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A case of atypical pyoderma gangrenosum

Ermira Vasili[1], *Entela Shkodrani*[1], *Liberta Labinoti*[2], *Alert Xhaja*[1]

1. Clinic of Dermatology, University Hospital Center "Mother Theresa", Tirane, Albania.
2. Unit of Dermatology, American Hospital of Tirana, Albania.

Corresponding author:

Dr. Ermira Vasili,

Clinic of Dermatology,
University Hospital Center
"Mother Theresa"

Tirane, Albania.

E-mail: *miravasili@hotmail.com*

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Abstract

Background: Pyoderma gangrenosum is a rare inflammatory disease of unknown etiology and unspecific histopathology. There are no clear-cut criteria for the diagnosis of this disease. The diagnosis is usually made based on clinical appereance, course of disease and possible, commonly coexisting disorders. In atypical cases the diagnosis is based on exclusion of other causes of similar appearing cutaneous ulcerations.

Main observations: The 67-year-old male patient, presented with a 15-year history of painful ulcers and vegetative lesions covered with sero-hemorrhagic and purulent secretions, localized on the dorsal surface of both hands leading to self-amputation of distal phalanges. We report a step-by-step The patient refers to have these complaints for more than 15 years. An extensive diagnostic procedure led to the diagnosis of pyoderma gangrenosum as a diagnosis of exclusion.

Conclusion: This report shows an atypical variant of an ulcerative disease. Pyoderma gangrenosum, a diagnosis of exclusion, was sustained based on an extensive diagnostic procedure. In this article we describe the step-by-step approach which let to this diagnosis.

Introduction

Pyoderma gangrenosum (PG) is a rapidly evolving, idiopathic, chronic, and potentially severely debilitating skin disease. PG is more frequent in female than male patients and may occur at any age, but onset is most common between the age of 40 and 60.[1,2]

Typical pyoderma gangrenosum is characterized by a deep ulceration with a violaceous border that overhangs the ulcer bed. These lesions most commonly occur on the legs, but they may occur anywhere on the body. Atypical variants of PG were described, occurring commonly on dorsal surface of the hands and characterized by a more superficial ulceration and a vesiculopustular component.[1,2]

There are no clear-cut criteria for the diagnosis. Histopathology is usually unspecific, but is commonly performed to exclude other causes of cutaneous lesions.[3]

We report a case of atypical, deep ulcerations on the dorsal surface of hands with self-amputation of digits.

Case report

The 67-year-old, otherwise healthy, male patient, had a 15-year history of erythema and ulcerations of both hands. The patient was a typist, there is no history of contact with animals or travels to tropical areas.

At admission he presented erythema, ulcerations, vegetations covered with sero-hemoragic and suppurated crusts accompanied by partial self-amputation and tissue destruction of distal phalanges (Fig. 1A). The fourth finger of his left hand had been amputated 4 years prior to admission with the suspicion of skin cancer but final pathology report did not support this diagnosis.

Initial working diagnoses included: skin tuberculosis, atypical mycobacterial infection, deep fungal infection, subcutaneous sarcoidosis, melidiosis, autoimmune diseases, complex regional pain syndrome, and Rosai Dorfman disease.

Bacteriology culture revealed proteus species. Pathology was unspecific, showing features of chronic granulation

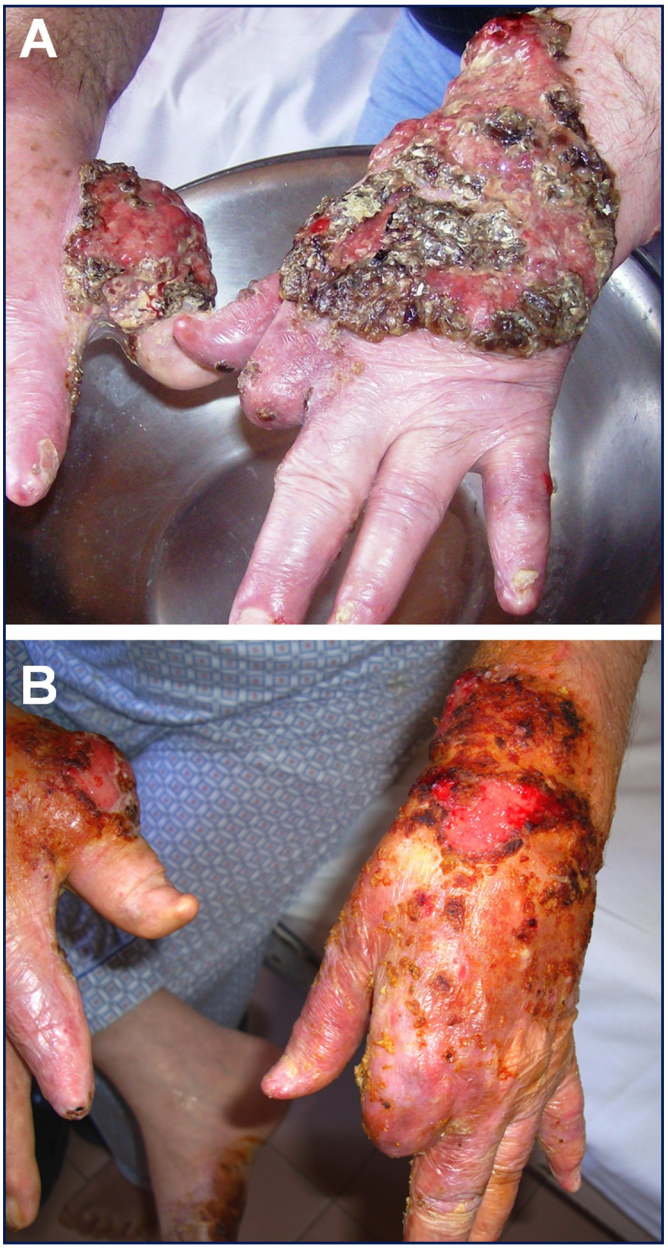

Figure 1

Ulcers and vegetative lesions covered with sero-hemorrhagic and purulent secretions. Self-ampuation and tissue destruction in distal phalanges. The fourth finger of his left hand had been amputated 4 years prior to admission (A). Improvement after therpy (B).

(2004) and proliferation of epithelial cells, inflammatory infiltrates (april 2007) and again chronic granulation (in June 2007). Additional pathology evaluation performed by Istituto Dermopatico Dell'Immacolata in Rome/Italy showed skin sections with ulcerative and infiltrative changes and dense dermal infiltrations with the predominance of T and B lymphocytes, neutrophiles, histiocytes, eosinophiles and plasma cells (Fig. 2 A, B).

Hand X-ray demonstrated osteoporosis and lack of distal phalanges. Culture results for fungi, performed on Sabouraut agar and Brain Heart infusion agar, were negative. Culture results for mycobacterium tuberculosi and other mycobacteriae on Lowenstein Medium Base were also negative. Culture results for mycobacterium tuberculosi and other mycobacteriae on Lowenstein Medium Base were also negative. The aspiration culture for burkholderia pseudomallei, was negative, what excluded the diagnosis of melidiosis.

PCR and reculture for atypical fungal infection and skin tuberculosis were all negative. Investigations included Gram, acid fast, Warthin-Starry, Gömöri methenamine silver, and Periodic acid-Schiff (PAS) staining of the biopsy specimen.

The Veneral Disease Research Laboratory test (VDRL) and the Treponema palliduman hemagglutination assay (TPHA) for syphilis were negative.

Mantoux test was negative.

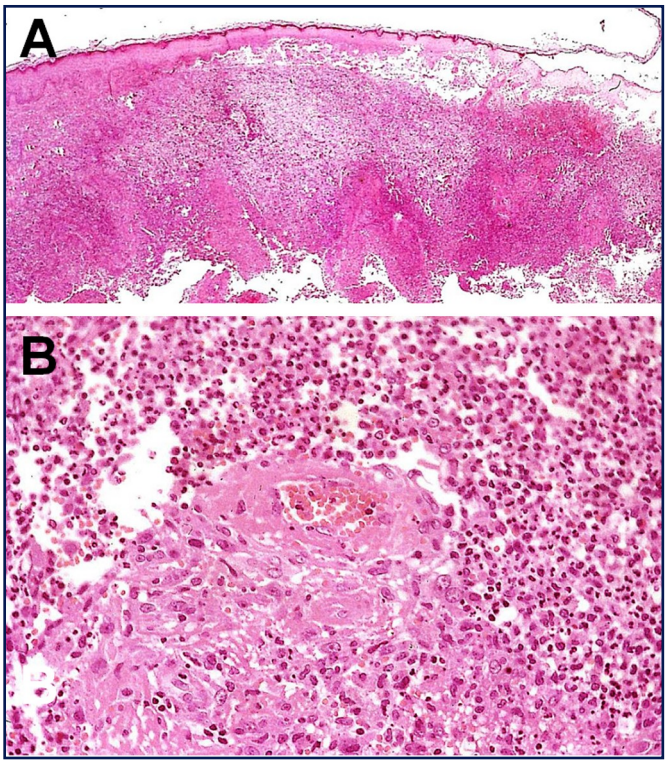

Figure 2

Dense dermal infiltrations with the predominance of T and B lymphocytes, neutrophile, histiocyte, eosinophiles and plasma cells. Hematoxylin-eosin (A, B).

Antinuclear antibodies, complement C3, C4, total hemolitic complement, Anti-dsDNA, rheumatoid factor were negative. Hepatitis B and C as well as human immunodeficiency wirus infections were excluded.

The neurological assessment was normal and in electromyography was normal. Arteriovenous Doppler scanning of his extremities was normal.

Additionally, pulmonary tbc and sarcoidosis were excluded based on chest X-ray and CT-scan.

All medications attempts with anti-bacterial and antifungal agents, including tazocin and itraconazol were not effective.

Taking into consideration the pathology result, exclusion of all enlisted diagnoses and failure to respond to anti-infectious agents the diagnosis of pyoderma gangrenosum was made as diagnosis of exclusion.

Methylprednisolone i.v. 80 mg per day with gradual decrease and shifting to oral cortisone was introduced. Clinical response was impressive and seen since after the first week. No adverse events were observed. After one month the patient was discharged with an impressive recovery. The patient is still under treatment with oral cortisone at a dose of 25 mg daily.

Discussion

Pyoderma gangrenosum is a rare inflammatory disease of unknown etiology. In more than half of cases, the disease is associated with extra-cutaneous diseases, such as inflammatory bowel disease, polyarthritis seronegative or seropositive, and hematologic malignancies.[4,5] Our patient had no underlying disease.

Typical cutaneous lesions of pyoderma gangrenosum are characterized by rapidly progressive deep ulceration. In atypical PG variant, lesions develop on dorsal surface of the hands and characterized by more superficial ulcerations and a vesiculopustular component. A vegetative variant of PG has also been described.[1,2]

In rare cases patients present with more than one type PG.[6] Our patient presented with an overlap of different types of pyoderma gangrenosum. He presented with lesions on the dorsal surface of hands and fingers with deep ulcerations and self-amputation of distal phalanges. These changes were accompanied by features characteristic for pyoderma vegetans and a vesiculopustular component with crusting, as in the superficial form of PG.

Histopathology of PG is usually unspecific. Usually massive neutrophilic infiltration, hemorrhage, and necrosis of the overlying epidermis is observed. Perivascular neutrophilic infiltrates are often present, but the full picture of vasculitis is generally absent. In the early disease or in new lesions a mixed cell infiltrate may be present. Late in the process, granulation tissue may be present.[1,2]

The diagnosis of PG is usually based on the clinical presentation. In doubtful cases the diagnosis is confirmed through a process of elemination of other causes of cutaneous ulcers.[7] Table 1 presents diseases which were excluded in the process of establishing the diagnosis in our patient. Occasionally coexistence of predisposing diseases[8,9] may be a useful hint for the diagnosis.

There are no unified guidelines for an uniformly effective treatment of pyoderma gangrenousum. Drugs being used in therapy of pyoderma gangrenosum include systemic corticosteroids and immunosuppressive drugs such as cyclosporine, azathioprine, cyclophosphamide, chlorambucil, cyclosporin, tacrolimus, mycophenolate mofetil, methotrexate and cyclophosphamide or intravenous immunoglobulins[10,11]. Lately immunosuppresive biological drugs, as infliximab, have been suggested for therapy of

Table 1

Causes of cutaneous ulcers, which were excluded in the process of establishing the diagnosis in our patient.

Diagnosis	Tests to exclude disease
Deep fungal infection Atypical fungal infection	Fungal culture on Sabouraut medium Warthin-Starry stain, Brain Heart infusion agar, Saboraud agar resulted negative. Gömöri methenamine silver stain Periodic acid Schiff (PAS) staining PCR for fungal DNA
Mycobacterium infection	Lowenstein glucose medium
Tubeculosis Cutis Sarcoidosis Lepra	**Mantoux test** Chest X-ray CT scan Skin biopsy Quantiferon **interferon** gamma **release assay**
Autoimmnune diseases/vasculitis	Antinuclear antibodies (AMA), Complement C3, C4, Anti-dsDNA, Antineutrophil cytoplasmic antibodies (ANCA)
Melidiosis	Aspiration culture for *pseudomonas pseudomallei*
Complex regional pain syndrome	Neurological assessment Electromyography
Syphilis	Serum evaluation for Veneral Disease Research Laboratory test (VDRL) *Treponema pallidum*an hemagglutination assay (TPHA)
HIV Infection	Serum evaluation for anti-HIV
Vascular pathology	Arteriovenous doppler scanning extremities bilateral
Skin cancer	skin histology
Rosai-Dorfmann disease	Exclusion of lymphadenopathy, hypergammaglobulinaemia or previous history of macules. papules or skin discoloration.

pyoderma gangrenosum associated with inflammatory bowel disease,[12] despite anecdotal cases of pyoderma gangrenosum occurring during infliximab therapy.[13]

In our case, application of systemic corticosteroids was sufficient to obtain rapid, significant improvement. Efficacy of immunosuppressive therapy may be considered as a final proof of the diagnosis of pyoderma gangrenosum.

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