Livedoid Vasculitis in a Patient With Sjogren Syndrome Successfully Treated With Methotrexate

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Clinical Medicine Insights: Case Reports
Volume 15: 1–3

DOI: 10.1177/11795476221088489

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ABSTRACT

INTRODUCTION: Cutaneous vasculitis occurs in a sizable minority of patients with Sjogren syndrome. In addition, their response to different modalities of therapy is variable.

CASE DESCRIPTION: We present a case of a 66-year-old female with Sjogren syndrome cutaneous vasculitis in whom combination treatment with Rituximab and Azathioprine failed to show a favorable response. However, methotrexate proved to be an excellent alternative.

DISCUSSION: In cutaneous vasculitis, in addition to the necessary local therapy applied to the affected limbs, methotrexate produced a complete response when other treatment modalities failed. Therefore, it may be advisable to use methotrexate to treat cutaneous vasculitis before trying Rituximab.

CONCLUSION: In cutaneous vasculitis associated with Sjogren syndrome, methotrexate can be an early effective therapeutic strategy.

KEYWORDS: Sjogren syndrome, Livedoid vasculitis, Rituximab, Methotrexate

RECEIVED: September 5, 2021. **ACCEPTED:** February 26, 2022.

TYPE: Case Report

FUNDING: The author(s) received no financial support for the research, authorship, and/or publication of this article.

DECLARATION OF CONFLICTING INTERESTS: The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Introduction

Sjogren syndrome cutaneous vasculitis occurs in approximately 10% of patients.[1-3] It typically involves capillaries, arterioles, and venules. Around half of the cases had a single episode of cutaneous vasculitis, while chronic recurring course tends to happen in the remaining half. Occasionally, cutaneous vasculitis is the initial presenting manifestation of the disease.[4]

Lesions are commonly distributed on the lower extremities. It is usually associated with antibodies to the Ro/SSA antigen.[5] The condition can be effectively managed with compression stockings, avoidance of prolonged standing, and hydroxychloroquine.[6,7] Patients who are refractory to these regimens or who have more severe symptoms may require oral prednisolone. Individuals with treatment-refractory attacks are treated with azathioprine or intravenous (IV) Rituximab at doses typically used to treat RA.[8]

This paper reports a case of Primary Sjogren syndrome with lower-limb cutaneous vasculitis resistant to hydroxychloroquine, azathioprine, and Rituximab. But it was subsequently successfully treated with methotrexate.

Case Description

Sixty-six-year-old female with a long-standing history of hypothyroidism referred to us by a dermatologist with a history of lower extremity rash and ulceration for the previous few months. She was taking levothyroxine 50 mcg. She was on aspirin 81 mg and pentoxifylline 400 mg 3 times a day without benefit when referred. She describes the rash as starting with burning-like pain that later ulcerates. She had a dry mouth all the time and drank a large quantity of fluid daily. She reported mild eye dryness as well. She had no history of venous thromboembolism. Physical examinations revealed multiple ulcerated atrophic plaques on the ankles and feet and a well-defined ulcer with an irregular border and fibrinous base over the left malleolus.

Laboratory examination revealed hemoglobin 13 g/dl (normal: 12-16 g/dl), platelet count 162 000 (normal: 150 000-450 000), and white blood cell count (WBC) 3000 mm^3 (normal: 4000-10 000 mm^3), with 86% neutrophils. Total protein was 66 g/dl, albumin 37.3 g/dl, and serum electrophoresis was unremarkable. The erythrocyte sedimentation rate (ESR) was 14 mm/hour, C-reactive protein (CRP) was 3 mg/dl (normal: 0.0-0.8 mg/dl). The liver function test, renal function test, coagulation profile, and urinalysis were unremarkable. Hepatitis B and C serology screening were negatives. Antinuclear antibodies (ANA) were elevated at 1:10 240. The anti-SS-A titer was positive at 90.28 units/ml. For complements, levels for C3 was 0.92 (normal range 0.8-1.6 g/l) and C4 was 0.32 (normal range 0.16-0.48 g/l). CH50 measured level was 77 (normal range 42-95 U/ml). However, rheumatoid factor, anti-double-stranded DNA (anti-dsDNA), anti-cyclic citrullinated peptide (anti-CCP), anti-neutrophil cytoplasmic antibodies (ANCAs), antiphospholipid antibodies, cryoglobulins, and inherited thrombophilia screen were negative. Schirmer test was performed ad revealed 5 mm/5 minutes on both eyes. Tear-film breakup time was performed as well and showed 8 seconds on both eyes. The patient refused to labial salivary gland biopsy. The diagnosis of Sjogren syndrome was made based on the findings mentioned above.

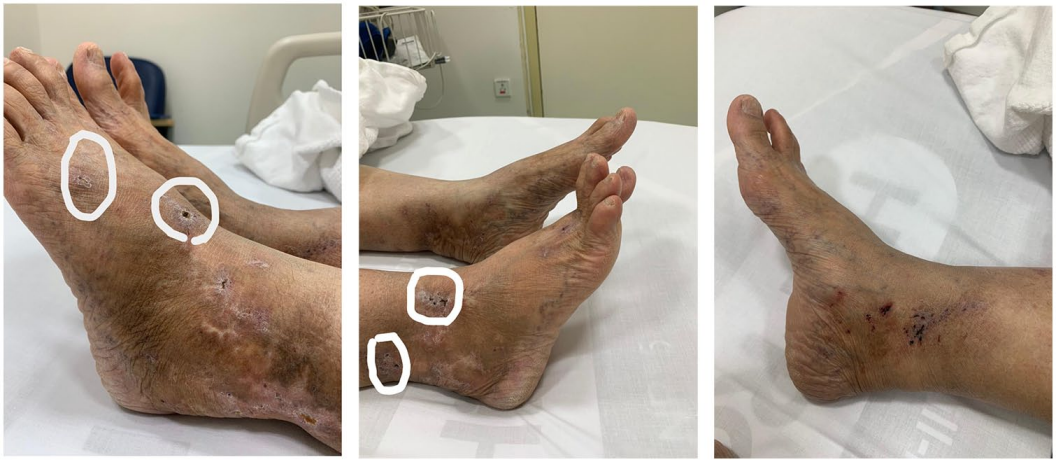

Figure 1. Images before starting Methotrexate.

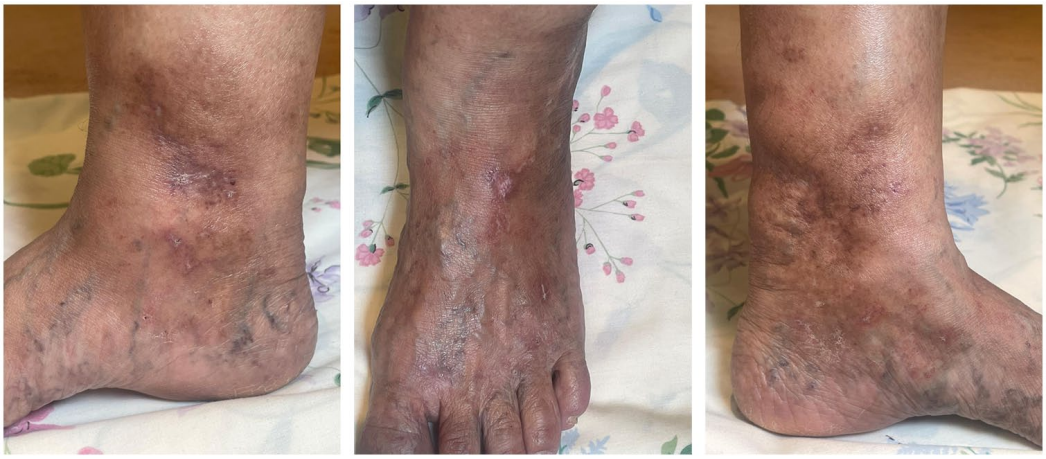

Figure 2. Images after 3 months of Methotrexate showing significant improvement.

Biopsy of the lesions revealed fibrinoid necrosis and focal fibrin thrombi inside the dermal blood vessels.

Before the presentation, her dermatologist tried to treat her with intravenous methylprednisolone 100 mg for 3 days and switched to oral prednisolone with partial improvement. However, the rash and ulceration reoccurred after the tapering of prednisolone. When she came to us, she was started on hydroxychloroquine 400 mg daily, and azathioprine 100 mg treatment was continued for 3 months. This regimen was not successful in treating the lesions. We decided to start Rituximab 1 g intravenously and repeated it after 2 weeks with partial response. She took 2 additional infusions of Rituximab over the subsequent 6 months for a total of 4 doses. However, the lesion continued, and new lesions developed. At that point, we stopped Rituximab and azathioprine due to lack of response and started methotrexate 10 mg along with folic acid 10 mg weekly orally. She reported an improvement in her condition and healing of ulcers in the lower extremities. She also had no new lesions. The picture before and after methotrexate therapy are shown in Figures 1 and 2.

Discussion

As presented in our case, cutaneous vasculitis in SSJ is a well-known manifestation. It can include palpable purpura, urticarial lesions, macules, papules, and ulceration of the overlying skin. The presence of cryoglobulins is a major contributor to vasculitis in SSJ. Its prevalence is estimated to be in 5% to 28% of patients with primary SSJ.[9] Since many therapeutic modalities are now available for hepatitis C, Primary SSJ has become the leading cause of cryoglobulinemic vasculitis.[10] Its presence is reported to cause more serious manifestations of systemic vasculitis in primary SSJ, which can involve medium-sized vessels resembling polyarteritis nodosa. It is also more to affect peripheral nerves and kidneys.[9] Another entity to consider in approaching vasculitis is drug-related causes. Nonetheless, in our case, cryoglobulins were not detected, and the only medication patient was using was levothyroxine for the last 20 years.

Treatment of cutaneous vasculitis is usually individualized to the varied etiology and degree of severity. Conservative measures, including resting the affected limb, elevation, and compression stockings, may help wound healing. In addition, topical

steroids and moisturizers can improve pruritus. However, these measures do not prevent the development of new lesions.

For severe, intractable, or chronic, recurring vasculitic lesions, systemic therapy is indicated. Unfortunately, there is no agreement in the literature on how to guide management. Therapeutic recommendations are based mostly on case reports, case series, and expert opinion.[11] Therefore, treatment should be tailored to the severity of the disease and its associated symptoms. Oral glucocorticoid (prednisolone) can be used for painful, ulcerative, or otherwise severe diseases. Their efficacy has been reported in various case series and reviews.[12-15] All previous measures were tried in our patient with little success. The dose of glucocorticoid administered by the referring dermatologist was even higher than those administered in some reported cases but without lasting benefit. As is well known, systemic glucocorticoid is not advisable as a long-term strategy due to its associated complications. Due to the failure of the previous regimen, hydroxychloroquine 400 mg was tried in our patient. Hydroxychloroquine has been reported to be beneficial in treating cutaneous vasculitis of Sjogren syndrome.[7]

However, the effect of hydroxychloroquine on skin lesions was not satisfactory. Azathioprine was reported to be effective in treating cutaneous vasculitis in an old report.[16] However, we tried a combination of hydroxychloroquine 400 mg daily and azathioprine 100 mg daily for 4 months. But this effort did not produce the desired effect. The application of Rituximab as a B-cell depleting agent has been investigated in primary SSJ, with varying levels of success.[17,18] Based on our experience, we used Rituximab initially despite the absence of rheumatoid factor and hypergammaglobulinemia. The patient refused to undergo a re-biopsy of the lesions. Yet, the persistence of the lesions, in addition to developing new ulcers, were satisfactory enough for us to presume its failure. Methotrexate produced a stronger effect on the healing of cutaneous ulcers and prevented new lesions.

In conclusion, methotrexate worked in our patient where other treatment modalities failed. Therefore, it may be advisable to use methotrexate to treat cutaneous vasculitis before trying Rituximab.

Author Contributions

Abdulkarim did literature reviwe and wrote the maniscript, Abdurahman supervised the maniscript.

Consent

Consent was secured to publish the findings of this case.

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