Actas Dermosifiliogr. 2011;**102(5)**:373-377

ACTAS
Dermo-Sifiliográficas

Full English text available at
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CASE REPORT

Lung Involvement in Pyoderma Gangrenosum: A Case Report and Review of the Literature

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Manuscript received April 11, 2010; accepted for publication December 8, 2010

KEYWORDS
Pyoderma gangrenosum;
Iodine;
Lung;
Wegener granulomatosis

Abstract Pyoderma gangrenosum is a neutrophilic dermatosis that, in addition to its characteristic skin manifestations, can cause visceral alterations. Our patient was a 34-year-old woman with pyoderma gangrenosum that was exacerbated by iodine and that also affected the lungs. Other published cases of lung involvement in pyoderma gangrenosum are reviewed and we discuss the possible exacerbation of this disease by iodine. Lung involvement is the most common extracutaneous manifestation of pyoderma gangrenosum and the main differential diagnosis is then with Wegener granulomatosis. It is important to remember the possible presentation of extracutaneous manifestations of pyoderma gangrenosum, including particularly lung involvement, in order to avoid subjecting a patient to aggressive diagnostic tests, at least in the initial stages.

PALABRAS CLAVE
Pioderma gangrenoso;
Yoduros;
Pulmón;
Granulomatosis de Wegener

Pioderma gangrenoso con afectación pulmonar: caso clínico y revisión de la literatura

Resumen El pioderma gangrenoso es una enfermedad perteneciente al grupo de las dermatosis neutrofílicas. Además de una clínica cutánea característica puede presentar manifestaciones viscerales. Presentamos el caso de una mujer de 34 años con un brote de pioderma gangrenoso exacerbado por yodo, con afectación pulmonar, y revisamos otros casos de pioderma gangrenoso con afectación pulmonar publicados hasta la fecha. Discutimos la posible implicación del yodo como factor de exacerbación del pioderma

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gangrenoso. Destacamos la afectación pulmonar como manifestación extracutánea más frecuente de esta entidad, y recordamos la granulomatosis de Wegener como principal diagnóstico diferencial del pioderma gangrenoso con afectación pulmonar. Es importante considerar la posible presentación de manifestaciones extracutáneas en el pioderma gangrenoso, entre las que destaca la afectación pulmonar, para evitar técnicas diagnósticas agresivas, al menos inicialmente.

Introduction

Pyoderma gangrenosum was first described by Brunsting et al in 1930.[1-4] It is a rare, noninfectious inflammatory disease of unknown etiology belonging to the group of neutrophilic dermatoses.[1,5] The disease has extracutaneous manifestations, including lung involvement,[6-9] and there are extrinsic factors that can exacerbate the symptoms.[10] We present a patient with pyoderma gangrenosum with lung involvement and review the cases published in the literature.

Case Description

The patient was a 34-year-old woman diagnosed with pyoderma gangrenosum 9 years earlier. During her initial episode of the disease, she presented a cavitating lung lesion for which the principal differential diagnoses were tuberculosis or lung manifestations of pyoderma gangrenosum. The tuberculin test was positive but sputum cultures were negative, and open lung biopsy of the lesion revealed necrotizing epithelioid granulomas. Ziehl-Neelsen stain and the polymerase chain reaction (PCR) were negative for *Mycobacterium tuberculosis*. Although the results of the tests performed were not compatible with tuberculosis, it was decided to administer a 6-month course of tuberculostatic treatment, due to the possibility of false negatives and the need for prolonged corticosteroid treatment in this patient. Four years later the patient presented a further episode of pyoderma gangrenosum that required oral corticosteroid therapy. Since that time the episodes have been less severe and have resolved with topical corticosteroids; the follow-up lung imaging studies have been normal.

Of note in her past history were long-standing iron deficiency anemia and a possible allergy to iodinated contrast media.

She came to our outpatient clinic for a 1-month history of painful, ulcerated lesions on the lower limbs that bled easily. At another hospital she had been prescribed azithromycin, 500 mg per day, potassium iodide in the form of a supersaturated solution, 8 mL every 8 hours, and potassium permanganate dressings. Twenty-four hours after starting the treatment, she developed numerous lesions on the trunk and limbs, together with reactivation of pre-existing lesions.

Physical examination revealed fever of 39°C, marked general malaise, pallor of the skin and mucosas, and widespread papules and pustules that became covered by hemorrhagic scabs. On the lower limbs and buttocks there were papulopustular lesions that coalesced into sunken, erythematous-violaceous ulcers with irregular borders and a base that was sometimes covered by fibrin (Figure 1). The reactivation of healed lesions from previous episodes of pyoderma gangrenosum presented with peripheral papulopustular lesions (Figure 2).

Blood tests revealed severe microcytic hypochromic anemia that required packed-cell transfusion, and methicillin-sensitive *Staphylococcus aureus* was isolated from the blood cultures. Antinuclear antibodies and perinuclear antineutrophil cytoplasmic antibodies (pANCA) were positive at low titers (nonsignificant), and cytoplasmic ANCA (cANCA) were negative. The chest radiograph showed 2 cavitating lesions in the right lung field compatible, among other possibilities, with septic emboli. In view of the radiographic findings, echocardiography was performed to exclude endocarditis; the study was normal. Thoracic

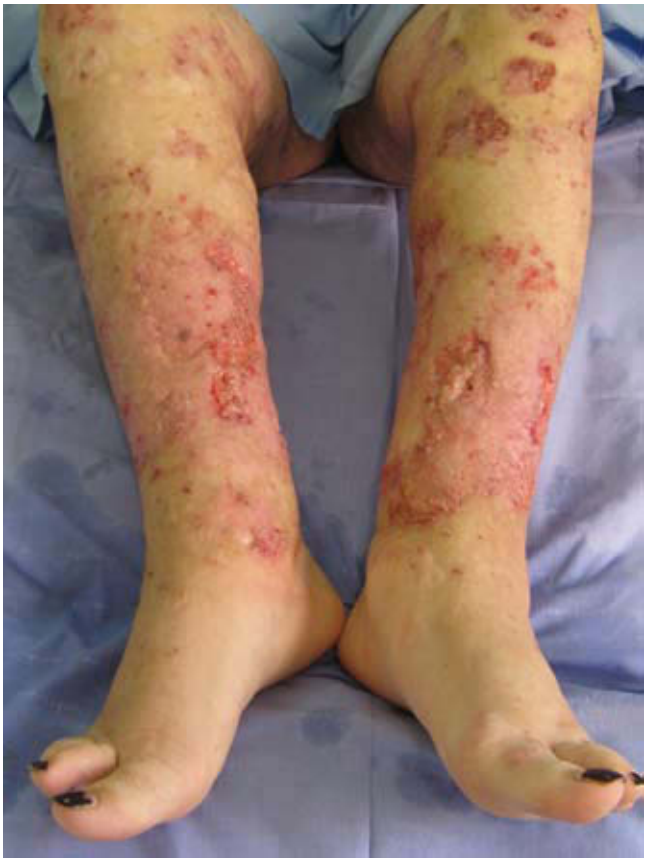

Figure 1 Deep ulcers with irregular borders on the lower limbs.

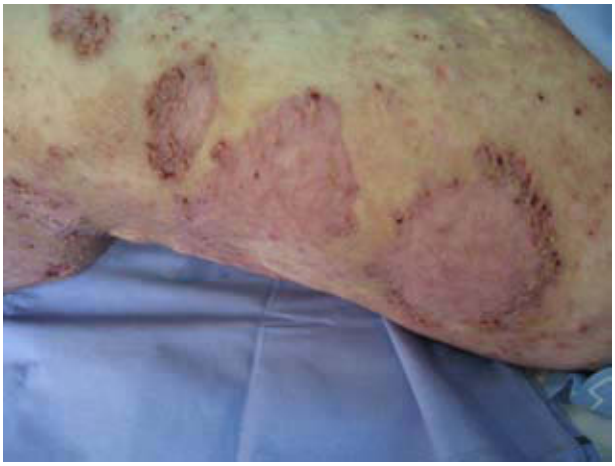

Figure 2 Scars of ulcers from previous episodes of pyoderma gangrenosum. The ulcers have a peripheral cribriform appearance and some have overlying papulopustular lesions.

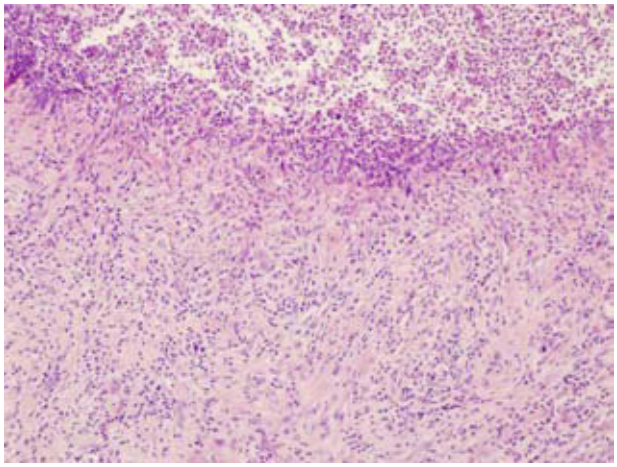

Figure 4 Lung biopsy. There is a palisading inflammatory infiltrate surrounding a central cavity with necrotic material, fibrin, and abundant neutrophils (hematoxylin-eosin, original magnification, 10).

computed tomography revealed the same cavitating lung lesions (Figure 3).

As the patient had been diagnosed with pyoderma gangrenosum and the lesions were similar to those typically observed in flare-ups, associated with the possibility of pathergy and the patient's poor general state of health, it was decided not to perform skin biopsy.

We reviewed the pathology of the lung biopsy performed 9 years earlier (Figure 4). The presence of necrotizing epithelioid granulomas with abundant neutrophils and the negative results for acid-alcohol-fast bacilli and PCR for *M tuberculosis* were compatible with lung disease secondary to pyoderma gangrenosum.

The patient was diagnosed with a probable iodine-induced exacerbation of pyoderma gangrenosum with associated lung involvement. In addition to topical dressing of the ulcers with fusidic acid and polyamide and silicone bandages, treatment was started with prednisone, 1 mg/kg/d, and intravenous imipenem, 1 g every 6 hours, and vancomycin, 1 g every 24 hours with subsequent dose adjustment according to the plasma levels of the drug. The skin lesions responded favorably, leaving cribriform scars. The chest radiograph performed at 4 months showed complete resolution of the lung lesions.

Figure 3 Thoracic computed tomography: cavitating image in the right middle lung field.

Discussion

There are 2 main problems in the case we present: the possible implication of iodine as a factor that exacerbated a flare-up of pyoderma gangrenosum and lung disease secondary to pyoderma gangrenosum.

Iodine-induced dermatitis can occur after oral, parenteral, or, less frequently, topical treatment with iodine. It is characterized by papulopustular lesions in areas with a high density of sebaceous glands. There are no pathognomic signs, nor is histology diagnostic. Resolution occurs spontaneously within 2 to 6 weeks after interrupting the treatment with iodine, and there is a residual postinflammatory hyperpigmentation. Treatment consists of avoiding iodine in the diet, in drugs, and in radiographic contrast media.[11-13]

Certain skin diseases, including pyoderma gangrenosum, are known to be exacerbated by iodine.[10]

Our patient has not restricted her dietary intake of iodine since her first reaction to the contrast medium, and, to date, she has developed no new lesions since the flare-up seen in our clinic. These observations would suggest that the skin manifestations were more likely due to a flare-up of pyoderma gangrenosum exacerbated by iodine rather than an iodine-induced dermatitis.

Pyoderma gangrenosum can affect the internal organs, most commonly the lungs, in which the typical findings are unilateral or bilateral nodules with or without necrosis. Lung involvement can also present with pleural effusion, lung abscesses, unilateral lung shadows, or interstitial pneumonitis.[6-9] Histology reveals nonspecific necrotizing

Table 1 Published Cases of Pyoderma Gangrenosum With Lung Involvement

Authors	Sex	Age, y	Lung Biopsy[a]	Lung Involvement	Hematologic Disorders	Reference
Kanoh S et al	M	54	Yes	Infiltrates. Ground-glass opacities. Consolidation	Myelodysplastic syndrome	Mayo Clin Proc. 2009;84:555-557
Rajan N et al	F	0.33	No	Wedge-shaped opacities	No	Pediatr Dermatol. 2009;26:65-69
Kitagawa KH et al	F	82	Yes	Mass	No	J Am Acad Dermatol. 2008;59:S114-116
Liu ZH et al	M	65	No	Nodules with and without cavitation	IgA myeloma	Eur J Dermatol. 2008;18:583-585
Field S et al	F	52	Yes	Consolidation. Cavitating nodules	No	Clin Exp Dermatol. 2008;33:418-421
Mirkamali A et al	-	-	-	Sterile lung abscess	Monoclonal IgA gammopathy	Med Mal Infect. 2007;37:835-839
Chahine B et al	F	33	Yes	Nodules with and without cavitation	Monoclonal dysglobulinemia	Presse Med. 2007;36:1395-1398
Chahine B et al	M	29	Yes	Emphysema. Cystic lesions. Micronodules	Acute monocytic leukemia	Presse Med. 2007;36:1395-1398
Bhat M et al	F	37	Yes	Pulmonary infiltrates	No	CMAJ. 2007;177:715-718
Takeuchi K et al	F	5	No	Diffuse opacities bilaterally	No	Eur J. Pediatr. 2003;162:344-345
Kanno T et al	M	76	-	Sterile lung abscess	-	Hinyokika Kiyo. 2002;48:565-568
Mlika RB et al	M	67	-	-	Lymphocytic leukemia	Int J Dermatol. 2002;41:65-68
Mlika RB et al	M	45	-	-	No	Int J Dermatol. 2002;41:65-68
Krüger S et al	F	45	Yes	Lung nodules with central necrosis	No	Chest. 2001;119:977-978
Riahi L et al	-	-	-	-	-	Ann Med Interne (Paris). 2001;152:3-9.
Brown TS et al	M	17	Yes	Abscess. Consolidation with central cavitation	No	J Am Acad Dermatol. 2000;43:108-112
Vadillo M et al	M	73	No	Pleural effusion	Myelodysplastic syndrome	Br J Dermatol. 1999;141:541-543
Wang JL et al	F	24	Yes	Opacity. Pleural effusion	No	Thorax. 1999;54:953-955
Fukuhara K et al	F	75	No	Infiltrate. Pleural effusion. Cavitating mass. Lung abscesses	No	Br J Dermatol. 1998;139:556-558
Grattan CE et al	F	28	No	Cystic lesions	No	Br J Dermatol. 1998;139:352-353
Peters FP et al	F	48	No	Lung infiltrates. Pleural effusion	Myelodysplastic syndrome	Ann Hematol. 1998;77:135-138
Kasuga I et al	M	50	Yes	Multiple nodules. Pleural effusion	No	Respir Med. 1997;91:493-495
Merke DP et al	M	0.75	Yes	Necrotizing tracheitis	No	J Am Acad Dermatol. 1996;34:681-682
Cartier H et al 101	M	54	-	Cavitating nodule	Monoclonal IgA gammopathy	Ann Dermatol Venereol. 1995;122:97-
Lebbé C et al	F	58	Yes	Opacity. Cavitating nodules	No	J Am Acad Dermatol. 1992;27:623-625
Vignon-Pennamen MD et al	M	38	No	Consolidation	No	Dermatologica. 1991;183:255-264
Vignon-Pennamen MD et al	F	60	Yes	Pleural effusion. Cavitating nodule	Monoclonal IgA gammopathy	Arch Dermatol. 1989;125:1239-1242
Gibson LE et al	F	66	Yes	Pulmonary infiltrates	Myeloproliferative syndrome	May Clin Proc. 1985;60:735-740
McCulloch AJ et al	F	53	Yes	Consolidation	No	Thorax. 1985;40:314-315
Moragon M et al	M	59	Yes	Pulmonary infiltrates	Myelodysplastic syndrome	Actas Dermosifiliogr. 1990;81:413-416
Poiraud C et al	M	56	No	Interstitial lung disease	Myelodysplastic syndrome	Ann Dermatol Venereol. 2010;137: 212-215

[a]Including cases of endobronchial biopsy. Abbreviations: F, female; Ig, immunoglobulin; M, male.

inflammatory granulomas with a neutrophilic infiltrate, as were observed in the lung biopsy in our patient.[2,8] The lung lesions can appear simultaneously with the skin manifestations, as in our case, or later.[2,9,14] An increase in the rate of hematologic tumors has been reported in patients with pyoderma gangrenosum with lung involvement.[15]

Through a search using the PubMed database, we performed a review of published cases of pyoderma gangrenosum with lung involvement (Table). Using the keywords "Pyoderma Gangrenosum"[Mesh term] OR "pyoderma gangrenosum"[Title] OR "pyoderma gangrenosum"[Text word] OR "pyoderma"[Text word] OR "Neutrophilic dermatoses" [Title] OR "Neutrophilic dermatoses" [Text word]) AND ("Lung"[Mesh term] OR lung[Text word] OR lung[Title] OR pulmonary[Text word] OR pulmonary[Title] OR cavitation[Text word] OR cavitary[Text word] OR tracheal[Text word] OR tracheobronquial[Text word] OR tracheitis[Text word], we obtained 91 articles. A similar search was performed using the EMBASE database, and finally free searches were performed in PubMed, Elsevier, and Dermabase. Those articles not related to the study subject were eliminated, as were articles without an abstract published in English or Spanish. The resulting 29 articles reported a total of 32 cases of pyoderma gangrenosum with lung involvement. Although publication bias could affect the results, the most frequent lung alterations were nodular lesions with or without cavitation, present in 11 patients. Hematologic tumors were reported in 13 cases, most commonly a myelodysplastic syndrome or a monoclonal gammopathy. Invasive procedures were used for diagnosis of the lung lesions in 16 cases.

The principal differential diagnosis of pyoderma gangrenosum with lung involvement is Wegener granulomatosis. In our case this possibility was excluded by the absence of nasopharyngeal and renal involvement, negative cANCA, and a favorable response to monotherapy with oral corticosteroids. The treatment of Wegener granulomatosis using corticosteroids without cyclophosphamide has a very poor prognosis.[2,6]

The medical history and other additional tests performed allowed us to exclude other causes of lung disease.

Conclusion

We present a case of pyoderma gangrenosum probably exacerbated by iodine and with concomitant lung involvement. From our review of the literature, we highlight the possible implication of iodine in exacerbations of pyoderma gangrenosum. We also note that, before a diagnosis of pyoderma gangrenosum is made, visceral involvement must be excluded using the medical history, physical examination, routine blood tests, chest radiograph, and other tests as indicated. Lung disease secondary to pyoderma gangrenosum should be suspected in cases of pyoderma gangrenosum associated with lung lesions. This suspicion could avoid subjecting patients to aggressive diagnostic procedures. The possibility of Wegener granulomatosis should be considered in cases of pyoderma gangrenosum with lung involvement resistant to corticosteroid treatment alone.

Conflict of Interest

The author declare that they have no conflicts of interest.

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