors commonly manifest themselves as painless and benign masses that are hard to differentiate from malignant masses on physical examination alone. However, benign soft-tissue tumors are more common than malignant ones. Malignant soft-tissue tumors, especially those in the musculoskeletal and dermatological system, are rare and account for less than 1 % of all neoplasms. Most of these tumors are mesodermal in origin, such as malignant fibrous histiocytomas, leiomyosarcomas, liposarcomas, synovial sarcomas, and malignant peripheral nerve-sheath tumors, etc. [1, 2]. Superficial soft-tissue lymphomas are extremely rare, with approximately only 1.4 % of all malignant lymphomas [3].

The usual appearance of lymphoma, including both Hodgkin disease and non-Hodgkin lymphoma, is as localized or generalized lymphadenopathy. Extranodal lymphoma is relatively rare, occurring in bone, gut, and tonsils, for example, but rarely in peripheral soft tissue [4–16]. According the revised European-American lymphoma classification [17], the classification of superficial soft-tissue lymphomas is similar to that of whole-body lymphomas and is divided into B-cell lymphoma (precursor B-cell and mature [peripheral] B-cell tumor), T-cell lymphoma (precursor T-cell and mature [peripheral] T-cell tumor), and Hodgkin lymphoma. Superficial soft-tissue lymphomas might be the result of hematogenous or lymphatic pathways, continuous extension from surrounding primary bony lymphoma, or (in rare cases) from the soft tissue or muscle itself [18–24]. The management of superficial soft-tissue lymphomas differs from that of other soft-tissue sarcomas, and the proper treatment for these malignant tumors depends on accurate histopathologic diagnosis; in malignant lymphoma, nonsurgical therapy can be curative [25]. There have been few imaging studies of primary soft-tissue lymphoma. Most have been plain radiographic, computed tomographic (CT), magnetic resonance, and positron emission tomographic studies [12]. High-resolution ultrasonography (HRUS) applied to soft-tissue lymphoma was only recently developed [26, 27].

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12.2 Technical Considerations

The gray scale ultrasonographic scanning should include both short and long axis views and evaluate the echogenicity, margin, and biggest diameter of the tumor. The echogenicity can be classified as high or low and as heterogeneous or homogeneous. Color Doppler ultrasonography was performed at various settings: the scale level and pulse repetition frequency were decreased; color gain was increased until color noise became apparent; and the probe pressure on the lesion was lowered to avoid compressing the small vessels and thereby causing disappearance of low–blood velocity signals [28]. A superficial soft-tissue mass is actually very sensitive to pressure. Therefore, we recommend that color Doppler ultrasound (CDU) and spectral analysis should be performed without pressure to obtain the most consistent results and will be the most sensitive to small vessel function. To achieve "pressureless" status, we recommended the use of a good supply of gel between the probe and skin. The Doppler spectral analysis technique was the same as the CDUS technique. CDUS findings were graded as 0 (no color signal), 1 (<5 spots or lines), 2 (5–15 color spots or lines), or 3 (>15 spots or lines).

The imaging systems will focus on the transducer, and we recommended using a high-frequency linear transducer with a lot of gel to put the lesion within the focus zone.

12.3 Pathology

Clinical presentations of superficial soft-tissue lymphomas could be classified as primary soft-tissue lymphoma, primary soft-tissue lymphoma with body involvement, and secondary soft-tissue lymphoma. Most of the superficial soft-tissue lymphomas occurred in the torso and lower limb [29].

The sonographic echogenicity and morphologic features of soft-tissue lymphoma usually presented as relatively homogeneous hypoechogenicity except for a panniculitis type lymphoma, possibly because most of the area of lymphocyte proliferation had less interface density to reflect the sound beam. Furthermore, most soft-tissue lymphomas had infiltrative margins, [28] which is related to the fact that lymphoma cells easily invade surrounding tissue except for the thick epimysium, and none had echo-free spaces within the tumor, suggesting that tumor necrosis is extremely rare in peripheral soft-tissue lymphoma. The homogeneously hypoechoic pattern of the lymphomas usually corresponded to the large-field, uniform cluster of lymphoma cells with correlation to histology (Fig. 12.1). In that pattern, acoustic impedances of the tumor were similar and differences in acoustic impedance were rare; therefore, the reflected echoes were less than those usually surrounding the soft tissue, resulting in homogeneous hypoechogenicity (Fig. 12.1). In lymphoma–cell infiltration and mixture of soft tissue (such as muscle fascicles), the acoustic impedance between uniform lymphoma cells and nonuniform soft tissue (perimysium or endomysium) varied and resulted in heterogeneous hypoechogenicity (Fig. 12.2). The appearance of soft-tissue lymphoma was variable and could be classified into five types: (1) big mass (>5 cm) (Fig. 12.1) (2) nodal (1–5 cm) (Fig. 12.3) or confluent nodal; (3) small nodular (<1 cm, most <5 mm) and disseminated (Fig. 12.4); (4) myositis (Fig. 12.2); and (5) panniculitis (Fig. 12.5). Most of the lymphomas were masses or nodal or confluent nodal.

Nodal or confluent nodal type means that lymphoma cells have infiltrated the lymph node, enlarging the node. In nodal-type lymphomas, the morphology of the lymph node (ovoid to round with a thin or absent echogenic central hilum) is usually preserved (Fig. 12.6). Therefore, the lymphoma may involve the superficial soft tissue, possibly by means of the lymphatic system, with proliferation in the lymph node. CDUS showed hypervascularity with proliferative vessels from the hilum and rarely from the peripheral capsule (Fig. 12.6).

Small nodular and disseminated lymphomas usually involve the salivary gland and have a diffuse, small and nodular pattern, which can be a result of cluster lymphocytic (hypoechoic) infiltration in the echogenic salivary gland (Fig. 12.4).

In the myositis type, the lymphoma usually grows via an infiltrative-like myositis if occurring within the muscle, rather than a focal process that usually presented on peripheral soft-tissue sarcoma. The sonographic pattern usually presents as heterogeneous hypoechogenicity with infiltration in the margin (Fig. 12.2). However, in some space-limited locations such as in the upper limb, rapid growth and infiltration within the muscle will result in compartment syndrome [12].

On modern HRUS equipment, the separation between adjacent normal adipose cells in subcutaneous fat lobules is difficult, the normal subcutaneous fat lobules therefore present as homogeneous hypoechogenicity except for some thick connective tissue bands. In the panniculitis form, the histologic examination showed that much lymphocytes proliferation and infiltration in the subcutaneous layer separated the small adipose cells from big fat lobules, increasing the number of the fat–soft tissue (lymphoma cells) interfaces and the amount of the sound beam reflected (Fig. 12.5c). Therefore, the infiltrated parts of the subcutaneous fat layer appear as variable homogeneous hyperechoic nodules (Fig. 12.7) distributed in the subcutaneous fat layer or occupied the whole layer of the subcutaneous layer (Fig. 12.5). Such homogeneous hyperechoic subcutaneous fat pattern could occur on other etiology, for example, when fluid or inflammatory cells (lymphocytes) infiltrate the subcutaneous fat layer. Therefore, the differential diagnosis should include entities such as subcutaneous edema (Fig. 12.8), hemorrhage, inflammatory myofibroblast cell tumor infiltration (Fig. 12.9), cellulites (Fig. 12.10), and panniculitis (Fig. 12.11). However, the panniculitic type is very rare in other malignant tumors such as malignantfibrous histiocytoma or other sarcomatous lesions. Subcutaneous panniculitis such as T-cell lymphoma is a rare disorder. Clinically, it is often confused with inflammatory panniculitis associated with connective tissue disease. Histologically, subcutaneous panniculitis-like T-cell

lymphoma is characterized by a lymphohistiocytic infiltrate confined primarily to the fat lobules in subcutaneous tissue.

Prominent hypervascularity in color Doppler sonography usually appears in peripheral soft-tissue lymphoma (Figs. 12.1b, 12.2b, and 12.7b). Although most other tumors (especially malignant tumors in peripheral soft tissue) are hypervascular, the degree of vascularity is more prominent in lymphomas than in other tumors [28–30]. The extreme hypervascularity in the lymphoma can be different from that in other types of soft-tissue sarcoma and result in no central necrosis in peripheral soft-tissue lymphoma. The spectral analysis showed that the resistive index of tumor vessels within the peripheral soft-tissue lymphoma was relatively low compared with that of normal vessels within the surrounding muscular tissue (Fig. 12.5b). The low resistive index was similar to that of vessels in other malignant soft-tissue tumors. Therefore, only the resistive index could not be differentiated from that of other soft-tissue sarcoma types. However, there were usually no arteriovenous shunts, which could be found in hemangiopericytoma, detected in peripheral soft-tissue lymphoma.

Patient survival is relatively independent to patient age, sex, tumor location or size, CDUS grade, or histology [30]. The prognosis of peripheral soft-tissue lymphoma possibly correlated to the cell type of lymphoma, tumor appearance, and clinical presentation; that is, poor prognosis in diffuse large B-cell lymphoma, myositis type, and secondary soft-tissue lymphoma [28, 30]

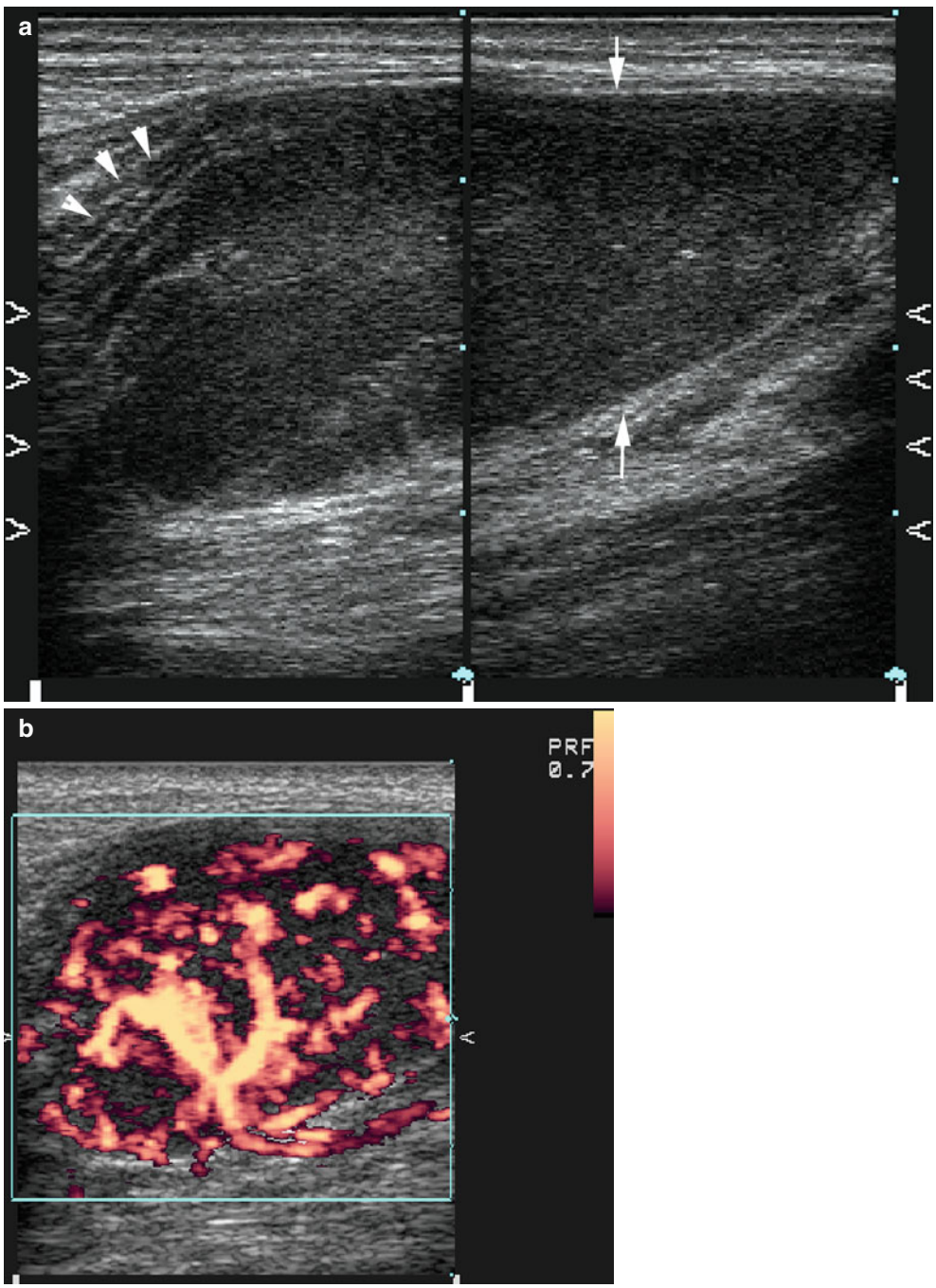

Fig. 12.1 A 60-year-old male patient complaining of a palpable mass over right calf. (**a**) Longitudinal section of the mass showing a homogeneous hypoechogenicity that infiltrated to the upper (*arrowheads*) and lower parts of the gastrocnemius muscle but well-defined margin in the anterior and posterior (*arrows*) aspect. (**b**) Power Doppler image showing hypervascularity in the tumor. This tumor turned out to be diffuse large T-cell lymphoma

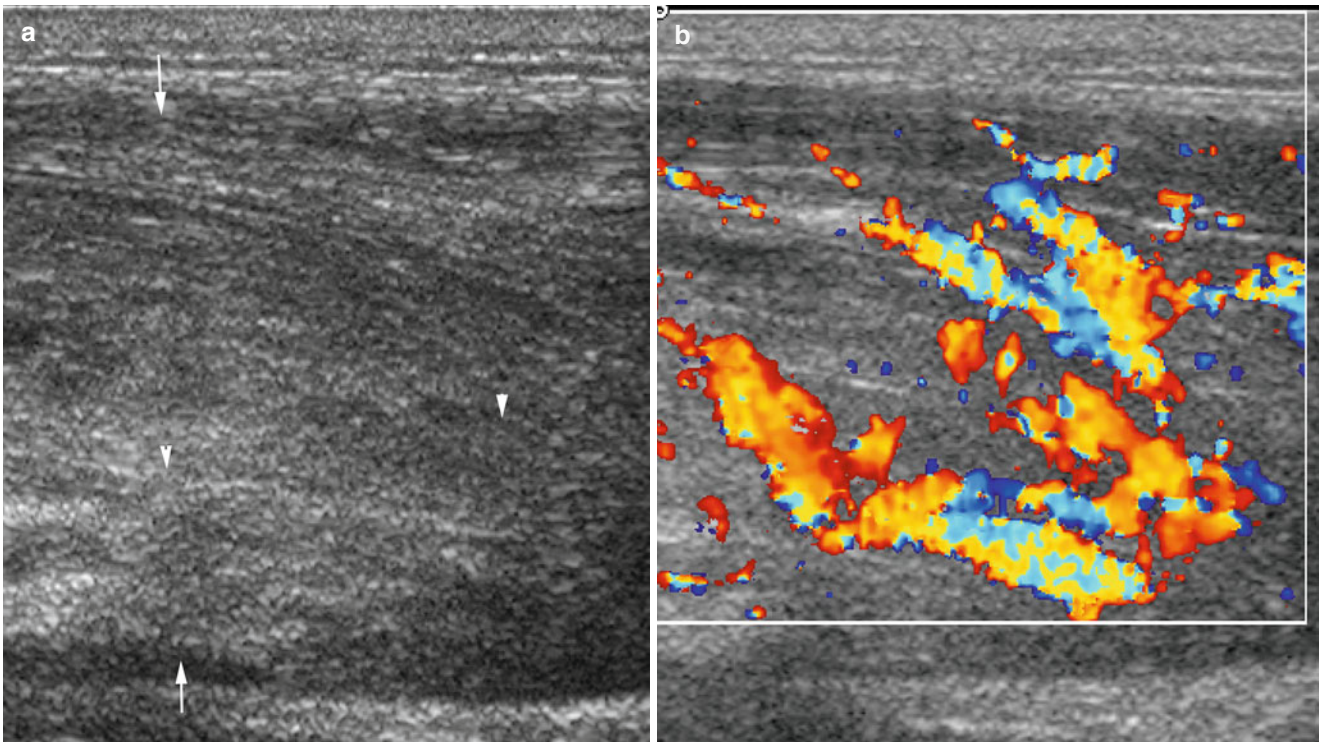

Fig. 12.2 A 79-year-old female patient complaining of severe swelling of the left arm. (**a**) Longitudinal section of left arm showing a heterogeneous echogenic lesion (*arrows*) infiltrating between the perimysium (*arrowheads*) in the muscle of the arm, as would be seen in a case of myositis. (**b**) Color Doppler ultrasound image showing hypervascularity in the tumor, that turned out to be diffuse large B-cell lymphoma

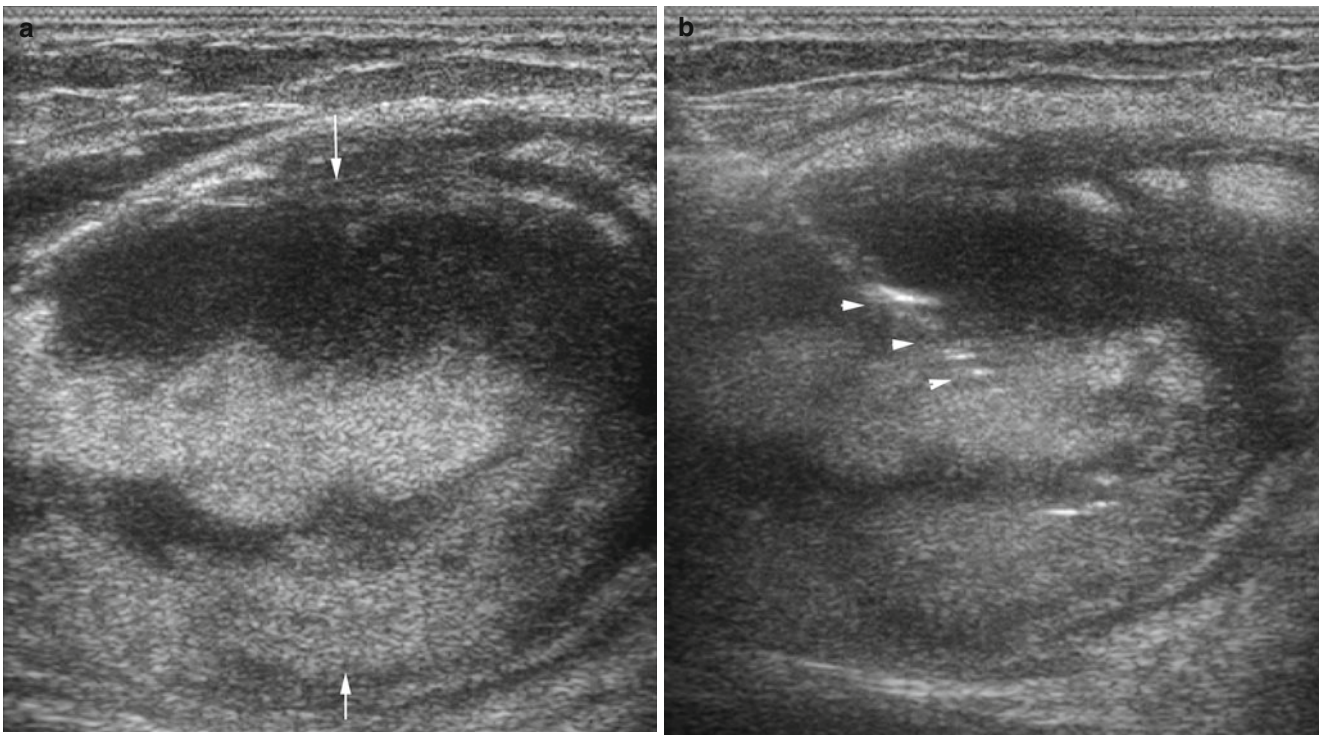

Fig. 12.3 A 77-year-old male, complaining of painless nodule in right inguinal region. (**a**) Grey-scale ultrasound image shows heterogeneous echoic nodule (*arrows*), mixed with hypoechoic and hyperechogenicity. (**b**) Ultrasound-guided core biopsy (*arrowheads*) through the hypoechoic and hyperechoic area. (**c**) Histologic photograph of specimen shows diffuse lymphoma cell infiltration and separated the adipose cell (*arrows*). This tumor turned out to be peripheral T-cell lymphoma

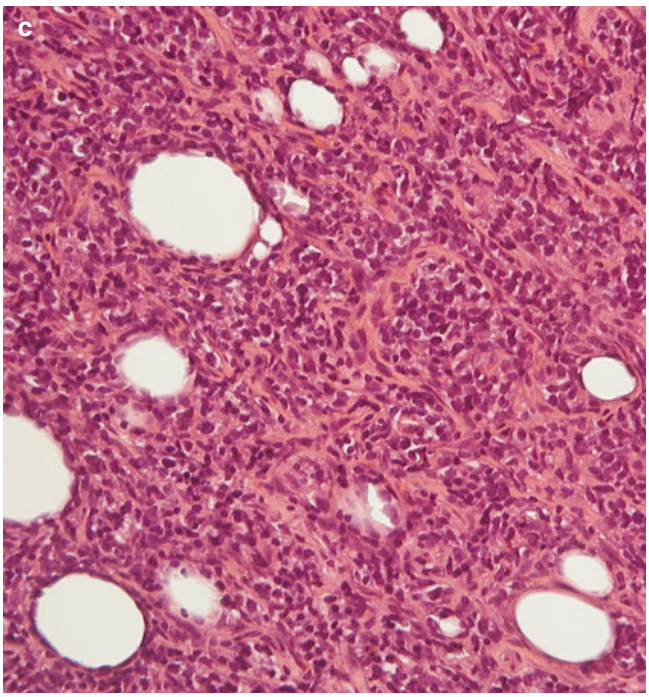

Fig. 12.3 (continued)

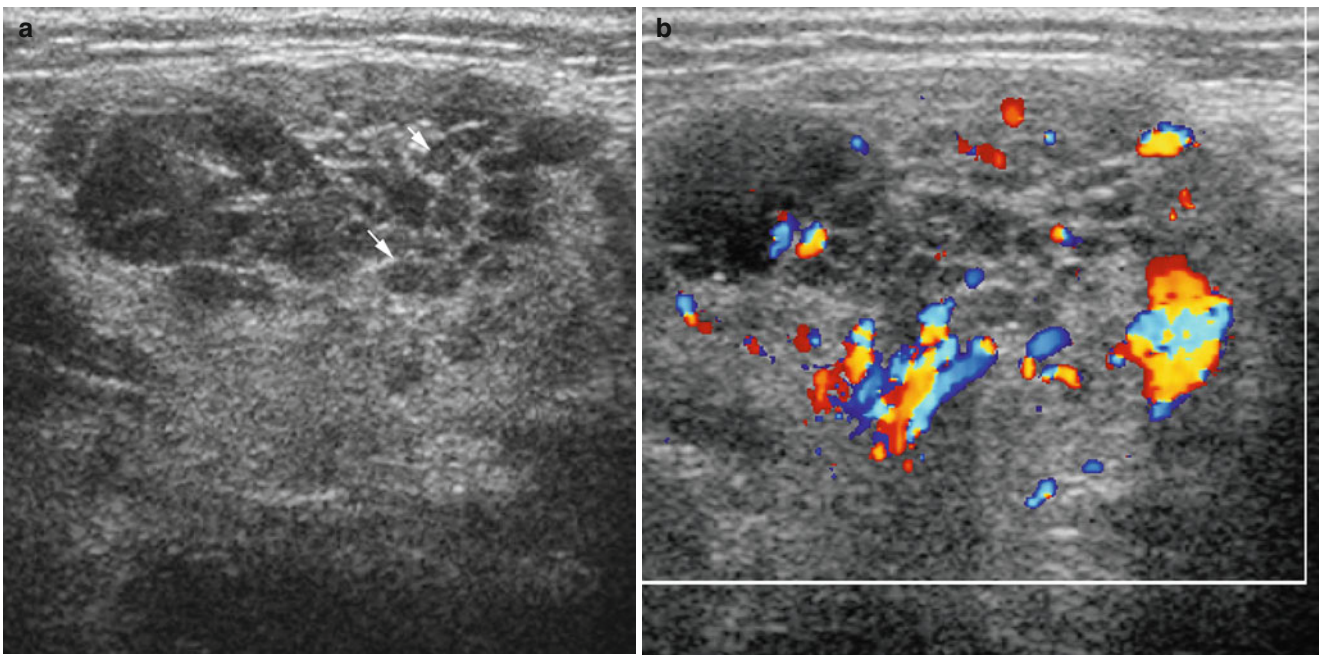

Fig. 12.4 A 53-year-old female patient complaining of swelling over billateral submandibular region. (**a**) Transverse section of left submandibular gland showing multiple small hypoechoic nodular lesions (*arrows*) within the echogenic submandibular gland. (**b**) Color Doppler ultrasound image showing prominent vascularity in left submandibular gland. Biopsy proved small B-cell lymphoma

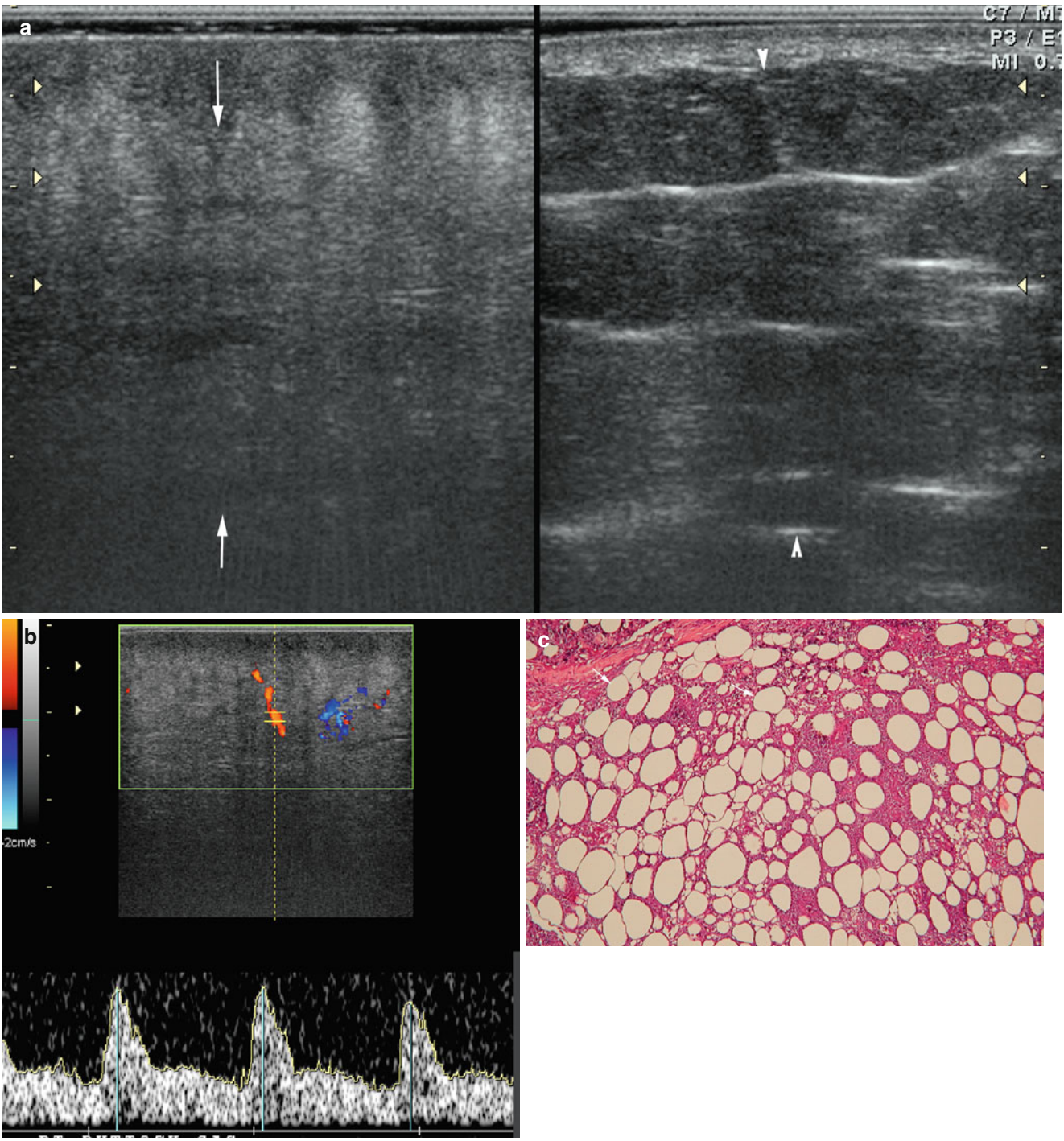

Fig. 12.5 A 25-year-old female patient complaining about painless nodule in right buttock region. (**a**) Grey scale ultrasound image shows homogeneous hyperechoic area (*arrows*) with infiltration in the subcutaneous layer compared with normal hypoechoic subcutaneous fat layer (*arrowheads*, left side). (**b**) Color Doppler ultrasound image shows grade 2 hypervascularity with low resistive index. (**c**) Histology image shows diffuse small lymphocyte infiltration and separated the adipose cells (*arrows*) in the subcutaneous layer. This lesion turned out to be T-cell lymphoma

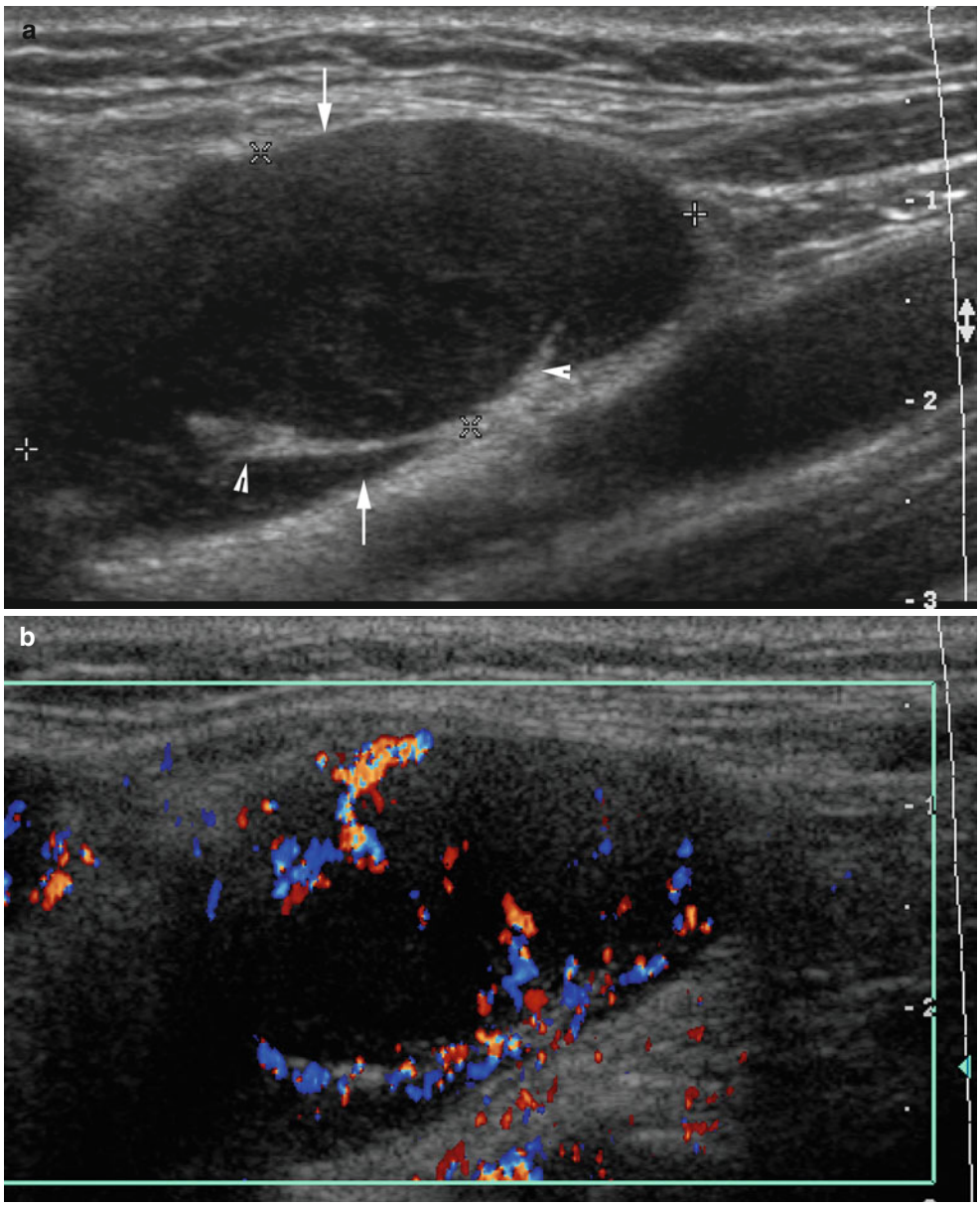

Fig. 12.6 A 57-year-old male patient complaining of firm mass in left neck that is movable for half a year. (**a**) Longitudinal section of left lateral neck showing an ovoid-shaped homogeneous hypoechoic nodule (*arrows*), size approximately 35 × 17 mm with compressed echogenic hilum (*arrowheads*). (**b**) Color Doppler ultrasound image showing vascularity from the hilum and capsule region. This turned out to be diffuse large B-cell lymphoma

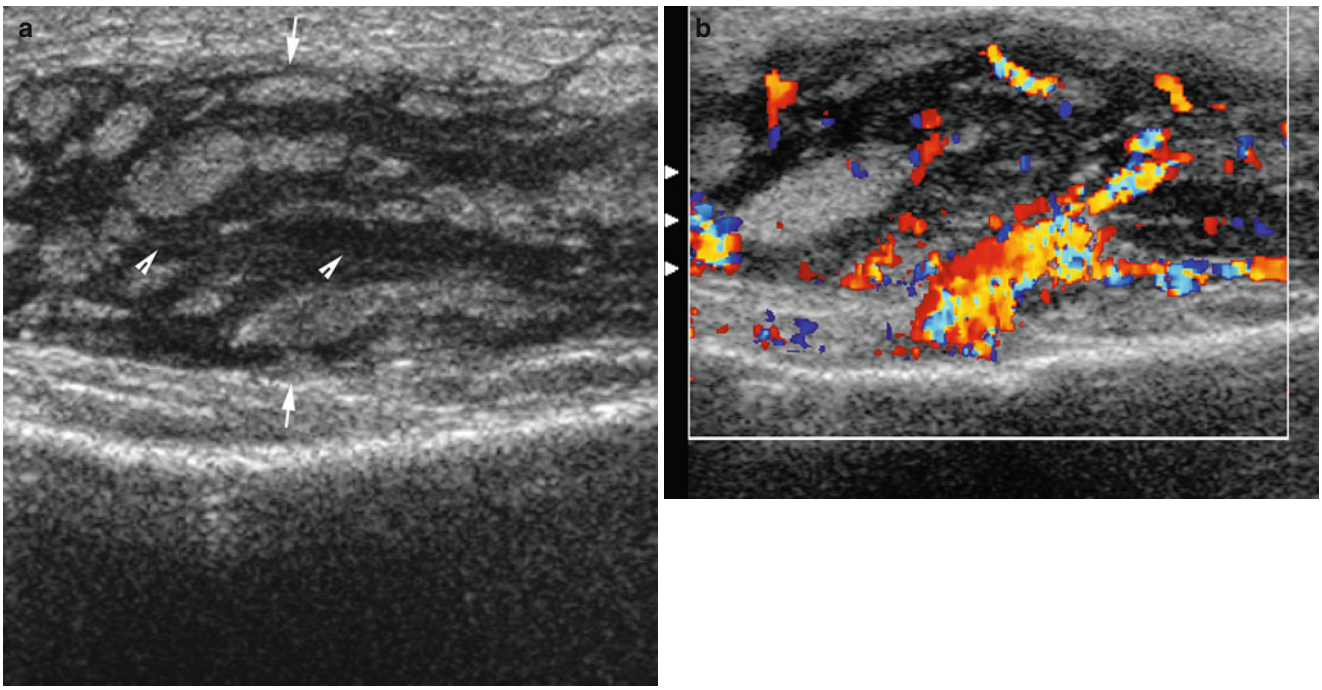

Fig. 12.7 A 72-year-old male patient complaining of painful mass over right anterior superior lower leg for 3 months. (**a**) Grey scale ultrasound image shows variable size homogeneous hyperechoic area (*arrows*) with thickening and hypoechogenicity of the septa (*arrowheads*) in subcutaneous fat layer. (**b**) Color Doppler ultrasound image showed grade 3 hypervascularity in the lesion. Sono-guide biopsy proved B-cell lymphoma

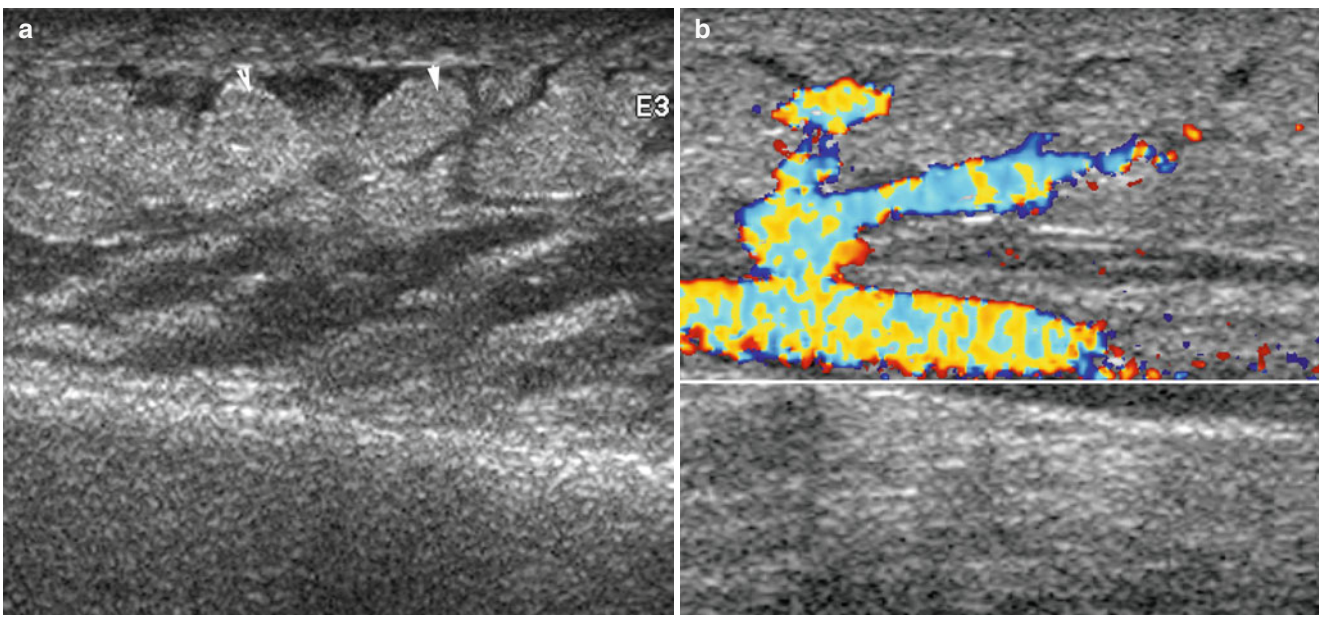

Fig. 12.8 A 58-year-old female patient complaining of bilateral lower leg edema. (**a**) Grey scale ultrasound image showing variable size homogeneous hyperechoic area (*arrowheads*) distributed in the subcutaneous fat layer. (**b**) Color Doppler ultrasound image showing grade 2 hypervascularity. This turned out to be lymphedema

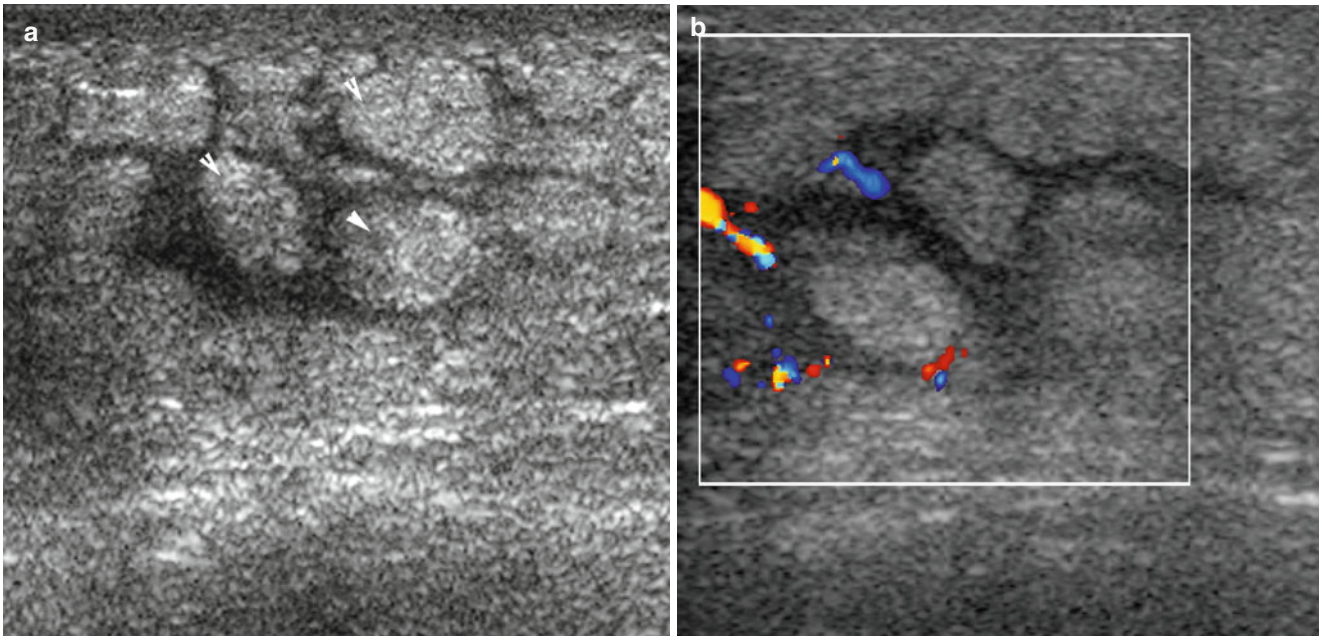

Fig. 12.9 A 57-year-old female patient complaining of palpable mass on left upper quadrant abdominal wall. a Grey scale ultrasound image showing variable size homogeneous hyperechoic nodules (*arrowheads*) distributed in subcutaneous fat layer. (**b**) Color Doppler ultrasound image showing grade 2 hypervascularity. Sono-guided biopsy proved to be inflammatory myofibroblastic tumor

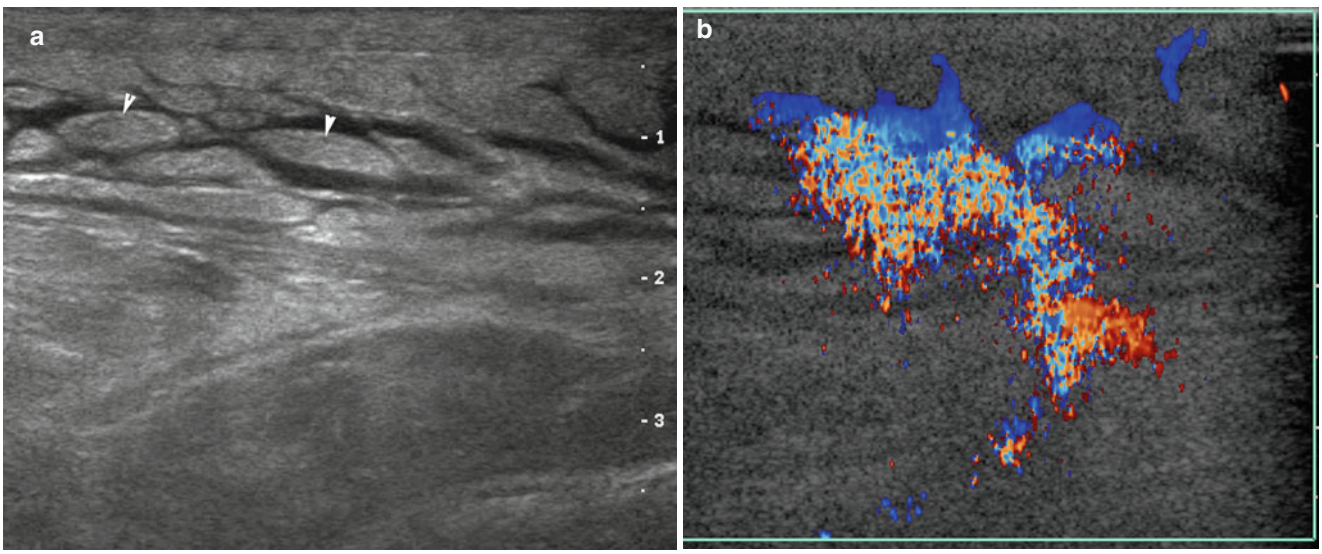

Fig. 12.10 A 40 y/o male patient complaint of painful swelling over left calf. (**a**) Grey scale ultrasonography showing variable size homogeneous hyperechoic nodules (*arrowheads*) distributed in subcutaneous layer. (**b**) Color Doppler ultrasonography showing grade 3 hypervascularity. This turned out to be cellulitis

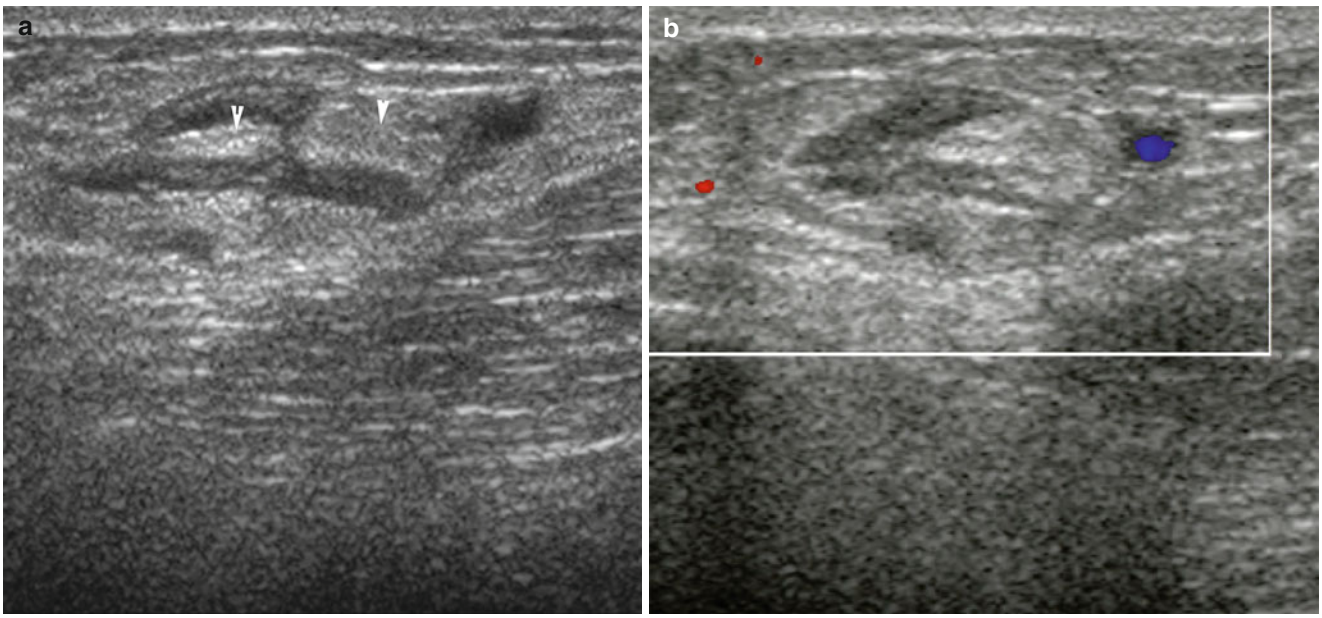

Fig. 12.11 A 27-year-old female patient complaining of painful nodule over RT upper lower leg that gradually enlarged within 2 weeks. (**a**) Grey scale ultrasound image showing heterogeneous echoic nodule (*arrowheads*) with ill-defined margin in RT upper leg subcutaneous layer. (**b**) Color Doppler ultrasound image showing grade 1 vascularity in the lesion. This turned out to be panniculitis

Conclusion

In conclusion, most of the superficial soft-tissue lymphomas were of the nodal or mass type. If the peripheral soft-tissue tumor appears as a nodal-type mass infiltrating the surrounding soft tissue, small nodular disseminated (<1 cm, most <5 mm), or a panniculitis-type lesion without signs of trauma or inflammation, lymphoma should be included in the differential diagnosis. The diagnostic protocol should begin with plain radiography, HRUS, CDUS, and then ultasound-guided biopsy. If malignancy is found, CT or magnetic resonance imaging should be performed for staging before treatment. The prognosis of patients with peripheral soft-tissue lymphoma is usually correlated with the clinical presentation and with tumor morphology, especially in patients with the myositis-type lymphoma and with secondary peripheral soft-tissue lymphoma.

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