

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

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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 erythematosus (SLE) patients. Rituximab can be effective in the treatment of PG. We report the case of 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.

Keywords: Pyoderma gangrenosum, Antiphospholipid syndrome, systemic lupus erythematosus, 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, subungual 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 erythematosus (SLE) patients [7-10]. 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 × 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.

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



FIGURE 1. Pyoderma gangrenosum (PG), before (1) and after treatment (4)

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.

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

With this set of symptoms, and also the joint pain that was present in the patient as well as anemia,

thrombocytopenia, and high ESR, it was investigated in terms of APS and SLE. In the evaluations, there was a high ESR, ANA+, a decrease in the level of complements, and IgG + antiphospholipid and IgG + anti-cardiolipin antibodies were reported. The patient was 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 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 the patient.

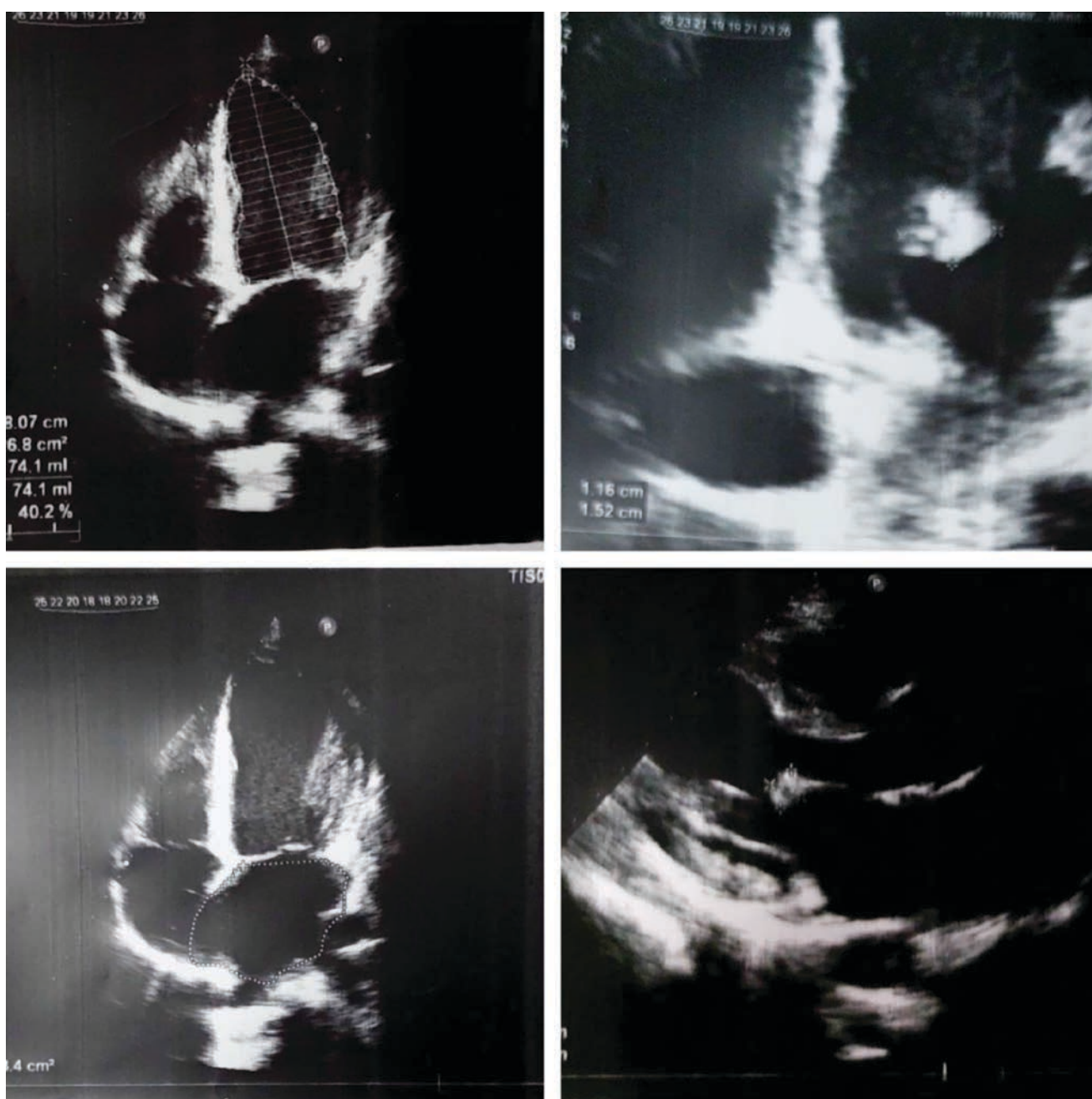


FIGURE 2. Echocardiography pictures about thickening mitral valve, echogen well defined mass at the tip of AMVL (11 in 15 mm), suggested to Libman-Sacks

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

Left ventricular ejection fraction (LVEF): 30-35%, mild left ventricle (LV) enlargement, moderate systolic dysfunction, global LV hypokinetic, no clots. Normal right ventricle (RV) size. Moreover, there was no mitral stenosis (MS), mild to moderate mitral regurgitation (MR), no pulmonary embolism (PE), no tricuspid stenosis (TS), mild tricuspid regurgitation (TR), thickening mitral valve Libman-Sacks (MVLS), echogenic well-defined mass at the tip of AMVL (11 in 15 mm), suggested to LSE. mild enlargement atrium, no pulmonary hypertension (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 (dsDNA) was + (24/18), fluorescent antinuclear antibody test (FANA) was +(1/320), C3:82/135, C4:10.1/40, complement total activity (CH50): 75/150, ESR:65, 24h urine protein 132 and was negative. Blood culture and wound culture were negative. CRP 1+, Hemoglobin: 8, platelets: 119000, WBC: 4140.

In total, the patient with PG, 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, PG, 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 could be seen. The wound was in the condition for the patient to be discharged. The patient's discharge medications included Cellcept, warfarin, prednisolone, and heart failure medications, which were adjusted under periodic follow-ups. Cardiac magnetic resonance imaging (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 [11]. 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 with disorders including arterial insufficiency, venous insufficiency, and neuropathy [12-16]. Studies of adults with cases of SLE reported that 5–8 percent of them had leg ulcers [14,17,18]. 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 is SLE (including hydroxychloroquine, cyclophosphamide, mycophenolate, methotrexate, and mofetil) which, 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.

CONCLUSION

PG is a rare but serious disease that requires careful attention and management. A delay in diagnosis can worsen the patient's condition. We present a case in which a patient with SLE and APS presented with extensive lesions consistent with PG. The successful treatment of the patient with rituximab shows its potential as a therapeutic option in the treatment of PG.

Patients consent:

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

Conflict of interest: none declared.

Financial support: none declared

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