Erythroderma is not all psoriasis: a case of Sézary syndrome

Introduction

Patients with severe erythroderma may be misdiagnosed with erythrodermic eczema and, as in this case, psoriasis. The authors describe a case of this unusual and life-threatening condition, a cutaneous T cell lymphoma (Sézary syndrome), and the management options for this condition.

Discussion

Sézary syndrome is a primary cutaneous T cell lymphoma, distinguished from the more common mycosis fungoides by the presence of erythroderma and malignant lymphoid cells in peripheral blood with an identical T cell clone to skin (Willemze et al, 2005). These atypical peripheral blood CD4 positive T lymphocytes (Sézary cells) have an aberrant T cell phenotype and characteristic cerebriform nuclear morphology.

Essentially, Sézary syndrome is a mature T cell leukaemia, which may rarely evolve from mycosis fungoides but can develop de novo. Although mycosis fungoides and Sézary syndrome are closely related, the precise pathogenetic relationship has yet to be clarified. Sézary syndrome is uncommon, representing 3–5% of cutaneous lymphomas (Vonderheid et al, 2002). It occurs most frequently in middle-aged males and is an aggressive condition with a median 5-year survival rate of 24% (Whittaker et al, 2003). More recently, a large report on 1502 patients detailed the survival outcomes and prognostic factors in mycosis fungoides and Sézary syndrome (Agar et al, 2010). Patients usually present with generalized erythroderma and intense pruritus. The differential diagnosis of erythroderma is extensive (*Table 1*); patients are potentially misdiagnosed with erythrodermic eczema and, in this case, psoriasis. Lymphadenopathy and recurrent skin ulceration with intercurrent infections occur. Tumour infiltration of the skin and profound immunodeficiency account for these later complications. Patients may die of infection rather than of tumour load. The most frequent sites of visceral involvement include oropharynx, lung and CNS.

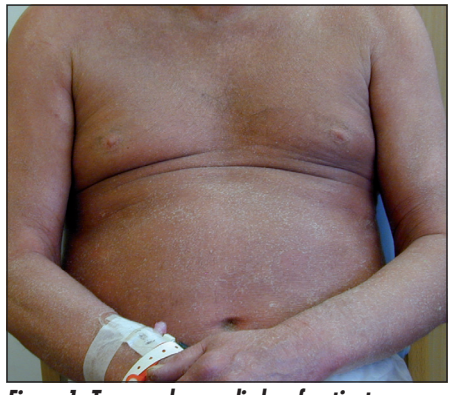


Figure 1. Torso and upper limbs of patient demonstrating extensive erythroderma.

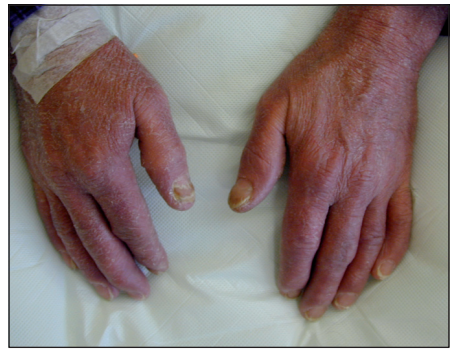


Figure 2. Skin and destructive nail features (onychodystrophia) typical of advanced Sézary syndrome.

Case Report

A 56-year-old man was admitted with cellulitis affecting the right hand. He was noted to have a high peripheral blood lymphocyte count (total white cell count 14.3 x 10^9/litre, lymphocytes 10.3 x 10^9/litre) with normal haemoglobin (15.3 g/litre) and platelet count (192 x 10^9/litre) and had severe erythroderma and associated pruritus. The patient had been previously treated for 2 years for extensive psoriasis with methotrexate. He had also received treatment for gout with colchicine and probenecid. The peripheral blood CD4+ lymphocytosis had been noted for 3 years.

A skin biopsy had revealed psoriaform hyperplasia and chronic dermal inflammation with a few eosinophils, but epidermotropism of CD4+ T cells was noted. Although these findings were initially felt to be suggestive of psoriasis, a subsequent clinical review concluded that the clinical and pathological features were consistent with cutaneous T cell lymphoma (Sézary syndrome), and identical T cell clones were detected in the skin biopsy and peripheral blood. Bone marrow revealed a lymphocytic infiltrate, amounting to 33% of all nucleated cells, with lymphocytes positive for CD4, CD2, CD3, CD5 and CD25, but negative for CD7 and CD8. Both human T-lymphotropic virus-1 and -2 infections were excluded.

A computed tomography whole body scan revealed bilateral axillary, inguinal and cervical lymphadenopathy, but a lymph node biopsy showed dermatopathic features only confirming stage III disease. However, the peripheral nodes became more prominent, and 5 months after the diagnosis, a positron emission tomographic scan suggested moderate to high positron emission tomogram avidity. A subsequent lymph node biopsy resulted in an infected and discharging groin abscess, but this biopsy revealed effacement of the nodal architecture with cytologically atypical CD4+ T cells. An identical T cell clone was present in the node. These findings indicated progression to stage IVA of the disease. The patient was pyrexial, experiencing intense pruritus with extensive erythroderma of the trunk and limbs (*Figure 1*). The hands were hyperkeratotic with extensive nail changes (*Figure 2*) and fissured plaques on the hands and feet. This was treated topically with mometasone (Elocon) to the body and clobetasone (Eumovate) to the face. Gabapentin was prescribed for pruritus and the patient commenced subcutaneous α-interferon at a dose of 3 MU three times per week and monthly extracorporeal photopheresis therapy with the subsequent addition of bexarotene.

Dr SW Dubrey *is Consultant Cardiologist and* **Dr G Rosser** *is Cardiology Specialist Registrar in the Department of Cardiology,* **Dr K Patel** *is Consultant Haematologist in the Department of Haematology, Hillingdon Hospital, Middlesex UB8 3NN, and* **Dr SJ Whittaker** *is Consultant Dermatologist, St John's Institute of Dermatology, St Thomas Hospital, London*

Correspondence to: Dr SW Dubrey (simon.dubrey@thh.nhs.uk)

Management of the mycosis fungoides and Sézary syndrome spectrum is a staged approach. The early stage of mycosis fungoides requires skin-directed therapies, such as corticosteroids, phototherapy (psoralen and ultraviolet radiation), topical chemotherapy and topical or systemic bexarotene (an agonist of the retinoid X receptor involved in the regulation of cell differentiation and proliferation) (Prince et al, 2009).

The patient required a combination of bexarotene, α-interferon and extracorporeal photopheresis. In photopheresis therapy, blood is extracted, treated with photoactivable drugs (psoralens), exposed to ultraviolet light and then returned to the patient (Zic, 2012). Photochemically damaged T cells appear then to induce cytotoxic effects on T cell proliferation.

Systemic chemotherapy, including single agent chlorambucil and multiagent regimens such as CHOP (cyclophosphamide, doxorubicin, vincristine and prednisolone), has short-lived responses. Immunomodulatory agents, proteasome inhibitors and monoclonal antibodies are under investigation. Several histone deacetylase inhibitors have gained approval (Whittaker et al, 2010), expanding treatment options and combination therapies. **BJHM**

Table 1. Differential diagnoses of erythroderma

Eczema
Psoriasis
Seborrheic dermatitis
Pityriasis rubra pilaris
Lichen planus
Drug induced (e.g. lithium, carbamazepine, antimalarials, gold, phenytoin, allopurinol)
Contact dermatitis (i.e. rubber, solvents, detergents)
Stasis dermatitis (gravitational eczema)
Bullous diseases (e.g. pemphigous, pemphigoid)
Human immunodeficiency virus (HIV) infection
Graft *vs* host disease
Connective tissue disease
Internal malignancy as a non-metastatic manifestation
Haematological malignancies (lymphoma, Hodgkin's disease, leukaemia)
Cutaneous T-cell lymphoma (Sézary syndrome)
Idiopathic (may account for as many as 30% of cases)

Agar NS, Wedgeworth E, Crichton S et al (2010) Survival outcomes and prognostic factors in mycosis fungoides/Sézary syndrome: validation of the revised International Society for Cutaneous Lymphomas/European Organisation for Research and Treatment of Cancer staging proposal. *J Clin Oncol* **28**(31): 4730–9

Prince HM, Whittaker S, Hoppe RT (2009) How I treat mycosis fungoides and Sézary syndrome. *Blood* **114**(20): 4337–53

Vonderheid EC, Bernengo MG, Burg G et al (2002) Update on erythrodermic cutaneous T-cell lymphoma: report of the International Society for Cutaneous Lymphomas. *J Am Acad Dermatol* **46**(1): 95–106

Whittaker SJ, Marsden JR, Spittle M et al (2003) Joint British Association of Dermatologists and UK Cutaneous Lymphoma Group guidelines for the management of primary cutaneous T-cell lymphomas. *Br J Dermatol* **149**(6): 1095–107

Whittaker SJ, Demierre MF, Kim EJ et al (2010) Final results from a multicenter, international, pivotal study of romidepsin in refractory cutaneous T-cell lymphoma. *J Clin Oncol* **28**(29): 4485–91

Willemze R, Jaffe ES, Burg G et al (2005) WHO-EORTC classification for cutaneous lymphomas. *Blood* **105**(10): 3768–85

Zic JA (2012) Photopheresis in the treatment of cutaneous T-cell lymphoma: current status. *Curr Opin Oncol* **24** (Suppl 1): S1–10

LEARNING POINTS

- Sézary syndrome can be a diagnostic challenge even for dermatologists.
- The presence of peripheral blood CD4+ lymphocytosis and characteristic Sézary cells helps to confirm the diagnosis.

Life-threatening constipation

An 80-year-old woman presented to the emergency department with sudden onset abdominal pain and vomiting. Her abdomen was soft with umbilical tenderness.

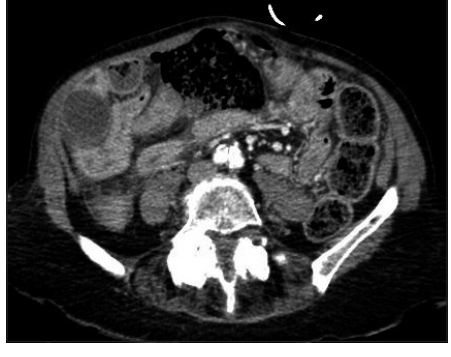
Laboratory tests revealed a leukocytosis of 16.7×10^9/litre, levels of amylase 189 IU/litre and lactate 7.4 mmol/litre, while other investigations were within normal range.

Dr Sumeet Hindocha *is F2 Doctor in the Department of Geriatrics, John Radcliffe Hospital, Oxford OX3 9DU and*
Dr Bob Soin *is Consultant Surgeon in the Department of General Surgery, Wexham Park Hospital, Slough*

Correspondence to: Dr S Hindocha (sumeet.hindocha@hwph-tr.nhs.uk)

Contrast computed tomography showed extensive faecal loading but no cause of her symptoms (*Figure 1*). Laparotomy revealed a 20 mm perforation of the transverse colon with free faeces in the peritoneal cavity.

Figure 1. Computed tomography scan showing extensive faecal loading.



Faecalomas cause ischaemic necrosis of the colon wall, leading to stercoral perforation. This is often plugged by omentum, causing signs of peritonitis to be absent. Chronic constipation and non-steroidal anti-inflammatory drug use are risk factors (Hollingworth and Alexander-Williams, 1991).

This case highlights the need for a high index of suspicion in cases of acute abdomen with a history of chronic constipation or non-steroidal anti-inflammatory drug use. Clinical suspicion of perforation is needed in light of unusual laboratory investigations, even in the absence of clinical and radiological evidence of perforation. **BJHM**

Hollingworth J, Alexander-Williams J (1991) Non-steroidal anti-inflammatory drugs and stercoral perforation of the colon. *Ann R Coll Surg Engl* **73**(6): 337–40