CASE REPORT

A case of deadly panniculitis

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SUMMARY

While the majority of panniculitides are benign in nature, there are rare instances when panniculitis presents as the initial sign of a complex disease state. We describe a case of panniculitis initially diagnosed as lupus profundus that was challenged when features of haemophagocytic lymphohistiocytosis became apparent. We illustrate how some key clinical features and newer investigations can help differentiate between benign and malignant panniculitis.

BACKGROUND

Panniculitis, which typically presents as tender subcutaneous nodules or plaques distributed on the torso and limbs, can have varying aetiologies.¹ This can range from reactive (eg, erythema nodosum) to autoimmune (eg, lupus erythematosus). The majority of causes are benign, but panniculitic features can also be indistinguishable from malignant mimics.² We report of a panniculitis presenting as lupus profundus (LP), but was subsequently determined to be a T cell malignancy.

CASE PRESENTATION

A 27-year-old woman of Vietnamese heritage with no known comorbidities presented to a tertiary emergency department after 6 weeks of severe facial swelling. She had a high-grade fever and general malaise. On examination, significant peri-orbital oedema with erythema and desquamation (figure 1A) was seen, as was indurated hyperpigmentation over her lower back (figure 1B) and chest. Hyperpigmented and deeply erythematous symmetrical indurated annular plaques with overlying scale were predominantly distributed over her distal extensor limbs (figure 1C). Large erosions were present over the hard palate; however, nails, hair and scalp appeared normal. Hepatosplenomegaly was noted.

INVESTIGATIONS

Investigations demonstrated anaemia, neutropenia, raised inflammatory markers (erythrocyte sedimentation rate 35 mm, C-reactive protein 32 mg/L and ferritin 3795 µg/L) and elevated liver enzymes. Antinuclear antibody titre was 1:640 homogenous pattern but extractable nuclear antigen and double stranded DNA were normal. A myositis-specific antibody, anti-PL-12, was positive with a markedly elevated lactate dehydrogenase (1153 U/L); however, creatine kinase was normal and no weakness was evident on examination. Infection screening was normal.

A right thigh punch biopsy demonstrated basal vacuolar changes and compact keratin with follicular plugging (figure 2A), lymphoplasmacytic inflammatory cell infiltrates and fat necrosis with sclerosis (figure 2B). This was consistent with a lobular panniculitis, and she was diagnosed with LP. She was treated with intravenous methylprednisolone 1 g daily initially, then prednisolone 50 mg daily on discharge.

DIFFERENTIAL DIAGNOSIS

After 4 weeks, there was only mild improvement in her hyperpigmentation, partial reduction in her facial swelling and an interim development of patchy scalp alopecia, despite the addition of hydroxychloroquine 200 mg two times a day. A CT scan of her chest, abdomen and pelvis demonstrated extensive subcutaneous thickening with abnormal subcutaneous fatty enhancement (figure 3). Poor response to high-dose prednisolone and deteriorating liver enzymes prompted alternative diagnoses, including clinically amyopathic dermatomyositis and lupus hepatitis. Mycophenolate mofetil 1 g BD was started.

Four weeks later, she presented jaundiced with a ferritin level of 14324 µg/L and severe liver enzyme derangement. The constellation of findings pointed towards a cytophagic histiocytic panniculitis (CHP), a rare syndrome with features of panniculitis and haemophagocytic lymphohistiocytosis (HLH). To further investigate, a soluble CD25 was done and demonstrated significant elevation at 14746 pg/mL (normal range: <1033 pg/mL), further supporting the presence of HLH as per the HLH-2004 trial diagnostic guidelines.³ She required an emergency admission to intensive care unit for coagulopathy with active melaena needing massive blood transfusions and multiple endoscopies.

An urgent review of her original skin biopsy for HLH was done. This revealed subtle but definite findings of a population of lymphoid cells showing atypia with nuclear irregularity and hyperchromasia, focally rimming the adipocytes (figure 4); a finding consistent with subcutaneous panniculitis-like T cell lymphomas (SPTCL) as per the WHO European Organization for Research and Treatment of Cancer classification for cutaneous lymphomas.⁴

A bone marrow biopsy confirmed haemophagocytosis. T-cell receptor (TCR) gene rearrangement studies detected a monoclonal TCR gamma rearrangement on her bone marrow identical to that in her skin, further supporting an SPTCL diagnosis. Hereditary HLH testing, with signaling-lymphocytic-activation-molecule-associated protein (SAP)

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Figure 1 (A) Oedema, erythema and desquamation. (B) Hyperpigmentation over the lower back. (C) Annular plaques over the upper limbs.

expression and natural killer (NK) cell degranulation assays, was negative.

OUTCOME AND FOLLOW-UP

Chemotherapy with cyclophosphamide, doxorubicin, etoposide, vincristine and prednisone (CHOEP) was commenced. Within a few days, facial swelling improved remarkably. Soon after, her jaundice resolved as her liver enzymes normalised. Over the succeeding year, she completed six cycles of CHOEP, salvage ifosfamide, carboplatin and etoposide (ICE) then BiCNU/carmustine, etoposide, Ara-C/cytarabine and melphalan (BEAM) chemotherapy followed by autologous stem cell transplantation. Currently in remission, she is being monitored by the haematology service.

DISCUSSION

As a presenting symptom, panniculitis can be problematic as malignant phenotypes are rare, while overlapping clinical and histological features are common.⁵ Determining the cause for a panniculitis is primarily a clinical undertaking though often relies on histopathology, more so when clinical signs are vague.

Our patient presented a diagnostic challenge as key clinical findings became apparent only later on. Her LP diagnosis was based on cutaneous findings with associated fever and anaemia; however in retrospect, the distribution of her panniculitis was inconsistent with LP as that tends to occur proximally.⁶ Another cause for suspicion was her lack of response to high-dose steroids, and her progressive ferritin rise and liver enzyme deterioration.

SPTCL is rare, but mistaking it for a benign panniculitides can lead to fatal consequences. The presentation of panniculitis with HLH, or CHP, is so closely linked to the disease that once CHP is suspected, it is imperative to search for evidence of SPTCL through histopathology, cell markers and gene rearrangement

Figure 2 (A) Basal vacuolar changes and compact keratin with follicular plugging. (B) Lymphoplasmacytic inflammatory cell infiltrates and fat necrosis with sclerosis.

Figure 3 CT scan of the abdomen showing abnormal subcutaneous fatty enhancement.

Figure 4 Lymphoid cells showing atypia with nuclear irregularity and hyperchromasia with focal rimming of adipocytes.

studies.⁷ HLH, on its own, has been found in up to 20% of haematological malignancies.⁸ While evidence of HLH can be seen histologically, a recent case report of an HLH presentation with multiple annular hyperpigmented plaques,⁹ identical to those seen on our patient, would suggest that cutaneous manifestations of HLH may also be present and should not be missed. Our experience has demonstrated that SPTCL should be kept as part of the panel of rare panniculitis mimics and should be considered in refractory cases of panniculitis, more so in patients with evidence of HLH. Newer diagnostic tests, such as soluble CD25 and TCR gene rearrangement studies, may help in identifying malignant processes in such cases.

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Contributors All of the authors listed have contributed significantly to this manuscript and are in agreement with its contents. Specifically, CY, CM and PH were all involved with direct management of the patient. In preparing of this manuscript, all three authors agreed upon the salient features of the case. CY was the lead author and created the first and final draft. CM contributed and edited the dermatological aspects of the case, including dermatological descriptions and parts

Learning points

- ▶ Haemophagocytic lymphohistiocytosis (HLH) may clinically present as multiple annular hyperpigmented plaques within the context of other HLH features.
- ▶ When panniculitis and HLH are present then an underlying malignancy should be investigated for and ruled out.
- ▶ Subcutaneous panniculitis-like T cell lymphoma should be kept as part of the panel of rare panniculitis mimics and should be considered in refractory cases of panniculitis.

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