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Case report

Cutaneous leukocytoklastic vasculitis in a patient with ankylosing spondylitis: A case report

Yida Xing [a,1], Chengjun Zhuang [b,1], Qian Yu [c], Changyan Liu [a], Mingxi Xu [a], Lin Zhao [a], Xiaodan Kong [a,*]

[a] Department of Rheumatology, The Second Affiliated Hospital of Dalian Medical University, China
[b] Department of Intensive Care Unit, The Second Affiliated Hospital of Dalian Medical University, China
[c] Wound Stoma Clinic, The Second Affiliated Hospital of Dalian Medical University, China

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ABSTRACT

Extra-articular manifestations (EAMs) in ankylosing spondylitis (AS) are common and most extra-articular manifestations such as acute iritis and inflammatory bowel disease are positively correlated with disease activity of AS. Vasculitis is an extra-articular manifestation of AS. However cutaneous leukocytoclastic vasculitis (CLV) is uncommon in AS patients. In this article, we report a case of a 66-year-old female patient who has had AS for long time. Although the patient's articular manifestations were stable, the aortic aneurysm and CLV continued to occur sequentially. This article reminds clinicians that even AS patients with stable articular manifestations should be followed up regularly. All extra-articular manifestations of AS patients should be taken seriously and treated as soon as possible under the guidance of rheumatoid immunologists.

1. Introduction

Spinal arthropathy (SpA) refers to a group of heterogeneous rheumatic diseases with common clinical and genetic features that are divided into the peripheral type or the axial type (ax-SpA), depending on the main affected body parts affected. Ankylosing spondylitis (AS), a form of ax-SpA, is a chronic, systemic, and autoinflammatory disease mediated by the immune system [1]. Back pain and increasing stiffness of the spine as well as inflammation of the hips, shoulders, peripheral joints, and fingers/toes, are the main clinical symptoms of the disease. Extra-articular symptoms such as acute iritis and inflammatory bowel disease (IBD) are also common in AS [2].

Cutaneous leukocytoclastic vasculitis (CLV) is uncommon in AS patients. CLV is characterized by nuclear dust or debris produced by polymorphonuclear leukocytes and an excess of red blood cells, necrosis of the small vessel walls, significant neutrophil infiltration in or around the wall of the arterioles, sepecially the posterior capillary vein, and occasionally lymphocyte infiltration [3]. Immunoglobulin and complement deposits on the arterial wall are observed in about 2/3 of CLV patients. Malignant tumors, idiopathic causes, systemic inflammation, and infection are among the causes of CLV [4]. Previous literature reports often associate CLV with AS disease activity and certain medications [5–14]. This case reports a patient with AS who developed CLV despite stable joint symptoms. The rash was well controlled by treatment with hormones and tripterygium glycosides.

* Corresponding author. The Second Affiliated Hospital of Dalian Medical University, No. 467 Zhongshan Road, Dalian, 116027, Liaoning, China.
E-mail address: xiaodankong2008@sina.com (X. Kong).
[1] YX and CZ contributed equally to this work.

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2. Case presentation

A 66-year-old female patient suffered from intermittent anterior uveitis, stiffness, and inflammatory low back pain for 9 years. Fig. 1 shows the patient's complete medical history. The HLA-B27 test was positive. In 2014, she was diagnosed with AS after a radiography showed bilateral sacroiliitis (Fig. 2A and B). Various nonsteroidal anti-inflammatory drugs (NSAIDs) provided the patient with relief from low back pain, stiffness, and heel pain in the initial phase. The patient's iritis recurred every two to three years. When acute iritis occurred, the patient received retrobulbar injections or topical glucocorticoid eye drops without visual damage. The patient was diagnosed with aortic aneurysm and secondary aortic regurgitation in 2015. That same year, she underwent ascending aortic angioplasty and artificial biological valve replacement for her aortic valve. In 2016, the patient received treatment with celecoxib, sulfasalazine, and thalidomide for worsening low back pain. After using the above medications, the patient's joint symptoms improved significantly and were discontinued in 2017. Since then, the patient had no significant inflammatory low back pain and the AS condition has remained stable. The patient's anterior tibial skin developed coin-sized scaly erythema in 2019, which burst but healed quickly without therapy. A coin-sized red rash appeared in the anterior tibial area of the patient's left leg in April 2021. A short time later, the rash broke open and caused an ulcer. She received antibiotic treatment (cephalosporins; details unclear) for two weeks in the outpatient hospital, but the skin ulcer became deeper and wider. In May 2021, she was hospitalized for these difficult-to-heal skin ulcers (Fig. 3A). The patient had no other complaints, such as fever, abdominal pain, diarrhea, or sores on the upper limbs, trunk, or facial skin. At that time, she was taking sulfasalazine 750 mg twice daily and celecoxib 200 mg once daily as normal medications. Pain and stiffness were effectively treated. The patient had an ascending aortic aneurysm for 5 year and carcinoma in her left upper lung for 17 years, which had been surgically removed. The patient is followed up every year in thoracic surgery, and thoracic CT shows no evidence of lung cancer recurrence. She was free of viral hepatitis, tuberculosis, hypertension, diabetes, intestinal disease, psoriasis, and other diseases.

White blood cell count was 5360/ml (3500–9500), hemoglobin was 11.4 g/dl (11.5–15), erythrocyte sedimentation rate (ESR) was 69 mm/h (2–20), C-reactive protein was 76.15 mg/dl (0–10), and serum albumin was 31 g/L (40–55), according to laboratory results. Creatine kinase (CK), liver function, serum electrolytes, a basic metabolic panel, and urinalysis were all within the normal range. Serum IgG levels were 17.16g/L [7–16] and serum IgA levels were 4.83g/L (0.7–4.0). Serum IgM, C3, and C4 levels were within the normal range. Serological tests for HIV and hepatitis B and C were also negative.

The patient's ANA test result was a speckled pattern at a titer of 320. Anti-dsDNA antibodies were negative, as were anti-Sm and polyangiitis antineutrophil cytoplasmic antibodies. Blood cultures, a nasopharyngeal swab for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), and tests for Legionella, cryptococcus, coccidioides, and histoplasma antigens were all negative on infectious examination. Ultrasonography of the heart valves revealed no vegetations. The intima-media of the left and right femoral popliteal arteries were thickened and had uneven plaque formation, but there was no thrombosis or luminal narrowing, according to ultrasound of both lower extremity arteries. Ultrasonography of the veins in both lower limbs showed them to be normal. The results of repeated rash secretion cultures were all negative. A skin biopsy revealed partial liquefaction and necrosis of fat cells and a high concentration of neutrophils and histiocyte infiltration in the cell septum, rarely plasma cells or eosinophils, and tiny cellulosic vascular necrosis with neutrophil infiltration. Several tiny foci of purpura-like red blood cells can be detected in the adipose tissue, and occasionally there are local inflammatory necrotic exudates consistent with leukocyte fragmentation vasculitis (Fig. 4). The patient received daily intravenous infusion of methylprednisolone 40 mg for one week and daily oral prednisone 40 mg after discharge. She continued to take sulfasalazine orally at the original dose and also took tripterygium glycosides orally, 20 mg twice daily. The

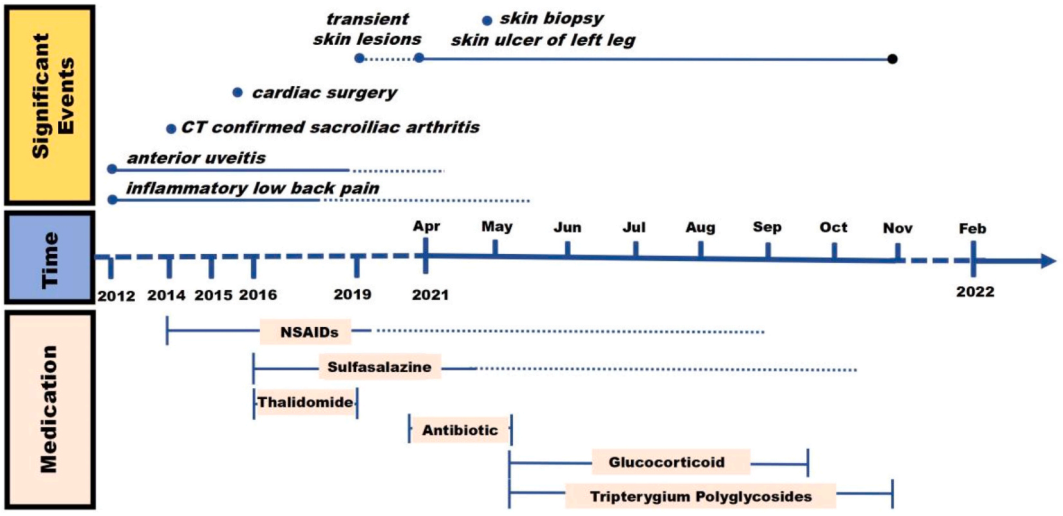

Fig. 1. Timeline of significant events and medication regiment for our case. Laboratory investigations and ongoing treatments. NSAIDs, nonsteroidal anti-inflammatory drugs. Cardiac surgery refers to aortic valve artificial biological valve replacement and ascending aortic angioplasty.

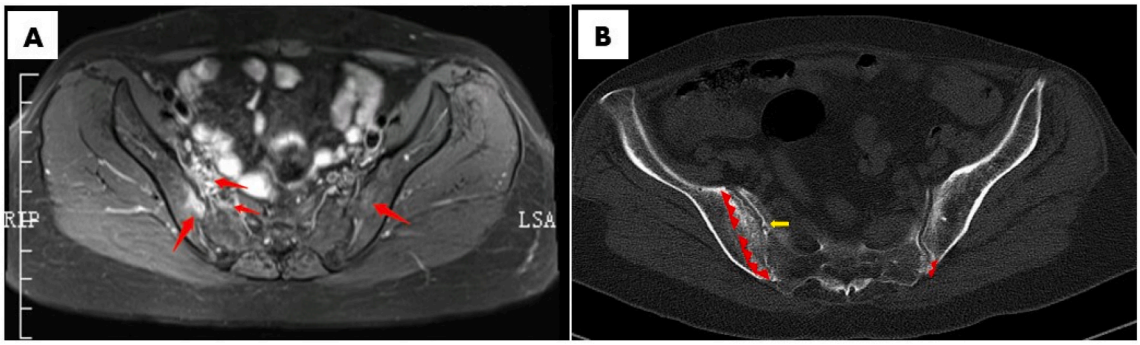

Fig. 2. (A) MRI of the sacroiliac joints revealed bilateral sacroiliitis. (B) Representative computed tomography (CT) images of in our case. Hyperosteogeny and sclerosis can be seen on the ilium surface of bilateral sacroiliac joints, and the joint surface of both sides was rough (red arrows). Insect erosion like bone destruction can be seen on both sides (yellow arrows), especially on the right.

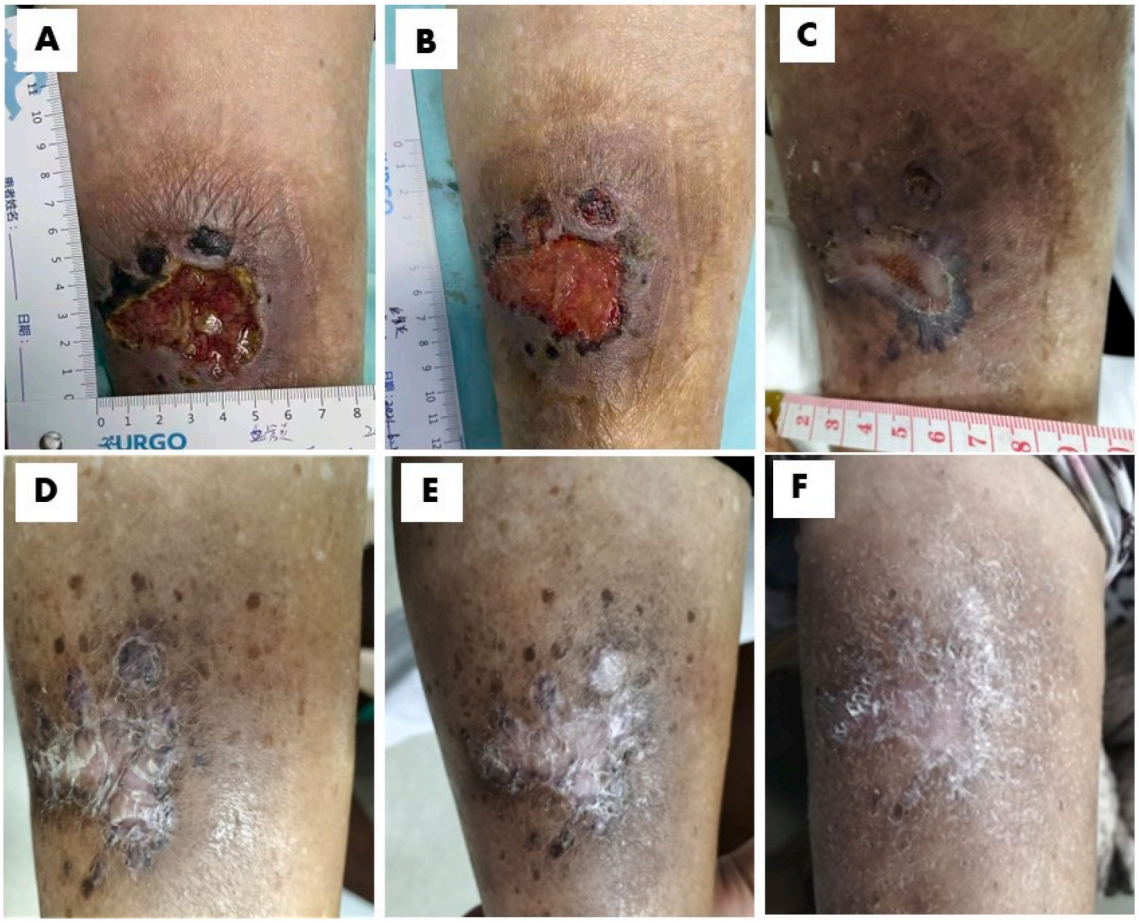

Fig. 3. The patient's left lower limb before and after treatment with glucocorticoids and tripterygium glycosides. (A) The patient's lower limbs at baseline with 2–5 mm of visible erythema with some ulceration. (B) The patient's lower limbs after 1 month of tripterygium glycosides administration showing improvement of skin ulcers. (C) The patient's lower limbs after 2 months of tripterygium glycosides treatment reveal complete remission of skin ulcers. (D–F) The patient's lower limbs have not developed skin ulcers after 3–5 months of treatment.

glucocorticoids were gradually reduced. One month, three months, and six months after the patient's discharge, we checked in with them. Blood tests, ESR and C-reactive protein were normal one month later, and serum albumin had increased to 37g/L (40–55). The skin lesions persisted for months until they finally healed (Fig. 3B–F), and the serum IgA level, C-reactive protein, and ESR were all within the normal range when we revisited her three and six months after she was discharged. The cutaneous vasculitis never returned,

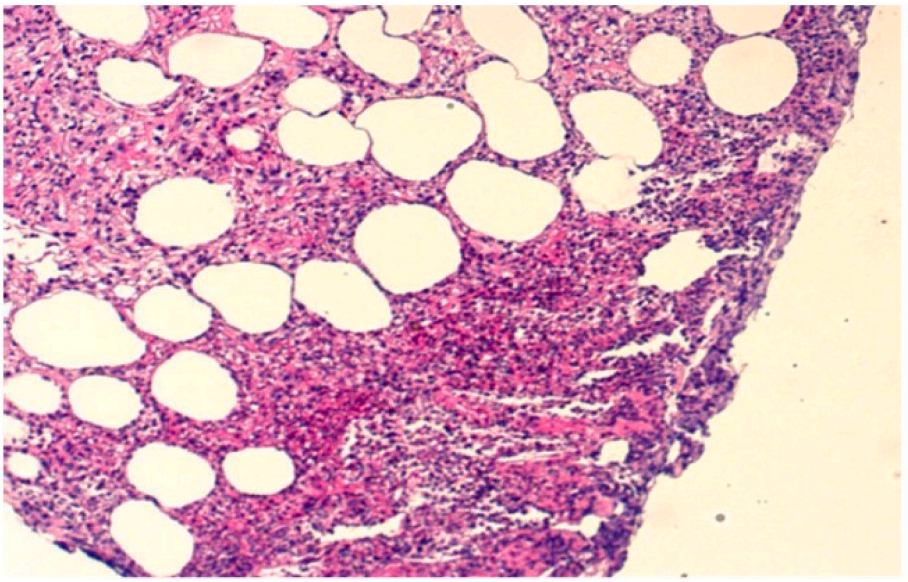

Fig. 4. Fat cells were partially liquefied and necrotic, a large number of neutrophils and histiocytes were found in the cell septum, plasma cells or eosinophils were rare, small vessel cellulose like necrosis with neutrophil infiltration can be seen, local epithelioid granuloma can be seen occasionally without necrosis, multiple small foci of purpura like red blood cells can be seen in the adipose tissue, and inflammatory necrotic exudates can be seen locally on the tissue surface. (H&E stain, 40 ×).

and the stiffness and pain were well controlled.

3. Discussion

We describe the case of a 66-year-old woman with AS with CLV characterized by symmetrical skin ulcers on the left lower extremity. As a patient with AS, she had both anterior uveitis and ascending aortic aneurysm. These organ involvements are common in Behcet's disease and ANCA-related vasculitis, but very rare in AS. Behcet's disease and ANCA can be excluded because the patient had no history of oral ulcers, vulvar ulcers, ILD, or renal involvement, and the ANCA antibody was negative. The patient's ANA test result was a speckled pattern at a titer of 320. However, the patient had no sicca symptoms. The diagnosis of Sjoegren's syndrome is therefore not sufficiently proven. She underwent surgical resection after being diagnosed with early stage lung cancer for 17 years. There was nothing to suggest a recurrence. After she began taking oral glucocorticoids and tripterygium glycosides, she noticed a decrease in the severity of her skin ulcers. And after a year, her anterior uveitis had not returned. To our knowledge, this is the first report of an AS patient who had concomitant CLV, anterior uveitis, and ascending aortic aneurysm. Ankylosing spondylitis complicated with uveitis is very common, especially anterior uveitis, which rarely causes visual loss. Our patient's anterior uveitis did not result in any visual loss either, which is consistent with the report in the literature.

Psoriasis, Henoch-Schonlein purpura, and nodular erythema are some examples of skin diseases that may be associated with AS. In addition, cutaneous vasculitis has been associated with the complication of AS. The etiology of cutaneous vasculitis is infection (including viruses, bacteria, streptococcus, staphylococci, parasites, fungi, mycoplasma, chlamydia, etc.), especially infection with hepatitis B virus, hepatitis C virus, and enteroviruses, which accounts for 15%–20%. Systemic inflammatory diseases (systemic lupus erythematosus, rheumatoid arthritis, Sjogren's syndrome, Behçet disease, and inflammatory bowel disease) account for 15%–20%. Drugs, such as nonsteroidal anti-inflammatory drugs, penicillin, sulfonamides, quinolones, cefaclor, dihydrocline, furosemide, insulin, oral contraceptives, tamoxifen, allopurinol, retinoic acid, and anti influenza vaccine accounting for 10%∼15% and malignancies (paraalbuminemia, myeloid and lymphoproliferative disorders and visceral solid tumors) account for 2–5% of cases, the remaining were idiopathic (45%∼55%) [3,4].

Patients who have mild vasculitis with only some sporadic purple spots but no systemic damage do not need special care. If the skin lesions involve severe skin or value ulcers or if the system is severely affected, more than an average dose of prednisone is required. As the rash improves, prednisone can be gradually reduced to a low dose. At the same time, hydroxychloroquine and Tripterygium wilfordii polyglycoside often have an ideal curative effect. Non-steroidal anti-inflammatory drugs are only useful for relieving joint symptoms. Cytotoxic drugs such as cyclophosphamide, methotrexate and azathioprine are generally not used to treat a single hypersensitive cutaneous vasculitis [15].

Cardiac damage is a common complication of ankylosing spondylitis [16]. Ascending aortic aneurysm, partial valve obstruction, and ventricular diastolic dysfunction can all be caused by lesions that may affect the myocardium and valves. Patients with AS suffer from chronic, recurrent immunologic inflammation that increases the likelihood that the heart will be affected. There is evidence that cardiac damage correlates to some degree with disease activity [17]. The patient we discussed is a postmenopausal woman who had

suffered from inflammatory low back pain for three years before developing an ascending aortic aneurysm. She was untreated for those three years and continued to be in an inflammatory state. Although the patient has no history of rheumatic fever, or hypertension, further clinical information and pathologic examination are needed to determine whether the patient's aortic regurgitation and ascending aortic aneurysm are related to AS. The risk of heart disease can be reduced by careful management of inflammation and vascular endothelial damage in AS patients. Perhaps the risk of heart disease can be reduced by careful treatment of inflammation and vascular endothelial damage in AS patients.

4. Conclusion

AS is an immune-mediated, long-lasting systemic disease that causes inflammation and a variety of extra-articular signs and symptoms. In addition to controlling joint symptoms and maintaining joint functionality, we should also pay more attention to extra-articular involvement. Equipment inspection and follow-up are crucial, especially in the elderly who do not show obvious articular symptoms. The prognosis of AS patients can be significantly improved by routine examination tracking inflammatory markers, actively reducing inflammation, and keeping an eye on the health of the target organs.

Ethics statement

The patient provided her written informed consent to participate in this study. Written informed consent was obtained from the individual(s) for the publication of any potentially identifiable images or data included in this article.

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Data availability statement

Data will be made available on request.

CRediT authorship contribution statement

Yida Xing: Writing – review & editing, Writing – original draft, Project administration, Funding acquisition, Data curation. **Chengjun Zhuang:** Writing – review & editing, Writing – original draft, Data curation. **Qian Yu:** Writing – original draft, Data curation. **Changyan Liu:** Writing – original draft, Data curation. **Mingxi Xu:** Writing – review & editing, Data curation. **Lin Zhao:** Writing – review & editing, Writing – original draft. **Xiaodan Kong:** Writing – review & editing, Writing – original draft, Project administration, Funding acquisition, Data curation, Conceptualization.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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