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Intravenous Immunoglobulin as Salvage Therapy in Refractory Pyoderma Gangrenosum: Report of a Case and Review of the Literature

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Key Words
Intravenous immunoglobulin · Treatment · Pyoderma gangrenosum

Abstract
Pyoderma gangrenosum is a neutrophilic dermatosis that occurs both as a primary disorder as well as secondary to an underlying disease. Due to its low prevalence there are limited data on therapeutics, particularly in refractory cases. Here, we discuss a case successfully managed with intravenous immunoglobulin and review the supporting literature.

Case Report

A 36-year-old woman presented with a 12 × 6 cm ulcer on her right leg (fig. 1). She stated that it had been present for 8 years and denied any history of malignancy, ulcerative colitis or rheumatic disease. Biopsy was diagnostic of pyoderma gangrenosum (PG) and prednisone 40 mg daily was initiated. Due to incomplete response, she required several steroid-sparing agents, including dapsone, methotrexate, cyclosporine, mycophenolate, infliximab, adalimumab and azathioprine. Despite this, the ulcers persisted and the prednisone could not be tapered below 20 mg daily. Intravenous immunoglobulin (IVIG) at 2 g/kg monthly was initiated with nearly complete improvement (fig. 2). The prednisone was tapered to 5 mg daily and IVIG was tapered to 2 g/kg every 12 weeks. She has since done well on azathioprine and low-dose prednisone and has had no recurrent lesions.

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Discussion

PG has an annual incidence of 3–10 per million persons, most commonly presents between 20 and 50 years of age and is more common in women. It is characterized by a neutrophilic infiltrate that is believed to be due to dysregulation of neutrophil function and altered innate immune responses. It frequently presents as painful ulcers that often follow surgery or trauma and is commonly misdiagnosed as infectious or ischemic lesions [1].

Initial therapy consists of corticosteroids, although steroid-sparing agents have been used, including dapsone, minocycline, methotrexate, cyclosporine, mycophenolate and TNFα inhibitors. IVIG is typically used after other treatments have failed. Careful wound care and avoidance of debridement and surgery is key [1].

We reviewed 20 cases of IVIG therapy in PG that are described in table 1 and table 2. Table 1 describes 13 cases that were treated with IVIG 2 g/kg (except for two in whom the dose was 1.5 and 2.5 g/kg, respectively). 12 of these achieved complete or nearly complete remission; 2 had disease recurrence that required repeated courses of IVIG. Both instances of recurrent disease responded to repeat treatment with IVIG. Table 2 describes 7 patients treated with lower-dose IVIG (0.5 g/kg). All had major or complete response, though all required continued corticosteroids, with 4 requiring additional immunosuppressive therapy.

Based on this case and our review of the literature, we believe that IVIG is a useful therapeutic option in refractory PG and can be considered in cases of resistance to or intolerance of standard immunomodulatory therapy.

This work was conducted at the University of Alabama, Birmingham, USA.

Disclosure Statement

The authors report no conflict on interest. There was no funding source.

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Table 1. Thirteen cases of IVIG therapy in PG (all IVIG courses were 2 g/kg unless noted otherwise)

Age, gender, ref.	Notable past medical history	Initial therapy	Initial IVIG courses	Initial response	Re-lapse	Therapy during IVIG treatment	Number of further IVIG courses	Subsequent response	Follow-up
35, F [2]	insect bite	PRD, DAP, CBT, TAC, CSA, MPD	2 (2 weeks apart)	nearly complete	no	PRD, CSA	none	N/A	clear at 8 months
48, M [3]	adrenal carcinoma, pemphigus vulgaris	PRD, MMF, CSA, DEX, THL	1	complete	yes	PRD, MMF	yes, 1 course	complete	clear at 5 months
17, F [3]	none noted	PRD, MPD, MMF, CSA	multiple (number and interval not given)	nearly complete	yes	CSA, MMF	yes	complete	clear at 15 months
37, F [4]	none noted	PRD, CSA	4 (monthly)	complete	no	PRD	none	N/A	clear at 4 months
55, M [5]	Ph^+ CML	PRD, MCN, DAP, AZA, MMF, SSKI, CSA	3 (monthly)	complete	no	PRD	yes, indefinite	complete	clear at 8 months
81, M [6]	trauma	CSA	6 (monthly)	significant	no	MPD	none	N/A	clear at 7 months, then died of cardiac arrest
58, M [7]	prostate carcinoma	PRD, MCN	6 (monthly)	significant	no	PRD	none	N/A	stable at 12 months
66, M [7]	CMML	BTM, TAC, PRD	6 (monthly)	significant	no	PRD	none	none	stable at 6 months
83, M [8]	none noted	CBT, MCN, PRL	5 (monthly)	significant	no	none	yes, 5 courses (bi-monthly)	complete	stable at 15 months
61, F [9]	RA, insect bite	PRD	3 (monthly)	marked	no	PRD	no	N/A	stable (unknown)
62, F [10]	none noted	CSA, GC	4 (monthly)[a]	complete	no	PRD	no	N/A	stable at 12 months
61, M [11]	MDS	PRL, MPD	2 (monthly)	marked	no	PRL, PRD	no	N/A	stable at 3 months
26, F [12]	twin pregnancy	DAP, MPD	4 (monthly)[b]	significant	no	MPD	no	N/A	stable (unknown)

The authors defined all clinical responses – there is no uniform standard for clinical response in PG.
AZA = Azathioprine; BTM = betamethasone (topical); CBT = clobetasol (topical); CMML = chronic myelomonocytic leukemia; CSA = cyclosporine A; DAP = dapsone; DEX = dexamethasone; GC = glucocorticoid (drug/route not specified); MCN = minocycline; MDS = myelodysplastic syndrome; MMF = mycophenolate mofetil; MPD = methylprednisolone; Ph^+ CML = Philadelphia chromosome-positive chronic myeloid leukemia; PRD = prednisone; PRL = prednisolone; RA = rheumatoid arthritis; SSKI = potassium iodide; TAC = tacrolimus (topical); THL = thalidomide.
[a] IVIG course 2.5 g/kg. [b] IVIG course 1.5 g/kg.

Table 2. Seven cases of IVIG therapy (0.5 g/kg) in PG (all data are from Kreuter et al. [13])

Age, gender	Associated disease	Concurrent immunosuppression	Treatment response
47, F	ankylosing spondylitis	SGC	complete
63, F	monoclonal gammopathy (IgA)	SGC, MMF, CSA	complete
31, M	ankylosing spondylitis	SGC, AZA, IFX	complete
79, F	monoclonal gammopathy (IgA)	SGC	complete
40, F	ulcerative colitis	SGC	major
49, F	ulcerative colitis	SGC, AZA, CSA	major
81, F	ulcerative colitis	SGC, CSA	complete

The authors defined all clinical responses – there is no uniform standard for clinical response in PG.
AZA = Azathioprine; CSA = cyclosporine A; IFX = infliximab; MMF = mycophenolate mofetil; SGC = systemic glucocorticoids.

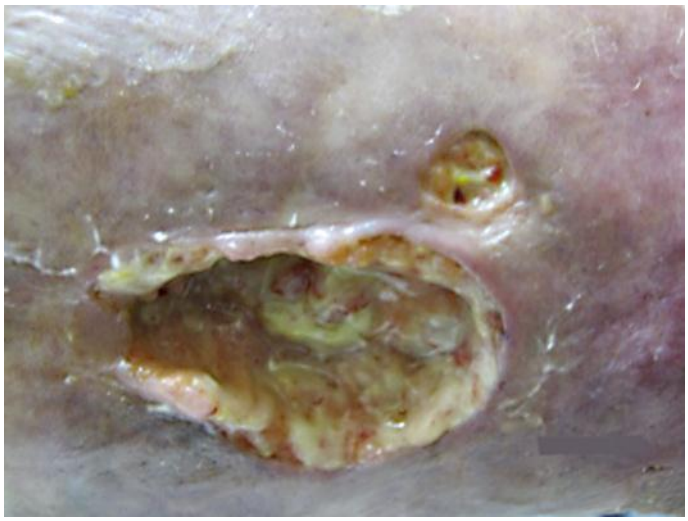

Fig. 1. PG lesion prior to IVIG therapy.

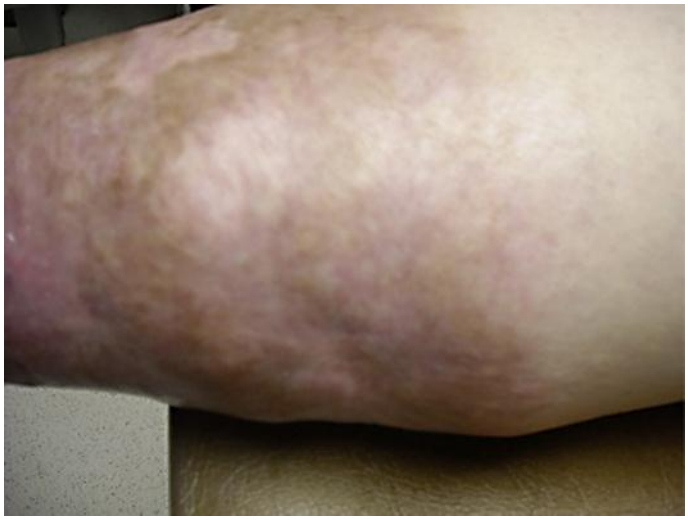

Fig. 2. PG lesion post IVIG therapy.