CASE REPORT

Subcutaneous panniculitis-like T-cell lymphoma with breast involvement: functional and morphological imaging findings

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ABSTRACT. Panniculitis-like T-cell lymphoma is a very uncommon subtype of cutaneous T-cell lymphomas. In this case report, we describe the morphological (CT and MRI) and functional (¹⁸F-FDG-PET and bone scan) imaging findings in a 35-year-old patient who suffered from slowly progressing multiple subcutaneous lesions caused by this rare disease.

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According to the World Health Organization–European Organization for Research and Treatment of Cancer (WHO–EORTC) classification, subcutaneous panniculitis-like T-cell lymphomas (SPTCLs) belong to the group of cutaneous T-cell and natural killer (NK)-cell lymphomas [1]. Less than 1% of all non-Hodgkin lymphomas (NHLs) are SPTCLs. Recent studies differentiate distinct subtypes of SPTCL each with a different prognosis [2]. Only a few reports describe the imaging of primary cutaneous T-cell lymphomas [3–8], even fewer with the imaging of subcutaneous involvement in SPTCLs [4, 9–11]. In this case report, we describe panniculitis-like T-cell lymphoma as a very rare cause of unclear subcutaneous soft-tissue indurations. We detail the morphological and functional CT, MRI, ¹⁸F-FDG-PET and bone scan findings relating to multiple panniculitic lesions in a 35-year-old female patient suffering from this uncommon subgroup of lymphoma.

Case report

A 35-year-old woman presented at the dermatology clinic complaining of an induration of the right breast that had appeared 3 weeks before and prompted her to visit a doctor. She reported that additional partially painful lumps and indurations beneath her skin had been present for 3 years. They were located in her upper arms and buttocks, and grew slowly. Furthermore, walking fast induced pain in her shin bones and lower legs.

A subcutaneous, poorly defined nodule (5 × 4 cm) was palpable in her right breast. Examination of her upper arms revealed multiple additional subcutaneous

plaques and nodules of sizes up to 2 cm. She had plaque-like subcutaneous indurations (12 × 7 cm) on both flanks. There were no ulcerated lesions. The patient had a strongly accelerated erythrocyte sedimentation rate (ESR; 70/80), mild anaemia (4.0 erythrocytes/μl) and a moderate increase in lactate dehydrogenase (LDH; 306 U/l). The other serum parameters and blood counts did not indicate abnormal pathological findings. The patient tested negative for HIV and syphilis.

Chest radiography and ultrasound of the abdomen were normal (not shown). CT of the neck, thorax and abdomen demonstrated normal lymph nodes and no visceral abnormality. The lesion in the right breast showed distinct CT contrast enhancement (Figure 1a). Widespread, contrast-enhancing subcutaneous plaques and nodules, as well as thickening of the skin, were confirmed and corresponded well with the clinical findings described above (Figure 1b). MRI of the right upper arm (Figure 2a, b) depicted low signal intensity on *T*₁ weighted images and strong homogeneous enhancement within the regions of the clinically palpable plaques after administration of contrast material. The muscles and bones were not affected. Because the patient complained of pain in her shin bones, a three-phase bone scan was performed. In the blood pool phase, focal tracer accumulation was found in the right breast and at the cutaneous level of both upper arms. A conspicuous diffuse bilateral accumulation of the tracer was also found in the dorsal and lateral subcutaneous tissue cranial to the iliac crests. The hyperaemic areas corresponded well with the CT findings of subcutaneous plaques and nodules (Figures 1b and 3a). The lower legs showed no abnormality. In the static phase, no skeletal pathology was detected (Figure 3b).

For further staging and to display the metabolism of the lesions, as well as for possible future therapy-response monitoring, FDG-PET was performed (Figure 4). Images were acquired 60 min post injection. Increased

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Figure 1. Contrast-enhanced CT scan of the thorax and the abdomen. (a) The coronal image shows an indistinctly confined hyperdensity of the subcutaneous fat and the adjacent tissue in the medial portion of the right breast (arrow). Note the thickening of the skin. (b) Axial CT image of the abdomen. Diffuse hyperdensities in the dorsolateral subcutaneous fat tissue and thickening of the skin are seen in both flanks. These correlated with the hyperaemic areas in the blood pool phase of the bone scan. No lymphadenopathy was found.

FDG uptake was observed in the right breast, both upper arms and flanks. No pathological lymph nodes were detected. The tibialis anterior muscles showed moderately increased metabolism, possibly reflecting concomitant myositis or myopathic changes. However, no muscle biopsy was carried out.

Histopathological assessment of a biopsy of the right flank displayed normal epidermis, subtle perivascular infiltrates in the skin and very dense lymphohistiocytic infiltrates in the subcutaneous tissue. Small and medium-sized lymphocytes showed a characteristic rim of fat cells (Figure 5). Immunohistological staining was positive for CD8 and negative for CD4 and CD56. Genetic testing indicated a clonal rearrangement of the T-cell receptor (TCR) alpha/beta genes. Indirect immunofluorescence showed positive staining for antinuclear antibodies (ANA; titre 1:10240) and was negative for

histones and double-stranded DNA. Lupus erythematosus profundus (LEP) appeared improbable according to the results of indirect immunofluorescence. Proof of monoclonal infiltrates and absence of other LEP markers were additional laboratory findings, that made the diagnosis of lupus even more unlikely, despite positive ANAs. The histopathological diagnosis was subcutaneous panniculitis-like T-cell lymphoma (SPTCL).

The patient was systemically well. Radiotherapy was not indicated because of the widespread subcutaneous involvement. The patient declined to accept chemotherapy according to the CHOP scheme (cyclophosphamide, doxorubicin, vincristine and prednisone), which was recommended by the medical oncologists. Instead, she wanted at first to observe the natural course of the disease and then start an auxiliary homoeopathic treatment. The patient refused further examinations in

Figure 2. MRI of the right upper arm. (a) Axial T_1 weighted image. In the lateral aspect, the subcutaneous fat exhibits an ill-defined hypointensity (arrow). (b) These infiltrates show a strong, homogeneous contrast enhancement (arrow) (coronal T_1 weighted fat-saturated image). Muscles and bones are not affected.

Figure 3. Bone scan. (a) Blood pool phase. In the early phase, 2 min post injection (p.i.), strong, diffuse tracer accumulation was observed in the right breast and bilaterally in the area of both flanks cranial to the iliac crests (white arrows). Focal accumulation was also found in both upper arms (black arrows). (b) Late phase. No skeletal tracer accumulation was detected 2.5 h p.i.

Figure 4. ^{18}F -FDG-PET images acquired 60 min post injection. Maximum intensity projection (MIP) images in ventral (V) and dorsal (D) projections: foci of increased FDG uptake were detected in the right breast (long black arrow). Multiple areas of increased FDG uptake were also displayed in the subcutaneous tissue of both flanks and upper arms. Note the moderately increased FDG uptake in both anterior tibialis muscles (short black arrow) possibly reflecting concomitant myositis. No lymphadenopathy was detected.

a specialised centre. The patient was seen only once more by her family doctor 2 years after onset of the disease and had only slowly progressing subcutaneous lesions. She again refused further treatment or monitoring.

Discussion

SPTCL was described as a new entity of cutaneous T-cell lymphomas by Gonzalez et al [12] in 1991. Recently, increasing evidence has been found to show that at least two types of SPTCL with different immunohistological manifestations and prognoses can be distinguished. In the new WHO-EORTC classification for cutaneous lymphomas, first used in 2005 [1], only cases with alpha or beta TCR phenotypes are classified as "SPTCL" whereas cases with gamma or delta TCR phenotypes now belong to the "cutaneous gamma/delta T-cell lymphomas (CGD-TCL) (provisional entity)", a subgroup of "primary cutaneous peripheral T-cell lymphoma, unspecified".

SPTL affects both sexes equally, and it may occur in young children as well as in adults. Patients clinically present with solitary or multiple subcutaneous plaques or nodules. The legs are the most common site of involvement. Fever or weight loss may be present. A severe complication is the haemophagocytic syndrome [12, 13] characterised by anaemia, leukaemia, thrombocytopenia and coagulation defects. Pancytopenia and bleeding complications may lead to a rapidly progressive, often lethal, course. Extra-cutaneous involvement is rare.

Histological findings are subcutaneous infiltrates of pleomorphic T cells and macrophages that can mimic benign panniculitis. Epidermis and dermis are mostly uninvolved. Rimming of single fat cells by T cells is a typical microscopic sign. SPTCLs show the following characteristic immunohistological phenotype: alpha/beta TCR⁺, CD3⁺, CD4⁻, CD8⁺, CD56⁻. Genetic analysis reveals clonal TCR gene rearrangements.

Figure 5. Histology (haematoxylin and eosin staining, 400 × magnification). The subcutaneous tissue biopsy sample shows dense lymphohistiocytic infiltrates. Pleomorphic lymphocytes showed a characteristic rim of single fat cells (red arrows).

By contrast, cases with a gamma or delta phenotype (CGD-TCL) are typically negative for CD4 and CD8 and positive for CD56. The T cells show clonal rearrangements of the TCR gamma gene. Epidermotropic, dermal, subcutaneous and combined histological involvements are known and angioinvasion can occur. Patients with CGD-TCL present with disseminated plaques and nodules that can ulcerate. In patients with panniculitis-type involvement, the haemophagocytic syndrome can also occur.

Patients with SPTCL show a 5 year survival rate of more than 80% [14], whereas patients with CGD-TCL have a poor prognosis (median survival 15 months) [15]. Because of the good prognosis of SPTCL without haemophagocytic syndrome, the EORTC Cutaneous Lymphoma Group proposed that the course of this disease is controlled with systemic corticosteroids as first choice, instead of the formerly used doxorubicin-based multi-agent chemotherapy (CHOP scheme) [2]. By contrast, patients with CGD-TCL should be treated with systemic chemotherapy. Some patients with solitary or localised skin lesions can be treated with radiotherapy or surgery [2].

Distinguishing SPTCLs from the differential diagnoses is often difficult. Aggressive cutaneous lymphomas, skin metastases and other malignant disorders, as well as various inflammatory and benign forms of panniculitis, have to be excluded. These can be classified into idiopathic (Weber-Christian disease), physical (cold, heat or chemical), rheumatological (systemic lupus erythematosus or rheumatoid arthritis) and dermatological (erythema nodosum) diseases. SPTCL and lupus erythematosus profundus with panniculitis (LEP) may be clinically indistinguishable. Some authors have proposed histopathological criteria for differentiation of these two entities [16], whereas others regard LEP and SPTCL as two varieties of one disease [17].

FDG-PET-CT is a powerful modality for the detection of nodal and visceral involvement in Hodgkin's (HD) and non-Hodgkin's lymphomas (NHL) [6, 18]. But only a few reports of subcutaneous imaging-based findings in SPTCL

[4, 9–11] and other cutaneous lymphomas exist in the literature [1, 3–5]. In a recently published small case series, the value of FDG-PET-CT in the evaluation of cutaneous T-cell lymphomas was discussed [4]. One patient with SPTCL was included in this study. The authors found that physical examination, in comparison with PET/CT, greatly underestimated disease burden. The thickness of the lesions could be measured exactly using CT, whereas PET delivered a semi-quantitative value for glucose metabolism. The authors concluded that these parameters could be used to create a more objective standardised skin score to assess tumour burden.

Our findings also confirm that CT and PET are valuable for determining the distribution, morphological patterns and metabolic activity of subcutaneous lesions in SPTCL. The bone scan was primarily indicated because of the pain in the lower legs and to rule out skeletal pathology. Although the blood pool phase of the bone scan depicted the distribution of subcutaneous involvement with surprising accuracy (most probably due to the inflammatory changes with continuous hyperaemia), FDG-PET/CT was found to be the most useful imaging modality.

MRI, potentially as whole-body MRI, may be considered as an alternative diagnostic tool. Lim et al [19] performed whole-body MRI for initial and follow-up evaluations in a child with SPTCL. In our patient, the subcutaneous nodules were hypointense in comparison with fat tissue in T_1 weighted imaging and showed a strong enhancement after administration of contrast material.

Soft-tissue ultrasound was not performed in our patient. Kang et al [9] described diffuse, ill-defined hyperechoic areas in three patients with SPTCL. The breast (as in our patient) is a rare site for SPTCLs in comparison with the extremities. To our knowledge, there is only one other case report describing a SPTCL manifesting as a breast mass [11].

In conclusion, our data indicate that SPTCL lesions can be accurately detected by FDG-PET and further characterised by multimodality imaging including CT and MRI. The value of FDG-PET (PET-CT) to monitor therapy response in this disease still needs to be defined. Although SPTCL is a rare disease, one should consider it as a differential diagnosis of panniculitis if diagnostic imaging detects unclear subcutaneous nodules or plaques.

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