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Case Report

All's Well that ends Wells': a case report of Wells' syndrome

善終為善：一宗威爾斯氏綜合徵的病例報告

ACC Chen 陳之傑, S Lee 李啓焱, RCF Chan 曾彩鳳, JYJ Choi 崔榮埈

We report a case of idiopathic Wells' syndrome in a 52-year-old male, who presented with pruritic, erythematous and annular plaques on his lower limbs, trunk and upper limbs. Histology revealed a dermal infiltrate of eosinophils with flame figures, consistent with Wells' syndrome. The lesions were resistant to treatment with prednisone, antihistamine and topical steroids, but resolved spontaneously after seven years.

我們報告一宗特發性威爾斯氏綜合徵的病例個案，一名求診的五十二歲男性患者，在其軀幹和四肢有著瘙癢的紅色環形斑塊。組織學顯示病灶真皮層中有嗜酸性粒細胞與火焰狀圖滲入，與威爾斯氏綜合徵吻合。病者患處在處方口服強的松、抗組織胺及外用類固醇治療後，無甚改善，但卻在七年後自癒。

Keywords: Wells' syndrome, eosinophilic cellulitis, prednisone, flame figures, spontaneous resolution

關鍵詞：威爾斯氏綜合徵、嗜酸性蜂窩組織炎、強的松、火焰狀圖、自癒

Department of Dermatology, Royal Prince Alfred Hospital, Sydney, NSW 2050, Australia
ACC Chen, MBBS, FRACGP

Department of Dermatology, Concord Repatriation General Hospital, Sydney, NSW 2139 and Central & Concord Clinical Schools, The University of Sydney, Australia
S Lee, DDM(Syd), FACD

Department of Dermatology, Concord Repatriation General Hospital, Sydney, NSW 2139, Australia
JYJ Choi, FRACP, FACD

Department of Anatomical Pathology, Concord Repatriation General Hospital, Sydney, NSW 2139, Australia
RCF Chan, MBBS(Hons), FRCPA

Correspondence to: Professor Stephen Lee AM

Department of Dermatology, Concord Repatriation General Hospital, The University of Sydney, NSW 2139, Australia

Introduction

Wells' syndrome, or eosinophilic cellulitis, is a rare disease with limited published case reports. The syndrome was first described by Wells in 1971.[1] Classically it presents as recurrent pruritic, erythematous and oedematous plaques or annular lesions that may resemble cellulitis. Peripheral blood eosinophilia is detected in approximately half of the cases. Typically, the histology of the lesions demonstrates a dermal infiltrate of eosinophils and scattered flame figures.[2] We describe a case of Wells' syndrome in a 52-year-old male that was resistant to treatment and had no identifiable cause or trigger.

Case report

Our patient was born in Italy and had migrated to Australia when he was seven years old. His only past medical problem was gout, for which he took allopurinol 300 mg daily. Allopurinol was initiated one year before the onset of the lesions. He drank approximately 50 g of alcohol per week and was a non-smoker. There was no family history of Wells' syndrome or other relevant medical problems.

In October 2005, our patient started experiencing a pruritic eruption. Multiple cutaneous lesions appeared on his lower limbs, which then spread to his trunk and upper limbs. The lesions began as erythematous papules that expanded centrifugally to become oedematous plaques with indurated edges (Figure 1a). Subsequently, the central portion of the lesions changed to a bluish colour then faded, giving the erythematous peripheries an annular appearance (Figures 1b & 1c). The lesions then gradually resolved. This cyclic and recurrent process took approximately one to two months. At a given time, our patient had developed multiple lesions in different stages of evolution on his body (Figure 1d). The patient was distressed as the lesions were disfiguring and itchy. Systemically however, he was well and afebrile.

In November 2005, he presented to his general practitioner with the eruption and was initially prescribed betamethasone valerate cream,

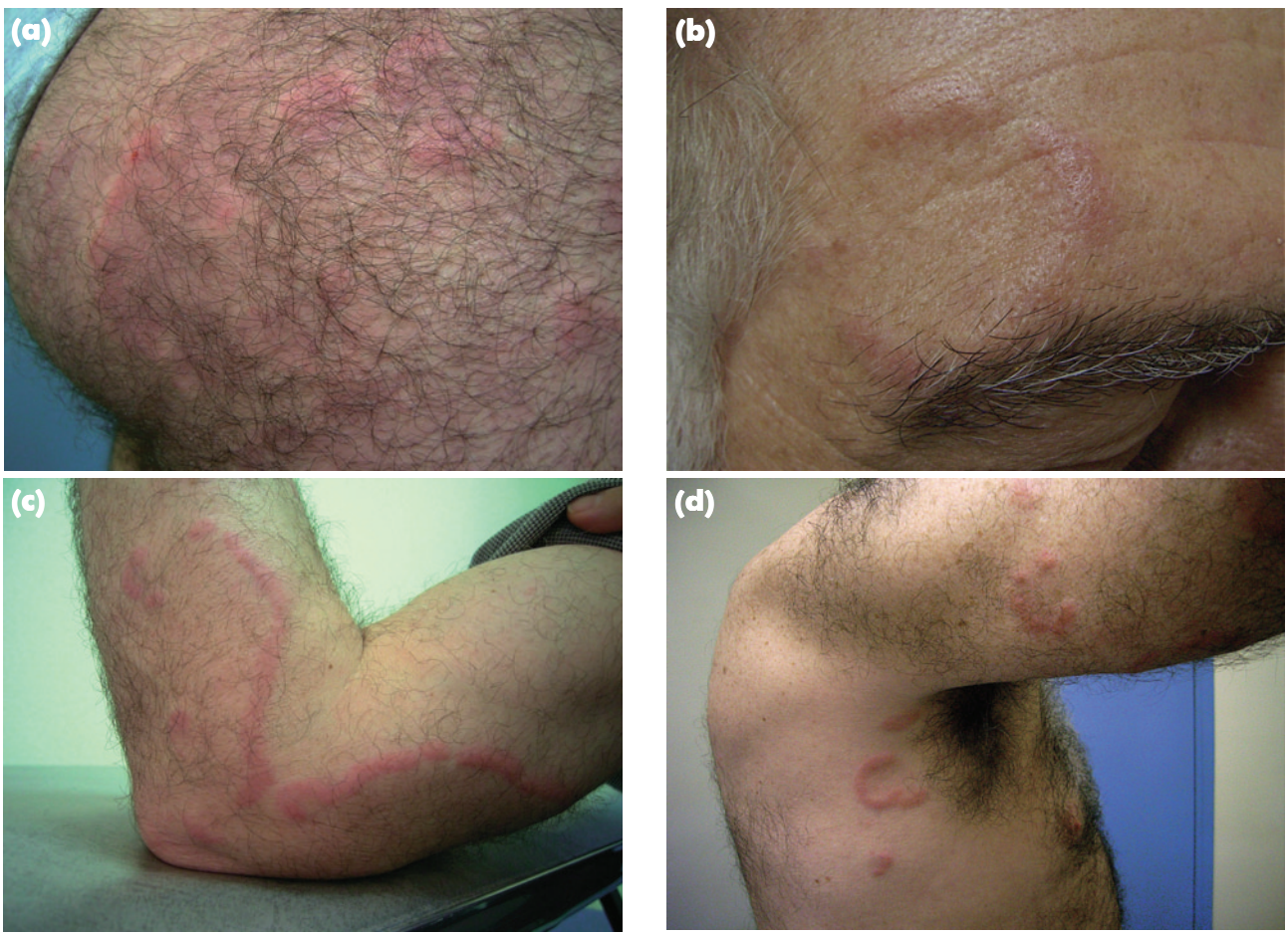

Figure 1. (a) Oedematous plaques on the right buttock. (b) An annular lesion on the forehead. (c) Annular lesions on the upper limb. (d) Multiple lesions on the upper limb and trunk in different stages of evolution.

followed by mometasone furoate cream and cetirizine orally. These reduced the pruritus but made no difference to the appearance of the lesions. In January 2006, he was seen at the Concord Repatriation General Hospital dermatology department. Initially the patient was suspected to have granuloma annulare or Wells' syndrome, and was investigated with blood tests and skin biopsies. The blood tests showed a borderline raised antinuclear antibody titre of 1:40 with a speckled pattern. However, double-stranded DNA antibody was negative. The rest of the blood tests were unremarkable, including a normal eosinophil count.

A punch biopsy from the left thigh showed a moderate infiltrate of eosinophils involving the superficial and deep dermis (Figure 2a). There were scattered flame figures, which represented eosinophilic granules encrusted on dermal collagen (Figure 2b). These changes were consistent with Wells' syndrome. Histological differential diagnoses included a drug reaction and a chronic urticarial process. No features of granuloma annulare were seen.

Our patient was started on prednisone 10 mg daily. Topically, betamethasone valerate cream was applied and oral cetirizine was taken as required for the pruritus. However, as the skin lesions continued to develop in the following weeks and no cause was found, prednisone was weaned off. After discussion with the patient, other oral therapeutic options were not trialled. In February 2006, allopurinol was stopped and he was advised to follow a restrictive diet, avoiding foods such as wine and cheese, as a trial. However, no noticeable improvement of the symptoms was observed. Indeed, the skin lesions became more widespread and annular lesions developed on his face. The facial lesions spontaneously resolved a few months later. There was no scarring. Seven years after the onset of the itchy skin lesions, in April 2012, the lesions began to clear without medical intervention, and after a couple of months they cleared altogether. At the time of writing of this case report, the patient remained free of symptoms and lesions.

Discussion

Wells' syndrome is rare and its aetiology is unknown. However, some authors have considered it to be a hypersensitivity reaction triggered by a variety of stimuli leading to

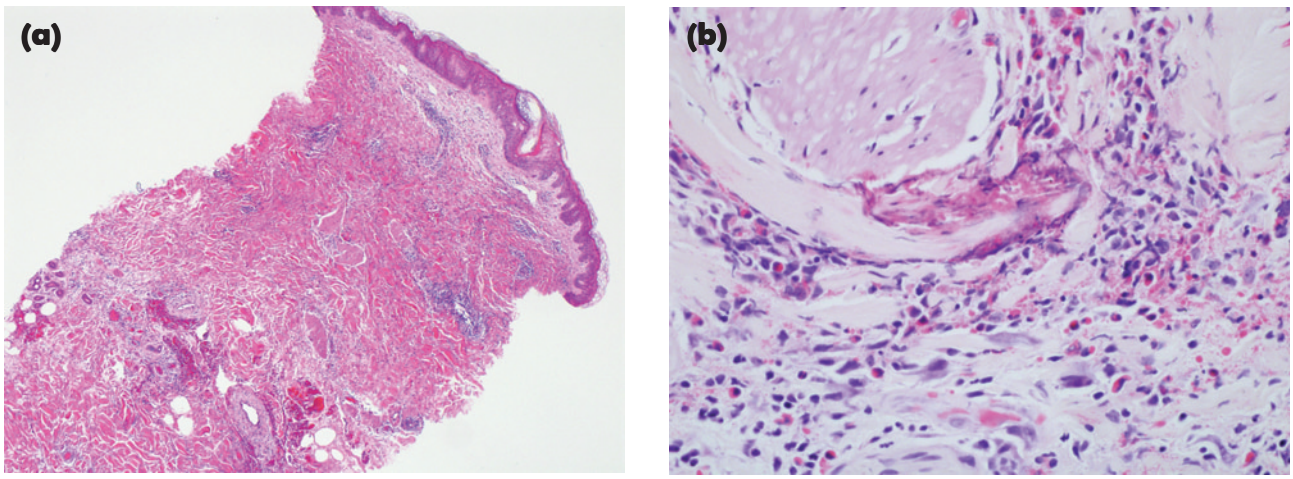

Figure 2. (a) Low magnification view showing an inflammatory infiltrate in the superficial to deep dermis (x20 magnification). (b) There is an infiltrate of eosinophils in the dermis, many of which are degenerate and degranulated. These eosinophilic granules are encrusted on a collagen bundle, forming a flame figure (centre of image) (x400 magnification).

eosinophil-induced cytotoxicity. Examples of the reported stimuli include insect bites or stings; thimerosal-containing vaccines; adalimumab; Churg-Strauss syndrome; malignancy; maternal exposure to danazol during pregnancy; and various infections such as varicella, molluscum contagiosum, Parvovirus B19, mumps, erysipelas, toxocariasis and onchocerciasis.[3] There may be a genetic component in the aetiology of Wells' syndrome: one paper reported a mother and her two sons all having had Wells' syndrome[4] and another paper reported three members in one family having had Wells' syndrome which was believed to have a dominant inheritance pattern.[5]

The skin lesions of Wells' syndrome can be multiple or few. The lesions may have different appearances. Reported clinical variants include plaques and annular, papulonodular, urticarial, bullous, papulovesicular and fixed drug eruption-like lesions. In adults, the most common presentation is erythematous annular lesions and in children plaques.[6] Histologically, three phases have been described. In the acute phase, the dermis is infiltrated by eosinophils and dermal oedema is present. In the subacute phase, the eosinophils degranulate and degenerate. The eosinophilic granules are deposited on collagen fibres, forming flame figures. Histiocytic reaction may be seen around the flame figures. In the regressive phase, eosinophils gradually decrease in number and histiocytes and giant cells are observed.[7,8] These histological findings are distinctive, but not pathognomonic.[9] In a Wells' syndrome case series, flame figures are observed in only around half of the cases.[6] Furthermore, dermal infiltration by eosinophils and flame figures can be seen in various other conditions such as insect bite reactions, drug reactions and bullous pemphigoid.[2,10] Accordingly, a diagnosis of Wells' syndrome relies on clinico-pathological correlation. Some patients with Wells' syndrome respond rapidly to oral steroids. However a minority of patients, as illustrated by our patient, are resistant to such therapy. Management should be aimed at conservative symptomatic relief and should not be too aggressive because the usual course of Wells' syndrome is self-limiting. A review of 19 cases estimated the mean duration of the disease to be five years for adults and three years for children.[6]

Conclusion

Whilst chronic urticaria is frustratingly common, authentic Wells' syndrome is rare. There have been less than one hundred reported cases worldwide. Nonetheless it needs to be included in the differential diagnosis of more common dermatoses such as resistant cellulitis, urticarial vasculitis, granuloma annulare, erythema annulare centrifugum, subacute cutaneous lupus and cutaneous lymphoma. A detailed history regarding triggers such as insect bites or stings, medications, associated medical problems and infections is essential to exclude other diseases which could mimic Wells' syndrome clinically and histologically. When managing a patient with Wells' syndrome, the dermatologist should be optimistic since a good outcome is possible. All that is Wells' may end well!

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