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A rare case of primary muscular non-Hodgkin's lymphoma and a review of how imaging can assist in its diagnosis

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ABSTRACT Primary malignant non-Hodgkin's lymphoma of the muscle is rare. Currently, imaging tools are necessary to enable its diagnosis. Herein, we report the case of a patient who presented with swelling and pain in the right thigh and pelvis. Computed tomography findings revealed isodense masses in the patient's right thigh and left iliacus muscle, leading to the initial diagnosis of either primary muscular lymphoma or soft tissue sarcoma. Further investigation with magnetic resonance imaging was done, and a biopsy was performed. The ensuing histological diagnosis was that of diffuse large B-cell lymphoma.

Keywords: primary, muscular lymphoma, imaging, diagnosis

INTRODUCTION

The extranodal type of non-Hodgkin's lymphoma is found in about 20%–30% of patients,[1] and primary muscular lymphoma is a rare disease that usually involves the lower extremities.[2] The presenting signs and symptoms may involve swelling, the presence of a mass, pain, or all three. The clinical diagnosis is nonspecific and the differential diagnosis includes tumours, haematomas or infections. While radiological modalities such as sonography, computed tomography (CT) and magnetic resonance (MR) imaging aid in the diagnosis of this disease, diagnosis using these modalities is not conclusive. A biopsy is necessary for a final and conclusive diagnosis. In this report, we describe a case of primary muscular non-Hodgkin's lymphoma encountered in our department, as well as review the imaging modalities that aid in the diagnosis of this rare disease.

CASE REPORT

A 45-year-old Thai woman presented to our hospital with a one-year and eight-month history of tenderness in her right thigh. She had received rehabilitative treatment, but continued to experience progressive muscular tenderness in her right thigh. One month prior to her presentation to our hospital, she experienced pain in her pelvis and discovered that her right thigh was larger than her left thigh. Physical examination of the patient was unremarkable, except for some swelling and the presence of a soft tissue mass in her right thigh. CT revealed enlargement of the patient's left pelvic, left buttock and right thigh muscles, as well as enhancement after contrast media injection (Fig. 1). The initial diagnosis was sarcoma, with a differential diagnosis of lymphoma. To evaluate the extent of the condition, the patient was referred to the Radiology Department for MR imaging, as well as to obtain a tissue diagnosis via ultrasonography-guided biopsy. The MR images revealed slightly hyperintense T1-weighted and T2-weighted masses involving multiple groups of muscles, including the right vastus lateralis, vastus intermedius, vastus medialis, adductor magnus, adductor longus, adductor brevis, pectineus, gluteus maximus, left iliacus, and gluteus medius and minimus muscles. These masses showed inhomogeneous

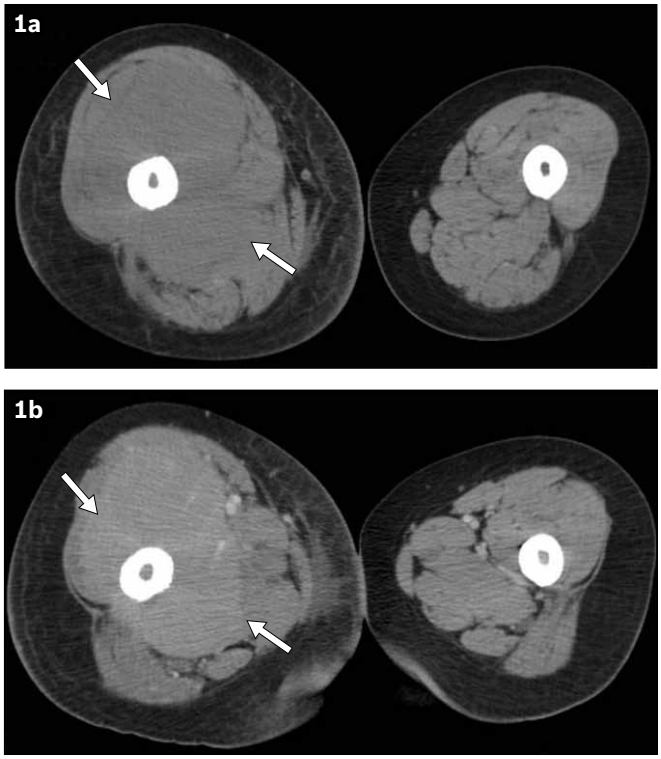

Fig. 1 CT images (a) without and (b) with contrast both show diffuse enlargement of the muscles in the right thigh, as well as homogeneous enhancement after contrast media injection (arrows).

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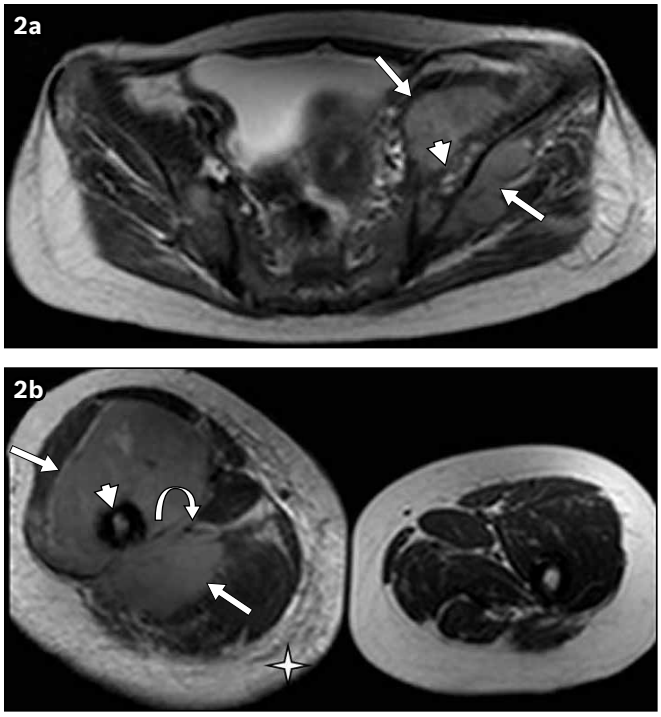

Fig. 2 T2-W MR images of the (a) pelvis and (b) thighs reveal hyperintense masses involving multiple groups of muscles in the left pelvis, left buttock and right thigh (arrows). Neurovascular bundle (curved arrows) and bone marrow (arrow heads) involvements, as well as skin thickening (star), are also observed.

enhancement after gadolinium administration. Neurovascular bundle involvement of the right thigh was also observed along with bone marrow involvement of the adjacent right femur. Skin thickening in the right thigh was also detected (Fig. 2). The MR findings favoured a diagnosis of muscular lymphoma, thus an ultrasonography-guided tissue biopsy was performed on the right thigh. Histological examination yielded a diagnosis of diffuse large B-cell lymphoma (Fig. 3).

The patient's condition was evaluated by means of a full haematological investigation, coupled with staging. Abdominal CT revealed a small lymphomatous nodule in the right kidney (Fig. 4) and bone scan showed increased uptake in the right femur. Other systemic and laboratory investigations (i.e. bone marrow biopsy, CT of the chest and brain, complete blood count, serum electrolytes, serum immunoglobulin, lactate dehydrogenase level, and liver function test) were negative. The malignancy was categorised as stage IV, according to the Ann Arbor system.[2] The patient underwent chemotherapy using the R-CHOP (rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin and prednisolone) regimen, and radiation therapy on the right femur to reduce bone pain. MR imaging after the eighth R-CHOP session revealed complete regression of the tumour, including all previous muscular, right femur and right kidney involvements (Fig. 5). However, the patient developed a right femur fracture, which was treated using an intramedullary nail. At the time of writing (i.e. 36 months following the patient's presentation to the hospital), the patient's lymphoma was in remission.

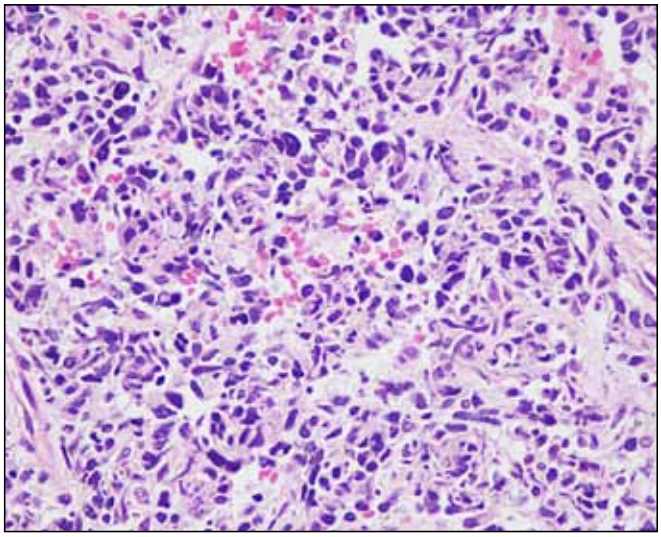

Fig. 3 Photomicrograph shows proliferation of large pleomorphic cells (Haematoxylin & eosin, × 100).

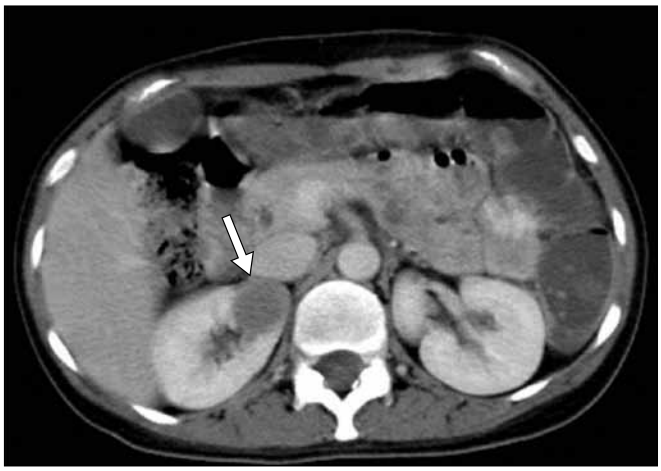

Fig. 4 Abdominal CT performed for staging shows the presence of a small lymphomatous nodule in the right kidney (arrow).

DISCUSSION

Primary extranodal lymphoma usually occurs in the central nervous system, gastrointestinal tract, respiratory system, skeletal system, skin and Waldeyer's ring.[3] Muscular lymphoma is extremely rare. In a study by Kransdorf, only 472 out of 38,484 (1.2%) patients in a 10-year period were reported to have extremity soft tissue lymphoma.[4] A Mayo clinic study found that only 8 out of 7,000 (0.1%) lymphoma cases involved muscular lymphoma in the extremities.[5] In a report by Glass et al, primary muscular lymphoma accounted for 0.5% of extranodal lymphomas.[6] Non-Hodgkin's lymphoma was reported to occur about 60 times more often in immunocompromised hosts (e.g. patients infected with human immunodeficiency virus; patients of an older age; patients with no prior history of receiving highly active antiretroviral therapy; and patients with a low CD4 count, particularly those with a count of less than 100 cells/mL) than in normal hosts, and a lymphomatous involvement of muscles was found in about 8.8% of cases.[7]

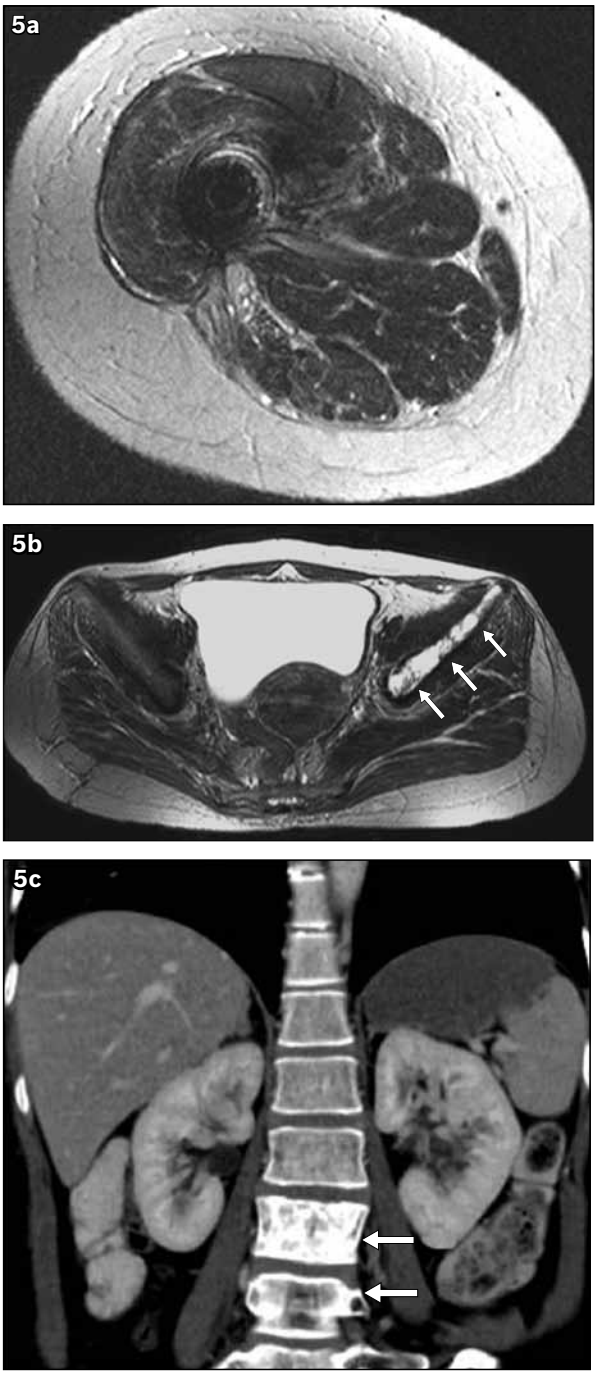

Fig. 5 (a & b) T2-W MR and (c) coronal CT images after treatment reveal complete regression of the tumour, including all previous muscular, right femur and right kidney involvements. Note the postradiation effect at the lower lumbar spine and left iliac bone (arrows).

Lymphomatous involvement of muscles typically occurs via one of three pathways.[8,9] Dissemination of the disease via the haematogenous or lymphatic pathway is classical. Another pathway occurs via extension from adjacent organs such as the bones or lymph nodes. The third pathway – as a primary extranodal disease – is very rare. The clinical symptoms of muscular lymphoma may include painful or painless enlargement of involved muscles.[9] The most common site of muscular involvement is the lower extremities, accounting for 50% of all reported cases.[2] A study by Suresh et al found lower extremity involvement in 13 of 24 (54%) cases of

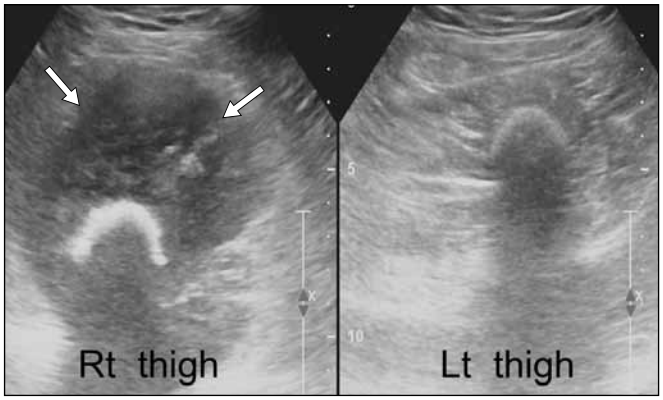

Fig. 6 Sonographic images of the right and left thighs show ill-defined hypoechoic masses, coarsened fibroadipose septa and swelling of muscle bundles (arrows) in the right thigh, as compared to the left thigh. Lt: left; Rt: right

primary muscular lymphoma.[8] One factor that may be related to the site of involvement is previous sites of injury. Primary muscular lymphoma occurring after leg injury,[10,11] near needle injected sites[12] and in homosexual men's rectums[13] have been reported. Since the lower extremities are vulnerable to injury, this may suggest a relationship between muscular lymphoma and mechanical stimulation.[2]

Imaging tools for the diagnosis of muscle lymphoma have been mentioned in several reports. Conventional radiography, which is usually unremarkable, may show soft tissue swelling without bone abnormality.[9,14] MR imaging is better than conventional radiography in detecting bone involvement due to its high sensitivity.[14] In cases of secondary bone involvement, radiography shows mixed osteolytic and osteoblastic lesions. However, these radiographic findings are not specific for the diagnosis of muscular lymphoma.

The sonographic findings of extranodal soft tissue lymphoma show ill-defined hypoechoic masses. For intramuscular lymphoma, the findings on ultrasonography usually only reveal coarsened fibroadipose septa and swelling of muscle bundles,[15] as was the case with our patient (Fig. 6). In other words, ultrasonography is a nonspecific imaging tool for the diagnosis of this disease.

Using CT, intramuscular lymphoma appears as a hypoattenuated or isoattenuated mass in the muscle. Varying enhancements will be observed after contrast administration, including enhancements that are similar to those observed in the muscle (i.e. vivid homogeneous or heterogeneous enhancements).[8] It is also possible to only observe the presence of a focal mass in the muscle or diffuse enlargement of the involved muscle, with or without loss of the fat plane.[14] As the findings from CT images are nonspecific, we are of the opinion that CT should only be used as an initial investigation and staging tool, and not for the diagnosis of muscular lymphoma. This is in agreement with most of the literature on muscular lymphoma.[8,9,14]

MR imaging is better than CT in the evaluation of soft tissue tumours as MR imaging offers higher soft tissue contrast

and multiplanar imaging view.[4] MR imaging is also superior to CT as it enables the evaluation of tumour extension, adjacent structure involvement and bone marrow condition. The signal intensity of intramuscular lymphoma may vary – it can be slightly hypointense, isointense and/or hyperintense relative to the muscle on a T1-weighted spin-echo image. On a T2-weighted spin-echo, the lymphoma is hyperintense relative to the muscle. On a postcontrast image, intramuscular lymphoma can be homogeneously or heterogeneously enhanced. However, findings of signal intensity and enhancement on MR imaging are nonspecific for intramuscular lymphoma. Several previous studies[8,9] have discussed some important MR imaging findings that may suggest that this disease is characterised by subcutaneous tissue involvement, adjacent skin thickening and neurovascular bundle involvement. Another very important finding is the involvement of more than one muscle compartment, which occurs naturally due to the infiltrative spreading of individual malignant cells, resulting in growth without respect to fascial boundaries.[8,9] These important findings were also detected in our patient and served as clues to assist the radiologist in excluding soft tissue sarcoma and diagnosing intramuscular lymphoma.

Recently, integrated positron emission tomography-CT (PET-CT) has been used in clinical practice. The lesions are demonstrated on fused PET-CT images using metabolic status and anatomical data. However, PET-CT does not have a role in the primary diagnosis of lymphoma because fluorodeoxy-glucose (FDG), which is used in PET, is associated with a false-positive uptake. Positive uptake can be seen in active inflammatory or infectious processes as a result of macrophage activity. False-negative results related to malignant neoplasms with low metabolic activity or tumours smaller than 1.0 cm in diameter also occur.[16] A study by Alavi et al reported a 13% false-positive rate and a 9% false-negative FDG uptake rate for cancer.[17] However, PET-CT has been widely applied in tumour staging and the evaluation of treatment response in many cancers, including malignant lymphoma.

Although MR imaging can assist in the diagnosis of muscular lymphoma, histological diagnosis is still necessary to avoid inappropriate surgery, as lymphomas respond well to chemotherapy. Once lymphoma is diagnosed, staging of the disease should be performed using CT of the neck, chest, abdomen and pelvis.

In conclusion, primary muscular lymphoma is rare, and MR imaging is an advantageous modality that assists in the diagnosis of this disease. The MR findings that are suggestive of primary muscular lymphoma include involvement of the multimuscular compartments, subcutaneous tissue and neurovascular bundle, and adjacent skin thickening. Tissue diagnosis is still crucial for a definitive diagnosis.

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