Diagnosis and management of eosinophilic cellulitis (Wells' syndrome): A case series and literature review

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INTRODUCTION: 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.
METHODS: A case series of eosinophilic cellulitis and a literature review are presented.
RESULTS: Patients with Wells' syndrome may present with a variety of nonspecific symptoms, such as fever, arthralgia and malaise, as well as myriad cutaneous lesions with associated erythema, presenting as blisters, bullae, papules and/or nodules. Several treatment modalities have been used to treat eosinophilic cellulitis and have been met with variable success rates; these include systemic corticosteroids, topical corticosteroids and antihistamines, with success rates of 91.7%, 50% and 25%, respectively.
CONCLUSIONS: A high degree of clinical suspicion must be exercised to diagnose this rare condition. Cellulitis with an atypical presentation or not responding to appropriate antibiotic treatment should trigger suspicion of Wells' syndrome. To date, the most successful treatment method is a short course of systemic corticosteroids.

Key Words: *Cellulitis; Eosinophilia; Eosinophilic cellulitis; Flame figures; Wells' syndrome*

Le diagnostic et la prise en charge de la cellulite à éosinophiles (syndrome de Wells) : une série de cas et une analyse bibliographique

INTRODUCTION : La cellulite à éosinophiles (syndrome de Wells) est une dermatite inflammatoire souvent diagnostiquée à tort comme une cellulite infectieuse en raison de sa présentation similaire. Le mauvais diagnostic retarde le traitement pertinent et suscite une utilisation inadéquate des antibiotiques.
MÉTHODOLOGIE : Les auteurs présentent une série de cas de cellulite à éosinophiles et une analyse bibliographique.
RÉSULTATS : Les patients ayant le syndrome de Wells peuvent présenter divers symptômes non spécifiques, tels que la fièvre, l'arthralgie et les malaises, de même qu'une myriade de lésions cutanées associées à un érythème, sous forme de vésicules, de cloques, de papules ou de nodules. Plusieurs modalités thérapeutiques ont été utilisées pour traiter la cellulite à éosinophiles et ont obtenu des taux de succès variés. Ainsi, les corticoïdes systémiques, les corticoïdes topiques et les antihistaminiques ont obtenu des taux de succès de 91,7 %, de 50 % et de 25 %, respectivement.
CONCLUSIONS : Il faut un fort degré de présomption clinique pour diagnostiquer cette maladie rare. La cellulite ayant une présentation atypique ou qui ne répond pas à une antibiothérapie convenable devrait soulever la possibilité de syndrome de Wells. Jusqu'à présent, la méthode thérapeutique la plus réussie consiste à administrer un court traitement aux corticoïdes systémiques.

Wells' syndrome, also known as eosinophilic cellulitis, was first described by Dr GC Wells in 1971 as a recurrent granulomatous dermatitis with eosinophila (1). It is a rare inflammatory dermatitis, with fewer than 200 cases reported in the literature. Clinically, it resembles bacterial cellulitis because patients usually present with a warm erythematous skin lesion. A seemingly common case of cellulitis with unclear source of infection on history, waxing and waning erythema of the skin, and a lack of response to antibiotic treatment should lead the physician to consider the diagnosis of Wells' syndrome. The diagnosis is corroborated by histopathological findings that include dermal edema, eosinophilic dermal infiltration and free eosinophilic granules coating collagen bundles ('flame figures').

In the present article, we review the literature and identify 32 idiopathic cases of this condition. Using these data, we created an algorithmic approach to aid in the diagnosis and treatment of Wells' syndrome. We also present our experience with two cases of eosinophilic cellulitis that were successfully treated with oral steroids. The present review is intended to increase awareness of Wells' syndrome, and to aid in diagnosis and treatment of this uncommon condition.

CASE PRESENTATIONS

Case 1

A healthy 23-year-old man presented with an acute onset of pruritic erythematous plaques, swelling and blistering of his right forearm (Figures 1 and 2). He experienced minimal pain, which was exacerbated with flexion and extension of his hand. He was afebrile (temperature is considered to be a vital sign), with vital signs within normal limits. He denied any history of trauma, recent travel, insect bites or intravenous drug use. A complete blood count revealed a white blood cell count within the normal range (7.88×10^9/L [normal 4.00×10^9/L to 10.00×10^9/L]); however, an elevated C-reactive protein level (6.3 mg/L [normal 0 mg/L to 5.0 mg/L]) was found, suggesting an inflammatory process. The patient was admitted with presumed bacterial cellulitis and was started on a course of intravenous cefazolin. The swelling and skin erythema further progressed along his right arm; thus, antibiotic coverage was broadened. At this time, the plastic surgery service was consulted to rule out necrotizing fasciitis. The diagnoses seemed unlikely given the clinical picture and conservative management with close observation.

Over the next several hours, the patient remained well, and the erythema of his right arm began to spontaneously improve, regressing from his shoulder down to his forearm. A computed tomography (CT) scan of the right arm demonstrated swelling limited to the subcutaneous tissue. A skin biopsy was performed and pathological findings consistent with Wells' syndrome were present (Figure 3). The complete blood count revealed peripheral eosinophilia, with a peak of 2.57×10^9/L (normal 0.10×10^9/L to 0.50×10^9/L). With the diagnosis of Wells' syndrome made from histology, all antibiotic treatment was discontinued, and the patient was treated with a course of oral steroids, which successfully resolved the patient's symptoms.

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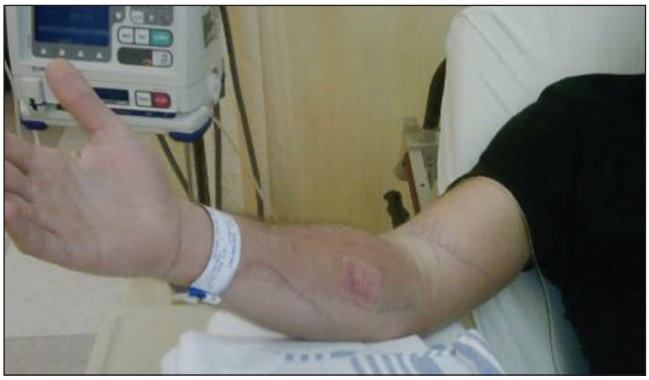

Figure 1) *Diffuse erythematous plaque of the right forearm*

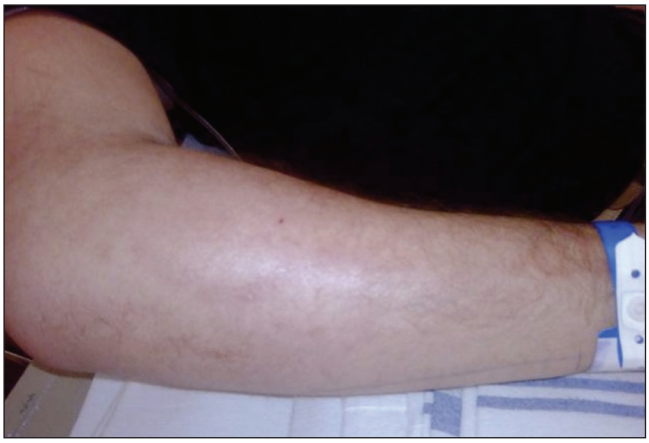

Figure 2) *Swelling of the right forearm*

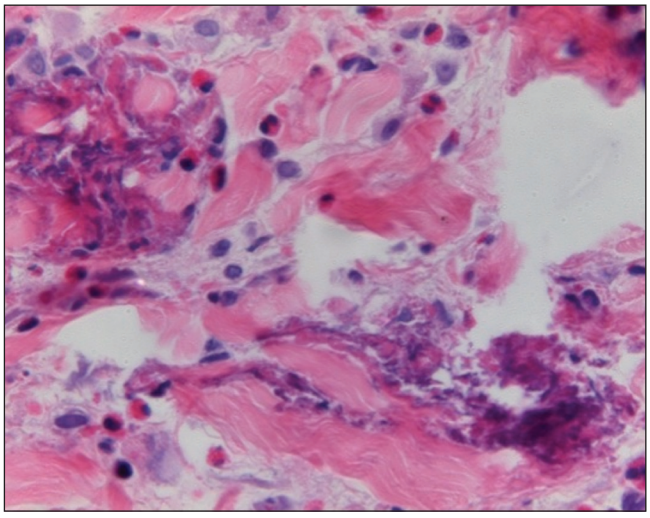

Figure 3) *Skin biopsy taken from the patient's right forearm. Flame figures, dermal edema and dermal infiltration by eosinophils consistent with Wells' syndrome. Hematoxylin and eosin stain, original magnification ×200*

Case 2

A healthy 44-year-old woman presented to the emergency department complaining of a painful 20 cm × 15 cm, pruritic, mildly tender, brown-violet nodular patch on her right thigh. The patient reported that the lesion had been enlarging over the 10 days before her presentation. The patient was diagnosed with bacterial cellulitis and was admitted to hospital for a course of intravenous antibiotics (cefazolin) as well as close observation. Over the following two days, the erythema continued to progress despite antibiotic treatment. Her white blood cell count was within normal limits (7.50×10^9/L). The plastic surgery service was consulted, and open fascial biopsies were performed at two different levels to rule out necrotizing fasciitis. Biopsies sent for frozen section showed no significant inflammatory changes in either specimen and a definitive diagnosis could not be made.

Throughout her course in hospital, the patient remained afebrile and cultures did not yield any bacterial growth. A CT scan of the patient's thigh was unremarkable. Due to the unusual history and presentation, absence of response to antibiotics and a nondiagnostic fascial biopsy, a skin biopsy was performed. A diagnosis of eosinophilic cellulitis was made based on histology. All antibiotic treatments were discontinued and the patient was subsequently treated with a course of oral steroids with successful resolution of the symptoms.

LITERATURE REVIEW

All published data regarding idiopathic Wells' syndrome from 1950 to 2010 were reviewed. The PubMed and Ovid MEDLINE database Embase were searched using the keywords "eosinophilic cellulitis" and "Wells' syndrome". Results were limited to English publications and to reports with adequate information on patient age, sex, symptoms, histological findings, blood counts and detailed treatment. The treatment data were analyzed, and success rates defined as complete resolution of symptoms were determined for each different treatment modality.

RESULTS

The search yielded 32 cases of idiopathic eosinophilic cellulitis, including the two cases described in the present review (2-29) (Table 1). There were 12 (37%) men and 20 (63%) women, with six (19%) cases reported in children. The mean (± SD) age was 33.6±22.5 years. Each of the cases presented with large erythematous plaques whereas only certain patients exhibited blisters (six of 32 [19%]), bullae (11 of 32 [34%]), papules (seven of 32 [22%]) and nodules (five of 32 [16%]). Seven of the 32 patients presented with systemic symptoms including fever, malaise and/or arthralgia. One-half of the patients exhibited localized lesion(s) (16 of 32 [50%]) and the remaining one-half exhibited diffuse lesions (16 of 32 [50%]). Hematological abnormalities, such as peripheral eosinophilia (20 of 32 [67%]) and leukocytosis (13 of 32 [41%]) were not uniformly present. Histopathological findings, such as 'flame figures', present in the majority of cases (96%), edema in the dermis and infiltration of the dermis by eosinophils, present in all 32 cases (100%), are considered to be the gold standard for diagnosis of Well's syndrome.

Multiple modalities have been used to treat Wells' syndrome with variable success. Oral steroids achieved the highest resolution rate (12 of 13 [92%]), whereas topical corticosteroids (three of six [50%]), and antihistamines (one of four [25%]) were met with less success. Four cases showed spontaneous clearance of lesions (four of 32 [12.5%]). Successful combination treatments have included oral steroids combined with antihistamines, and oral steroids combined with topical steroids. Antibiotics have been generally shown to be ineffective, although the use of minocycline resolved symptoms in one case (n=1) (2,3). Other reported therapies that have shown some success on a smaller scale include antimalarial drugs (n=1) (4), cyclosporine (n=2) (2), dapsone (n=1) (5), psoralen with ultraviolet A therapy (n=1) (6) and oral steroids combined with antibiotics (n=2) (7,8). The natural history of Wells' syndrome includes recurrence, which occurred in 13 of 23 cases (56%) at a mean follow-up time of 11±8 months.

DISCUSSION

Based on the case reports reviewed, Wells' syndrome is often misdiagnosed and, thus, inappropriately treated. As such, the diagnosis of eosinophilic cellulitis should be part of the differential diagnosis for any cellulitis presenting with atypical features (Table 2). The natural course of disease can be divided into two stages. Initially, it presents as burning or pruritus, as well as localized or diffuse cutaneous erythematous plaques. These lesions are mildly tender, with patients

TABLE 1
Idiopathic eosinophilic cellulitis (EC): Literature review

Author (reference), year	Age, years/ sex	Systemic symptoms	Location: local (L) or diffuse (D)	Particular presentation	Blood count (WBC, eosinophils), $\times 10^9$/L	Histological examination of the dermis	Treatment: (–) Did not relieve symptoms; Partial partially relieved symptoms; (+) relieved symptoms	Recurrence
Present case 1	23/male	Yes	Right forearm (L)	Blisters	Normal WBC 7.88 Eosinophilia 2.57	Flame figures Edema Eosinophilic infiltration	(–): Antibiotics (penicillin, clindamycin, vancomycin and cefazolin) (+): Oral steroids	N/A
Present case 2	44/female	No	Right thigh (L)	Brown-violet nodular	Normal WBC 7.50 Eosinophilia 0.20 (2.7%)	N/A	(–): Antibiotics (cefazolin, vancomycin, imipenem) (+): Oral steroids	No recurrence at 6 months
Howes et al (4), 2008	52/female	Yes: lethargy and arthralgia	Trunk, limbs, face (D)	Papules, nodules	Both normal	No flame figures Edema Eosinophilic infiltration	(+): Oral hydroxychloroquine 300 mg/day and indomethacin 25 mg	N/A
Green et al (9), 2007	91/female	No	Both arms (L)	Bullae	Normal WBC 11.0 Eosinophilia 1.8 (16.4%)	Flame figures Edema Eosinophilic infiltration	(+): Oral steroids (prednisone) and anti-histamine (cetirizine)	N/A
Arca et al (7), 2007	20/male		Both arms, both feet (L)	Bullae	Leukocytosis 15.0 Normal eosinophils 0.2 (1.3%)	Flame figures Edema Eosinophilic infiltration	(+): Oral steroids (prednisolone 60 mg/day) and antibiotics (Tetracycline)	No recurrences for EC, but developed eosinophilic pustular folliculitis 2 months after
Van der Straaten et al (10), 2006	6/male	Yes: febrile	Both legs (L)	Blisters	Leukocytosis 21.5 Eosinophilia 4.2 (20%)	Flame figures Edema Eosinophilic infiltration	(–): Rest and ibuprofen (+): Spontaneously	Recurrence after 6 months
Feliciani et al (11), 2006	88/female	N/A	Trunk, abdomen, lower limbs, arms (D)	Bullae	Both normal	Flame figures Edema Eosinophilic infiltration	(+): Oral steroids (prednisolone 40 mg/day)	No recurrences in 3-year follow-up
Gilliam et al (12), 2005	1/female	No	Lower limbs, left arm (L)	Bullae	Leukocytosis 30.0 Eosinophilia 14.4 (48%)	Flame figures Edema Eosinophilic infiltration	(–): Antibody (oxacillin) (+): Oral steroid 2 mg/kg combined with topical steroids (triamcinolone)	No recurrences in 1-year follow-up
Ling et al (13), 2002	45/female	No	Chest, abdomen, ankle (D)	Bullae	Leukocytosis 13.3 Eosinophilia 6.18	No flame figures Edema Eosinophilic infiltration	(+): Topical corticosteroids (+): Oral steroid (Prednisolone 30 mg daily) and anti-histamine (certirizine)	No recurrences in 1-year follow-up
Ling et al (13), 2002	24/male	No	Limbs, trunk, ears and scalp, hands, involved also tongue and throat (D)	Bullae	Both normal	Flame figures Edema Eosinophilic infiltration	(+): Oral steroids (prednisolone 40 mg daily)	N/A
Holme et al (14), 2001	39/male	No	Both hands, both legs (L)	Nodules, blisters	WBC N/A Eosinophilia 0.7	Flame figures Edema Eosinophilic infiltration	(–): Antibiotics (flucloxacillin, azithromycin) (+): Topical steroids (betamethasone valerate 0.1%)	N/A

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TABLE 1 – CONTINUED

Author (reference), year	Age, years/sex	Systemic symptoms	Location: local (L) or diffuse (D)	Particular presentation	Blood count (WBC, eosinophils), $\times 10^9$/L	Histological examination of the dermis	Treatment: (–) Did not relieve symptoms; Partial: partially relieved symptoms; (+) relieved symptoms	Recurrence
Herr and Koh (2), 2001	25/male	N/A	Lower abdomen (L)	Nodules	Both normal	Flame figures Edema Eosinophilic infiltration	(–): Oral steroids (prednisolone) Partial: antibiotics (minocycline) and topical steroids (triamcinolone) (+): Cyclosporine 100 mg/day	No recurrences in 10 months follow-up
Herr and Koh (2), 2001	42/male	N/A	Right lower abdomen (L)	None	Leukocytosis 12.2 Eosinophilia 3.49 (28.6%)	Flame figures Edema Eosinophilic infiltration	(–): Dapsone, anti-histamine (certirizine) and topical steroids (+): Cyclosporine (100 mg/day)	No recurrences in 1 year follow-up
Weiss et al (15), 2001	17/female	No	Lower extremities, back, chest, abdomen (D)	Papules	Normal WBC 8.0 Eosinophils (N/A)	Flame figures Edema Eosinophilic infiltration	(+): Oral steroids (Prednisolone 40 mg/day)	N/A
Selvaag et al (16), 2000	43/female	Yes: Febrile and malaise	Face (L)	Papules, nodules	WBC (N/A) Normal eosinophils 0.46	Flame figures Edema Eosinophilic infiltration	(+): Oral steroids 30 mg/daily	N/A
Aroni et al (17), 1999	12/female	No	Both legs (L)	Papules	WBC (N/A) Eosinophilia (no value)	Flame figures Edema Eosinophilic infiltration	(+): Anti-histamine (certirizine 10 mg 3×/day)	No recurrences in 1 year follow-up
Espana (18), 1999	24/female	No	Right foot and both arms (L)	Blisters	Leukocytosis 21.0 Eosinophilia 9.45 (45%)	Flame figures Edema Eosinophilic infiltration	(+): Oral steroids (Prednisone 30 mg/day), dapsone 100 mg/day	Recurrences after 15 months
Ferreli et al (19), 1999	49/female	No	Both arms (L)	None	Both normal	Flame figures Edema Eosinophilic infiltration	(+): Topical corticosteroid	Recurrences after 2 months with a 1 year follow-up
Stam-Westerveld et al (3), 1998	75/female	No	Hands, wrists, face, lower legs (D)	Blisters	Normal WBC 7.9 Eosinophilia 1.57 (19.7%)	Flame figures Edema Eosinophilic infiltration	(+): Antibiotics (Minocycline 100 mg/day)	Recurrences after 1 month with a 9-month follow-up
Diridl et al (6), 1997	29/female	N/A	Lower extremities and lower back (D)	None	WBC (N/A) Normal eosinophils 8%	Flame figures Edema Eosinophilic infiltration	Partial: Topical steroids and oral steroids (+) prolonged PUVA therapy (Psoralen + UVA)	Recurrences after 7 months
Tassava et al (20), 1997	41/female	No	Forearms, abdomen, upper thighs (D)	Bullae	Normal WBC 9.3 Eosinophilia 1.0	Flame figures Edema Eosinophilic infiltration	Partial: Topical steroid and antibiotic (+): Oral steroid (prednisone 60 mg/day)	N/A
Garty et al (21), 1997	Newborn/ female	No	Scalp, trunk, legs and dorsal feet, right abdomen (D)	Nodules, bullae	Leukocytosis 15.0 Eosinophilia 3.7	Flame figures Edema Eosinophilic infiltration	(–): Antibiotic, topical steroid (+): Spontaneously	Recurrences after 18 months

TABLE 1 – CONTINUED

Author (reference), year	Age, years/sex	Systemic symptoms	Location: local (L) or diffuse (D)	Particular presentation	Blood count (WBC, eosinophils), $\times 10^9$/L	Histological examination of the dermis	Treatment: (–) Did not relieve symptoms; Partial: partially relieved symptoms; (+) relieved symptoms	Recurrence
Lee and Nixon (23), 1994	56/female	No	Abdomen, back (D)	None	Normal WBC 6.6 Normal eosinophils 1%	Flame figures No edema Eosinophilic infiltration	(–): Topical steroids (–): Anti-histamine (+): Oral steroids (prednisolone 25 mg/day) combined with anti-histamine (acyphroheptadine, cetrizine) Dapsone was given, which allowed lowering the dose of prednisolone	No recurrence
Goh (24), 1992	25/male	No	Face, arms, legs (D)	None	Normal WBC 8.5 Eosinophilia 15%	Flame figures Edema Eosinophilic infiltration	(+): Oral steroids (prednisone 30 mg/day)	Recurrences after 6 months
Coldiron and Robinson (25), 1989	25/female	No	Face (L)	Bullae	WBC, N/A Normal eosinophils 8%	Flame figures Edema Eosinophilic infiltration	(–): Antibiotics (+): Topical steroids and oral steroids (prednisone) (+): Was given continuous low-dose prednisone (5mg/day)	Recurrences 2 times/year in a 4-year follow-up
Newton and Greaves (26), 1988	39/female	No	Hand, axillae and groins, limbs (D)	Papules	Leukocytosis, No value Eosinophilia 1.2	Flame figures Edema Eosinophilic infiltration	(–): Dapsone (+): Oral steroids (Prednisolone 20 mg/day)	Recurrences (no follow-up time)
Horn et al (8), 1985	36/female	N/A	Both wrist and thighs (D)	None	Leukocytosis 15.0 Eosinophilia 0.75 (5%)	Flame figures Edema Eosinophilic infiltration	(+): Oral steroids (prednisone 20 mg/day)	Recurrences after 2 years
Wong et al (27), 1984	28/male	No	Left arm and both limbs and feet (D)	None	Leukocytosis 16.2 Eosinophilia 2.92 (18%)	Flame figures No edema Eosinophilic infiltration	(–): Antihistamine, NSAID, antibiotics (+): Oral steroid (prednisolone 40 mg/day)	No recurrences (no follow-up time)
Saulsbury et al (28), 1983	7/male	Yes, febrile	Right upper eyelid, right side of the face, right hand, forearm (D)	Blisters	Leukocytosis 17.7 Eosinophilia 8.50 (48%)	Flame figures Edema Eosinophilic infiltration	(–): Antibiotics (ampicilin) (+): Spontaneously	Recurrences after 2 months and after 6 months
Neilsen et al (29),1981	11/male	Yes: febrile and arthralgia	Face, abdomen, upper extremities (D)	Papules, bullae	Leukocytosis 14.8 Eosinophilia 2.78	Flame figures Edema Eosinophilic infiltration	Partial: Prednisone (80 mg/day) (+): Spontaneously	No recurrence (no follow-up time)
Marks (5), 1980	28/female	Yes, febrile	Trunk and limbs (D)	None	Normal WBC 10.5 Eosinophilia 1.16 (11.0%)	Flame figures Edema Eosinophilic infiltration	(–): Griseofulvin (+): Dapsone 200 mg/day	Recurrences after 3 weeks in a 4-month follow-up

N/A Not available; NSAID Nonsteroidal anti-inflammatory drug; PUVA Psoralen with ultraviolet A; WBC White blood cell

subsequently developing cutaneous edema. In addition to erythema, papules, nodules, blisters or bullae may occur. The second stage is characterized by a progressive involution of the lesions, which occurs over a period of two to eight weeks (7), and can result in morphea-like residual skin atrophy and hyperpigmentation (12).

Once the diagnosis of Wells' syndrome is suspected based on clinical findings, it is corroborated by histopathological examination of a skin biopsy specimen. Histological findings vary depending on the time when the biopsy is taken; they are divided into three chronological stages (30). First, the acute stage is marked by dermal infiltration of granulocytes, predominantly eosinophils, and by dermal edema. Second, the subacute stage is characterized by the formation of palisading groups of eosinophils and histiocytes surrounding a core of collagen containing free eosinophilic granules and cellular debris, also known as flame figures. The final (resolution) stage shows gradual disappearance of the eosinophils, leaving histiocytes and giant cells

TABLE 2
Differential diagnosis (DDx) of eosinophilic cellulitis

DDx	Clinical findings	Histological findings	Standard treatment
Wells' syndrome (Eosinophilic cellulitis)	Pruritus or burning sensation Erythematous plaques +/– Peripheral eosinophilia No tenderness	Eosinophilic infiltration of dermis Flame figures Dermal edema Absence of vasculitis	Oral steroids, characteristically unresponsive to antibiotics
Bacterial cellulitis	Erythematous plaque Tenderness	Nonspecific neutrophilic and lymphocytic infiltrate Dermal edema	Oral or intravenous antibiotics
Churg-Strauss syndrome (allergic granulomatosis)	ANCAs (<50% of cases) Peripheral eosinophilia Palpable purpura Systemic involvement (cardiac, renal and GI)	Vasculitis Flame figures (+/–) Extravascular granulomas Eosinophilic infiltration of dermis	Oral steroids (with or without chemotherapy [cyclophosphamide]), with addition of steroid-sparing agents for maintenance
Compartement syndrome	Pain Pallor Swelling Paraesthesia Erythema Tense compartment Elevated compartment pressure	Fibrocytic activity (remodelling) Dermal edema Lymphocytic infiltration of dermis	Fasciotomy
Necrotizing fasciitis	Tenderness High fever Erythema and edema of skin followed by necrotic tissue formation Blisters (+/–)	Necrosis of superficial fascia Polymorphonuclear infiltration of dermis and fascia Fibrinous thrombi or arteries and veins coursing through the fascia Microorganisms within destroyed fascia and dermis	Surgical debridement Intravenous antibiotics

(+/–) Absent/present; ANCA Antineutrophil cytoplasmic antibodies; GI Gastrointestinal

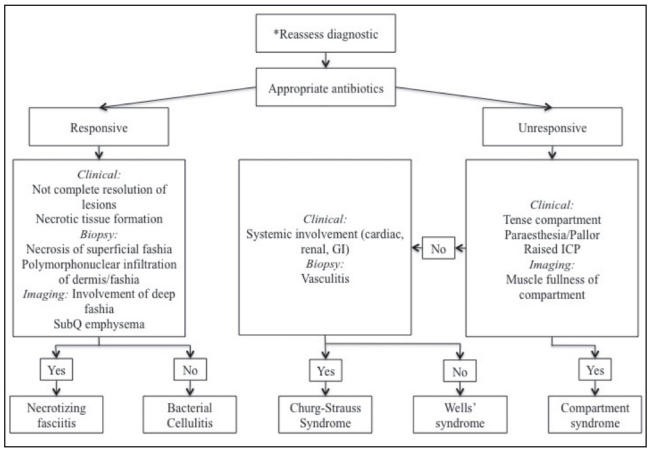

Figure 4) *Algorithm 1. Derived for the management of Wells' syndrome. GI Gastrointestinal; ICP Intracranial pressure; SubQ Subcutaneous. *See Figure 5*

surrounding the flame figures and forming granulomas. Vasculitis is not a feature of Wells' syndrome (13). Flame figures, while distinctive, are not pathognomic of Wells' syndrome, and may also be found in Churg-Strauss syndrome, parasitic infections, follicular mucinosis, herpes gestationis (20) and spider bites (10). As such, a clinical and histopathological correlation is necessary for diagnosis.

Although many theories have been proposed, the etiology of Wells' syndrome remains unknown. Some authors implicate specific triggers in the development of the syndrome, such as insect bites, viral or bacterial infections, drug eruption and thimerisol-containing vaccines (13,31-34). Others have suggested links with hematological disorders, lymphoproliferative malignancies and carcinoma (1,8,35). Although most of the reported cases suggest a triggering event or an underlying disorder, some do not and appear to be idiopathic. The pathogenesis of Wells' syndrome is also not well defined, with some evidence pointing to a type IV hypersensitivity reaction in response to a variety of exogenous and endogenous stimuli (7).

Many treatments have been used for Wells' syndrome with variable success. It should be first noted that antibiotic therapy is characteristically ineffective in the treatment of Wells' syndrome. The most common and effective treatment are oral steroids, most often oral prednisone 2 mg/kg per day for one week, then tapered over two to three weeks. For cases of persistent and frequently recurrent eosinophilic cellulitis, Coldiron et al (25) suggest a therapeutic approach of low-dose (5 mg) alternate-day oral prednisone. Topical corticosteroids also demonstrated efficacy, but should be considered in cases of limited diseases or for residual lesions. There are two cases in the literature of successful treatment of steroid-resistant Wells' syndrome with low-dose cyclosporine, suggesting the use of cyclosporine for recalcitrant disease (15). Antihistamines can be administered to relieve pruritus (23), but they are ineffective in clearing cutaneous lesions. Dapsone, a medication with both antibacterial and anti-inflammatory properties, has been used effectively alone and as an adjunct to systemic steroids to spare the negative side effects of long-term high-dose steroid use (23). For cases of eosinophilic cellulitis with an underlying cause, treating the underlying condition has led to resolution of the syndrome, such as treatment of an associated viral infection with acyclovir (33) or an underlying malignancy with radiation therapy (36). Even with appropriate therapy, patients can expect multiple recurrences (31). Using the available evidence (level 4), algorithm 1 (Figure 4) presents a treatment approach, while an approach to the differential diagnosis of eosinophilic cellulitis is presented in algorithm 2 (Figure 5).

CONCLUSION

To our knowledge, the present report represents the most comprehensive literature review to date addressing the diagnosis and management of Wells' syndrome. This uncommon condition is a cutaneous inflammatory syndrome that runs a benign course, heals with slight hyperpigmentation resembling morphea, and patients have a high probability of recurrence (56%). Wells' syndrome should be kept in mind as part of the differential diagnosis of any atypical presentation of cellulitis not responsive to antibiotics. Although peripheral eosinophilia is common, this is not sufficient for diagnosis of the syndrome. Correlation of clinical features and histopathological examination of a skin biopsy is necessary to obtain definitive diagnosis. We reviewed published

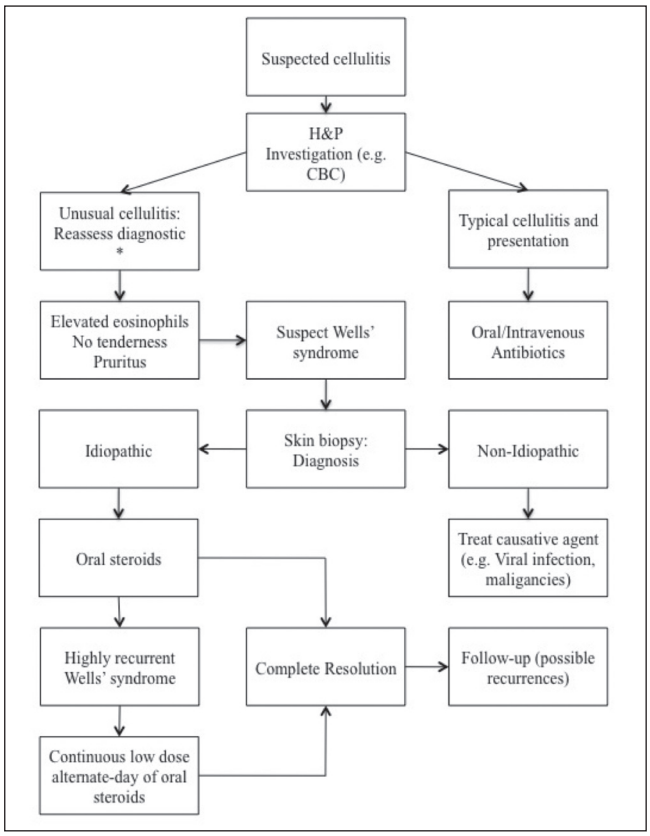

Figure 5) *Algorithm 2. Derived for the differential diagnosis of Wells' syndrome. CBC Complete blood count; H&P History and physical examination*

cases of idiopathic eosinophilic cellulitis since 1950 and found that the most successful treatment choice was oral steroids, with a 92% success rate. However, treating the underlying cause is important if one is present and alternate-day low-dose oral steroids is suggested in cases of highly recurrent Wells' syndrome. Finally, we presented two algorithms to improve diagnostic accuracy and management of this often misdiagnosed condition.

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