

Recurrent nodules in the calves: A sign of tuberculosis

Nódulos recorrentes na panturrilha: um sinal de tuberculose

Bruno Rodrigues¹, Filipa Carvalho², Jose Matilla³, João Araújo²

¹ Serviço de Nefrologia, Hospital Professor Doutor Fernando Fonseca, Amadora, Portugal.

² Serviço de Medicina Interna, Hospital Professor Doutor Fernando Fonseca, Amadora, Portugal.

³ Serviço de Cirurgia Cardio-Torácica, Hospital Pulido Valente, Lisboa, Portugal.

ABSTRACT

Aims: To describe a case of erythema induratum of Bazin, classified as a tuberculid, or skin lesion with similar histological features to true cutaneous tuberculosis, in which the relation with *Mycobacterium tuberculosis* cannot be easily demonstrated.

Case Description: A 60-year-old woman presented with recurrent multiple nodules in the legs. Skin examination revealed violaceous painless nodules, some of them ulcerated, with a serous fluid, located on both legs in an asymmetric way, predominantly in the calves. Lesions disappeared spontaneously for brief periods. Skin biopsies revealed septal and lobular panniculitis with epithelioid granulomata and vascular necrosis. Tuberculin skin test was positive. Culture of the cutaneous lesions and polymerase chain reaction to *Mycobacterium tuberculosis* were negative, but mediastinal lymph nodes collected through mediastinoscopy were cultivated and positive to *Mycobacterium tuberculosis*. Therapy with isoniazid, rifampicin, pyrazinamide and ethambutol were administered. After two months under therapy the skin lesions healed. The clinical and histopathological features and the strong positive tuberculin skin test have strongly suggested the diagnosis of erythema induratum of Bazin. Positive culture for *Mycobacterium tuberculosis* and the remission of the lesions with antituberculosis therapy confirmed the diagnosis.

Conclusions: Clinicians must be aware of the differential diagnosis of recurrent skin lesions, including the erythema induratum of Bazin. In this case, association with tuberculosis was confirmed by positive culture of mediastinal lymph nodes for *Mycobacterium tuberculosis* and remission of the lesions with antituberculosis therapy.

KEY WORDS: ERYTHEMA INDURATUM/histopathology; BAZIN'S DISEASE; TUBERCULOSIS, CUTANEOUS/diagnosis; TUBERCULID; TUBERCULOSIS, LYMPH NODE; MYCOBACTERIUM TUBERCULOSIS; CASE REPORTS.

RESUMO

Objetivos: descrever um caso de eritema induratum de Bazin, classificado como tuberculíde, lesão cutânea com características histológicas semelhantes à tuberculose cutânea, mas na qual a relação entre o *Mycobacterium tuberculosis* não é facilmente demonstrada.

Descrição do Caso: uma mulher de 60 anos de idade apresentou-se com múltiplos nódulos recorrentes nos membros inferiores. O exame da pele revelou nódulos indolores, violáceos, alguns deles ulcerados, com um líquido seroso, localizados em ambas as pernas, de forma assimétrica e com predomínio nas panturrilhas. As lesões apresentavam um aparecimento paroxístico, com remissão espontânea por breves períodos. Foi realizada biópsia cutânea que revelou paniculite septal e lobular com granulomas epitelióides e necrose vascular. O teste tuberculínico foi positivo. A cultura das lesões cutâneas e a reação em cadeia da polimerase para *Mycobacterium tuberculosis* foram negativos, mas foi realizada biópsia de linfonodos por mediastinoscopia, cuja cultura foi positiva para *Mycobacterium tuberculosis*. Foi iniciada terapêutica específica com isoniazida, rifampicina, pirazinamida e etambutol. Após dois meses de tratamento houve remissão das lesões. As características clínicas e histopatológicas e o teste tuberculínico fortemente positivo sugeriram o diagnóstico de eritema indurado de Bazin, sendo este confirmado pela cultura de linfonodos positiva para *Mycobacterium tuberculosis* e pela remissão das lesões com a terapêutica antituberculose.

Conclusões: o clínico precisa estar atento para o diagnóstico diferencial de lesões cutâneas recorrentes, incluindo neste o eritema induratum de Bazin. Neste caso, a associação com a tuberculose ficou confirmada pela cultura dos linfonodos mediastinais positiva para *Mycobacterium tuberculosis* e remissão das lesões com a terapêutica antituberculose.

DESCRIPTORIOS: ERITEMA ENDURADO/histopatologia; DOENÇA DE BAZIN; TUBERCULOSE CUTÂNEA/diagnóstico; TUBERCULÍDE; TUBERCULOSE DOS LINFONODOS; MYCOBACTERIUM TUBERCULOSIS; RELATOS DE CASOS.

Recebido: julho de 2011; aceite: novembro de 2011

Endereço para correspondência/Corresponding Author:

BRUNO RODRIGUES
Hospital Fernando Fonseca, IC 19 Venteira
2720-276 Amadora, Portugal
Telefone: (00351) 914307273
E-mail: bfgrodrigues@gmail.com

INTRODUCTION

Cutaneous tuberculosis can be divided into true cutaneous lesions and tuberculids. The former show a wide spectrum of morphological presentations and the presence of *Mycobacterium tuberculosis* (*M. tuberculosis*) can be demonstrated by special staining, culture or polymerase chain reaction (PCR). Tuberculids are skin lesions with similar histological features to true cutaneous tuberculosis, but the presence of *M. tuberculosis* cannot be demonstrated, although there is evidence to suggest that it acts as an etiologic factor.¹ These lesions include erythema induratum of Bazin (EIB), lichen scrofulosorum and some cases of papulonecrotic tuberculid, and are considered to be the result of cutaneous hypersensitivity reactions from an extracutaneous focus of *M. tuberculosis* infection.²

When Bazin first described this lesion in 1861, tubercle bacillus had not been yet identified. The link between EIB and tuberculosis was described later, in the beginning of the 20th century, by French dermatologists. By the same time clinical case reports of patients without evidence of tuberculosis infection were made by English authors, leading to the controversy around its etiology, and the establishment of a new terminology – Whitfield erythema, to which Montgomery, in the United States, proposed renaming to “nodular vasculitis”.²

In recent years, a consensual view is arising, considering this concepts as parts of the same disease, which is considered to be a reactive disorder related to different etiologic factors, one of them being tuberculosis.³ The identification of *M. tuberculosis*

by PCR in the skin lesions have definitely brought evidence to this relationship.⁴⁻⁷

The diagnosis of EIB is made by suggestive clinical morphology and histopathological features, strongly positive tuberculin skin test for Purified Protein Derivative (PPD), and positive epidemiology for tuberculosis. The response to antituberculous drugs confirms the diagnosis.^{1,4,8} Detection of *M. tuberculosis* DNA by PCR on the biopsy specimen supports the diagnosis, but a negative result does not exclude it.²

Here we report a case of this controversial entity, frequently misdiagnosed, in order to draw attention of clinicians to its existence. The study is accomplished according to the Helsinki Declaration in its latest version, and a written informed consent was obtained from the patient.

CASE DESCRIPTION

A 60-year-old woman presented with recurrent multiple nodules in her legs for four years. The patient had a history of hypertension and paroxistic atrial fibrillation medicated with warfarin, amiodarone, amlodipine, trimetazidine and lisinopril. Cough, weight loss, fever, chills, exposure to tuberculosis or recent travels were denied.

Skin examination revealed violaceous painless nodules, some of them ulcerated, with a serous fluid, located on both legs in an asymmetric way and predominantly in the calves (Fig. 1). The patient had been medicated with prednisone for two occasions, with remission of the lesions, which reappeared when corticoids were stopped. Lesions also disappeared spontaneously for brief periods.



Figure 1. Violaceous, ulcerated, painless nodule located in the leg.

Complete blood count, liver and renal function and antineutrophil cytoplasmic antibody were normal. Sedimentation rate was 40 mm/h and antinuclear antibody was positive 1/320. Skin biopsies revealed septal and lobular panniculitis with epithelioid and palisading granulomata and vascular necrosis. Culture and PCR to *M. tuberculosis* were negative.

Chest X-Ray identified mediastinum enlargement. Chest computer tomography scan showed multiple adenopathies around the carina. Abdominal and renal ultrasonography and arterial and venous Doppler of the legs were normal. Bronchofibroscope was normal, and smear of expectorated sputum did not reveal acid-fast bacilli. Transbronchial biopsy showed an unspecific inflammatory infiltrate, without granulomas. PPD test was positive with an erythematous induration of 22 mm.

The patient was submitted to a mediastinoscopy to collect lymph nodes, which culture was positive to *M. tuberculosis* (Bactec MGIT960 and Lowenstein-Jensen). Therapy with 300 mg of isoniazid, 600 mg of rifampicin, 1500 mg of pyrazinamide and 1200 mg of ethambutol was daily administered for two months, followed by 300 mg of isoniazid and 600 mg of rifampicin for another four months. After two months under therapy, the skin lesions healed with remaining hyperpigmentation.

DISCUSSION

Since EIB is not frequent, physicians are not always alert to this entity. The presence of inflammatory nodules that involve primarily the legs have a complex differential diagnosis, sometimes difficult or impossible on clinical aspects alone. A group of diseases share the same characteristics, namely erythema nodosum, nodular vasculitis, and recurrent idiopathic thrombophlebitis. Histopathological features are important in order to get more information, that may not be pathognomonic but may help towards the diagnosis.⁵ Schneider et al.,⁹ studying 20 skin biopsies of patients with well documented EIB, defined two histopathological patterns, one having focal septolobular panniculitis in association with a muscular artery or small vessel with primary neutrophilic vasculitis, and a second with diffuse septolobular panniculitis with primary neutrophilic vasculitis. The presence of poorly developed, palisading, and lipophagic granulomas predominated in both groups.⁹ In the present case, it was the presence of palisading granulomas with vasculitis that first drew attention to the diagnosis. Vasculitis has been extensively investigated by Segura et al.,³ in a review of 101 biopsies from 86 patients; some

type of vasculitis was found in 90% of the cases, being the small venules of the fat lobule the most frequent vessels affected.³

This patient, as usual, had a strongly positive reaction to PPD but no signs of active tuberculosis. Since late 1990's several authors have reported the presence of *M. tuberculosis* DNA identified in the EIB lesions by PCR, fact that relaunched the discussion of this controversial entity.⁶ In this case PCR test to *M. tuberculosis* was negative, and further steps were needed to prove the existence of a latent tuberculosis infection. The presence of adenopathies around the carina indicated a mediastinoscopy, an invasive procedure with associated risks. After a carefully analysis of risk versus benefits, and following the patient's information and consent, the medical team decided to perform the procedure. A lymph node specimen was collected and *M. tuberculosis* was identified in tissue culture. Treatment was started in a standard regimen, with an excellent outcome.

The clinical characteristics of the lesion and the histopathological features were crucial for the suspicion of diagnosis, and the strong PPD test, positive cultures and good response to antituberculous treatment were fundamental to its confirmation.

REFERENCES

1. Barbagallo J, Tager P, Ingleton R, et al. Cutaneous tuberculosis: diagnosis and treatment. *Am J Clin Dermatol.* 2002;3:319-28.
2. Mascaró JM Jr, Baselga E. Erythema induratum of bazin. *Dermatol Clin.* 2008;26:439-45.
3. Segura S, Pujol RM, Trindade F, et al. Vasculitis in erythema induratum of Bazin: a histopathologic study of 101 biopsy specimens from 86 patients. *J Am Acad Dermatol.* 2008;59:839-51.
4. Rademaker M, Lowe DG, Munro DD. Erythema induratum (Bazin's disease). *J Am Acad Dermatol.* 1989;21:740-5.
5. Cho KH, Lee DY, Kim CW. Erythema induratum of Bazin. *Int J Dermatol.* 1996;35:802-8.
6. Schneider JW, Jordaan HF, Geiger DH, et al. Erythema induratum of Bazin. A clinicopathological study of 20 cases and detection of Mycobacterium tuberculosis DNA in skin lesions by polymerase chain reaction. *Am J Dermatopathol.* 1995;17:350-6.
7. Yen A, Rady PL, Cortes-Franco R, et al. Detection of Mycobacterium tuberculosis in erythema induratum of bazin using polymerase chain reaction. *Arch Dermatol.* 1997;133:532-3.
8. Ho CK, Ho MH, Chong LY. Cutaneous tuberculosis in Hong Kong: an update. *Hong Kong Med J.* 2006;12:272-7.
9. Schneider JW, Jordaan HF, Geiger DH, et al. Erythema induratum of Bazin. A clinicopathological study of 20 cases and detection of Mycobacterium tuberculosis DNA in skin lesions by polymerase chain reaction. *Am J Dermatopathol.* 1995;17:350-6.