

Bullous Presentation of Idiopathic Wells Syndrome (Eosinophilic Cellulitis)

Dear Editor,

A 44-year-old female presented with pruritic oedematous papules and plaques with vesiculobullae formation over her face, trunk and limbs over 1 week (Fig. 1). She denied fever and other associated symptoms, drug intake, or insect bites. Her medical history was unremarkable. Complete blood count analysis revealed the presence of eosinophilia ($0.81 \times 10^9/L$, normal $0.04\text{--}0.40 \times 10^9/L$). Levels of urea and electrolytes, and the results of liver function tests and chest radiography were normal. Antinuclear antibodies were absent, indicating that an autoimmune rheumatic disease was less likely. Stool specimens were negative for the presence of parasites.

A skin biopsy was performed and histology findings were that of intense upper dermal oedema with subepidermal blister formation, and a dense superficial and deep perivascular and interstitial infiltrate of predominantly eosinophils with some lymphocytes (Figs. 2-4). Vessel walls were intact. Direct immunofluorescence revealed non-



Fig. 1. Erythematous papules and plaques with formation of bullae.

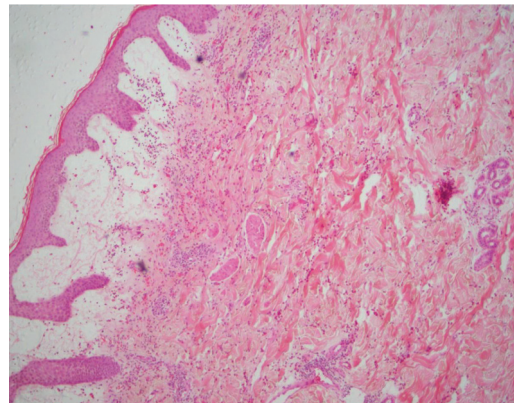


Fig. 2. Intense upper dermal oedema with subepidermal blister formation (hematoxylin and eosin, magnification, $\times 40$).

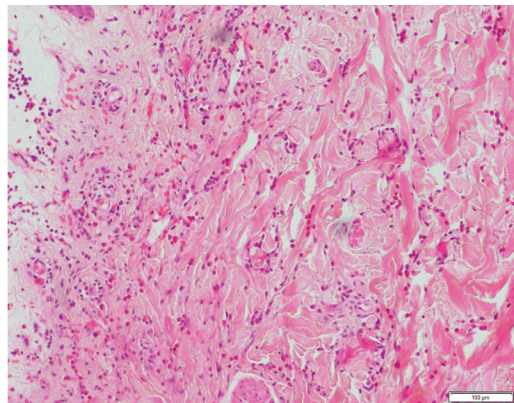


Fig. 3. Dense superficial and deep perivascular and interstitial infiltrate with many eosinophils and some lymphocytes (hematoxylin and eosin, magnification, $\times 100$).

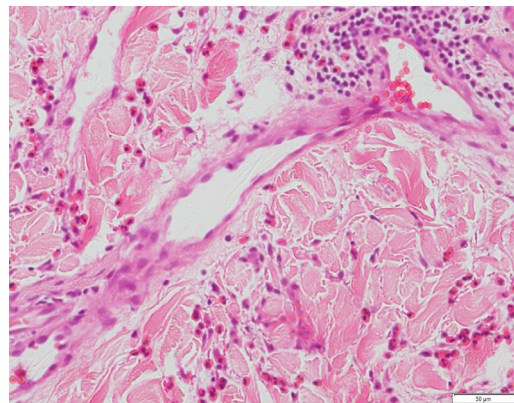


Fig. 4. Close-up view of the perivascular eosinophilic infiltrate with adjacent intact vessel walls (hematoxylin and eosin, magnification, $\times 200$).

specific findings of granular C3 deposition in the walls of several blood vessels. Serum indirect immunofluorescence was normal, which excluded an autoimmune blistering disorder. Based on the clinical presentation, presence of blood eosinophilia, and histopathological features, a diagnosis of Wells syndrome was made. The patient was treated with oral prednisolone 20 mg/day in a tapering dose over 3 weeks, with resolution of the lesions and normalisation of the blood eosinophil count. No new lesions appeared during treatment and subsequent 6 months of follow-up. Further investigations for occult malignancies did not yield significant abnormalities.

Discussion

Wells syndrome, or eosinophilic cellulitis, is a rare inflammatory dermatosis first described by George Wells in 1971 as a recurrent granulomatous dermatitis with eosinophilia. Patients typically present with recurrent well circumscribed erythematous plaques resembling cellulitis but are unresponsive to antimicrobial therapy. The course of the disease tends to be benign. Peripheral blood eosinophilia may be observed in 50% of patients, with levels fluctuating with the disease course, returning to normal during clinical remission. The condition is characterised by clinical polymorphism, and has been categorised into 7 variants: plaque-type, annular granuloma-like, papulonodular, fixed drug eruption-like, urticarial, bullous, and papulovesicular presentations.¹

Histologic findings are that of marked superficial and deep perivascular and interstitial infiltrate of eosinophils and lymphocytes. Epidermal reaction is the most variable aspect, ranging from a normal epidermis to minimal to moderate epidermal spongiosis, with or without vesiculation.² Flame figures may be present, formed by widespread degranulation of eosinophils and aggregation of eosinophil granules among dermal collagen bundles. While flame figures are associated with Wells syndrome, they are not pathognomonic and may occur in other conditions with a eosinophil-rich infiltrate, such as arthropod bite reactions, parasitic or fungal infections, drug hypersensitivity reactions, bullous pemphigoid, and eosinophilic pustular folliculitis.

The pathogenesis of Wells syndrome is uncertain. The hallmark of the disease is dysregulated tissue eosinophilia, which appears to be driven by a functional disorder of T lymphocytes. Immunophenotyping studies of peripheral T cells have shown increased CD3+ and CD4+ T cells.³ These lymphocytes spontaneously release interleukin 5, which drives eosinophilic accumulation in a Th2 immune response. Eosinophils then degranulate in the dermis causing oedema and inflammation. A plethora of proposed triggers has been reported, such as arthropod bites, drugs, thiomersal-containing vaccines, herpes simplex and human

immunodeficiency viruses, and parasitic infestations. Associations with haemato-oncological diseases and solid neoplasms have also been described.

Wells syndrome usually improves with non-aggressive therapies. Systemic corticosteroids are the first-line treatment, with the recommended starting dose of prednisolone 1-2 mg/kg per day and continuing with 5 mg/day, or initiating with 2 mg/kg for 5-7 days followed by a gradual taper for 2-3 weeks.⁴ For mild cases, potent topical corticosteroids may be used. Variable results have been reported with antihistamines, griseofulvin, and photochemotherapy (PUVA). There have been anecdotal reports of successful treatment with cyclosporine, dapsone and interferon- α .⁵⁻⁷ Any underlying precipitating event should be treated, if possible.

The bullous presentation of Wells syndrome is rare in the literature, and an association with lymphoproliferative diseases has been described in previous reports.^{8,9} In our patient, an initial search for underlying malignancies was unyielding. We recommend that such cases be monitored for interval development of haemato-oncological diseases, with relevant investigations arranged based on the symptoms and signs of the patient.

Conclusion

Wells syndrome is a rare inflammatory dermatosis with clinical polymorphism, and distinctive but non-specific histopathological features. We have described a case of the rare bullous variant of Wells syndrome, in the absence of an obvious precipitant.

Skin lesions clinically resembling cellulitis without improvement to antibiotics in association with blood eosinophilia should suggest a possible diagnosis of Wells syndrome. Although peripheral eosinophilia is common, this is not sufficient for the diagnosis of the syndrome. Correlation of clinical features, the course of skin lesions, as well as histopathological examination of a skin biopsy is important to obtain a definitive diagnosis of eosinophilic cellulitis.

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