CASE REPORT

Ackerman syndrome: a rare cause of arthritis with dermatitis

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SUMMARY

We present a case of a middle-aged woman who presented with acute onset of non-erosive oligoarthritis and cutaneous lesions. Her laboratory work up revealed mild anaemia with positive antinuclear antibody. Her skin biopsy confirmed the presence of interstitial granulomatous dermatitis. She was treated with a successful trial of non-steroidal anti-inflammatory agents. Interstitial granulomatous dermatitis with arthritis (IGDA), or Ackerman syndrome, is an under-recognised cause of arthritis with dermatitis. This is primarily due to the varied clinical presentation of the skin lesions and the non-specific laboratory findings. Our aim is to highlight the pivotal role of skin biopsy as part of the diagnostic assessment of patients who present with arthritis and concomitant skin lesions.

BACKGROUND

Ackerman syndrome is an uncommon and under-recognised cause of arthritis with dermatitis. It is associated with various autoimmune conditions. The clinical and laboratory findings are mainly non-specific, and the most important diagnostic tool for this condition is a skin biopsy.

CASE PRESENTATION

A 35-year-old Indian woman with no significant medical history presented with a 1-week history of low-grade fever, dysuria, yellow-mucoid vaginal discharge, rash, oral ulcers and left knee joint swelling. There was no ocular involvement. There was no preceding history of diarrhoea or flu-like illness. There was no history of joint pain, myalgia, photo-sensitive rash, alopecia, venous thromboembolism

episodes, obstetric complications, haematological or renal diseases. She did not have any preceding constitutional symptoms such as weight loss, night sweats, chronic fever, cough or haemoptysis prior to the onset of this episode of illness. She denied any recent use of medications. There was no history of recent travel or contact with anyone ill. She was married with two children. She was a strict vegetarian, non-smoker and denied alcohol consumption.

On examination, the patient's vital signs were as follows: temperature 37.2°C, blood pressure 120/70 mm Hg, heart rate 86 bpm, respiratory rate 18 bpm and oxygen saturation by pulse oximetry 100% in room air. Her left knee and ankle were warm, swollen and tender. There was no calf tenderness present. Dermatological assessment revealed the presence of symmetrically-distributed indurated erythematous to violaceous annular plaques all over her body surface, excluding the palms and soles. The plaques were non-tender, non-pruritic, had well-demarcated borders and measured 1–2 cm (figure 1). She also had oral ulcers present in her inner lip and buccal cavity. Ophthalmological examination was normal. Other systemic examinations, including a pelvic examination, were unremarkable.

INVESTIGATIONS

The laboratory work up for the patient is given in table 1.

Chest, abdomen and pelvis imaging was reported as normal. Ultrasound Doppler of the lower limbs did not show any sign of deep vein thrombosis.

Figure 1 Image of right upper extremity (A) and bilateral lower extremities (B) of the patient showing the skin lesions.

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Table 1 Results of the laboratory investigation

Laboratory parameter	Patient's result
WCC	4.8×10 ³ /μL
Hb	11.1 g/dL (normocytic normochromic)
Platelet	255×10 ³ /μL
Ferritin	64 ng/mL
PT	12 s (11–14), INR 1.1
APTT	30 s (28–41)
D-dimer	0.68 mg/L (<0.5)
ESR	38 mm/1 h
CRP	40 mg/dL
PCT	0.04 pg/mL
Blood culture ×2	Negative
Liver function test	Normal
Renal function test	Cr 0.5 mg/dL, Urea 11 mg/dL, electrolytes: normal Urine analysis: 10–15 WCC, few epithelial cells, no casts, proteinuria or RBC Urine culture: negative
Uric acid	1.7 mg/dL
CPK	59
Thyroid function test	Normal
HBA1c	6.4%
HIV, HBsAg, HCV, VDRL	Negative
High vaginal swab	2–4 WCC/hpf Epithelial cells/hpf: 2+ No pathogen isolated
Knee aspirate	Yellowish turbid fluid Blood: not visible Coagulum: not visible WCC count/cm ² : 2000 (75% lymphocyte) RBC count/cm ² : 100 Gram stain: no organisms seen Culture: negative
T-spot test	Indeterminate
Mantoux skin test	<5 mm induration
Autoantibodies	Antidouble stranded DNA Ab: negative ANA: positive, 1/80 speckled pattern Rheumatoid factor, anti-CCP: negative c-ANCA, p-ANCA: negative Antiphospholipid Ab, anticardiolipin, β 2 glycoprotein: negative

ANA, antinuclear antibody; APTT, activated partial thromboplastin time; c-ANCA, cytoplasmic antineutrophil cytoplasmic autoantibody; CPK, creatine phosphokinase; CRP, C reactive protein; ESR, erythrocyte sedimentation rate; HBA1c, glycated haemoglobin; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; hpf, high power field; INR, international normalised ratio; p-ANCA, perinuclear antineutrophil cytoplasmic autoantibody; RBC, red blood cell; VDRL, Venereal Disease Research Laboratory WCC, white cell count.

Ultrasound scan of the neck showed multiple well-defined, oval shaped and hypoechoic bilateral cervical lymph nodes with normal echogenic hilum. The thyroid gland was normal. The patient was offered excisional lymph node biopsy, however, she refused to undergo the procedure at that time.

A skin punch biopsy was taken from one of the skin lesions.

DIFFERENTIAL DIAGNOSIS

- ▶ Reactive arthritis
- ▶ Disseminated gonococcal infection
- ▶ Systemic lupus erythematosus
- ▶ Rheumatoid arthritis

TREATMENT

As the knee aspirate was not suggestive of septic arthritis, the initial clinical impression was reactive arthritis or disseminated

Figure 2 Low-power view of the skin punch biopsy (×40) of the epidermis, dermis and panniculus.

gonococcal infection. The patient was therefore empirically treated with a course of ceftriaxone and azithromycin along with non-steroidal anti-inflammatory drugs. During the course of hospital stay her left ankle also became painful and swollen.

Later, the result of the skin biopsy returned, showing diffuse interstitial granulomatous dermatitis with lichenoid interface dermatitis (figure 2). The epidermis showed a maintained basket weave horny layer and foci of parakeratosis mounds without neutrophils. The basal layer showed foci of interface dermatitis with vacuolar degeneration, spongiosis, few necrotic keratinocytes and lymphocytic exocytosis. The basement membrane was not thickened. The papillary dermis showed mild oedema, pigment incontinence and scant extravasated red blood cells. The papillary and deeper dermis showed scattered foci at different levels of ill-defined necrotising interstitial epithelioid granulomas composed of epithelioid histiocytes with debris karyorrhectic material, lymphocytes and few neutrophils (figure 3). They involved the interstitial collagen bundles with minimal necrobiosis, smooth muscle bundles and tissue around sweat ducts/glands. No eosinophils, plasma cells or giant cells were seen. The small blood vessels were intact overall. There was no evidence of fibrin thrombi. The panniculus-dermis interface was focally involved by non-specific chronic inflammation, probably secondary to the adjacent dermis. The subcutaneous fat tissue was, otherwise, uninvolved.

Figure 3 High-power view (×400) of the reticular dermis.

Mucin stains (Colloid iron and Alcian blue) showed minimal mucin deposition in and around granulomatous collections. The larger blood vessels were intact and uninvolved. Special stains for acid-fast bacilli (ZN and Fite) and for fungi (PAS and GMS) were negative.

The patient was discharged on a 4-week course of a non-steroidal anti-inflammatory agent.

OUTCOME AND FOLLOW-UP

The patient was followed-up after a month. She reported that the arthritis had improved significantly and the rash had acquired a faint brown macular appearance. The cervical lymph nodes were not palpable.

DISCUSSION

Interstitial granulomatous dermatitis (IGD) belongs to a subgroup of non-infectious granulomatoses. It is a distinct histopathological entity that is associated with a number of autoimmune conditions, including rheumatoid arthritis,¹ systemic lupus erythematosus,^{2–6} autoimmune thyroiditis,⁷ antiphospholipid syndrome,⁸ etc. It is, therefore, postulated to have an immune-mediated aetiology.⁹ There are a few isolated case reports linking IGD to underlying malignancies.^{10 11}

When IGD occurs in association with arthritis, it is known as interstitial granulomatous dermatitis with arthritis (IGDA), or Ackerman syndrome. This uncommon condition was initially described by Ackerman in 1993.¹² His description initiated a series of case reports that described similar patients. IGDA typically affects middle-aged women. The dermatological manifestations are extremely variable and include multiple, symmetric, erythematous to violaceous papules, nodules or plaques. However, the hallmark of this condition is the characteristic 'rope-sign', in the form of palpable subcutaneous linear cords that typically occur in the axilla. Nevertheless, this finding occurs only in a minor subgroup of patients.¹³ The joint manifestation is commonly in the form of non-erosive, seronegative arthritis or arthralgia; this may occur at any stage of cutaneous manifestation, that is, prior to, during or even after the onset of dermatological eruptions.⁹ The laboratory abnormalities include ANA positivity, elevated ESR, mild anaemia and leucopaenia.¹³

Owing to the rarity of the condition, the experience for treatment of IGDA is not well established and response to various therapeutic agents is limited to scattered case reports in the literature. The associated conditions, for example, SLE or rheumatoid arthritis, could have a significant role in influencing the choice of agents. Treatment options include non-steroidal anti-inflammatory drugs,¹⁴ topical steroids,^{13 15} systemic steroids^{6 16 17} or any combination of these agents.^{8 18} Other available options for more resistant cases include methotrexate,¹⁹ anti-TNF agents,^{20 21} tocilizumab,²² ustekinumab²³ and IVIG.²⁴

Nevertheless, the specific indication for each class of therapeutic agent is still not clearly defined.

The prognosis of IGDA is variable. At times it could be a self-limiting condition with a documented spontaneous resolution.²⁵ On the other hand, it may have an undulating course with frequent flares that are resistant to various therapeutic agents.⁹

Contributors KH wrote the manuscript. LT and NAS reviewed the manuscript. BAAH reviewed the histopathological details of the case. All authors reviewed and approved the final version.

Competing interests None.

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REFERENCES

- Hu S, Cohen D, Murphy G, et al. Interstitial granulomatous dermatitis in a patient with rheumatoid arthritis on etanercept. *Cutis* 2008;81:336–8.
- García-Rabasco A, Esteve-Martínez A, Zaragoza-Ninet V, et al. Interstitial granulomatous dermatitis in a patient with lupus erythematosus. *Am J Dermatopathol* 2011;33:871–2.
- Gulati A, Paige D, Yaqoob M, et al. Palisaded neutrophilic granulomatous dermatitis associated with systemic lupus erythematosus presenting with the burning rope sign. *J Am Acad Dermatol* 2009;61:711–14.
- Marmon S, Robinson M, Meehan SA, et al. Lupus-erythematosus-associated interstitial granulomatous dermatitis. *Dermatol Online J* 2012;18:31.
- Wong HK, Kaffenberger BH, Zirwas M. A palpable erythematous cord over the trunk in a patient with systemic lupus erythematosus. Interstitial granulomatous dermatitis (IGD). *JAMA Dermatol* 2013;149:609–14.
- Blaise S, Salameire D, Carpentier PH. Interstitial granulomatous dermatitis: a misdiagnosed cutaneous form of systemic lupus erythematosus? *Clin Exp Dermatol* 2008;33:712–14.
- Antunes J, Pacheco D, Travassos AR, et al. Autoimmune thyroiditis presenting as interstitial granulomatous dermatitis. *An Bras Dermatol* 2012;87:748–51.
- Lee HW, Chang SE, Lee MW, et al. Interstitial granulomatous dermatitis with plaques associated with antiphospholipid syndrome. *Br J Dermatol* 2005;152:814–16.
- Verneuil L, Domp Martin A, Comoz F, et al. Interstitial granulomatous dermatitis with cutaneous cords and arthritis: a disorder associated with autoantibodies. *J Am Acad Dermatol* 2001;45:286–91.
- Schreckenberg C, Asch PH, Sibilia J, et al. [Interstitial granulomatous dermatitis and paraneoplastic rheumatoid polyarthritis disclosing cancer of the lung]. *Ann Dermatol Venerol* 1998;125:585–8.
- Swing DC Jr, Sheehan DJ, Sangüeza OP, et al. Interstitial granulomatous dermatitis secondary to acute promyelocytic leukemia. *Am J Dermatopathol* 2008;30:197–9.
- Ackerman AB, Guo Y, Vitale P, et al. *Clues to diagnosis in dermatopathology*, Vol 3. Chicago: ASCP Press, 1993:309–12.
- Peroni A, Colato C, Schena D, et al. Interstitial granulomatous dermatitis: a distinct entity with characteristic histological and clinical pattern. *Br J Dermatol* 2012;166:775–83.
- Comte C, Guillot B, Durand L, et al. [Interstitial granulomatous dermatitis with arthritis: four cases]. *Ann Dermatol Venerol* 2008;135:38–43.
- Warycha MA, Fangman W, Kamino H, et al. Interstitial granulomatous dermatitis in a child with chronic uveitis. *J Am Acad Dermatol* 2008;58(5 Suppl 1):S100–2.
- Long D, Thiboutot DM, Majeski JT, et al. Interstitial granulomatous dermatitis with arthritis. *J Am Acad Dermatol* 1996;34:957–61.
- Lee KJ, Lee ES, Lee DY, et al. Interstitial granulomatous dermatitis associated with autoimmune hepatitis. *J Eur Acad Dermatol Venerol* 2007;21:684–5.
- Bañuls J, Betloch I, Botella R, et al. Interstitial granulomatous dermatitis with plaques and arthritis. *Eur J Dermatol* 2003;13:308–10.
- Dubey S, Merry P. Clinical vignette. Interstitial granulomatous dermatitis (Ackerman's syndrome) in SLE presenting with the 'rope sign'. *Rheumatology (Oxford)* 2007;46:80.
- Ahmed ZS, Joad S, Singh M, et al. Interstitial granulomatous dermatitis successfully treated with etanercept. *Am J Case Rep* 2014;15:94–6.
- Zoli A, Massi G, Pinnelli M, et al. Interstitial granulomatous dermatitis in rheumatoid arthritis responsive to etanercept. *Clin Rheumatol* 2010;29:99–101.
- Schanz S, Schmalzing M, Guenova E, et al. Interstitial granulomatous dermatitis with arthritis responding to tocilizumab. *Arch Dermatol* 2012;148:17–20.
- Leloup P, Aubert H, Causse S, et al. Ustekinumab therapy for severe interstitial granulomatous dermatitis with arthritis. *JAMA Dermatol* 2013;149:626–7.
- Alghamdi R, Bejar C, Steff M, et al. Intravenous immunoglobulins as a treatment of interstitial granulomatous dermatitis with arthritis. *Br J Dermatol* 2012;167:218–20.
- Aloi F, Tomasini C, Pippione M. Interstitial granulomatous dermatitis with plaques. *Am J Dermatopathol* 1999;21:320–3.

Learning points

- In patients with skin and joint manifestations, skin biopsy is a valuable diagnostic intervention.
- Consider the possibility of interstitial granulomatous dermatitis with arthritis (IGDA), or Ackerman syndrome, in the differential diagnosis of cutaneous lesions with arthritis.
- Owing to association of IGDA with other autoimmune conditions, a full work up for underlying autoimmune or malignancy is warranted.

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