CASE REPORT

Abundant macroscopic fat in intra-abdominal lymph nodes involved in the course of a patient with chronic lymphocytic leukaemia: presentation of imaging findings with biopsy correlation

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ABSTRACT. The presence of a small amount of macroscopic fat is not unusual in the hilar region of normal lymph nodes. However, abundant replacement of the lymph node with fat is highly unusual and may appear as metastatic lymph node disease in the course of fat-predominant liposarcomas or in the case of coeliac disease complicated by cavitating lymph node syndrome. In this case report, a patient with chronic lymphocytic leukaemia/small lymphocytic lymphoma who demonstrated an increasing abundance of macroscopic fat in the diseased lymph nodes is presented. To the best of our knowledge, the imaging findings of abundant fat in lymph nodes in the course of lymphoma have not been reported before. The presence of macroscopic fat may be seen in the presence of actively involved lymph nodes in the presence of chronic lymphocytic leukaemia.

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Enlargement of abdominal lymph nodes in patients with lymphoma is common, and appropriate staging and treatment is dependent on detection and correct localisation on imaging. We present the radiographic and histopathological findings in a patient with chronic lymphocytic leukaemia/small lymphocytic lymphoma (CLL/SLL) who presented with bulky and enlarging macroscopic fat in involved, enlarged intra-abdominal lymph nodes. The presence of large amounts of fat in abdominal lymph nodes is rare and, to the best of our knowledge, has not been reported in the setting of lymphoma.

Case report

A 47-year-old afebrile male patient presented for surveillance of CLL/SLL. He presented 5 years earlier with fatigue, painless enlargement of cervical lymph nodes and elevated white blood cell counts. Diagnosis was confirmed via bone-marrow biopsy and flow cytometry. The patient completed appropriate cycles of rituximab (Rituxan; Genentech, San Francisco, CA)/fludarabine (Fludara; Bayer Schering Pharma AG, Berlin, Germany) and Rituximab/Cyclophosphamide (Endoxan; Baxter, Deerfield, IL)/vincristine (Oncovin; Eli Lilly and Company, Indianapolis, IN)/prednisolone-based che-

motherapy. Chemotherapy was stopped after 38 months when blood counts normalised and the patient was free of symptoms, and surveillance protocols were then initiated. Review of the CT scans at the time of the original diagnosis showed enlarged intra-abdominal lymph nodes (Figure 1). Subsequent scans showed progressive enlargement and increasing areas of intranodular macroscopic fat. Based on clinical improvement and a negative workup for additional malignancies, findings were interpreted as benign.

At the time of presentation (13 months surveillance), abdominal CT scans demonstrated progressive enlargement and increased fatty infiltration in multiple lymph nodes (Figure 2). The degree of progressive fatty infiltration triggered a percutaneous biopsy of the largest lymph node to rule out atypical presentation of relapse or an additional malignancy (*i.e.* liposarcoma). The biopsy was done under CT guidance and multiple core and fine needle aspiration samples were obtained from the non-fatty portions of the lesion. Histological examination showed a diffuse monomorphic lymphoid infiltrate adjacent to benign fibroadipose tissue (Figure 3a). High-power examination of the infiltrate demonstrated sheets of monomorphic small lymphocytes (Figure 3b). Immunophenotyping flow cytometry confirmed that the tumour tissue was identical to the prior diagnostic samples. This immunophenotype is identical to the patient's prior flow cytometric results and is diagnostic of CLL/SLL. There was no evidence of additional malignancies or sarcoma.

To further delineate the biological properties of this fatty infiltration, 18F-fluodeoxyglucose (FDG) positron emission tomography (PET) imaging was performed and

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Figure 1. Image from patient's first intravenous contrast-enhanced CT scan at the time of the diagnosis demonstrating the largest intra-abdominal adenopathy (arrow) below the level of the aortic bifurcation.

showed low FDG uptake in all of the intra-abdominal lymph nodes. These features are consistent with an overall hypometabolic status of fatty and lymphoid infiltrates in these nodes. After tissue confirmation of CLL/SLL, the patient was started on chemotherapy 4 months after the biopsy. He was still on chemotherapy 8 months after the biopsy but was otherwise doing well with stable disease.

Discussion

Detection of enlarged conglomerated lymph nodes in multiple body compartments, including the abdomen, is a common finding in various subtypes of lymphoma. Both Hodgkin's lymphoma and non-Hodgkin's lymphoma (NHL) may cause extensive intra-abdominal lymphadenopathy, although this finding is more common in patients with NHL [1]. Intra-abdominal lymphoma classically presents in the mesentery as massively enlarged and conglomerated lymph nodes without infiltration of normal structures. Associated symptoms are explained by the local mass effect and a highly specific radiological presentation for mesenteric lymphoma is the so-called "sandwich sign" [2]. This mnemonic refers to the cross-sectional imaging appearance of homogeneous soft-tissue masses ("the bread") around mesenteric fat, arteries and veins ("the filling").

Abdominal involvement in lymphoma patients is highly variable. Solid organ involvement and lymphadenopathy may both be detected in the same patient [1]. In solid organ involvement, focal lymphomatous lesions generally tend to enhance less than the involved organ. Progressive size increases may outgrow the vascular supply and central areas of necrosis may be seen [1]. Calcification in lymph nodes and solid organ lesions is rare at the time of diagnosis before treatment of lymphoma unless associated with amyloidosis. Almost all of the solid or hollow organs in the abdomen may be involved by the disease with varying frequencies [1]. Massive lymphadenopathy is one of the most common features of CLL, although not specific for this subtype. The size and number of the lymph nodes depend on the patient's clinical status and treatment.

The presence of a small amount of macroscopic fat is a well-known imaging feature in the hilum of normal lymph nodes in the abdomen and elsewhere. However, exaggerated presence of fat in a lymph node is unusual and rarely seen. The best-known example of the presence of macroscopic fat tissue in a lymph node is the cavitating lymph node syndrome in the course of coeliac disease [3]. The classic finding in this disease is a fat-fluid level, and fat can be easily detected with CT or MRI. However, the absence of retroperitoneal lymphadenopathy, the relatively small size of the affected lymph nodes or alternatively the lack of coeliac disease in the patient's history typically allows differentiation of coeliac disease from mesenteric involvement by lymphoma. The patient was also re-evaluated for a potential occult malignancy like liposarcoma, but the lack of other malignancies on re-evaluation and the long-term follow-up was deemed to be reassuring for the absence of any additional malignancy.

Low-attenuation mesenteric lymphadenopathy on CT can also be seen in mycobacterial infections, Whipple's disease and some necrotic metastases, including germ cell tumours. However, macroscopic fat has not been reported before in these patients. Intestinal malignancies may also cause low-attenuating lymphadenopathies but they are rarely as extensive as seen in lymphoma, and the primary lesion is usually well visualised or becomes clinically manifest even if there is extensive lymphadenopathy. Again, coeliac disease is another consideration with its unique appearance of fat-fluid levels in the lymph nodes on CT when it is associated with mesenteric cavitating lymph node syndrome, as described above.

Figure 2. CT scan in April 2010. (a) Axial CT image showed the progressively enlarging lymph node (same lymph node as demonstrated in Figure 1) with increasing fat content (arrows). (b) Same lymph node (arrowheads) and other macroscopic fat containing lymph nodes (arrows) in the abdomen on a coronal reformatted image.

(a)

(b)

Figure 3. Histopathology. (a) Low-power view shows benign fibroadipose tissue adjacent to lymphatic tissue. The lymph node architecture is effaced and there are no proliferation centres ($\times 20$). (b) High-power view shows sheets of monotonous small lymphocytes with rounded nuclei, clumped chromatin, scant cytoplasm, inconspicuous to small nucleoli, and infrequent mitotic figures. Larger lymphoid cells (prolymphocytes/paraimmunoblasts) or proliferation centres are not present ($\times 200$).

To the best of our knowledge, enlarging macroscopic fatty areas in involved abdominal lymph nodes of lymphoma patients have not been described before. We are aware of one similar report on a rapidly enlarging auxiliary lymph node in a patient with large cell (histiocytic) diffuse lymphoma mimicking lymphoma relapse [4]. However, the lymphoma in our patient is biologically distinct and active disease was detected on histopathology in contrast to this previously reported patient. Specifically, CLL represents the most common type of leukaemia, typically affects the bone marrow and presents with marked peripheral blood involvement (e.g. $>5 \times 10^9 \text{ l}^{-1}$ lymphocytes). In contrast, SLL affects primarily lymph nodes. Histologically and immunophenotypically, SLL and CLL are identical and represent extremes of a highly variable B-cell malignancy [5]. CLL mostly occurs in older people; however, it can occur in any age group, as in this case. Typically, the disease takes months to years to progress and the cells are produced at much higher rates than normal. This chronic nature of the disease requires tailoring of therapy to ensure maximum effectiveness, which is typically assessed via the individual patient's physical status.

The pathophysiology of the unusual appearance of the lymph nodes in this case remains unclear. In general, white fat in abdominal and retroperitoneal lymph nodes is not rare [6]; however, the presentation as a mass-like lesion is very uncommon [7]. Given that fat in lymph nodes can undergo considerable hyperplasia in obese patients (referred to as lipolymph nodes), it is safe to assume that external triggers can disturb an otherwise dynamically balanced coexistence of adipocytes and lymphatic elements in lymph nodes [7]. Interestingly, we noted that in both reported cases the fatty areas gradually developed after completion of therapy. Based on the well-established association of fatty infiltration with atrophy described in a variety of organs [8–11], we propose that there may be a relation between therapy-induced atrophy of lymphatic tissues (i.e. lymphoma) and subsequent expansion of the fibroadipose elements. The propensity of adipocytes to fill a vacuum, in a sense, left by an atrophic process is well established [12] and referred to as *Vakutwuucherung* [13] or *adipositas ex vacuo* [14, 15]. Despite these sound speculations, we cannot explain the seemingly rare presentation of such drastic effects in an otherwise well-established disease entity.

Conclusion

We believe that progressively enlarging macroscopic fat densities may be observed in enlarging intra-abdominal lymph nodes of patients with lymphoma, the presence of which does not necessarily indicate another associated disease. Irrespectively, we advocate meticulous clinical evaluation before attributing benignity in the setting of lymphoma.

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