

# Journal Pre-proof

[[Translated article]]Pyoderma Gangrenosum and Systemic Lupus Erythematosus: An Uncommon Association

J Lorca-Spröhnle A Casanova-Esquembre C Labrandero-Hoyos A Pérez-Ferriols



PII: S0001-7310(25)00661-1

DOI: <https://doi.org/doi:10.1016/j.ad.2025.10.014>

Reference: AD 4481

To appear in: *Actas dermosifiliograficas*

Received Date: 25 July 2023

Accepted Date: 4 February 2024

Please cite this article as: Lorca-Spröhnle J, Casanova-Esquembre A, Labrandero-Hoyos C, Pérez-Ferriols A, [[Translated article]]Pyoderma Gangrenosum and Systemic Lupus Erythematosus: An Uncommon Association, *Actas dermosifiliograficas* (2025), doi: <https://doi.org/10.1016/j.ad.2025.10.014>

This is a PDF file of an article that has undergone enhancements after acceptance, such as the addition of a cover page and metadata, and formatting for readability, but it is not yet the definitive version of record. This version will undergo additional copyediting, typesetting and review before it is published in its final form, but we are providing this version to give early visibility of the article. Please note that, during the production process, errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

© 2025 AEDV. Published by Elsevier España, S.L.U.

Refers to AD\_4421

Carta científico-clínica

## Pioderma gangrenoso y lupus eritematoso sistémico: una asociación infrecuente

[[Translated article]]Pyoderma Gangrenosum and Systemic Lupus Erythematosus: An Uncommon Association

AUTORES:

Lorca-Spröhnle, J.<sup>1</sup>  
Casanova-Esquembre, A.<sup>1</sup>  
Labrandero-Hoyos, C.<sup>1</sup>  
Pérez-Ferriols, A.<sup>1</sup>

INSTITUCIÓN:

<sup>1</sup>Departamento de Dermatología, Consorcio Hospital General Universitario de Valencia, España.

AUTOR DE CORRESPONDENCIA:

Javier Lorca Spröhnle,  
javierlorcasprohnle@gmail.com

*To the Editor,*

Pyoderma gangrenosum (PG) is a neutrophilic dermatosis (ND) that is frequently associated with systemic diseases. Its association with systemic lupus erythematosus (SLE) is, however, exceptionally rare. We describe a case in which PG preceded the diagnosis of SLE and highlight therapeutic aspects.

A 59-year-old woman with a past medical history of hypertension, type 2 diabetes mellitus, and bipolar disorder presented to the emergency department with a painful lesion on the right leg of 2 weeks' duration which, despite levofloxacin and amoxicillin-clavulanate, enlarged and ulcerated. The history did not identify other relevant systemic symptoms.

On examination, the patient was dehydrated, hypotensive (80/55 mmHg), and tachypneic (31 breaths/min), with a single ulcerated plaque showing depressed erythematous–violaceous borders (Figure 1). Laboratory tests showed hemoglobin 11.4 g/dL, leukocytes  $11.2 \times 10^3/\mu\text{L}$ , neutrophils  $9.6 \times 10^3/\mu\text{L}$ , platelets  $414 \times 10^3/\mu\text{L}$ , and C-reactive protein 12.6 mg/dL. CT revealed marked edema of subcutaneous and muscle tissue. She was admitted and started on IV normal saline and empiric antibiotics with piperacillin–tazobactam plus gentamicin.

The following day she developed chest pain. Repeat labs showed hemoglobin 8.5 g/dL, leukocytes  $0.3 \times 10^3/\mu\text{L}$ , neutrophils  $0.1 \times 10^3/\mu\text{L}$ , platelets  $267 \times 10^3/\mu\text{L}$ , D-dimer 35,336 ng/mL, and a positive direct Coombs test. Peripheral smear, CT angiography, and transthoracic echocardiogram were normal. A biopsy was taken from the lesion edge, and a single 100 mg IV bolus of methylprednisolone was administered along with filgrastim.

On hospital day 2, prednisone 1 mg/kg/day was begun, and daily wound care with wet compresses and a barrier cream containing copper and zinc sulfate was performed (Figure 2). Notable improvement was observed from day 4 and continued during hospitalization. However, on day 5, thrombocytopenia emerged.

Histopathology showed a dense neutrophilic infiltrate in the dermis. PAS stain was negative. Antinuclear antibodies (ANA) were elevated (titer 1:1280) with anti–double-stranded DNA antibodies 83 IU/mL. All microbiologic cultures obtained during hospitalization tested negative, and antibiotics were discontinued on day 10. On day 15, due to progressive improvement, she was discharged on hydroxychloroquine and a tapering course of prednisone. Despite complete re-epithelialization of the lesion at the 1-month follow-up (Figure 3), she required readmission for a flare of lupus nephritis, which confirmed the SLE diagnosis. Therapy was adjusted and belimumab initiated, with no PG recurrences at 1-year follow-up.

We presented an unusual case in which PG preceded fulfillment of EULAR/ACR criteria for SLE diagnosis.<sup>1</sup> In a review by Magdoud et al. of 25 PG–SLE cases, 72% received the SLE diagnosis before PG onset, whereas in 12% PG preceded SLE diagnosis.<sup>2</sup> Additionally, patients with PG and SLE tend to be younger than those with PG without SLE. Nevertheless, this association appears not to significantly impact SLE prognosis and seems independent of disease activity.<sup>2</sup>

Successful management of PG associated with SLE involves reducing inflammation and optimizing wound healing while simultaneously treating the underlying disease. Our literature review (Table 1) incorporates therapeutic aspects not previously addressed in depth. First, we found heterogeneity in both treatments employed and clinical responses.<sup>2–8</sup> The most widely used drugs were prednisone (72.7%) and cyclosporine (42.4%). Although complete remission was achieved in most cases (75.7%), relapses occurred up to 2 years later, underscoring the need for continued clinical surveillance. Second, data on topical treatment are limited. Angiogenesis—fundamental for wound healing—is largely regulated by vascular endothelial growth factor (VEGF). It has been suggested that copper may positively influence VEGF expression via pathways similar to tissue hypoxia, and that topical copper sulfate might accelerate contraction and closure of dermal wounds.<sup>9</sup> Conversely, although aggressive surgical debridement is generally discouraged in PG, in our case we used a strategy of meticulous, sequential selective debridement of necrotic tissue. Importantly, the scarcity of detailed information hampers meaningful comparisons among therapeutic approaches and the formulation of precise management recommendations to treat these injuries.

In conclusion, the heterogeneity of therapeutic approaches to SLE-related PG emphasizes the need for individualized treatment protocols, highlighting the importance of a deeper understanding of topical and systemic therapies to optimize management.

### Conflicts of interest

None declared.

### References

1. Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, et al. 2019 European league against rheumatism/American college of rheumatology classification criteria for systemic lupus erythematosus. *Arthritis rheumatol.* 2019;71(9):1400–12. doi:10.1002/art.40930
2. Magdoud O, Souissi A, Chelly I, Haouet S, Mokni M. Pyoderma gangrenosum et lupus érythémateux systémique : une association rare [Pyoderma gangrenosum and systemic lupus erythematosus: A rare association]. *Rev Med Interne.* 2020;41(1):54-57. doi:10.1016/j.revmed.2019.08.001
3. Hania A. Pyoderma gangrenosum in a patient with systemic lupus erythematosus: case report. *J Med Cases.* 2014;5(8):455–458. [Google Scholar]
4. Teoh SC, Sim CY, Chuah SL, Kok V, Teh CL. Pyoderma gangrenosum and cobalamin deficiency in systemic lupus erythematosus: a rare but non fortuitous association. *BMC Rheumatol.* 2021;5(1):7. Published 2021 Mar 3. doi:10.1186/s41927-021-00177-4
5. Beynon C, Chin MF, Hunasehally P, et al. Successful Treatment of Autoimmune Disease-Associated Pyoderma Gangrenosum With the IL-1 Receptor Antagonist Anakinra: A Case Series of 3 Patients. *J Clin Rheumatol.* 2017;23(3):181-183. doi:10.1097/RHU.0000000000000511
6. Choi YJ, Yoo WH. Pyoderma gangrenosum masquerading as an ulcer related to antiphospholipid antibodies in a patient with systemic lupus erythematosus. *Lupus.* 2018;27(13):2174-2176. doi:10.1177/0961203318793705
7. 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. Published 2021 Mar 13. doi:10.1155/2021/8869914
8. Ahmadi K, Aflaki E, Akbarzade Jahromi M, Dastgheib L. Successful treatment of classic pyoderma gangrenosum with intralesional infliximab injection: A case report. *Australas J Dermatol.* 2023;64(3):e252-e255. doi:10.1111/ajd.14072

9. Sen CK, Khanna S, Venojarvi M, Trikha P, Ellison EC, Hunt TK, et al. Copper-induced vascular endothelial growth factor expression and wound healing. *Am J Physiol Heart Circ Physiol*. 2002;282(5):H1821-7. doi: 10.1152/ajpheart.01015.2001

Journal Pre-proof

Figure 1. Clinical appearance at emergency department presentation.

A warm, erythematous–edematous plaque with MP central necrotic ulcers involving the right leg in a semicircumferential pattern.



Figure 2. Clinical evolution of the lesion.

Daily wound care consisted of wet compresses with zinc, copper, and aluminum–potassium sulfates, followed by careful mechanical debridement of necrotic tissue and application of collagenase to remaining slough. Islands of spared and surrounding skin were protected with a barrier cream containing copper and zinc sulfate, then covered with a silver alginate dressing and bandage. Clinical appearance at 48 hours (A) and 96 hours (B) after initiation of the comprehensive approach shows clear improvement in erythema, edema, and ulceration. By day 5 (C) the response remained favorable and progressive. At day 10 (D), re-epithelialization was evident both concentrically from lesion borders and eccentrically from islands of spared skin inward over debrided areas.

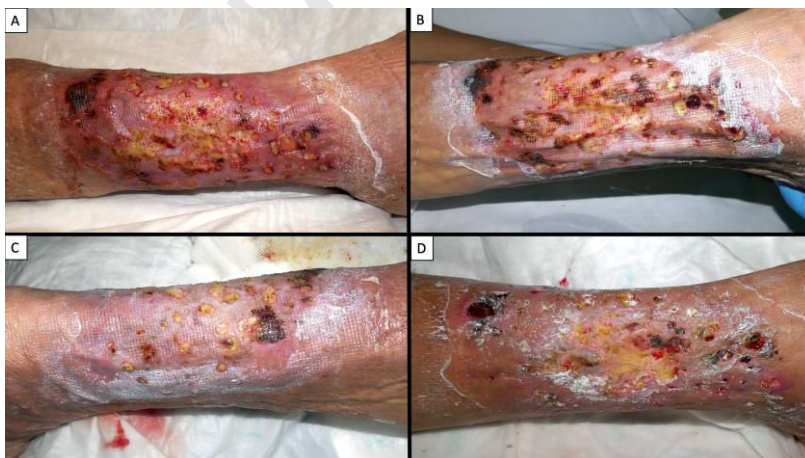




Figure 3. Clinical appearance at 1 month of treatment.

Complete re-epithelialization of the entire lesion without signs of ulceration or necrosis.



Table 1. Cases of PG-related SLE

No.	Reference	Sex / age	Site (number of lesions)	Timing of PG onset relative to SLE diagnosis	SLE activity at PG onset	Topical treatment	Pharmacologic treatment	Response (months)	Recurrence (follow-up)
1	Present clinical case	F/59	Leg (1)	1 month before	No activity	Wet compresses with Cu/Zn sulfates, debridement, collagenase, barrier cream with Cu/Zn sulfates, silver alginate dressing	MPD-IV; PDN	CR (1)	No (1 year)
2	Magdoud [2019]	F/43	Thighs, shoulders, hands (6)	4 years after	Active signs	ND	PDN	CR (1)	No (6 months)
3	Lebrun [2018]	F/32	Face (3)	1 year after	No activity	ND	TCS; MINO	CR (6)	No (3 years)
4	Lebrun [2018]	F/37	Leg (MP)	10 years after	Active signs	ND	PDN; MTX	CR (1)	No (3 years)
5	Gonzalez-Moreno [2015]	M/46	Leg (1)	After	Active signs	ND	TCS; PDN; CsA	CR (3)	ND
6	Gonzalez-Moreno [2015]	F/63	Leg (1)	After	No activity	ND	TCS; IV tacrolimus	ND	ND
7	Gonzalez-Moreno [2015]	F/42	Leg (1)	After	No activity	ND	TCS; PDN; AZA	CR (3)	Yes (2 years)
8	Gonzalez-Moreno [2015]	F/46	Leg (MP)	After	No activity	ND	TCS; CsA; AZA; MMF; IVIG	CR (ND)	Yes (ND)
9	Gonzalez-Moreno [2015]	M/36	Foot (MP)	After	Active signs	ND	ILC; PDN; AZA; DDS; CF; MMF	CR (ND)	ND
10	Hamzi [2013]	F/35	Leg (1)	18 years after	No activity	ND	ND	ND	ND
11	Canas [2010]	ND/48	Leg (1)	2 years after	ND	ND	PDN; CsA; ASA; WF	CR (ND)	ND
12	Canas [2010]	ND/28	Leg (1)	4 years after	Active signs	ND	PDN; CsA; ASA; WF	CR (ND)	ND
13	Canas [2010]	ND/50	Foot (1)	Simultaneous	ND	ND	PDN; CsA; ASA; WF	CR (ND)	ND
14	Husein-ElAhmed [2010]	M/36	Foot (1)	8 years after	No activity	ND	MMF	CR (1)	No (ND)
15	Masatlioglu [2009]	F/35	Leg (1)	Simultaneous	Active signs	ND	PDN; HCQ	CR (1)	ND
16	Masatlioglu [2009]	F/47	Thigh (1)	10 months before	Active signs	ND	CsA; TCS	CR (2)	No (6 months)



No.	Reference	Sex / age	Site (number of lesions)	Timing of PG onset relative to SLE diagnosis	SLE activity at PG onset	Topical treatment	Pharmacologic treatment	Response (months)	Recurrence (follow-up)
17	Hind [2008]	F/1	Face, upper and lower limbs (MP)	Simultaneous	Active signs	ND	MPD-IV; PDN; AZT; CsA; IVIG; TLD; IFX	NR	Died
18	Reddy [2007]	M/34	Legs (MP)	After	Active signs	ND	PDN; AZT	CR (1)	No (3 months)
19	Waldman [2005]	F/35	Lower limbs (MP)	5 years before	ND	ND	PDN; CsA; MMF	CR (11)	Yes (8 months)
20	Sakamoto [2002]	F/55	Trunk/shoulders (MP)	3 years after	Active signs	ND	CsA	CR (ND)	No (ND)
21	Schmid [1998]	F/64	Legs (2)	11 years after	Active signs	ND	PDN; CsA	NR	Died
22	Holbrook [1996]	F/57	Leg (1)	2 years after	No activity	ND	MPD-IV; PDN; MTX	CR (6)	No (ND)
23	Roger [1993]	F/25	Foot (1)	1 month after	Active signs	Dextranomer followed by sterile hydrocolloid	MPD-IV; CF; PDN	CR (4)	No (10 months)
24	Hostetler [1993]	F/27	Trunk, buttocks, knees (MP)	13 years after	No activity	ND	ND	ND	ND
25	Pinto [1991]	F/35	Leg (1)	15 years after	Active signs	ND	MPD-IV; PDN	CR (1)	No (4 months)
26	Peterson [1984]	F/48	Intergluteal and inguinal folds (6)	Simultaneous	Active signs	ND	TCS	CR (2)	No (ND)
27	Olson [1971]	F/15	Leg (MP)	1 year before	ND	ND	PDN	ND	Yes (2 years)
28	Hania [2014]	F/53	Leg (2)	17 years after	No activity	ND	PDN	CR (6)	ND
29	Teoh [2021]	M/35	Scrotum, legs (MP)	Simultaneous	Active signs	ND	PDN; HCQ; MTX; cyanocobalamin	CR (1)	ND
30	Beynon [2017]	F/57	Leg (1)	After	ND	Hydrofiber and hydrocolloid dressings	MPD-IV; PDN; TLD; CsA; MMF; ANAK	PR (11)	ND
31	Choi [2018]	F/61	Leg (1)	8 years after	No activity	ND	PDN; CsA	CR (6)	No (1 year)
32	Ibrahim [2021]	F/55	Leg (1)	After	Active signs	ND	PDN; DDS; MTX; MMF; CsA; IVIG	PR (24)	ND
33	Ahmadi [2023]	F/40	Leg (1)	After	No activity	Saline solution, mupirocin, petrolatum gauze	PDN; MPD-IV; CsA; AZT; intralesional IFX	CR (3)	ND

ASA: acetylsalicylic acid; ANAK: anakinra; AZA: azathioprine; CF: cyclophosphamide; CsA: cyclosporine; Cu/Zn: copper/zinc; DDS: dapsone; HCQ: hydroxychloroquine; ILC: intralesional corticosteroids; IFX: infliximab; IVIG: IV immunoglobulins; SLE: systemic lupus erythematosus; M: male; F: female; MINO: minocycline; MMF: mycophenolate mofetil; MP: multiple; MPD-IV: IV methylprednisolone; MTX: methotrexate; ND: not available; PDN: prednisone; PG: pyoderma gangrenosum; CR: complete response; PR: partial response; TCS: topical corticosteroids; TLD: thalidomide; WF: warfarin.

Source: Adapted from Magdoud et al. (2019)<sup>2</sup>.



ELSEVIER

Advancing human progress *together*

Journal Pre-proof