Journal of International Case Reports
Case Report | Pages: 04-09
Volume 3 | Issue 1 (Jan-Mar 2024)
Published Date: January 29, 2024

Systemic Lupus Erythematosus in Patient with Pyoderma Gangrenosum: A Case-Based Literature Review

Aseel Abuhammad[1*]
Qais Z F Hamarsha[1]
Iman khamayseh[1]
Osama N. Dukmak[1]
Mohammed Alkhanafsa[2]
Laith Alamlih[3]

[1]Faculty of Medicine, Al-Quds University, Jerusalem, State of Palestine
[2]Internal Medicine Department, Hamad Medical Corporation, Qatar
[3]Rheumatology, Hebron University, Hebron, State of Palestine

Received Date: December 11, 2023; Accepted Date: December 26, 2023; Published Date: January 29, 2023

[*]**Corresponding author:** Aseel Abuhammad, Faculty of Medicine, Al-Quds University, Main Campus, Abu dis, P.O. Box 89, Jerusalem, State of Palestine.

Citation: Aseel Abuhammad, Qais Z F Hamarsha, Iman khamayseh, Osama N. Dukmak, Laith Alamlih, and et al. Systemic Lupus Erythematosus in Patient with Pyoderma Gangrenosum: A Case-Based Literature Review. ICARE. 2024;3(1):4-9

Abstract

Pyoderma Gangrenosum (PG) is a rare skin disorder that includes blisters, bullae, and ulcers, which can rapidly grow. Systemic Lupus Erythematosus (SLE) in association with PG is rarely reported, and the occurrence of PG earlier is relatively uncommon. A 33-year-old female patient known to have pyoderma gangrenosum presented with a 3-year history of polyarthralgia and morning stiffness involving both the hand and knee. She also complained of mouth ulcers, photophobia, fatigue, and sweating. Laboratory results disclosed anemia, leukopenia, and neutropenia. The autoimmune screen showed a positive ANA. Based on the clinical findings and positive immunologic studies, she was diagnosed with systemic lupus erythematosus. Initially, her general condition improved with an immunosuppressant, but the patient stopped her medication after three months of treatment. Although SLE is uncommon to develop after PG, our case report shows that clinicians should consider it in any patient with a known history of PG who presents with obvious symptoms of an autoimmune disease.

Keywords: Systemic Lupus Erythematosus (SLE); Pyoderma Gangrenosum (PG); Case Report

Introduction

Pyoderma Gangrenosum (PG) is an ulcerative cutaneous disease that frequently accompanies various systemic autoimmune conditions. Although PG is well known to be idiopathic, the coexistence of autoimmune conditions reaches 50% to 70% [1]. Inflammatory Bowel Disease (IBD) is the most common condition associated with PG. But PG is also linked to a wide range of other illnesses,

including hematological malignancies, IgA monoclonal gammopathies, and Rheumatoid Arthritis (RA). Pyoderma gangrenosum diagnosis should be made carefully after excluding other similar conditions with cutaneous ulcerations, which include infectious disease, cancer, vasculitis, venous disorder, and trauma.

Systemic Lupus Erythematosus (SLE) and pyoderma gangrenosum rarely co-exist. [1] We report a rare case of PG preceding the diagnosis of SLE. We also performed a literature review of previously published cases.

Case Presentation

A 33-year-old female patient developed fatigue and polyarthralgia that involved the Metacarpophalangeal (MCP) and Proximal Interphalangeal (PIP) joints, right shoulder, right elbow, and both ankles and knees over a few years. She reported having morning stiffness lasting more than half an hour. Her pain is greater in the morning and with rest. She also reported recurrent mouth ulcers, Raynaud's phenomenon, photosensitivity, dry eyes, and hair loss for the last few months before presentation. She denied any history of abdominal pain, diarrhea, bleeding per rectum, recurrent sinusitis, or any respiratory symptoms. Her past medical history is significant for autoimmune hypothyroid disease. She was also diagnosed with PG 10 years before her presentation, which was based on the classical presentation of ulcerative skin nodules that was confirmed with a skin biopsy. The problem started as a chronic, non-healing ulcer in her right foot, which was followed by similar lesions over both hands. She was treated at first with steroids and frequent dressing, which resulted in resolution but with scars. One of the most severe attacks affected her right foot, where there was a loss of skin with tendons and soft tissue visible over the bones. Following that, she was treated with allograft cover, azathioprine, and tapering steroids, which resulted in very good control of her disease. At that time, blood tests were conducted to exclude other medical conditions. The C-reactive protein (CRP) was not elevated, and neither was there an elevation of the white blood cells. Ferritin was normal, and haemoglobin was 10 g/dl with normal leukocyte and platelet counts. The serology screen for vasculitis or systemic diseases was negative. The Antinuclear Antibody (ANA) titer was slightly elevated at 1: 1320; however, the Rheumatoid Factor (RF) was not elevated. Her cholesterol and triglyceride levels were normal. Thyroid function tests revealed an elevated Thyroid-Stimulating Hormone (TSH); however, Free Thyroxine (FT4) and Free Triiodothyronine (FT3) were normal. Thyroid antibody testing showed elevated TSH receptor antibodies, Microsomal Thyroid Antibodies (MAK), and Antibodies against Thyroglobulin (TAK).

Unfortunately, the patient was not compliant with her treatment and follow-up, and she developed a recurrence of the disease because of that. She is a smoker. She has a family history of SLE (her niece) and palindromic rheumatism (her sister), but no family history of IBD. When she presented to the clinic, she was not taking any medications.

On examination, the patient had multiple joint tenderness, affecting mainly the PIP and MCP joints, without significant swelling and no foot ulceration. She had residual scarring at areas of pyoderma gangrenosum resolution on both the hand and right foot (Figure 1).

Figure 1: Residual scarring at the area of pyoderma gangrenosum resolution on the right hand.

Laboratory investigations revealed microcytic anemia of 9.3 g/dL hemoglobin with MCV of 66.7, leukopenia of 2,600/mm3, and neutropenia of 0.75/mm3. Autoimmune screening showed positive ANA at a titer of 1:160, positive lupus anticoagulant, and negative for ENA (Extractable

Nuclear Antigen Antibodies) panel, RF, and anti-cyclic Citrullinated Peptide (anti-CCP). Both inflammatory markers, Erythrocyte Sedimentation Rate (ESR) and CRP, were normal. The liver function test and kidney function test were in the normal range. Complement C3 and C4 were normal. The serological tests for various infectious agents (HBsAg and anti-HCV ab tests) were negative (Table 1).

Table 1: Laboratory Investigations.

Laboratory test	Value	Normal values
Complete blood count		
WBC count	2,600/mm^3 (L)	4,500-11,000/mm^3
Hemoglobin	9.3 g/dL (L)	12.1-15.1 g/dL
MCV	66.7	80-100 fl
Platelets	280 /mm3	150 - 500 /mm3
Neutrophils	0.75 /mm3(L)	1.4 - 8 /mm3
Lymphocytes	1.42 /mm3	0.9 - 5.2 /mm3
Rheumatologic workup		
CRP	0.5 mg/dL	0.0-0.8 mg/dL
ESR	17 mmHg	0-20 mm/hour
ANA screen	Positive	< 0.8 Negative
C4 complement level	Normal	10–40 mg/dL
C3 complement level	Normal	55–120 mg/dL
Anti-dsDNA	Negative	Negative
AntiSM	Negative	Negative
Nucleolar	Negative	Negative
Rheumatoid factor	Negative	<40 U/mL
Anti-CCP	Negative	Negative
Infection workup		
HBsAg	Negative	-
Anti-HCV Ab	Negative	-

L: Low Value; WBC: White Blood Count; MCV: Mean Corpuscular Volume; CRP: C-Reactive Protein; ESR: Erythrocyte Sedimentation Rate; ANA: Antinuclear Antibody; CCP: Cyclic Citrullinated Peptides; HB: Hepatitis B; HCV Ab: Hepatitis C Antibody; Anti-SM: Anti Smith antibody; Anti-dsDNA: Anti-double stranded DNA.

Based on clinical features and laboratory investigations, our patient was diagnosed with SLE and started on azathioprine 100 mg daily, hydroxychloroquine 5 mg/kg daily, and prednisolone 10 mg daily. She developed a skin rash, and she stopped taking hydroxychloroquine as she believed it caused an allergic skin reaction.

Discussion

We present a case of a 33-year-old woman who had previous severe ulcerative PG disease and was also diagnosed with SLE. Thus far, there are no approved, reported diagnostic, clinical, or pathological criteria to diagnose PG. Su et al. have proposed diagnostic criteria requiring two major and two minor diagnoses (Table 2),
maintaining PG as a diagnosis of exclusion [2]. Our case fulfilled the two major criteria and three minor criteria proposed by these groups. Few cases of PG associated with SLE have been reported to date. In most cases, PG develops years after the diagnosis of SLE [3].

Table 2: Diagnostic tool for pyoderma gangrenosum

Major criteria
Rapid progression of a painful necrolytic cutaneous ulcer with an irregular, violaceous, and undermined border
Other causes of cutaneous ulceration excluded
Minor criteria
History of pathergy or cribriform scarring clinically
Associated systemic disease (inflammatory bowel disease, arthritis, IgA gammopathy, or underlying malignancy)
Classic histopathological findings
Treatment response (rapid response to systemic steroid treatment - 50% improvement in 1 month)

We have reviewed published articles in PubMed up to August 2022, searching for similar coexistence. The following keywords were used in different combinations: “Pyoderma gangrenosum" AND “autoimmune diseases” OR “systematic lupus erythematosus" OR “cutaneous lupus erythematosus” OR "arthritis." We included the full paper articles and excluded the abstracts. We extracted the

following data: age, time of PG onset compared to SLE diagnosis, location of PG, types of lesions, medical management, histopathology, and the time to complete resolution of PG.

Following a review of the literature, 27 cases of PG with SLE were found [1,3-19]. Two of them later have SLE overlap with Sjogren's syndrome; five have SLE and Antiphospholipid Syndrome (APS); and one has SLE and ulcerative colitis (Table 3). The main features of the 27 cases of PG associated with SLE and our additional patient are summarized in Table 3.

Table 3: Literature review and summary of clinical characteristics in SLE patients with PG

Measure	**N**	**%**
Number of patients, n	28	
Age, year, median	36.5 (25-64)	
Sex		
Female	20	71.4
Male	5	17.8
Unknown	3	10.7
Time of PG onset compared to SLE diagnosis		
After	19	67.8
Before	3	10.7
Simultaneous	6	21.4
Time to complete resolution of PG		
Within 1months	7	25
Within 6 months	5	17.8
Within 2 years	1	3.5
Unknown	15	53.5
Location of PG		
Leg	14	50
Foot	5	17.8
Face	2	7.1
Trunk/chest/ shoulder	2	7.1
Thigh/ scrotum/lower abdomen	3	10.7
Unknown	3	10.7
Type of lesion		
Papule then ulcer Ulcer	20	71.4
Bulla/Pustules	3	10.7
Nodular	2	7.1
Papule then ulcer	1	3.5
Unknown	3	10.7
Autoimmune related disorder		
Antiphospholipid Syndrome (APS)	5	17.8
Sjogren syndrome	2	7.1
Autoimmune hepatitis	1	3.5
Inflammatory Bowel Disease (IBD)	1	3.5
Received treatment with hydroxychloroquine		
Yes	11	39.2
No	11	39.2
Unknown	6	21.4
Histopathology		
Polymorphonuclear	11	39.2
Nonspecific pattern	5	17.8
Marked inflammatory infiltration	4	14.2
Leukocytoclastic vasculitis	4	14.2
Mononuclear cells	1	3.5
Unknown	6	21.4

PG: Pyoderma Gangrenosum Note; SLE: Systemic Lupus Erythematosus.

PG affects patients of all ages, with an equal incidence between men and women, and a large percentage of ages were between 20 and 50 years. However, women were affected more than men with a non-malignancy-associated PG [20]. This is consistent with our results, where many PG patients with SLE are female (19F/5M).

Our patient had ulcerative PG like most reported patients. However, in some cases, the disease started with papules, bullae, or pustules. There was no histologic difference found between PG associated with SLE and PG related to other conditions. That exhibited a high degree of neutrophil infiltration in most cases.

Among the 27 cases of SLE-associated PG reported in the literature, most of the patients (70.3%) had been diagnosed with SLE before the onset of PG. Both diseases appeared simultaneously in 6 cases, whereas PG was observed before

the first symptom of SLE in only 2 cases. One of these two cases was diagnosed with SLE after 10 months of PG onset. However, this delay is most probably related to the patient, as she postponed her appeal to the rheumatology department [14]. The other was diagnosed with SLE after 8 years of the onset of PG when she started to develop shortness of breath. She was admitted to the hospital and diagnosed with autoimmune pneumonitis, hemolytic anemia, and lupus nephritis. She was successfully treated with oral corticosteroid monotherapy [11].

After about ten years since the start of PG, our patient developed symptoms of SLE. Corticosteroid therapy, surgical debridements with allograft cover, and azathioprine therapy were effective means of managing her PG disease.

Conclusion

PG can accompany many autoimmune conditions. We describe a rare association between PG and SLE, which should be kept in mind among other conditions while dealing with such patients. A careful history and physical exam are essential to the proper diagnosis and treatment of such patients. Additionally, autoimmune diseases can follow the development of idiopathic PG disease. Therefore, careful surveillance is needed to detect the future development of autoimmune disease in the setting of PG.

Declaration

Source of funding: The study did not receive any funding.

Ethical approval: This study is exempt from ethical approval at our hospital.

Consent

Written informed consent was obtained from the patient for reporting this case and its associated images. The consent is available for review on request.

Authors' contributions

- **Data collection:** Aseel Abuhammad
- **Writing the manuscript:** Aseel Abuhammad
- **Study concept or design:** Aseel Abuhammad
- **Review & editing the manuscript:** Laith Alamlih
- **Guarantor:** Laith Alamlih

- **Provenance and peer review:** Not commissioned, externally peer-reviewed
- **Declaration of competing interest:** There is no conflict of interest to declare
- Methods: This case has been reported in line with Care criteria [21]

References

1. Teoh SC, Sim CY, Chuah SL, Kok V, Teh CL. Pyoderma gangrenosum and cobalamin deficiency in systemic lupus erythematosus: a rare but nonfortuitous association. BMC Rheumatol. 2021;5(1):7.
2. George C, Deroide F, Rustin M. Pyoderma gangrenosum - a guide to diagnosis and management. Clin Med (Lond). 2019;19(3):224-8.
3. 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.
4. González-Moreno J, Ruíz-Ruigomez M, Callejas Rubio JL, Fernández RR, Centeno NO. Pyoderma gangrenosum and systemic lupus erythematosus: a report of five cases and review of the literature. Lupus. 2015;24(2):130-7.
5. Peterson LL. Hydralazine-induced systemic lupus erythematosus presenting as pyoderma gangrenosum-like ulcers. J Am Acad Dermatol. 1984;10(2 Pt 2):379-84.
6. Pinto GM, Cabecas 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.
7. Hostetler LW, von Feldt J, Werth VP. Cutaneous ulcers in a patient with systemic lupus erythematosus. Arthritis Rheum. 1993;36(1):91-3.
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. Holbrook MR, Doherty M, Powell RJ. Post-traumatic leg ulcer. Ann Rheum Dis. 1996;55(4):214-5.

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. Waldman MA, Callen JP. Pyoderma gangrenosum Preceding the diagnosis of systemic lupus erythematosus. Dermatology. 2005;210(1):64-7.
12. 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.
13. Hind A, Abdulmonem AG, Al-Mayouf S. Extensive ulcerations due to pyoderma gangrenosum in a child with juvenile systemic lupus erythematosus and C1q deficiency. Ann Saudi Med. 2008; 28(6):466-8.
14. Masatlioglu SP, Goktay F, Mansur AT, Akkaya AD, Gunes P. Systemic lupus erythematosus presenting as pyoderma gangrenosum in two cases. Rheumatol Int. 2009;29(7):837-40.
15. Canas CA, Duran CE, Bravo JC, Castaño DE, Tobón GJ. Leg ulcers in the antiphospholipid syndrome may be considered as a form of pyoderma gangrenosum and they respond favorably to treatment with immunosuppression and anticoagulation. Rheumatol Int. 2010;30(9):1253-7.
16. Husein-ElAhmed H, Callejas-Rubio JL, RF Raquel, Norberto OC. Effectiveness of mycophenolic acid in refractory pyoderma gangrenosum. J Clin Rheumatol. 2010;16(7):346-7.
17. 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.
18. Mansour HE, Arafa SG, Shehata WA. Systemic lupus erythematosus with inflammatory bowel disease-ulcerative colitis: case report. Lupus. 2018;27(7):1198-201.
19. Ibrahim I, Shereef H, Hashim A, Habbal H, Mahmood R, Mohamed MA. Winning the Battle after Three Years of Suffering: A Case of a Refractory Pyoderma Gangrenosum Treatment Challenge. Case Rep Rheumatol. 2021;2021:8869914.
20. Marzano AV, Borghi A, Wallach D, Cugno M. A comprehensive review of neutrophilic diseases. Clin Rev Allergy Immunol. 2018;54(1):114-30.
21. Gagnier JJ, Kienle G, Altman DG, Moher D, Sox H, Riley D, et al. The CARE guidelines: consensus-based clinical case reporting guideline development. BMJ Case Rep. 2013:2013:bcr2013201554.