

and after remission. *J Neurol Neurosurg Psychiatry* 2003; 74:1003–4.

- 7 Brelinski L, Cottencin O, Guardia D *et al.* Catatonia and systemic lupus erythematosus: a clinical study of three cases. *Gen Hosp Psychiatry* 2009;31:90–2.
- 8 Perisse D, Amoura Z, Cohen D *et al.* Case study: effectiveness of plasma exchange in an adolescent with systemic lupus erythematosus and catatonia. *J Am Acad Child Adolesc Psychiatry* 2003;42:497–9.
- 9 Daniels J. Catatonia: clinical aspects and neurobiological correlates. *J Neuropsychiatry Clin Neurosci* 2009; 21:371–80.

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Wells' syndrome (eosinophilic cellulitis) secondary to infliximab

SIR, George Wells first described this syndrome in 1971 as a 'recurrent granulomatous dermatitis with eosinophilia' [1]. It is an uncommon inflammatory dermatosis of unknown aetiology, with few cases reported worldwide. Wells' syndrome is characterized by a pruritic rash, which usually follows a relapsing and remitting course, and distinct histology showing an infiltrate of eosinophils within the dermis. Pruritus can be intractable and unresponsive to anti-histamines. Affected individuals typically present with erythematous plaques over a 2- to 3-day period and plaques usually resolve without scarring over 2–8 weeks [2]. This condition is rarely associated with systemic involvement, but peripheral blood eosinophilia is common [3]. We describe the case of a woman treated with infliximab for RA who developed Wells' syndrome.

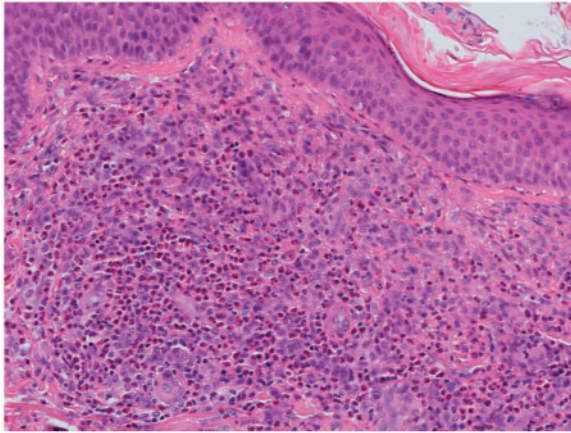
A 69-year-old woman with seropositive RA of 18 years duration presented with a 6-month history of an intensely pruritic intermittent rash over her back and abdomen (Fig. 1). The rash had appeared 1 week after an infliximab infusion, following which infusions were withheld for 12 weeks. The rash then remitted and another infliximab infusion was given; consequently, the rash returned. The patient complained of disabling pruritus, despite the use of various anti-histamines and topical emollients, but systemically was well. The patient had received infliximab infusions every 6 weeks for almost 9 years for control of RA. She had also been taking oral prednisolone since diagnosis. There had been no change in her usual medications and she could not recall receiving any recent courses of antibiotics or over-the-counter medications. There was no recent foreign travel or history of insect bites or stings. There was also no suggestion of latent malignancy or infection upon systemic enquiry. Clinical examination showed an extensive rash over her trunk and back and skin-coloured papules with an erythematous rim. Investigations revealed a mild peripheral eosinophilia of 0.67×10^9 cells ($0.04\text{--}0.4 \times 10^9$ cells/l) and slightly elevated inflammatory markers. The eosinophil count had been

Fig. 1 Photograph showing lesions on the patient's back.



intermittently mildly elevated for some months, with the total percentage of eosinophils of 5.3% at its peak (1–4%). A punch biopsy of a posterior lesion was performed. Histology showed a dense infiltrate of lymphocytes, histiocytes and abundant eosinophils in the dermis, perivascular areas and around sweat glands, consistent with Wells' syndrome (Fig. 2).

Seven clinical variants of Wells' syndrome have been documented: plaque type, annular granuloma-like, urticaria-like, papulovesicular, bullous, papulonodular and fixed drug eruption-like [3]. The pathophysiology of the lesions in Wells' syndrome remains unknown. It has been suggested that excess production of IL-5 occurs, which drives eosinophilic accumulation in a local Th2 immune response [4]. A variety of triggering factors have been identified, such as insect bites or stings [5], chronic inflammatory diseases [6] and neoplasias. More commonly it is idiopathic, drug-related, or associated with immunological, myeloproliferative or infectious disorders [7]. Although a distinct entity, it has been suggested that Wells' syndrome may be associated with rare multisystem eosinophilic disorders, such as Churg–Strauss syndrome and hypereosinophilic syndrome [7]. Prognosis for Wells' syndrome is excellent and most patients recover without difficulty, although lesions may recur later. The patient was treated with topical steroids and infliximab was

Fig. 2 Dense infiltrate of eosinophils within the dermis.

withheld. Following this, the lesions began to remit but took some weeks to resolve fully.

Wells' syndrome may be a side effect of anti-TNF treatment. There have been two reports of anti-TNF-induced Wells' syndrome in patients treated with adalimumab [8] and etanercept [9]. To the authors' knowledge, this is the first report of Wells' syndrome due to infliximab. We postulate that, in the absence of the introduction of any new pharmaceutical agent, the patient developed Wells' syndrome in response to chronic exposure to infliximab. Infliximab is a chimeric biological agent and post-marketing surveillance has demonstrated skin rash as a moderately common side effect. We suggest that infliximab induces hypereosinophilia via a hypersensitivity reaction to the chimeric antibody. It is likely that the long duration of CS treatment the patient had been on had suppressed the pathological process underpinning Wells' syndrome. The process was probably unmasked through a reduction in the CS dose. Furthermore, although the British Society of Rheumatology Biologics Register (BSRBR) has 10 years of data on the safety profile of infliximab, it is still a relatively recent addition to the RA armoury and, as such, long-term data are still being compiled. Wells' syndrome may be a complication of continuous use of anti-TNF agents, and the previous reports of its occurrence in patients on etanercept and adalimumab lend weight to this assumption. Physicians should therefore remain diligent regarding cutaneous reactions in patients on anti-TNF agents, particularly in cases where the skin rash waxes and wanes as a result of treatment.

Rheumatology key message

- Wells' syndrome can be caused by anti-TNF and should be considered in patients with rash.

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References

- 1 Wells GC. Recurrent granulomatous dermatitis with eosinophilia. *Trans St Johns Hosp Dermatol Soc* 1971;57:46–56.
- 2 Green WH. Recurrent, pruritic dermal plaques and bullae. *Arch Dermatol* 2007;146:791–6.
- 3 Carlesimo M, Fidanza L, Mari E *et al.* Wells' syndrome with multiorgan involvement mimicking hypereosinophilic syndrome. *Case Rep Dermatol* 2009;1:44–8.
- 4 French LE, Shapiro M, Junkins-Hopkins JM *et al.* Eosinophilic fasciitis and eosinophilic cellulitis in a patient with abnormal circulating clonal T cells: increased production of interleukin 5 and inhibition by interferon alfa. *J Am Acad Dermatol* 2003;49:1170–4.
- 5 Wood C, Miller AC, Jacobs A *et al.* Eosinophilic infiltration with flame figures. *Am J Dermatopathol* 1986;8:186–93.
- 6 Sakaria SS, Ravi A, Swerlick R, Sitaraman S. Wells' syndrome associated with ulcerative colitis: a case report and literature review. *J Gastroenterol* 2007;42:250–2.
- 7 Caputo R, Marzano AV, Vezzoli P, Lunardon L. Wells' syndrome in adults and children – a report of 19 cases. *Arch Dermatol* 2006;142:1157–61.
- 8 Boura P, Sarantopoulos A, Lefaki I *et al.* Eosinophilic cellulitis (Wells' syndrome) as a cutaneous reaction to the administration of adalimumab. *Ann Rheum Dis* 2006;65: 839–40.
- 9 Winfield H, Lain E, Horn T, Hoskyn J. Eosinophilic cellulitis-like reaction to subcutaneous etanercept injection. *Arch Dermatol* 2006;142:218–20.

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Inflammatory cytokine expression in the skin lesions of tumour necrosis factor receptor-associated periodic syndrome

SIR, TNF receptor-associated periodic syndrome (TRAPS) is a rare autosomal-dominant disorder characterized by recurrent episodes of fever, myalgia, abdominal pain, conjunctivitis and skin eruptions that occur either spontaneously or after minor triggers. This syndrome is associated with missense mutations in *TNFRSF1A*, the gene encoding the 55 kDa TNF receptor [1]. Although the pathogenesis of TRAPS has not been fully elucidated, serum levels of inflammatory cytokines such as TNF- α , IL-6 and IL-1 β were elevated in TRAPS, and patients