A Rare Manifestation of Primary Sjögren’s Syndrome with Pyoderma Gangrenosum: Case Report

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ABSTRACT

Objective: Sjögren’s Syndrome (SjS) is a systemic autoimmune disease typically presenting with sicca symptoms. However, a limited number of case reports in the literature have described rare initial presentations with pyoderma gangrenosum (PG). This report aims to underscore this infrequent association between PG and SjS by presenting another illustrative case.

Case: This case report elucidates the diagnosis and treatment of primary Sjögren’s syndrome (pSS), focusing on the ulcerated lesion that manifested on the leg of a 54-year-old female patient with no underlying health conditions. The findings are discussed in the context of the existing literature.

Discussion: SjS is a multisystemic autoimmune disease characterized by lymphocyte infiltration and damage to tissues, especially exocrine glands. Although sicca symptoms are typically the initial clinical findings, PG can rarely manifest as the primary symptom, presenting as an ulcerative skin lesion predominantly located on the lower extremities. There is currently no standard treatment recommendation in the existing guidelines for this rare condition.

Conclusion: The co-occurrence of PG and SjS is uncommon, yet it may serve as a warning for associated systemic diseases, such as SjS. Treatment may involve a combination of corticosteroids and disease-modifying antirheumatic drugs (DMARDs).

Keywords: Sjögren’s syndrome, pyoderma gangrenosum, leg ulcer, skin ulcer

INTRODUCTION

Sjögren’s Syndrome (SjS) is a systemic autoimmune disease characterized by the infiltration of lymphocytes into exocrine glands, particularly the lacrimal and salivary glands. It can manifest as a primary disease or as a secondary condition associated with another autoimmune connective tissue disorder or systemic disease. Although the first findings are mostly sicca symptoms, the heterogenous nature of SjS as a multisystemic disease may affect gastrointestinal, pulmonary, neurologic, articular, and cutaneous organs (1, 2). Rare examples of this multisystemic involvement include case reports in the literature declaring first clinical presentations with cerebellar degeneration, pulmonary amyloidosis, membranous nephropathy, or pyoderma gangrenosum (PG) (3-12).

PG is an uncommon neutrophilic dermatosis characterized by painful ulcerative skin lesions that can occur on any cutaneous site but predominantly in the lower extremities (13). This condition typically initiates as a small papule or pustule, progressively enlarging and ulcerating, featuring an acneiform and serpiginous necrotizing red-blue border (14-16). The pathogenesis of pyoderma gangrenosum remains unclear but appears to result from a multifaceted interplay of genetic predisposition, neutrophil dysfunction, and inflammatory mediators (17). The clinical course can vary, encompassing rapidly progressing disease to more indolent forms.

While the diagnosis of PG is primarily clinical, the significance of laboratory tests and histopathological examinations lies in identifying any associated diseases. Apart from the primary disease, PG can be seen in half of patients secondary to inflammatory bowel diseases, malignancies, and rheumatological diseases (15).

In the literature, only a limited number of cases have reported the uncommon association between PG and SjS. This paper details a noteworthy instance where the primary clinical presentation of SjS is pyoderma gangrenosum.
CASE

A 54-year-old female patient with no comorbidities presented to the dermatology clinic due to a lesion that started as an eruption on the front surface of the right leg a month ago but rapidly turned into a painful ulcer (Figure 1). Despite receiving amoxicillin-clavulanate treatment for 10 days, no improvement was observed in the ulcer, and she was referred to our clinic for etiological investigation due to the lesion's compatibility with pyoderma gangrenosum (PG).

In the rheumatological evaluation, the patient reported no joint pain, photosensitivity, Raynaud's phenomenon, oral aphthae, genital aphthae, or diarrhea, but she had been experiencing dry eyes and dry mouth for a year. Physical examination revealed no active arthritis or arthralgia, lymphadenopathy, or hepatosplenomegaly. Cardiovascular, respiratory, and neurological system examinations were normal. Abdominal examination did not reveal any specific findings. Apart from the ulcer on the leg, there were no other physical examination findings.

Laboratory tests showed normal liver and kidney functions. Hemoglobin level was 11.3 g/dL, white blood cell count was 8,100 mm³, platelet count was 180,000 mm³, sedimentation rate was 43 mm/s, and C-reactive protein (CRP) was 5.4 mg/dL. PPD skin test and serological tests for hepatitis B/C virus and HIV were negative. Immuno- genic tests revealed a speckled positive antinuclear antibodies (ANA) at a titer of 1/320, positive anti-Ro/SSA and anti-La/SSB, and negative anti-sm, anti-dsDNA, anti-Scl70, anti-Jo 1, antineutrophil cytoplasmic antibodies (ANCA), anti-cyclic citrullinated peptide (anti-CCP), and rheumatoid factor (RF). The Schirmer test was 3 mm bilaterally. Salivary gland biopsy, which was performed due to the positivity in anti-Ro/SSA and anti-La/SSB, showed more than 50 lymphocytes in 3 foci (Focus score 3). The wound culture from the ulcer did not yield any growth, while the tissue biopsy result of the ulcer was reported as neutrophilic dermatosis consistent with pyoderma gangrenosum.

The patient was diagnosed with Primary Sjögren’s Syndrome according to the 2016 American College of Rheumatology/European League Against Rheumatism (ACR/EULAR) classification criteria and was started on methylprednisolone 60 mg/day, followed by the addition of hydroxychloroquine 200 mg/day and azathioprine 100 mg/day. As significant improvement in the skin lesion was observed after 3 weeks, the methylprednisolone dose was gradually reduced, reaching a maintenance dose of 6 mg/day at the 3rd month. Hydroxychloroquine and azathioprine were continued at the same doses.

Figure 1. Pyoderma gangrenosum, which starts as an eruption in the right lower extremity and turns into acneiform and necrotizing ulcer formation with serpiginous border.
DISCUSSION

Pyoderma Gangrenosum (PG) is classified within the spectrum of neutrophilic dermatoses (NDs), characterized by skin lesions demonstrating a significant inflammatory reaction primarily composed of neutrophils without any evidence of infection upon immunohistological examination. The pathophysiology of NDs remains unclear, but there is an association with various systemic diseases such as myeloproliferative disorders, monoclonal gammapathies (predominantly of the IgA type), inflammatory bowel diseases, and autoimmune connective tissue diseases.

Sjögren’s Syndrome (SjS) is an autoimmune connective tissue disease that affects multiple systems beyond the exocrine glands. It may present with various manifestations in the gastrointestinal, hematopoietic, central and peripheral nervous systems, joints, and skin. Skin findings associated with SjS may include xeroderma, purpura, Raynaud's phenomenon, and urticarial vasculitis (2).

The co-occurrence of primary Sjögren’s syndrome with pyoderma gangrenosum is an infrequent phenomenon documented in the literature. Among the seven previously reported cases (6-12), five were women, and the majority of cases occurred between the fourth and sixth decades of life. Except for a 25-year-old female patient (11), all cases were diagnosed with pSS before the occurrence of PG. Our patient is the second case in the literature who presented with PG without a prior diagnosis of SjS.

PG lesions are commonly found on the lower extremities (13) but can occur on any cutaneous site, including the scalp, face, perioral and perioral areas, arms, hands, trunk, genital, perianal, and peristomal regions. In all case reports showing PG-SjS association, the location of the lesions is the lower extremities, as in our case. These lesions typically start as inflammatory papules or pustules and progress to necrotic painful ulcers. Biopsy taken from these ulcers shows significant neutrophilic infiltration, necrosis, and abscess formation. While the most common type among the four major defined subtypes of PG is the ulcerative (classical) form, it also occurs in bullous (atypical), pustular, and vegetative forms (18). In the differential diagnosis, traumatic ulcers, cutaneous infections, vasculitis, malignancies, ulcers secondary to vascular occlusion disorders, or ulcerative inflammatory disorders like cutaneous Crohn’s disease and ulcerative necrobiosis lipoidica must be considered (19).

Although no standard treatment is defined in the guidelines on this issue, most patients in the literature responded well to methylprednisolone (5 to 60 mg/day according to the severity of clinical symptoms) and azathioprine (20 mg/kg/day) and/or hydroxychloroquine (200 mg/day) combination (6,7,9,10,12). A patient with rheumatoid arthritis and secondary SjS was treated with rituximab and methotrexate (8), while cyclosporine and methylnprinosilone combination was the chosen therapy for another patient (11). Consistent with these results, our patient also responded well to corticosteroid and disease-modifying antirheumatic drugs (DMARDs) combination.

CONCLUSION

The co-occurrence of pyoderma gangrenosum (PG) and Sjögren’s Syndrome (SjS) is exceptionally uncommon, and this case represents the inaugural instance documented in the literature where PG serves as the initial presentation of Sjögren’s syndrome. Despite the atypical nature of PG as a presenting symptom, this case serves as a valuable indicator for clinicians that SjS should be contemplated as a potential cause of pyoderma gangrenosum. Intriguingly, the combination of corticosteroids and disease-modifying antirheumatic drugs (DMARDs) has proven to be an effective treatment for pyoderma gangrenosum in patients with Sjögren’s syndrome.

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Ethical approval: The present study was conducted in strict accordance with the principles outlined in the Declaration of Helsinki. Ethical approval for the study was obtained from the appropriate ethics committee, and all participants provided informed consent before participating in the study.

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