PYODERMA GANGRENOSUM AND FULL-THICKNESS BURNS: IS THERE A PROBLEM OF DIFFERENTIAL DIAGNOSIS?

Napoli B., D'Arpa N., Conte F.

Division of Plastic Surgery and Burns Therapy, ARNAS, Civic Hospital, Palermo, Italy

SUMMARY. A case is presented of pyoderma gangrenosum, describing its characteristic features with particular reference to the phenomenon of pathergy, which considerably limits the surgical approach to the disease. After an account of the numerous skin ulcerations that have to be taken into consideration in order to make a differential diagnosis, it is noted that pyoderma gangrenosum can only on rare occasions be confused with a full-thickness granulating burn.

Introduction

Pyoderma gangrenosum is a rare disease that hardly ever comes to the notice of a plastic surgeon. This is because the phenomenon of pathergy (onset of disease after even only a banal trauma in a high percentage of cases) that is its characteristic feature limits the surgical indications to cases with bone or tendon exposure or to serious vegetating forms.[1-3]

Surgical excision of the lesion and free skin graft can be followed not only by its enlargement but also by the appearance of a new lesion at the skin removal site, unless systemic steroid coverage is performed.[4]

The diagnosis of pyoderma gangrenosum is not however simple, and it often goes unrecognized; also, it is frequently wrongly diagnosed instead of other types of skin ulceration, which has important effects on the appropriate treatment and therefore on its evolution.[5]

We describe here the case of a female patient suffering from pyoderma gangrenosum who was however admitted with a diagnosis of full-thickness burns.

Clinical case

P.M., aged 65 yr, female. The patient was admitted on 20 August 2004 with a vast loss of granulating cutaneous substance surrounded by erythematous skin in the anterior region of the left thigh. On admission the patient reported prolonged contact with synthetic ice dating from ten days before, treated topically with mupirocin. Topical antibiotic treatment (two microbiological swabs revealed pollution of the lesion by *Pseudomonas aeruginosa*) was accompanied by intravenous administration of steroids (methylprednisolone 1 g per day for two days followed by 500 mg per day for three days, and then 250 mg per day for another three days).

On 22 September 2004 the fully recovered patient was discharged and instructed to follow oral steroid therapy in scalar doses for a further two weeks (an initial 50 mg dose of prednisone, progressively decreasing). Tests performed during hospitalization did not reveal any underlying systemic pathology. The patient did not present any recidivations.

Discussion

Pyoderma gangrenosum may present as a cutaneous pathology or, in some 50% of cases, it may occur in patients with systemic pathologies present before, at, or after diagnosis.[1]

The condition has two main clinical variants. The classic variant is characterized by a deep ulcer with undermining purple edges.

Although the lesions may appear in any part of the body, they are usually located in the lower limbs. The atypical variant of pyoderma gangrenosum presents a vesicular/pustular component at the edge of the lesion consisting of an erosion or superficial ulceration most frequently on the back of the hands or of the extensor surface of the forearm and on the face. The ulcerative lesion is generally accompanied by pain, which may require treatment.[1] Pyoderma gangrenosum has also been reported to affect extracutaneous areas.[6-8]

The diagnosis of pyoderma gangrenosum is based on the morphology of the lesions, the clinical course, and the presence, if any, of an associated systemic pathology - there are no pathognomonic laboratory tests and histological findings that may be useful to exclude other pathologies are not specific, as they are those of non-infective neutrophilic dermatoses lacking neutrophilic invasion of the vascular walls (without vasculitis). With reference to histological findings in pyoderma gangrenosum, there is a perivascular dermal infiltrate of neutrophils, generally ex-

tending to the subcutis and associated with a mixed interstitial infiltrate of lymphocytes and histiocytes.[1]

There are numerous skin ulcerations (*Table I*) that have to be taken into consideration in order to make a differential diagnosis, for which numerous factors are useful: anamnestic and epidemiological factors, clinical aspects, laboratory findings, and histology.[5,9]

Conclusions

The frequent association of pyoderma gangrenosum with diseases characterized by immune disorders and its response to immune modulating agents suggest an immune aetiopathogenesis. It is not however known in what way various conditions with distinct immunological abnormalities lead to a common final course that finally induces neutrophil infiltration and tissue destruction.

To this regard, an aetiological role of interleukin-8 has been suggested - this is a powerful polypeptide exerting chemotactic action on neutrophils that is overexpressed in skin ulcers in patients suffering from pyyoderma gangreosum.[10]

With regard to treatment, a wide variety have been used - anti-infective chemotherapy, sulphasalazine, high-dosage intravenous human immunoglobulin, Infliximab.

However, systemic corticosteroids (prednisone *per os* or methylprednisolone in venous boli) are drugs of first choice that may or may not be associated with immunosuppressive drugs (cyclosporin, azathioprine, mycophenolate, cyclophosphamide, chlorambucil, tacrolimus) as steroid-sparing agents, which can in fact be used alone.

The general treatment can be associated with local treatment.[1,4,6,7,11-13] For this purpose the application of cultured autologous keratinocytes has also been used.[14,15] Full-scale surgical treatment, as we have seen, is contraindicated, and correct therapy depends on correct diagnosis. Numerous conditions, as we know, have to be distinguished: a differential diagnosis occasionally has to be made in cases of full-thickness burns. In the case we describe here, the initial doubt was probably due to poor anamnestic investigation. It can also be hypothesized that the cutaneous damage was secondary to the prolonged application of synthetic ice, which acted as a pathergic stimulus.

Table I - Differential diagnosis

Infections
Ecthyma
Gangrenous ecthyma
Cutaneous tuberculosis
Ulcers due to nontubercular mycobacteria
Tertiary syphilis
Herpes virus ulcers
Deep mycoses
Amoebiasis
Cutaneous Leishmaniasis
Necrotizing systemic vasculitis
Wegener's granulomatosis
Cryoglobulinaemia
Polyarteritis nodosa
Rheumatoid arthritis
Proliferative processes
Langerhans cell histiocytosis
Cutaneous T-cell lymphoma (mycosis fungoides)
Leukaemia cutis
Reaction to drugs
Hydroxyurea
Warfarin
Granulocyte colony-stimulating factor
Bromine and iodine
Isotretinoin
Other pathologies
Antiphospholipid syndrome
Dermatitis artefacta (Munchausen syndrome)
Trigeminal trophic syndrome
Sweet's syndrome
Calciphylaxis

RÉSUMÉ. Les Auteurs décrivent un cas de pyoderma gangrenosum avec ses aspects caractéristiques, faisant particulière attention au phénomène de la pathergie, qui limite considérablement l'approche chirurgicale à cette maladie. Après avoir décrit les nombreuses ulcérations cutanées qui doivent être prises en considération avant de faire un diagnostic différentiel, ils soulignent que les cas où le pyoderma gangrenosum peut être confondu avec une brûlure granuleuse à toute épaisseur sont rares.

BIBLIOGRAPHY

1. Jackson J.M., Callen J.P.: Pyoderma gangrenosum, www.emedicine.com/DERM/topic 367.htm
2. Swinson B.D., Morrison C.M., Sinclair J.S.: Pyoderma gangrenosum - a complication of breast biopsy. Ulster Med. J., 71: 66-7, 2002.
3. Yong-Kwang T., Friednash M., Aeling J.L.: Acute pyoderma gan-

grenosum does not require surgical therapy. Arch. Fam. Med., 7: 377-80, 1998.
4. Bhat R.M.: Management of pyoderma gangrenosum - an update. Indian J. Dermatol. Venereol. Leprol., 70: 329-35, 2004.
5. Weenig R.H., Davis M.D.P., Dahl P.R., Su W.P.D.: Skin ulcers misdiagnosed as pyoderma gangrenosum. New England J. Med., 347: 1412-8, 2002.
6. Miserocchi E., Modorato G., Foster C.S., Brancato R.: Ocular and extracutaneous involvement in pyoderma gangrenosum. Ophthalmology, 109: 1941-3, 2002.
7. Wang J.-L, Wang J.-B, Zhu Y.-J.: Pyoderma gangrenosum with lung injury. Thorax, 54: 953-5, 1999.
8. Perkins G.D., Moudgil H., Jones R.: Pyoderma gangrenosum. Thorax, 55: 345, 2000.
9. Rugarli C.: "Medicina Interna Sistemica", vol. II (4th ed.), Masson, Milan, 2000.
10. Oka M., Berking C., Nesbit M., Satyamdorthy K., Schaider H., Murphy G., Ichihashi M., Sauter E., Herlyn M.: Interleukin-8 overexpression is present in pyoderma gangrenosum ulcers and leads to ulcer formation in human skin xenografts. Lab. Invest., 80: 595-604, 2000.
11. Wollina U.: Pyoderma gangrenosum. Orphanet Encyclopedia, www.orpha.net/data/patho/GB/uk-PG.pdf, Sept. 2003.
12. Ortiz Ponce J.M.: Pioderma gangrenoso. www.gacetamedica.8m.com/122/artic.10.htm
13. Bartolucci P., Ramanoelina J., Cohen P., Mahr A., Godmer P., Le Hello C., Guillevin L.: Efficacy of the anti-TNF-alpha antibody Infliximab against refractory systemic vasculitides: An open pilot study on 10 patients. Rheumatology, 41: 1126-32, 2002.
14. Wollina U., Karamfilov T.: Treatment of recalcitrant ulcers in pyoderma gangrenosum with mycophenolate mofetil and autologous keratinocyte transplantation on a hyaluronic acid matrix. J. Eur. Acad. Dermatol., 14: 187-90, 2000.
15. Limova M., Mauro T.: Treatment of pyoderma gangrenosum with cultured keratinocyte autografts. J. Dermatol. Surg. Oncol., 20: 833-6, 1994.

This paper was received on 3 June 2005.

Address correspondence to: Dr B. Napoli, Divisione di Chirurgia Plastica e Terapia delle Ustioni, ARNAS, Ospedale Civico, Via C. Lazzaro, 90127 Palermo, Italy. Tel.: 0039 091 6663631; fax: 0039 091 596404; e-mail: mbcpa@medbc.com

G. WHITAKER INTERNATIONAL BURNS PRIZE – PALERMO (Italy)
Under the patronage of the Authorities of the Sicilian Region for 2007

By law n. 57 of June 14th 1983 the Sicilian Regional Assembly authorized the President of the Region to grant the "Giuseppe Whitaker Foundation", a non-profit-making organisation under the patronage of the Accademia dei Lincei with seat in Palermo, a contribution for the establishment of the annual G. Whitaker International Burns Prize aimed at recognising the activity of the most qualified experts from all countries in the field of burns pathology and treatment.

Law n. 23 of December 2002 establishes that the prize becomes biannual.

The next prize will be awarded in 2007 by the month of October in Palermo at the seat of the G. Whitaker Foundation.

The amount of the prize is fixed at Euro 20,660.00.

The Adjudicating Committee is composed of the President of the Foundation, the President of the Sicilian Region, the Representative of the National Lincei Academy within the G. Whitaker Foundation, the Dean of the Faculty of Medicine and Surgery of Palermo University or his nominee, a Representative of the Italian Society of Plastic Surgery, three experts in the field of prevention, pathology, therapy and functional recovery of burns, the winner of the prize awarded in the previous year and a legal expert nominated in agreement with the President of the Region as a guarantee of the respect for the scientific purpose which the legislators intended to achieve when establishing the prize.

Anyone who considers himself/herself to be qualified to compete for the award may send by January 31st 2007 his detailed curriculum vitae to: Michele Masellis M.D., Secretary-Member of the Scientific Committee, G. Whitaker Foundation, Via Dante 167, 90141 Palermo, Italy.