CASE REPORT

A rare case of fever of unknown origin: subcutaneous panniculitis-like T-cell lymphoma (SPTCL)

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Accepted 5 August 2015

SUMMARY

A 26-year-old man presented with high-grade fever, chills, productive cough and episodic abdominal pain of 6 months duration. Physical examination revealed that the patient was febrile and had multiple, ill-defined, tender, indurated, erythematous nodules and plaques over the trunk and thighs. Systemic examination and investigations revealed bilateral exudative pleural effusion with an increased adenosine deaminase (ADA) level. Pulmonary tuberculosis was suspected and the patient was started on a standard four-drug antitubercular regimen. Since his fever persisted, biopsy of the plaque over the trunk was performed, which showed lobular panniculitis with atypical lymphoid cells. Immunohistochemistry showed atypical lymphoid cells, which were CD3 and CD8 positive and CD4 negative. Based on the clinical features, skin biopsy and immunohistochemistry, the diagnosis of subcutaneous panniculitis-like T-cell lymphoma was made. The patient was treated with chemotherapy followed by bone marrow transplantation, and 4-year follow-up showed complete remission of lymphoma.

BACKGROUND

T-cell lymphoma with clinicopathological features suggesting panniculitis frequently associated with a haemophagocytic syndrome (HPS) and an aggressive clinical course was described by Gonzalez *et al.*¹ Subcutaneous panniculitis-like T-cell lymphoma (SPTCL) is a rare cytotoxic T-cell lymphoma of the skin comprising <1% of all non-Hodgkin's lymphomas.² It can present with prolonged fever and weight loss, mimicking tuberculosis, which is very common in this part of the world. A high

degree of suspicion and skin biopsy is mandatory for early diagnosis.

CASE PRESENTATION

A 26-year-old man presented with high-grade intermittent fever with chills, weight loss, productive cough and episodic abdominal pain of 6 months duration. Physical examination showed that the patient was febrile with mild pallor. There were numerous, tender, erythematous, indurated nodules and plaques measuring 1–8 cm over the trunk (figure 1) and anterior aspect of the thighs. There were no ulcerations over the nodules and plaques. Small bilateral axillary lymph nodes were palpable.

INVESTIGATIONS

Chest X-ray showed bilateral pleural effusion. The effusion was exudative with lymphocyte predominance and an elevated level of adenosine deaminase (ADA). Based on the above clinical presentation and investigations, pulmonary tuberculosis was considered and standard antituberculous treatment (ATT) was initiated. However, the ATT was stopped after 2 weeks as the high-grade fever persisted with significant increase in hepatic transaminase levels. Subsequently, biopsy of the indurated plaque over the trunk was performed, which showed atypical lymphocytes infiltrating the lobules of the subcutaneous fat. The epidermis and dermis were not involved (figure 2). The atypical lymphocytes were seen rimming the individual adipocytes (figure 3). Numerous apoptotic bodies were observed. The atypical lymphocytes were CD3 (figure 4) and CD8 positive (figure 5) with a high MIB index (figure 6). They were CD20 and CD30 negative.

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To cite: Ganesh Y, Yadala V, Reddy IS, *et al.* *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-211355

Figure 1 Multiple erythematous plaques and nodules on the trunk.

Figure 2 H&E ×10 stain showing no involvement of epidermis and dermis.

Figure 3 H&E x20 stain showing infiltration of subcutaneous fat by neoplastic lymphocytes with hyperchromatic nuclei. Necrosis is present. Adipocytes are rimmed by neoplastic lymphocytes.

The histopathological examination (HPE) was consistent with SPTCL. Bone marrow biopsy was within normal limits and there was no evidence of haemophagocytosis. Epstein-Barr virus serology was negative. Whole body positron emission tomography CT (PET-CT) revealed mediastinal, para aortic and pelvic lymph nodal involvement with extensive cutaneous and subcutaneous nodules, which showed increased fluorodeoxyglucose (FDG) uptake.

DIFFERENTIAL DIAGNOSIS

Erythema nodosum was the initial impression after clinical examination.

Panniculitis secondary to tuberculosis was considered because of chronic fever with exudative lymphocytic predominant pleural effusion associated with high erythrocyte sedimentation rate and raised ADA level.

The patient's antinuclear antibody profile was negative, which ruled out lupus panniculitis.

Finally, histopathological examination of the skin nodule revealed SPTCL.

TREATMENT

The patient received four cycles of CHOP (cyclophosphamide, adriamycin, vincristine and prednisolone) chemotherapy but had progression of disease, for which he received three cycles of

Figure 5 Immunohistochemistry showing CD8 positive neoplastic cells.

an ICE (ifosfamide, carboplatin and etoposide) regimen with complete response. He was scheduled for autologous peripheral blood stem cell transplant (PBSCT).

OUTCOME AND FOLLOW-UP

There was a logistic delay in autologous PBSCT. Meanwhile, the patient developed progression of disease confined only to skin. He was given electron beam radiotherapy to the skin lesions, with good response. Later, autologous PBSCT was performed (in the year 2011). He is, to date, in complete remission.

DISCUSSION

SPTCL is a rare cytotoxic α/β T-cell lymphoma characterised by primary involvement of subcutaneous tissue.³ According to the 2005 classification of lymphoma, the designation SPTCL should be considered exclusively for those patients showing α/β neoplastic T lymphocytes. Subcutaneous lymphomas exhibiting γ/δ T lymphocytes are termed as primary cutaneous γ/δ T-cell lymphoma.⁴ Clinically, α/β T-cell lymphoma is more indolent than γ/δ T-cell lymphoma, which is more aggressive. The usual clinical presentation is with nodules and plaques over the trunk and extremities. Constitutional symptoms such as fever are common in SPTCL. Our patient had fever for 6 months, and the diagnosis of SPTCL was made only after skin biopsy was performed.

Skin biopsy and immunohistochemistry play a crucial role in the diagnosis. SPTCL shows lobular panniculitis with atypical

Figure 4 Immunohistochemistry showing CD3 positive neoplastic cells.

Figure 6 Immunohistochemistry showing very high MIB-1 index.

lymphocytes arranged in a rim-like fashion around the individual adipocytes. Necrosis of adipose tissue with foamy histiocytes and apoptotic bodies is invariably present. The neoplastic T lymphocytes are CD3 and CD8 positive, and CD20, CD30 and CD56 negative. PET using [18F] FDG plays an additional role in the diagnosis and helps to evaluate the extent of the disease.⁵ Treatment options include systemic steroids, cyclosporin and chemotherapy regimens such as CHOP. Autologous PBSCT is effective in patients showing haemophagocytosis⁶ or for progression/recurrence of disease.

Learning points

- The differential diagnosis in a young patient with fever of unknown origin with multiple skin nodules should include subcutaneous panniculitis-like T-cell lymphoma as the possible cause of fever.
- Skin biopsy and immunohistochemistry should be considered early in such patients to confirm the pathogenic cause of the fever of unknown origin (FUO).
- Positron emission tomography CT can play a significant role in evaluating a patient with FUO.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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