A case report of Pyoderma gangrenosum (PG) associated with Antiphospholipid syndrome (APS) and systemic lupus erythematous (SLE)

By Sonia Hosseini Anbaran

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A case report of Pyoderma gangrenosum (PG) associated with Antiphospholipid syndrome (APS) and systemic lupus erythematous (SLE)

Yousef Mohammadi Kebar[1] Leili Avesta[2]; Elham Nezhadseifi[1]; Sonia Hosseini Anbaran[3]; Mahdi Mohammadzadeh shahla[4],Maryam Bahramnezhad[5]

[1]Department of Internal Medicine, Ardabil University of Medical Sciences, Ardabil, Iran

[2]Department of Cardiology, Ardabil University of Medical Sciences, Ardabil, Iran

[3]Medical doctor, internal medicine resident, Ardabil University of medical science, Ardabil, Iran

[4]Young Researchers and Elite Club, Ardabil Branch, Islamic Azad University, Ardabil, Iran

[5]Imam Khomeini Hospital, Ardabil University of medical science, Ardabil, Iran

Abstract

Pyoderma gangrenosum (PG) is a noninfectious, inflammatory, ulcerative neutrophilic dermatosis that mainly involves the extensor surfaces of the legs. PG characteristically presents as a painful wound with suppurative as well as attenuated borders. PG-like wounds have been rarely reported in patients with APS and systemic lupus erythematous (SLE) patients. Rituximab can be effective in the treatment of PG. We report a woman with SLE and APS who developed extensive and progressive lesions consistent with PG that showed rituximab can be a potential treatment for it.

Key words:

Pyoderma gangrenosum, Antiphospholipid syndrome, systemic lupus erythematous, rituximab

Introduction

Pyoderma gangrenosum (PG) is a noninfectious, inflammatory, ulcerative neutrophilic dermatosis that mainly involves the extensor surfaces of the legs. PG characteristically presents as a painful wound with suppurative as well as attenuated borders (1, 2). The pathophysiology of PG is not well known, and it may include genetics, abnormal phagocytosis, neutrophilic abnormalities (trafficking, adhesion, and chemotaxis), and innate as well as adaptive immune system dysregulation (3). It is often accompanied by inflammatory arthropathies, inflammatory bowel diseases (IBD) as well as hematologic malignancies (4, 5). Antiphospholipid syndrome (APS) has been related to various cutaneous abnormalities such as phlebitis, subungueal splinter hemorrhages, cutaneous necrosis and infarctions, livedoid vasculitis, livedo reticularis, Degos's disease (malignant atrophic papulosis), as well as skin ulcerations (6). PG-like wounds have been rarely reported in patients with APS and systemic lupus erythematous (SLE) patients (7-11). We report a woman with SLE and APS who developed extensive and progressive lesions consistent with PG.

Case presentation

The patient is a 35-year-old woman who came with a complaint of leg ulcer.

The patient's wound was caused by an insect bite 3 years ago and has gradually become larger. Currently, it has a yellow discharge and measures 3 x 4 cm with a black border and an erythematous center. It is located in the distal part of the leg. It is placed on the left and it is considered PG.

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The patient's vital signs are stable: blood pressure: 120/80, heart rate: 87, respiratory rate: 16, body temperature: 36.8.

On auscultation of the heart, a murmur of 3/6 is heard in the mitral center. The lungs are clear on auscultation. The abdomen is soft. There is no tenderness. There is no arthritis in the examination of the joints. DTR is normal, muscle forces are normal.

2years ago, the patient had a spontaneous abortion at 8 weeks. She had 1 episode of DVT 2 years ago. 1 year ago, she suffered from left hemiparesis and was diagnosed with ischemic CVA. At the same time, in the echocardiography, there was vegetation on the surface Atrial AMVL and Libman-Sachs endocarditis (LSE) have been discussed and treated.

With this set of symptoms, as well as anemia, thrombocytopenia, and high ESR, it was investigated in terms of APS and lupus diseases. In the evaluations, there was a high ESR, ANA+, a decrease in the level of complements, and IgG + antiphospholipid and IgG + anticardiolipin antibodies were reported. has been treated with hydroxychloroquine 200 mg once daily, prednisolone 10 mg daily, Cellcept 500 mg once every 12 hours, warfarin 5 mg once daily, Aspirin 80 mg once daily, Lasix 40 mg It was once a day

Due to the arbitrary discontinuation of the drugs, the patient had a recurrence of the left leg ulcer and was admitted to the hospital again. In the evaluation of the leg ulcer, according to the

dimensions of the ulcer, its painfulness, non-infectiousness, and the necrotic margin, PG was suggested to him.

In the patient's new echocardiography, the following were reported:

LVEF: 30-35%, mild LV enlargement, moderate systolic dysfunction, global LV hypokinetic, no Clot. Normal RV size. No MS, mild to mod MR,no PE,No TS,mild TR,thickening MVLS,echogenic well defined mass at the tip of AMVL(11 in 15 mm),suggested to LSE.mild enlargement atrium, no PH,no pericardial effusion

In new lab tests: Lupus anticoagulants was +, Cardiolipin antibodies was negative, beta-2 glycoprotein 1 antibodies IgG was +(28/18), anti-double stranded DNA was + (24/18), C3 :82/135, C4:10.1/40, CH50: 75/150, FANA: +(1/320), ESR:65, 24h urine protein 132 and was negative. Blood culture and wound culture was negative.CRP 1+, Hemoglobin: 8 platelets: 119000 WBC: 4140.

In total, the patient with pyoderma gangrenosum, a history of DVT, 1 spontaneous abortion, 1 ischemic CVA, LSE, heart failure in the background and positive diagnostic tests, was diagnosed with SLE, APS, pyoderma gangrenosum, LSE, and heart failure.

The patient was treated with prednisolone at a dose of 1 mg/kg; Cellcept 500 mg tablets every 12 hours, enoxaparin and warfarin. He took 1000 mg rituximab 2 times with an interval of 2 weeks. Hydroxychloroquine tablets were discontinued due to corneal thinning. Heart failure was treated with captopril, empagliflozin, carvedilole, Aldactone, and aspirin. Daily wound dressing was performed by wound specialists along with local treatment measures to heal the wound. Finally, after 2 months, the patient was in good general condition and significant improvement. The wound was discharged. The patient's discharge medications included Cellcept, warfarin,

prednisolone, and heart failure medications, which were adjusted under periodic follow-ups. Cardiac MRI was recommended.

Discussion

Epidemiological features of PG include its global distribution; it is usually more common in women and mainly affects the age group of twenty to fifty years (12). SLE is related to lower limb ulceration. Wounds in SLE patients occur probably secondary to thrombophilia states or vasculitis, such as attendance of APS, whereas the cause of lower limb ulcers is more common disorders including arterial insufficiency, venous insufficiency, and neuropathy (13-16). Studies of adults with cases of SLE reported that 5–8 percent of them had leg ulcers (16-18). Most of the patients who had SLE and PG at the same time, like our patient, had SLE before PG (19). Although in rare cases, PG has developed before SLE (18). SLE and APS are commonly associated and are considered closely related diseases (20). Thrombosis is one of the main manifestations of APS. We prescribed warfarin for our patient because of its anti-inflammatory effects. Another common manifestation of APS is heart valve involvement, and the most important abnormality is LSE, which occurs mostly in the mitral and aortic valves (21). Like our patient, who had LSE along with APS. The diagnosis of PG can be challenging because of the clinical overlap with other diseases and conditions, the variable manifestations of PG, and the lack of specific laboratory and histopathological findings. Currently, the diagnosis of PG is often based on the morphology of the wounds, ruling out other conditions, the clinical course, and the response to some medications such as calcineurin inhibitors and steroids (22). PG has no gold standard treatment (23). Because the pathogenesis is not fully understood, the therapeutic approach is often empirical, and there is no particular nor permanently effective treatment (24). Presently, according to expert opinions, immunosuppressive agents and glucocorticoids form the

basis of PG therapy (25). Remarkably, capable of regulating the activity of connective tissue diseases, like SLE (including hydroxychloroquine, cyclophosphamide, mycophenolate, methotrexate, and mofetil) According to the literature, has been effective in treating skin lesions caused by neutrophils (26-30). Infliximab is also used in treatment-resistant cases (31). Matthew et al. (32) showed that rituximab can be effective in the treatment of PG. This was a case report of a young man who had widespread cutaneous ulcerations, including involvement of two-thirds of his face, for 6 years. The patient had tried numerous treatments over the previous six years, such as oral and intravenous corticosteroids, minocycline, ciprofloxacin, and infliximab, but none of them was effective. Administering 600 mg of intravenous rituximab per week for 6 months was able to completely cure the disease. In conclusion, we evaluated a 35-year-old woman with a history of DVT, CVA, and PG. After clinical and laboratory investigations, we diagnosed her with APS and SLE, and initiated treatment with corticosteroids, warfarin, and rituximab. In subsequent follow-ups, we observed a significant improvement in the ulcer and control of other disease symptoms, and no recurrence of the ulcer in subsequent visits.This case shows that rituximab can be a potential treatment for PG. It is important to consider PG in the differential diagnosis of leg ulcers in patients with APS.

***Signed informed consent was obtained from the patient regarding the use of patient information for the purposes of writing a case report publication.**

References:

1. Kaffenberger BH, Hinton A, Krishna SG. The impact of underlying disease state on outcomes in patients with pyoderma gangrenosum: A national survey. J Am Acad Dermatol. 2018;79(4):659-63.e2.
2. Ravi M, Trinidad J, Spaccarelli N, Kaffenberger B. The impact of comorbidity identification on outcomes in patients with pyoderma gangrenosum: A retrospective cohort study of previously hospitalized patients. J Am Acad Dermatol. 2022;87(1):194-7.
3. Alavi A, French LE, Davis MD, Brassard A, Kirsner RS. Pyoderma Gangrenosum: An Update on Pathophysiology, Diagnosis and Treatment. Am J Clin Dermatol. 2017;18(3):355-72.
4. Marzano AV, Ishak RS, Saibeni S, Crosti C, Meroni PL, Cugno M. Autoinflammatory skin disorders in inflammatory bowel diseases, pyoderma gangrenosum and Sweet's syndrome: a comprehensive review and disease classification criteria. Clin Rev Allergy Immunol. 2013;45(2):202-10.
5. Vacas AS, Torre AC, Bollea-Garlatti ML, Warley F, Galimberti RL. Pyoderma gangrenosum: clinical characteristics, associated diseases, and responses to treatment in a retrospective cohort study of 31 patients. Int J Dermatol. 2017;56(4):386-91.
6. Gibson GE, Su WP, Pittelkow MR. Antiphospholipid syndrome and the skin. J Am Acad Dermatol. 1997;36(6 Pt 1):970-82.
7. Babe KS, Jr., Gross AS, Leyva WH, King LE, Jr. Pyoderma gangrenosum associated with antiphospholipid antibodies. Int J Dermatol. 1992;31(8):588-90.
8. Roger D, Aldigier JC, Peyronnet P, Bonnetblanc JM, Leroux-Robert C. Acquired ichthyosis and pyoderma gangrenosum in a patient with systemic lupus erythematosus. Clin Exp Dermatol. 1993;18(3):268-70.
9. Pinto GM, Cabeças MA, Riscado M, Gonçalves H. Pyoderma gangrenosum associated with systemic lupus erythematosus: response to pulse steroid therapy. J Am Acad Dermatol. 1991;24(5 Pt 2):818-21.
10. Sakamoto T, Hashimoto T, Furukawa F. Pyoderma gangrenosum in a patient with bullous systemic lupus erythematosus. Eur J Dermatol. 2002;12(5):485-7.
11. Schmid MH, Hary C, Marstaller B, Konz B, Wendtner CM. Pyoderma gangrenosum associated with the secondary antiphospholipid syndrome. Eur J Dermatol. 1998;8(1):45-7.
12. von den Driesch P. Pyoderma gangrenosum: a report of 44 cases with follow-up. Br J Dermatol. 1997;137(6):1000-5.
13. Alegre VA, Winkelmann RK. Histopathologic and immunofluorescence study of skin lesions associated with circulating lupus anticoagulant. J Am Acad Dermatol. 1988;19(1 Pt 1):117-24.
14. Nahass GT. Antiphospholipid antibodies and the antiphospholipid antibody syndrome. J Am Acad Dermatol. 1997;36(2 Pt 1):149-68; quiz 69-72.
15. Cardinali C, Caproni M, Bernacchi E, Amato L, Fabbri P. The spectrum of cutaneous manifestations in lupus erythematosus--the Italian experience. Lupus. 2000;9(6):417-23.
16. Callen JP. Management of skin disease in patients with lupus erythematosus. Best Pract Res Clin Rheumatol. 2002;16(2):245-64.
17. Hochberg MC. Updating the American College of Rheumatology revised criteria for the classification of systemic lupus erythematosus. Arthritis Rheum. 1997;40(9):1725.
18. Waldman MA, Callen JP. Pyoderma gangrenosum Preceding the diagnosis of systemic lupus erythematosus. Dermatology. 2005;210(1):64-7.
19. Lebrun D, Robbins A, Hentzien M, Toquet S, Plee J, Durlach A, et al. Two case reports of pyoderma gangrenosum and systemic lupus erythematosus: A rare but nonfortuitous association? Medicine (Baltimore). 2018;97(34):e11933.
20. Tincani A, Andreoli L, Chighizola C, Meroni PL. The interplay between the antiphospholipid syndrome and systemic lupus erythematosus. Autoimmunity. 2009;42(4):257-9.

21. Mohammadi Kebar Y, Avesta L, Habibzadeh A, Hemmati M. Libman-Sacks endocarditis in patients with systemic lupus erythematosus with secondary antiphospholipid syndrome. Caspian J Intern Med. 2019;10(3):339-42.
22. Fitz NM, Rudikoff D. Pyoderma gangrenosum. Mt Sinai J Med. 2001;68(4-5):287-97.
23. Miller J, Yentzer BA, Clark A, Jorizzo JL, Feldman SR. Pyoderma gangrenosum: a review and update on new therapies. J Am Acad Dermatol. 2010;62(4):646-54.
24. Ruocco E, Sangiuliano S, Gravina AG, Miranda A, Nicoletti G. Pyoderma gangrenosum: an updated review. J Eur Acad Dermatol Venereol. 2009;23(9):1008-17.
25. Cozzani E, Gasparini G, Parodi A. Pyoderma gangrenosum: a systematic review. G Ital Dermatol Venereol. 2014;149(5):587-600.
26. Hau E, Vignon Pennamen MD, Battistella M, Saussine A, Bergis M, Cavelier-Balloy B, et al. Neutrophilic skin lesions in autoimmune connective tissue diseases: nine cases and a literature review. Medicine (Baltimore). 2014;93(29):e346.
27. Hamzi AM, Bahadi A, Alayoud A, El Kabbaj D, Benyahia M. Skin ulcerations in a lupus hemodialysis patient with hepatitis C infection: what is your diagnosis? Iran J Kidney Dis. 2013;7(3):191.
28. Husein-ElAhmed H, Callejas-Rubio JL, Ríos Fernandez R, Ortego Centeno N. Effectiveness of mycophenolic acid in refractory pyoderma gangrenosum. J Clin Rheumatol. 2010;16(7):346-7.
29. Reddy V, Dziadzio M, Hamdulay S, Boyce S, Prasad N, Keat A. Lupus and leg ulcers--a diagnostic quandary. Clin Rheumatol. 2007;26(7):1173-5.
30. Masatlioğlu SP, Göktay F, Mansur AT, Akkaya AD, Güneş P. Systemic lupus erythematosus presenting as pyoderma gangrenosum in two cases. Rheumatol Int. 2009;29(7):837-40.
31. Salehzadeh F, Mohammadikebar Y, Enteshary A, Ghanbarpour O, Mirzarahimi M. Infliximab in treatment of idiopathic refractory childhood pyoderma gangrenosum (PG). Biologics. 2019;13:97-9.
32. DaCunha M, Siscos S, Downing M, Tarantino I, Hall J. Pyoderma gangrenosum controlled with rituximab. JAAD Case Rep. 2019;5(7):593-5.