A Red Flag in Shades of Grey:
Dedifferentiated Liposarcoma and its Sonographic Appearances

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INTRODUCTION

Soft tissue sarcomas (STSs) are a heterogenous group of rare malignancies of mesenchymal origin (Crombe *et al.,* 2023). They make up ~1% of all adult malignancies and can occur anywhere in the body (Dangoor *et al.,* 2016). In Ireland, an average of 176 cases of STSs are diagnosed per annum and are slightly more common in women than men (Bhatt *et al.,* 2016), with >50 histological STS subtypes possible (Dangoor *et al.,* 2016). Liposarcoma is the most common STS (25%), followed by undifferentiated sarcoma (22%) and leiomyosarcomas (17%) (Crombe *et al.,* 2023). STSs appear to be sporadic, with only specific risk factors currently identified: previous radiation therapy, advancing age and specific genetic disorders (ibid, 2023).

Liposarcoma typically presents as a painless, growing mass in the extremities (Amer *et al.,* 2020). Despite its painless and sometimes indolent nature, liposarcoma has a poor prognosis, with 5-year survival rates estimated at 58% dependent on tumour grade and stage (ibid, 2020). Due to their relative rarity, the diagnostic confounder of common benign entities (100X more common), and misconception that STSs must present with pain and rapid growth, STSs may fail to be recognised (Eastley, Green and Ashford, 2016). Given increasing incidence with age and an aging population, STSs are likely to become more common (ibid, 2016).

For soft tissue masses, ultrasound (US) is the indicated first-line modality (Royal College of Radiologists (RCR), 2024). STS imaging may involve US in the first instance, but masses deep to fascia preclude its use due to inherent limitations (Jacobson *et al.,* 2022). Adequate characterisation is by means of contrast-enhanced MRI (Jacobson *et al.,* 2022; RCR, 2024). However, definitive diagnosis may be limited by non-specific imaging features and difficulty in differentiating low from high grades, with accurate MRI diagnosis pre-biopsy reported in 20-25% of cases (Manaster, 2013).

This case presents a high-grade liposarcoma masquerading as a seemingly more superficial and smaller mass. Despite recognised limitations in deep soft tissue masses, US added value and played an important role in diagnosis for this patient.

PATIENT BACKGROUND

An 82-year-old female presented to A&E with an ~4cm hard, fixed inner thigh mass. The patient noticed the mass three months previously and reported a relatively rapid interval size increase, with no noteworthy pain or history of trauma.

Due to the heterogeneity of STSs, definitive classical symptoms are difficult to summarise; but a lump that is large (>4cm), increasing in size and painless are universally considered red flags (Amer *et al.,* 2020). Initial x-rays were requested to rule out bony involvement (Figure 1).

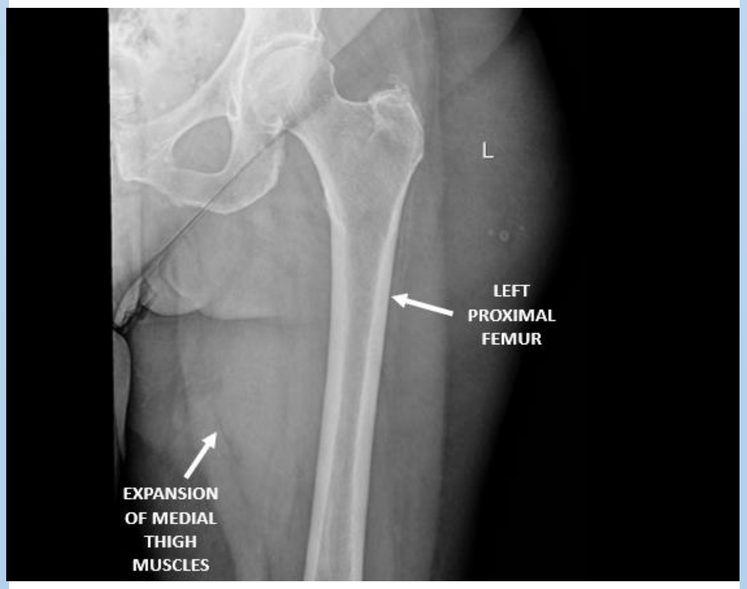

Figure 1. AP proximal femur x-ray demonstrating subtle non-specific expansion of the medial upper thigh muscles without evidence of calcification, fatty density or phlebolith formation.

A focussed US examination of the area of concern was requested by A&E clinicians to further assess.

ULTRASOUND EXAMINATION

The area of concern was scanned using a curvilinear transducer at 5.8MHz, as it was a larger, deeper lesion than what it presented superficially (Jacobson *et al.,* 2022). The patient was consulted for a targeted clinical history, which was documented in the sonographer's report; key in soft-tissue mass sonography (ibid, 2022). The mass was mildly tender on sonopalpation, with its sonographic appearances demonstrated in Figures 2-6.

ULTRASOUND EXAMINATION

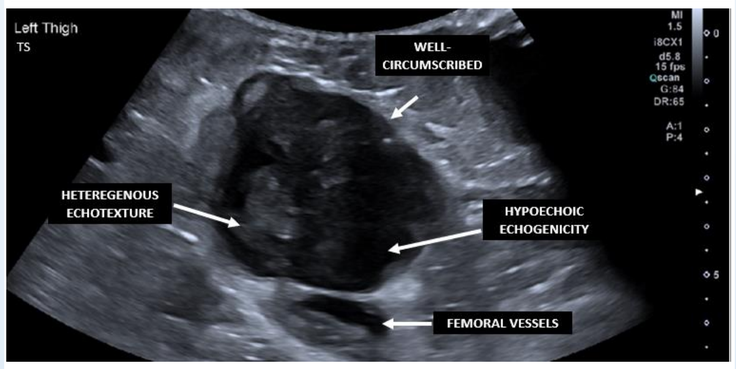

Figure 2: A solid, heterogeneous mass was identified. It was hypoechoic to surrounding muscular structures, well-circumscribed and expansile; typical sonographic findings of STS (Jacobson *et al.,* 2022). The mass was located anterior to the femoral vessels without obvious involvement. Vessel encasement is an independent predictor of local recurrence and has surgical implications (Crombe *et al.,* 2023).

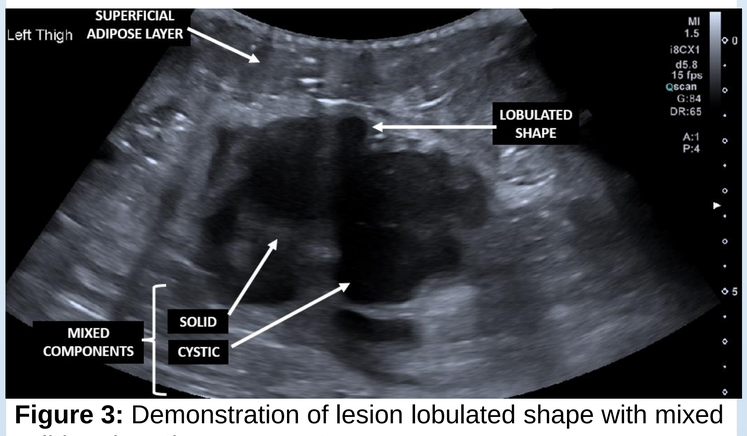

Figure 3: Demonstration of lesion lobulated shape with mixed solid and cystic components.

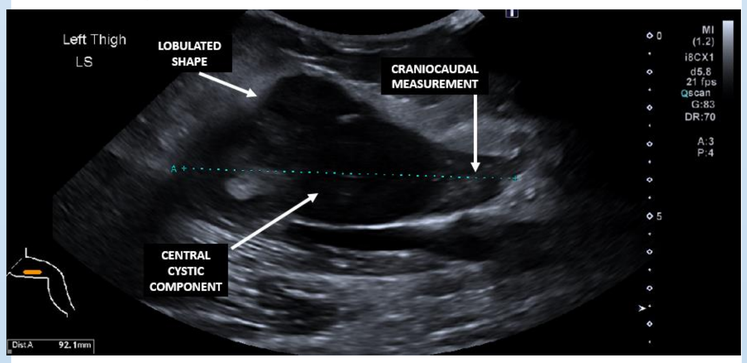

Figure 4: Lesion maximal dimensions were 9.2 x 4.2 x 5.6 cm (CC, AP, TS): concerningly larger than it appeared superficially. A body marker indicated the area of concern: the proximal to mid-thigh; a location typical of liposarcomas (Jacobson *et al.,* 2022). As rates of local recurrence are dependent on tumour size, accurate measurements are crucial (Crombe *et al.,* 2023). The central cystic component was concerning for malignant necrosis secondary to rapid lesion growth (Jacobson *et al.,* 2022); a common finding in large, high-grade STS (Dangoor *et al.,* 2016).

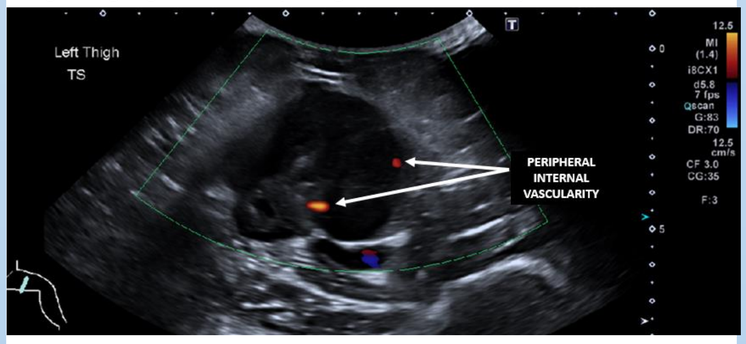

Figure 5: Colour Doppler interrogation of the lesion with reduced PRF for increased sensitivity to flow (12.5cm/s) demonstrated concerning internal vascularity, with a vascularised discrete lesion indicating its neoplastic nature (Jacobson *et al.,* 2022).

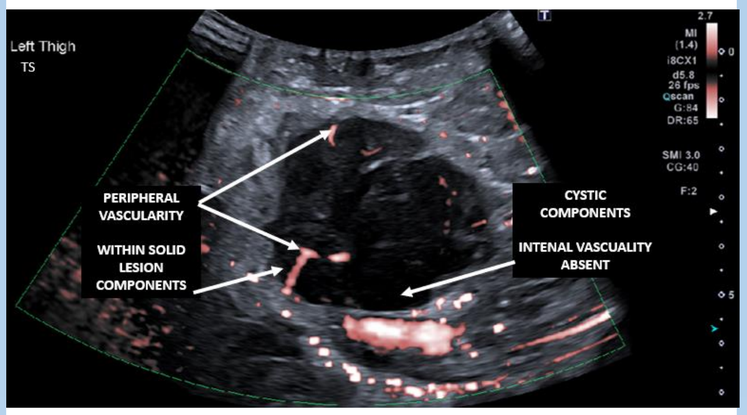

Figure 6: The mass was interrogated using Superb Microvascular Imaging (SMVI), as it is sensitive to lower velocity flow rates. Internal vascularity was identified; most evident in solid, peripheral components, concerning for malignant angiogenesis (Toprak *et al.,* 2014).

A sagittal cine loop demonstrated the lesion relative to surrounding structures and was deemed to be within the anterior muscle compartment. Sonographic appearances combined with patient history were noted as highly concerning for soft tissue neoplasm. Urgent contrast-enhanced MRI, specialist referral, and biopsy were advised.

SUBSEQUENT IMAGING

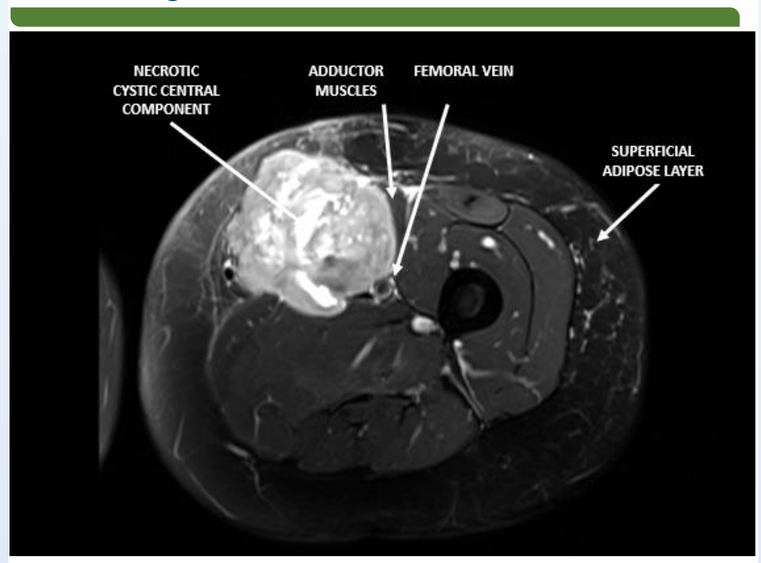

Figure 7: Axial T2-weighted MRI of left femur with fat saturation. A central fluid component, deemed likely necrotic, was noted. Intra-tumoral necrotic signal and heterogeneity on T2WI predicts high probability of grades 2 and 3 STS (Crombe *et al.,* 2023). The lesion was centred on the adductor muscles and now compressed the femoral vein posteriorly without evidence of thrombosis or osseous involvement.

Further MRI sequences demonstrated a large 12 x 6.5 x 6.5 cm soft tissue lesion that enhanced post-gadolinium administration, most marked peripherally. The interval increase in size may be due to modality discrepancies, evolving lesion expansion over four weeks, or both. The above was again consistent with a large soft-tissue neoplasm.

DIAGNOSIS & TREATMENT

An urgent core biopsy was performed. Histological analysis revealed rapid transition to poorly differentiated neoplastic tissue composed of pleomorphic, round, and spindled cells, which replaced and entrapped local adipocytes with a brisk mitotic rate. Adjacent fat necrosis was noted. Using immunochemistry, tissue was positive for MDM2 protein amplification. These findings were characteristic of high-grade dedifferentiated liposarcoma (Crombe *et al.,* 2023).

At the time of writing, the patient is awaiting staging CT-TAP to guide treatment. Mainstay treatment for non-metastatic liposarcoma involves limb-sparing en-bloc surgical resection aiming for clear margins and adjuvant radiation therapy (Amer *et al.,* 2020). Adjuvant chemotherapy is typically of limited use due to inherent tumour chemo-resistance but may be utilised in context of pulmonary metastasis. Unfortunately, high-grade dedifferentiated liposarcoma has a poor estimated median survival of 48 months (ibid, 2020).

CONCLUSION

US is considered the first line imaging modality for the assessment of soft-tissue masses. However, its utility in lesions deep to the fascia of the extremities is limited. Although not capable of the total lesion characterisation of contrast-enhanced MRI, US allowed identification of highly suspicious lesion features and established significant clinical concern. US added value in the management of this liposarcoma in a safe, rapid, and cost-effective manner.

Deep malignancies may masquerade as being more superficial and can present to US. Due to heterogeneity of STSs, their relative rarity and common benign confounders, sonographers must be aware of clinical and sonographic red flags and acknowledge the value of a targeted clinical history.

Clinical & Sonographic Red Flags for Liposarcoma

M	**M**argins: often ill-defined, infiltrative	**R**	**R**apidly growing, non-mobile, firm, focal mass (often painless)	**F**	**F**ascia: deep to it
E	**E**chotexture: heterogenous: solid & cystic	**E**	**E**chogenicity: hypoechoic	**L**	**L**ung metastasis: chest pain, haemoptysis, SOB
D	**D**oppler: internal vascularity	**D**	**D**imensions: >5cm	**A**	**A**ge (>60 years)
				G	**G**et CE-MRI & biopsy!

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