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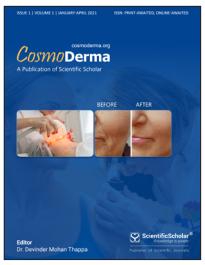

Case Report

An itchy mystery: A rare case of Wells syndrome

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ABSTRACT

Eosinophilic cellulitis (Wells syndrome) is an inflammatory dermatitis that is often misdiagnosed as infectious cellulitis due to its similarity in presentation. Misdiagnosis leads to delay of correct treatment and inappropriate use of antibiotics. The clinical eruption is characterized by varying morphology and severity and usually follows a relapsing remitting course. The classical histopathologic picture is of eosinophilic infiltrate of the dermis along with the presence of "flame figures." Limited number of cases have been reported in the literature. We describe one such case which posed as a diagnostic dilemma.

Keywords: Wells syndrome, Eosinophilic cellulitis, Flame figures, Wheals

INTRODUCTION

Wells syndrome is a rare disease with unknown etiopathogenesis. George Wells first identified this condition as a recurrent granulomatous dermatitis with eosinophilia in 1971.[1] It has been commonly misdiagnosed as cellulitis and wrong diagnosis often results in patient's dissatisfaction.

It is characterized by clinical features of cellulitis and a histopathologic picture of eosinophilic infiltrate of the dermis, along with the presence of "flame figures."[2] Although other clinical presentations such as urticarial, papulonodular, and vesicobullous lesions have been documented, slightly itchy, recurring cellulitis-like plaques are the predominant clinical presentation of eosinophilic cellulitis.[2]

Herein, we describe one such report with classical features of Wells syndrome which posed as a diagnostic challenge.

CASE REPORT

A 30-year-old male presented with multiple recurrent painful and itchy, edematous plaques, and wheals over trunk and extensors since 1 year [Figure 1]. Over a span of 3 months, they progressed to annular indurated erythematous plaques with well-defined violaceous borders associated with recurrent angioedema episodes. He was previously diagnosed with recurrent lower limb cellulitis a year ago, which failed to resolve despite medical therapy and fasciotomy. He also gave history of large fluid filled lesions over dorsum of hands and thighs that burst spontaneously with residual hyperpigmentation and scarring 4 months ago [Figure 2]. These cutaneous manifestations were in tandem with recurrent bouts of fever and arthralgia.

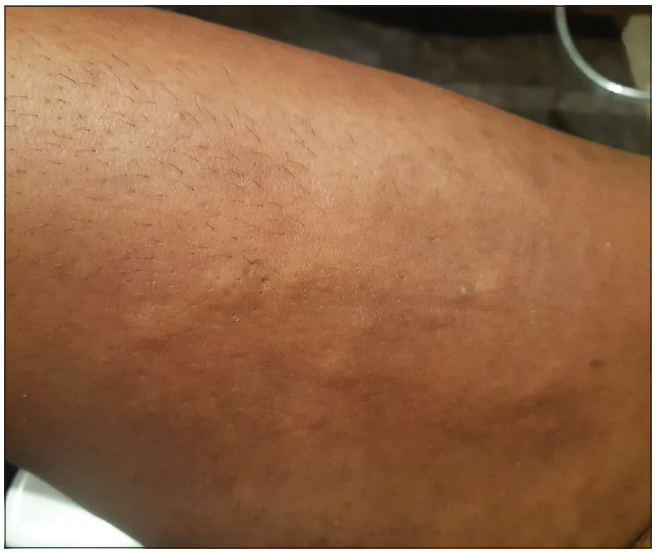

Figure 1: Clinical photograph of 30-year-old male with urticarial wheals over medial aspect of the right thigh.

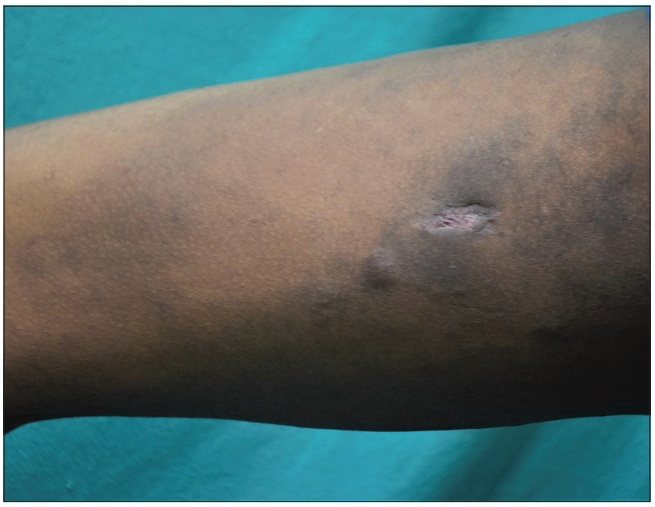

Figure 2: Atrophic scar tissue surrounded by post inflammatory hyperpigmentation that developed following spontaneous rupture of fluid-filled lesion over right thigh.

Histopathological examination revealed eosinophilic spongiosis, dense eosinophilic infiltration in perivascular region, and interstitial dermis extending up to the subcutaneous tissue. Several flame figures (collagen fibrils coated with eosinophilic granule proteins) were visualized [Figure 3].

Investigations revealed a normal complete hemogram except for raised total leukocyte count of 18,200 cells/mm^3 and peripheral blood eosinophilia (absolute eosinophil count = 10,600 cell/mm^3). Liver and renal parameters were within normal range. Urine and stool routine examination were normal. Infective serology (human immunodeficiency virus, hepatitis B surface antigen, hepatitis C virus, and venereal disease research laboratory) was unremarkable. However, 24-h urine protein was raised (228.2 mg/24 h). Complement levels (C3, C4) were normal and antinuclear antibody was negative.

A diagnosis of Wells syndrome was made and patient was started on prednisolone 40 mg (0.5 mg/kg/day) daily orally and patient showed complete clearance of lesions within a month. No new lesions appeared in the next 6 months during the follow-up visits. The patient was subsequently maintained on dapsone, after gradual tapering of the steroid.

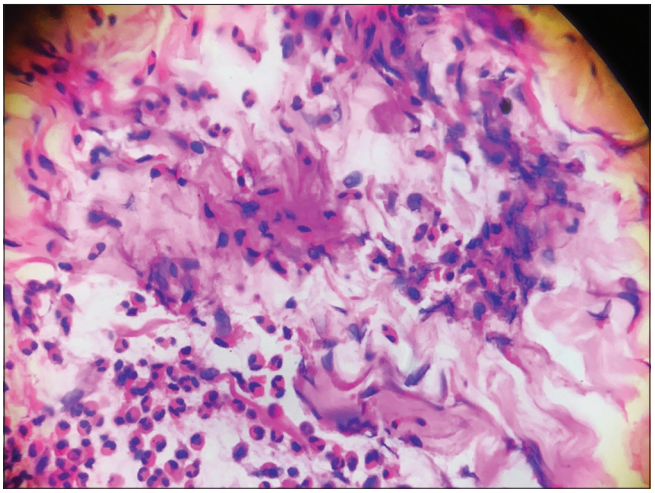

Figure 3: Histopathology (Hemotoxylin and Eosin staining) × 400 magnification, depicting numerous eosinophils and "flame figures."

DISCUSSION

Wells syndrome is an uncommon dermatosis with recurrent, erythematous, and urticarial plaques that become indurated and subsequently heal with mild pigmentation.[3] There is a wide range in the clinical and histological presentation of the disease, depending on the nature and location of the infiltrate. While some authors consider Wells syndrome to be a histopathological reaction pattern,[4-6] others consider it to be a distinctive clinical diagnosis.

Eosinophilia in dysregulated tissue is thought to be brought on by the Wells syndrome pathophysiology. There is a higher percentage of CD3+ and CD4+ T-cells, according to investigations on peripheral T-cell immunophenotyping. Interleukin 5, which is involved in the etiology of blood and tissue eosinophilia, is spontaneously released in substantial numbers by these cells. The eosinophils then degranulate in the dermis, causing edema and inflammation. With immunofluorescent stains, eosinophil major basic protein is identified in the granules of the flame figures.[2]

Many triggers have been reported including insect bites, viral infections (parvovirus B19, herpes simplex virus, varicella-

zoster virus, and mumps virus), parasitic infections (Ascaris, *Toxocara canis*, Giardia), bacterial or fungal infections, drugs (antibiotics, non-steroidal anti-inflammatory drugs, thiazide diuretics, anti-TNF, and biomedicines), and vaccines. Wells syndrome has also been linked to other illnesses, including hematologic malignancies (chronic myeloid leukemia, chronic lymphocytic leukemia, polycythemia vera, non-Hodgkin lymphoma), malignant tumors, ulcerative colitis, and eosinophilic granulomatosis with polyangiitis (Churg–Strauss syndrome).[7]

The diagnosis of the Wells syndrome is based on the clinical features and the course of the disease, especially its recurrences and the histopathologic features of eosinophilic infiltration of the dermis. The relationship of Wells syndrome to other idiopathic disorders with eosinophils is unknown.

On histopathological evaluation, a dermal infiltrate of histiocytes, eosinophils, and eosinophilic granules occurs between collagen bundles, which form the classic "flame figures." Flame figures are not pathognomonic of Wells syndrome and can be found in other disorders with a eosinophil-rich infiltrate such as insect bites, pemphigoid, and Churg–Strauss syndrome.[2] The stages of histopathological changes described include an early phase exhibiting dermal edema, and diffuse dermal infiltration of eosinophils, a subacute phase with a characteristic infiltrate of phagocytic histiocytes together with flame figures where amorphous or granular eosinophilic material adheres to collagen and a chronic phase showing fewer eosinophils, histiocytes, and giant cells between collagen bundles along with remaining flame figure.[3] The flame figures may disappear after the acute stage with the granulomatous infiltrate becoming more obvious.

Wells syndrome has a well-defined diagnostic criterion postulated as follows [Table 1].[3]

Table 1: Diagnostic criteria proposed for Wells syndrome.

Major (two of four required)	Minor (at least 1 required)
1. Diverse clinical picture to include any of the previously reported variants • Plaque-type • Annular-granuloma-like • Urticaria-like • Papulovesicular • Bullous • Papulonodular • Fixed-Drug Eruption-like 2. Relapsing, remitting course 3. No evidence of systemic disease 4. Histology: eosinophilic infiltrates, no vasculitis	1. Flame figures 2. Histology: Granulomatous change 3. Peripheral eosinophila not persistent and not greater than>1500/μL 4. Triggering factor (e.g. drug)

Our patient had met all major criteria and minor criteria of blood eosinophilia (<1500/uL) along with flame figures on histopathology. Wells syndrome usually improves dramatically with low-dose systemic glucocorticoids. Dapsone, interferon-alpha, cyclosporine, antihistamines, or minocycline have also proved effective.[2]

Following a step wise meticulous history taking and examination the clinician must rule out the diagnosis of the Wells syndrome, and histopathologic examination should be done for confirmation.

It has been commonly confused with disorders such as urticaria, urticarial vasculitis, and hypocomplementemic urticarial vasculitis. The case is being reported for its rarity with lesser than 200 cases that have been published in the literature.[8]

CONCLUSION

Wells syndrome has proven to be a great masquerader with close differentials of common conditions like urticaria. It is imperative for the treating clinician to pick up the diagnostic clues early to prevent inadvertent use of antibiotics and to initiate the right therapy at an early stage to achieve remission.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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