DOI: http://dx.doi.org/10.3315/jdcr.2012.1113

Journal of Dermatological Case Reports

PHOTOLETTER TO THE EDITOR

Localized pyoderma gangrenosum after interferon-alpha2b injections

José M. Mir-Bonafé[1], *Susana Blanco-Barrios*[1], *Alberto Romo-Melgar*[1], *Ángel Santos-Briz*[2], *Emilia Fernández-López*[1]

1. Department of Dermatology, University Hospital of Salamanca, Paseo de San Vicente 58-182, 37007, Salamanca, Spain;
2. Department of Pathology, University Hospital of Salamanca, Paseo de San Vicente 58-182, 37007, Salamanca, Spain.

Corresponding author:
José M. Mir-Bonafé, MD, Department of Dermatology, University Hospital of Salamanca, Paseo de San Vicente 58-182, 37007, Salamanca, Spain. E-mail: *jmirbonafe@gmail.com*

Abstract

We present a male patient with polycythemia vera (PV) in whom pyoderma gangrenosum (PG) was induced by subcutaneous injections of interferon-α2beta (IFN-α2b).

The patient presented with a 6 cm wide necrotic ulcer on the external aspect of his left thigh, which was surrounded by an erythematous and indurated plaque. He also had a simetrical but smaller 2 cm of size ulcer on the external aspect of the right thigh. Histopathological examination showed a massive perivascular and interstitial inflammatory infiltrate. It was vastly composed of neutrophils and secondary formation of interstitial neutrophilic microabscesses was also observed.

To our knowledge only two cases of PG secondary to IFN-α2b injections have been reported, none of them in a patient with PV. Physicians should be aware of these IFN-α2b-related local adverse effects as they might become extremely severe. Immediate local discontinuation of drug administration is mandatory. In order to avoid these complications, alternating injection sites is highly advisable. (*J Dermatol Case Rep*. 2012; 6(3): 98-99)

Key words:

adverse event, injection, interferon, polycythemia vera, pyoderma gangrenosum, ulcer

We report the case of a 61-year-old male diagnosed with PV in 1992. Due to lack of response with hydroxiurea 1000 mg daily, subcutaneous interferon-α2beta (IFN-α2b) injections (18 million U/day) were added on September 2006. He alternated injection sites on buttocks, thighs, abdomen, shoulders and arms.

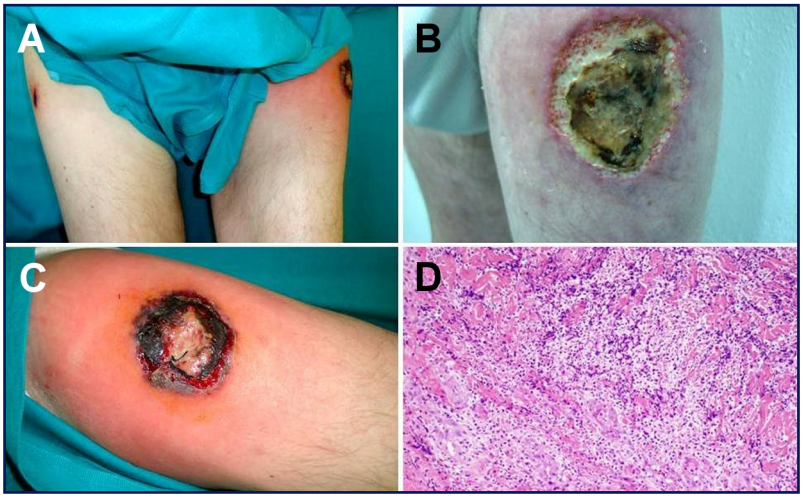

Figure 1

(A) Symmetrical necrotizing ulcers at the sites of injection. (B) Enlarged lesion one week after interferon discontinuation. (C) Inflammatory signs had largely diminished in 2 weeks approximately. (D) Perivascular inflammatory infiltrate, interstitial neutrophilic aggregates and leukocytoclasia (Hematoxylin & Eosin, X 100).

On April 2011 he attended the Emergency Department because of the onset of two skin lesions on his right and left thighs, six and seven days before, respectively (Fig. 1A). He reported that they had appeared 24 hours after IFN-α2b injections. They were extremely painful and were enlarging rapidly. A 6 cm wide necrotic ulcer surrounded by an erythematous, indurated plaque was observed on the lateral aspect of the left thigh (Fig. 1B). Symmetrically, on the right thigh a smaller 2 cm wide ulcer was present. Blood tests did not reveal any data other than his PV-related basal parameters and increased acute-phase reactants (C reactive protein: 5.02 mg/dl). Platelet and leukocyte counts, coagulation, tumor-associated antigens, basal renal values, serum creatinine, BUN, LDH, indirect bilirrubin, ANA, ENA, ANCA, cryoglobulins as well as antiphospholipid and anticardiolipin antibodies were normal. His blood pressure values were normal. Fever was absent. Tissue cultures for bacteria and fungi resulted negative. A skin biopsy of the larger plaque's edge was performed. Histopathological examination showed spongiotic epidermis and a dense perivascular and interstitial inflammatory infiltrate within upper and mid-dermis. It was vastly composed by neutrophils with prominent leukocytoclasia and secondary neutrophilic microabscesses (Fig. 1D). No eosinophils or granulomas were noted. Signs of leukocytoclastic vasculitis were noted. Small muscular arteries in the subcutaneous tissue were unremarkable. Gram and periodic acid-Schiff stain did demonstrate neither bacteria nor fungi. Our patient was diagnosed with PG secondary to IFN-α2b injections.

The drug was immediately discontinued. In addition, oral prednisone 60 mg/day and betamethasone-gemtamicin cream were prescribed. Two weeks after the beginning of therapy, margins of necrosis were progressively replaced by granulation tissue from borders to centre (Fig. 1C). Prednisone was gradually reduced (10 mg per week) until it was stopped after a total of 14 weeks' therapy. The patient is currently receiving ruxolitinib for PV with no reported side effects or recurrences of skin lesions after 1 year of follow-up.

Although PG is idiopathic in 25-50% of cases, it has also been related to underlying systemic disorders.[1] PG secondary to drugs is unusual. Isotretinoin[2] and granulocyte colony-stimulating factors[3] have been communicated. In the setting of IFN-α2b, PG is extremely rare and only two cases have been reported. Montoto *et al*[4] published in 1998 the first case of PG secondary to IFN-α2b. Recently, Yurci *et al*[5] have described a patient in whom exacerbation of psoriasis and occurrence of PG were observed 8 weeks after the commencement of IFN-α2b and ribavirin therapy for hepatitis C. Here we communicate a patient who developed severe lesions of PG at the site of IFN-α2b injections for PV. This association had not been reported in a patient with PV. On the other hand, other localized side effects as blisters, granulomas, embolia cutis, lupus-like pattern, and alopecia have also been communicated. Immediate local discontinuation of drug administration is mandatory. In order to avoid these complications, alternating injection sites is highly advisable.

References

1. Verma S, Field S, Murphy G. Photoletter to the editor: Oral ulceration in pyoderma gangrenosum. *J Dermatol Case Rep*. 2011; 5: 34-35. PMID: 21894254.
2. Tinoco MP, Tamler C, Maciel G, Soares D, Avelleira JC, Azulay D. Pyoderma gangrenosum following isotretinoin therapy for acne nodulocystic. *Int J Dermatol*. 2008; 47: 953-956. PMID: 18937662.
3. Ross HJ, Moy LA, Kaplan R, Figlin RA. Bullous pyoderma gangrenosum after granulocyte colony-stimulating factor treatment. *Cancer*. 1991; 68: 441-443. PMID: 1712666.
4. Montoto S, Bosch F, Estrach T, Blade J, Nomdedeu B, Nontserrat E. Pyoderma gangrenosum triggered by alpha2b-interferon in a patient with chronic granulocytic leukemia. *Leuk Lymphoma*. 1998; 30: 199-202. PMID: 9669691.
5. Yurci A, Guven K, Torun E, Gursoy S, Baskol M, Akgun H, Ozbakir O, Yucesoy M. Pyoderma gangrenosum and exacerbation of psoriasis resulting from pegylated interferon alpha and ribavirin treatment of chronic hepatitis C. *Eur J Gastroenterol Hepatol*. 2007; 19: 811-815. PMID: 17700270.