Pulmonary manifestations of Pyoderma gangrenosum

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Summary

Introduction > Pyoderma gangrenosum is an uncommon ulcerative cutaneous disorder. Extracutaneous localizations are rare. Respiratory system involvement has been described in a few cases, but the pulmonary features reported were highly variable.

Case > We report two cases of patients with Pyoderma gangrenosum combining cutaneous and pulmonary manifestations. One case presented multiple nodular lesions, some with cavitation. The underlying disease was varicella-zoster virus infection. The second presented pneumonitis with bronchiolar micronodules.

Discussion > Few cases have reported Pyoderma gangrenosum with pulmonary involvement, which appears to be manifested mainly as nodules or interstitial lung disease. The principal differential diagnosis is Wegener’s granulomatosis.

Résumé

Manifestations pulmonaires du Pyoderma gangrenosum

Introduction > Le Pyoderma gangrenosum est une affection cutanée, ulcéra- tive et rare. Les localisations extra-cutanées associées sont rares. Des atteintes respiratoires liées au Pyoderma gangrenosum ont été décrites dans un nombre limité de cas; elles sont très variées.

Observation > Nous rapportons 2 cas de Pyoderma gangrenosum présentant l’association d’atteintes cutanée et pulmonaire. Le premier cas présentait des lésions nodulaires multiples, dont certaines étaient cavitaires. La maladie sous-jacente était une varicelle suggérant que le Pyoderma gangrenosum peut être déclenché par cette infection virale. Dans le deuxième cas, il y avait une pneumopathie avec des micronodules bronchiolaires.

Discussion > Des rares cas d’atteinte pulmonaire au cours du Pyoderma gangrenosum ont été rapportés. Cette affection est souvent de type nodulaire, ou de type interstitiel. Il est important de distinguer ces lésions de la maladie de Wegener.
Pyoderma gangrenosum is an uncommon ulcerative cutaneous disorder that develops most often on the lower extremities. Extracutaneous localizations are rare and mainly involve the respiratory system. We report two cases of Pyoderma gangrenosum with both cutaneous and pulmonary manifestations.

Case 1
A 33-year-old woman was admitted in May 2002 with acute fever, a vesicular cutaneous eruption, and dyspnea. Her medical history was notable principally for salpingitis. She had been smoking for several years (9 pack-years) and was exposed to wood dust at work.

At admission, the patient reported cutaneous lesions for the past four weeks, which began two weeks after exposure to chickenpox. The ensuing vesicular cutaneous eruption developed in the same sequence as and resembling chickenpox. The skin lesions deteriorated, and she began coughing up purulent sputum. Physical examination revealed typical Pyoderma gangrenosum: multiple deep necrotic ulcerations topped with purple borders, on the legs, arms and thorax (Figure 1). These ulcerations — none located in the mucosa — were painful and bled easily. Pulmonary auscultation revealed bilateral crackles. Otherwise, there were no abnormalities. Chest radiography revealed multiple pulmonary nodules. Computed tomography (CT) showed nodules of different sizes, some with cavitation, as well as mediastinal lymph nodes (Figure 2). The abdominal CT scan was normal. The WBC count was 11x10^9/L with a differential count of 88% granulocytes; the erythrocyte sedimentation rate (ESR) was 110 mm in the first hour; fibrinogen 9 g/L and C-reactive protein 233 mg/L. Serum protein electrophoresis showed double IgG kappa monoclonal dysglobulinemia. Search for Bence-Jones proteinuria was negative. Neither the myelogram nor the bone marrow biopsy revealed any abnormalities; C3 and C4 fractions, beta-2-microglobulinemia, LDH and angiotensin converting enzyme levels were normal. Rheumatoid factor and antineutrophil cytoplasmic antibodies (ANCA) were not detected. Repeated bacterial, mycobacterial and fungal cultures from sputum and bronchoalveolar lavage (BAL) were negative. The lung function test was normal. Varicella-zoster virus serology was positive for IgG and IgM. The BAL differential cell counts were: 67% macrophages, 22% neutrophils and 9% lymphocytes. Histopathological examination of bronchial biopsies showed no specific inflammation. Histopathological examination of the open lung biopsy showed necrotic lesions and infiltration with neutrophils and monocytes; no vasculitis or granulomatous features were seen. Cutaneous biopsy was not performed because of the risk of aggravating the lesions.

Concluding that the patient presented Pyoderma gangrenosum involving skin and lungs, we began corticosteroid treatment with prednisolone at a dose of 1 mg/kg/day. Cutaneous and pulmonary lesions improved and completely healed within a few weeks with progressive tapering of corticosteroid therapy. For the past two years, the patient has not received any corticosteroid therapy and has not shown any sign of relapse.

Case 2
The second case involved a man who was first admitted in May 1988, at the age of 29 years, for a suicide attempt. He had a 2-pack-year smoking history, having stopped smoking many years earlier. He had no notable medical history. Chest radiography revealed bilateral emphysema with a micronodular pulmonary pattern. WBC showed a neutrophil count of 13.3x10^9/L. ESR was 110 mm in the first hour. The patient refused a further work-up at that time. A year later, he was admitted for weight loss and night sweats. Physical examination was normal, while inflammatory markers (ESR, C-reactive protein) were again elevated. HIV serology was negative, as was screening for antinuclear antibodies and rheumatoid factor. The chest CT showed numerous bronchiolar micronodules and moderate cystic lesions (Figure 3). Lung function tests showed a restrictive pattern: total lung capacity was 62% of theoretic value. Repeated bacterial, mycobacterial and fungal cultures of sputum and endoscopic samples were negative. Open lung biopsy revealed interstitial fibrosis, lipophagic granuloma and alveolitis with neutrophilic infiltrate. A mediastinoscopy-sampled lymph node showed sinus histiocytosis.

The patient began oral corticotherapy, which led to clinical improvement for 18 months. In May 1991, the patient was hospitalized for pneumonia. A new CT scan showed new consolidations with mediastinal and hilar lymph nodes. Bronchoalveolar lavage (BAL) fluid from the middle lobe contained 23% lymphocytes, 77% macrophages and monocytes, and < 1% granulocytes. Several antibiotic regimens remained ineffective.
Skin lesions then began to appear. We took a biopsy sample from subcutaneous nodules of the left leg and right finger. After these two skin stresses, extensive necrotic lesions with a purple border developed at these traumatized locations. Cutaneous biopsy showed superficial erosion with underlying dense dermal neutrophilic infiltrate and no evidence of vasculitis. On treatment with prednisolone 1 mg/kg/day, the cutaneous lesions improved and pulmonary symptoms decreased over a 3-year period. In September 1994, however, he developed severe anemia and thrombopenia, with hemoglobin at 7 g/dL and a platelet count of 58x10^9/L. The leukocyte count increased to 38x10^9/L with a differential cell count of 19% neutrophils, 25% monocytes, 29% myelocytes and 13% blasts. Testing of bone marrow aspirate showed acute monocytic leukemia with 8% blasts, 8% myeloblasts and 3% promyelocytes, and karyotyping revealed monosomy 7. The patient could not receive an allograft because of pulmonary fibrosis and was treated with hydroxyurea. In March 1995, he was admitted for acute respiratory distress due to right pleural effusion and aggravation of fibrosis. The pleural effusion was caused by progression of the leukemia. He died three weeks after admission. Death was attributed to complications of leukemia, and no postmortem examination was performed.

Discussion

We report here two cases of *Pyoderma gangrenosum*, one with multiple cavitary lesions and another with infiltrative lung disease. Pulmonary features are, albeit rarely, associated with *Pyoderma gangrenosum* — mainly nodules and cavitations, but also interstitial lung disease. Corticosteroid treatment is adequate in most cases. Prognosis depends on the associated diseases. The principal differential diagnosis is Wegener’s granulomatosis; in the absence of evidence of either it or cutaneous lesions, a lung biopsy is necessary. The etiology and pathogenesis of *Pyoderma gangrenosum* are currently unknown. Many abnormal immune responses have been described in patients with it, including both humoral and cell-mediated defects. Complement abnormalities, immune complex deposition and the possible existence of circulating factors that influence lymphocyte function have been described. *Pyoderma gangrenosum* also occurs in immunocompromised patients [1]. *Pyoderma gangrenosum* occurs in 30-60% of patients with inflammatory bowel disease [1, 2]. It has also been reported in other conditions, such as Behçet syndrome, hematologic and rheumatoid diseases, hepatopathies, visceral carcinoma and immune disorders such as HIV infection.
More recently, the possible relation to hepatitis C virus has been discussed [3, 4]. *Pyoderma gangrenosum* can appear before the onset or detection of an associated disease, and patients should be re-evaluated periodically even after the disease has healed.

Many conditions have been confused with *Pyoderma gangrenosum*, resulting in delayed diagnosis, inappropriate treatment and unnecessary surgery. The differential diagnosis depends on the stage and site of the disease and whether it is a typical or atypical form. Early lesions of classic *Pyoderma gangrenosum* may present as an inflammatory pustule or nodule and might suggest folliculitis, gonococcemia, furunculosis, inflamed epidermal cyst, erythema nodosum, vasculitis or thrombophlebitis. When an inflammatory ulcer is present, the differential diagnosis includes a variety of infections, vascular ulcers, neoplasms and reactions to ingested or external agents. Vasculitic conditions such as polyarteritis nodosa, rheumatoid arthritis, Wegener’s granulomatosis and Churg-Strauss syndrome can also cause ulceration that could be confused with *Pyoderma gangrenosum*, and neuropathic ulcers occur in association with diabetes on weight-bearing surfaces [1].

In the first case, *Pyoderma gangrenosum* was associated with chickenpox, that is, varicella zoster virus infection. This suggests that pulmonary involvement could be due to the chickenpox or could be one of the systemic manifestations of typical cutaneous *Pyoderma gangrenosum*. The possible involvement of the Chickenpox virus (morphologically identical to varicella-zoster virus) in the pathogenesis of *Pyoderma gangrenosum* was noted in 1974 and 1979 [5, 6]. A previous report describes multiple pulmonary nodules four months after recovery from chickenpox [7]. Active chickenpox pneumonia mimicking pulmonary metastasis has also been described [8]. In the present case, the high levels of IgM- and IgG-specific antibodies against varicella-zoster virus that we observed strengthened our hypothesis that chickenpox might trigger *Pyoderma gangrenosum*.

Infection must always be sought and then ruled out. A cutaneous biopsy should be performed to eliminate other types of ulceration. The risk of precipitating new lesions or causing existing disease to expand into the site of trauma as a “pathergic reaction to biopsy” must be considered, but is outweighed by the need to reach a diagnosis and rule out other diseases insofar as possible. In our second case, the skin biopsy was considered a precipitating factor in new lesions [9].

Histological analysis of the pulmonary lesions in *Pyoderma gangrenosum* shows typical necrotic chronic nonspecific inflammatory granulomas with neutrophilic and lymphocytic infiltration, similar to cutaneous neutrophilic infiltrates [1]. These lesions are frequently seen in Wegener’s granulomatosis. However, in our cases, it was ruled out by the absence of nasopharyngeal or renal lesion and the pathology findings of the open lung biopsy [10].

**Conflicts of interest:** none

References