

SHORT COMMUNICATION

Lymphomatoid Plaquiosis – A CD30⁺ Lymphoproliferative Rash Exhibiting a Predilection for Recurrence on the Same Skin SitesChester Lai^{1,2}, Ciara Haddadeen^{1,2}, Shin-Young Cho^{1,2}, Adam Fityan^{1,2}, Andrew Bates³, Jeffrey Theaker⁴ and Eugene Healy^{1,2}¹Department of Dermatopharmacology, University of Southampton, Mail point 825, Level F, South Block, Southampton General Hospital, SO16 6YD Southampton, Departments of ²Dermatology, ³Medical Oncology and ⁴Histopathology, University Hospital Southampton NHS Foundation Trust, Southampton, UK. E-mail: c.y.lai@soton.ac.uk

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Aberrations in cutaneous T-cell immunology may result in rashes that recur at the same or similar sites in the skin, and include fixed drug eruption, psoriasis and mycosis fungoides (MF). Here we describe a patient with an unusual presentation of a cutaneous CD30⁺ lymphoproliferative disorder, manifesting as a rash with a tendency to repeatedly appear at the same skin locations before spontaneously clearing. The rash differed clinically from lymphomatoid papulosis (LyP) in that it arose as recurrent plaques which cleared without scarring, and therefore we have termed this condition ‘lymphomatoid plaquiosis’.

CASE REPORT

A 68-year-old man presented with a 47-year history of an episodic rash consisting of itchy, red scaly patches and plaques. Prior to taking up residence in our region in 2007, he had attended his previous local dermatology department, and due to the complexity of his case and the absence of a definite diagnosis, had attended numerous regional clinical dermatology meetings. Upon presentation to our department, his skin was unaffected, but he mentioned that on each occasion his rash recurred predominantly on the same sites, and showed photographs from 2003 and 2006 (Fig. 1) which seemed to support his view. He mentioned that the skin condition relapsed anytime between 2–7 month intervals, and lasted for 5 days to 2 weeks, after which the rash would clear completely without treatment.

The patient later attended a regional clinical dermatology meeting and, despite no obvious precipitant drug, the consensus opinion from the photographs and history included fixed drug eruption, possibly to salicylates or a food colouring, as the most probable diagnosis. The patient was encouraged to attend

the dermatology department when the rash recurred but failed to do so (principally because the rash did not trouble him as it always resolved spontaneously). However, in 2012, he was seen when the rash was present on his trunk and limbs in the same sites as in his earlier photographs, and the clinical diagnosis proposed at that stage was cutaneous T-cell lymphoma. Skin biopsies were taken; histology showed acanthosis, spongiosis, parakeratosis, and an infiltrate dominated by large pleomorphic lymphoid blast cells, but also containing small lymphocytes, neutrophil polymorphs and occasional eosinophils in the upper/mid-dermis (Fig. S1¹). Immunohistochemistry showed that the large atypical lymphocytes expressed CD30 as well as CD3 but not CD4, CD5 or CD8. Occasional lymphocytes, neutrophils and blast cells permeated into the epidermis, however there were no overt features of MF, such as clear lymphocyte cytological atypia in the smaller lymphoid cells nor epidermotropism/Pautrier abscesses indicating that the histological appearances in isolation were considered more consistent with LyP. T-cell receptor gene PCR showed clonal rearrangements in the TCR beta DBJ-C, VBJ-A, VBJ-B and TCR gamma VJG-A loci, confirming the diagnosis of a cutaneous CD30⁺ lymphoproliferative disorder. A repeat biopsy was performed from the same skin site when the rash was not active; this showed occasional CD3⁺ upper dermal lymphocytes but no atypical CD30⁺ lymphocytes and no evidence of lymphocyte cytological atypia or epidermotropism (Fig. S2¹).

DISCUSSION

Primary cutaneous CD30⁺ lymphoproliferative disorder is a form of cutaneous T-cell lymphoma (1), which includes LyP and primary cutaneous anaplastic large cell lymphoma. In the current case, the histological features were consistent with LyP but the patient’s rash did not appear typical of this diagnosis nor of primary cutaneous anaplastic large cell lymphoma. LyP commonly presents as a recurrent papular rash, but the rash in our case consisted of plaques rather than papules, so we have termed this condition ‘lymphomatoid plaquiosis’.

An interesting feature of the rash was its tendency to reappear at the same skin locations. The differential diagnoses in this case included other causes of rashes that are known to recur in the same skin sites; these include fixed drug eruption, MF and psoriasis (2). Fixed drug eruption usually appears as erythematous

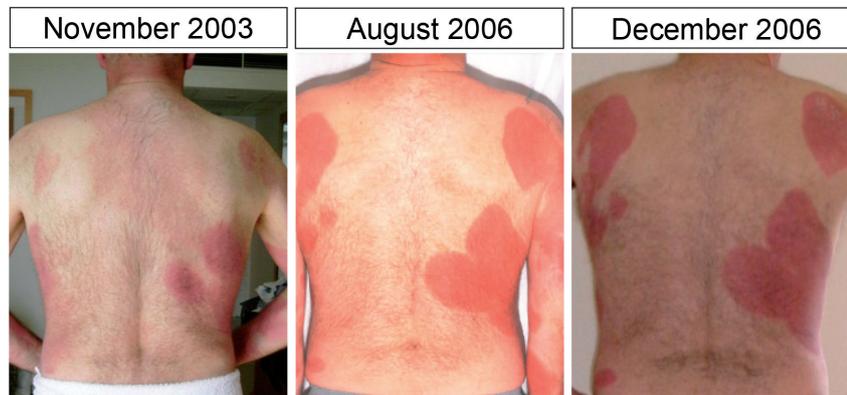


Fig. 1. The appearances of the rash during flares in November 2003, August 2006 and December 2006.

plaques which resolve after discontinuation of the offending drug, and recur in the same sites when rechallenged with the drug. In resolved fixed drug eruption skin lesions, CD8⁺ T cells capable of producing interferon- γ and TNF- α remain present in the epidermal basal layer (3). In our case, a drug eruption was discounted as a cause because no precipitant drug could be identified as the patient did not take any regular medications that could explain a recurrent rash over 47 years.

Another type of drug eruption that could account for the clinical appearances in the current case is drug-induced CD30⁺ pseudolymphoma, which has been reported to manifest as a rash consisting of scaly erythematous plaques on the trunk and extremities (4, 5). Causative medications known to induce CD30⁺ pseudolymphoma include carbamazepine, amlodipine, valsartan, gemcitabine and gold; however, drug-induced pseudolymphoma is not known to exhibit a recurrent clinical course with intervals of complete remission (4, 6).

Another differential diagnosis was MF, a disease characterised by malignant skin-resident effector memory T cells which are non-motile and can persist long term in the skin, giving rise to recurrence in the same skin sites. Indeed, recently-described pores in the epidermal basement membrane seem to act as conduits which allow these malignant T cells to enter into the epidermis (7). In our case, MF with CD30⁺ transformation was considered, however, this diagnosis is typically associated with signs of clinical progression, and throughout the long history of the condition, the rash did not show signs of progression to tumour stage and the patient remained systemically well. In addition, whilst this cannot be excluded on the basis of the biopsy material, the histology did not demonstrate clear morphological evidence of underlying MF.

Psoriasis is another T-cell-mediated inflammatory skin disease which often recurs in the same locations. Suarez Fariñas et al. (8) showed that in clinically-resolved psoriatic lesions there were residual dermal CD8⁺ T cells, persistent alterations in expression of psoriasis-related inflammatory genes, and morphological changes in lymphatic vessels that could explain the tendency of psoriasis to recur at the same site after treatment.

The sessile nature of skin resident memory T cells may explain the clinical presentation in the current case, with plaques appearing in fixed anatomical sites in the skin, but the reasons for the episodic flares and spontaneous remissions remain unclear. The repeat skin biopsy taken when the rash was in remission showed that CD30⁺ atypical lymphocytes were absent; this could theoretically be explained by apoptosis via Fas signalling following activation of CD30 (9). It is pos-

sible that the rash may have resulted from antigenic stimulation via Langerhans' cells causing activation, clonal expansion and subsequent apoptosis of malignant skin resident memory T cells (10). The generalised nature of our patient's rash would suggest that any antigenic stimulus is likely to have been of a systemic nature in order to generate the recurrent rash on several skin sites at the same time. One possible antigenic stimulus is recurrent subclinical reactivation of viral infection, such as Epstein-Barr virus (EBV), which has been reported to induce CD30 expression (11, 12). In addition, the clinical picture in this case highlights the need to add lymphomatoid plaquiosis to the list of episodic rashes which can recur at the same skin site.

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