Pulmonary Tuberculosis Presenting with Cutaneous Leukocytoclastic Vasculitis

P. Mínguez, E. Pintor, R. Burón, B. Díaz-Pollán, J.J. Puche, J.C. Pontes

Summary

This case report deals with a rare association: tuberculosis and cutaneous leukocytoclastic vasculitis. The patient was a 36-year-old man with no significant past medical problems. He presented with a palpable purpura on both legs, low-grade fever, cough and expectoration, progressive dyspnea due to a massive left pleural effusion and a symmetric swelling on his ankles and wrists. Skin biopsy yielded a histological diagnosis of leukocytoclastic vasculitis and the primary diagnosis was only achieved after performing a pleural biopsy, which unequivocally showed the presence of *Mycobacterium tuberculosis*. This case shares many features with the few cases already reported in the medical literature. Possible pathogenic mechanisms are reviewed and discussed in detail.

Key Words

Tuberculosis · Leukocytoclastic vasculitis · Immune complexes

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Introduction

There are many causes of hypersensivity vasculitis (Table 1) and the antigens most frequently involved in the reaction are drugs, chemical products and microorganisms [1]. *Mycobacterium tuberculosis* has been included in the list since 1967, when *Parish* et al. showed the existence of antigens of this bacterium in nodular vasculitis lesions from two patients with tuberculosis (TB) [2]. However, only a few reports on this association can be found in the past 30 years and the pathophysiology and etiopathogenic mechanisms are still unclear.

Case Report

A 36-year-old man, a company manager, presented with 15 days of low-grade fever, cough and expectoration, progressive dyspnea and a symmetric swelling of his elbows and knees that resolved spontaneously in a few days to appear later on his ankles and wrists, together with a cutaneous eruption on both legs. There was no associated medication use. He had a previous history of heavy smoking (20–40 cigarettes/day for 15 years).

Physical examination revealed a palpable confluent purpura on the lower limbs (Figure 1), symmetric arthritis of ankles and wrists and diminished ventilation in his left lung. The rest of the examination was unremarkable. Initial investigations showed an ESR of 61 mm/h and a white cell count of 10.4 cells/nl. Blood biochemistry and urine analysis were normal. Other investigations performed during admission were as follows: Plasma immunological study: ANA, ANCA, rheumatoid factor and other autoantibodies (anti-RNP, anti-DNA, anti-Ro, anti-La, anticardiolipin antibodies) were negative. Complement: normal. ASLO: 103 mg/dl (normal < 200 mg/dl). C-reactive protein : 6.5 mg/dl. Cryoglobulins: negative. Immunoglobulins: slight increase in IgA. Viral serology: negative for hepatitis B and C and HIV. Chest x-ray (Figure 2a): infiltrate in left apex. Huge left pleural effusion that occupied two-thirds of the hemithorax (a diagnostic paracentesis was then performed). Pleural fluid: 1,200 cells/mm^3, 99% lymphocytes; glucose 98 mg/dl, LDH 143 U/l, proteins 5.8 g/dl, ADA 34 U/l; Ziehl-

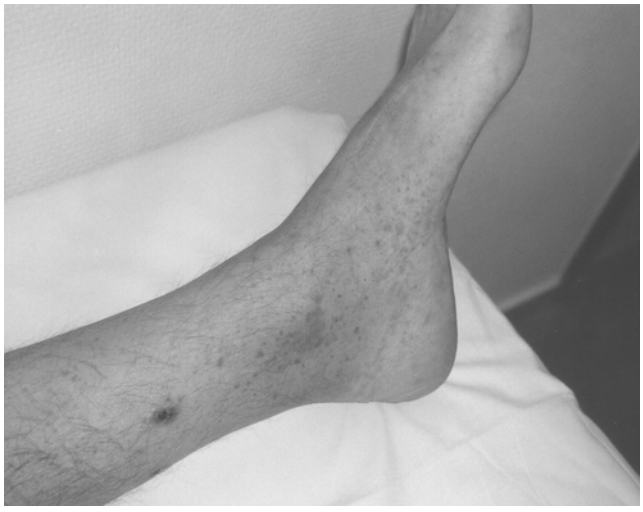

Figure 1
Macroscopic view of the cutaneous vasculitis lesions on the legs.

P. Mínguez *(corresponding author)*
Dept. of Internal Medicine III, University Hospital San Carlos, Avda. Martín Lagos s/n, E-28040 Madrid, Spain; Phone: +34-91-3303832
E. Pintor, R. Burón, B. Díaz-Pollán, J.J. Puche, J.C. Pontes
Dept. of Internal Medicine, University Hospital San Carlos, Avda. Martín Lagos s/n, E-28040 Madrid, Spain

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Neelsen staining failed to show acid-fast bacilli in pleural fluid or sputum. Skin PPD test was positive (13 mm). Thorax and abdomen CT scan (Figure 2b): massive left pleural effusion which collapsed the left lower lobe, small pre-vascular lymphadenopathy in mediastinum, multiple nodular lesions on both pulmonary upper lobes, normal liver and kidneys. Skin biopsy (Figure 3): leukocytoclastic vasculitis. Pleural biopsy: granuloma and positive staining for acid-fast bacilli. Sputum culture eventually grew *M. tuberculosis*.

From the first day of admission the patient received antiinflammatory treatment (acetylsalicylic acid, 4 g/day); the arthritis resolved in a few days as well as his low-grade fever, but the cutaneous lesions persisted.

The patient received standard anti-TB therapy with isoniazid (300 mg/day), rifampicin (600 mg/day) and ethambutol (1,200 mg/day). Over the next month, the skin eruption gradually subsided, as well as the pleural effusion. By then, the patient was completely asymptomatic and tolerated the treatment well.

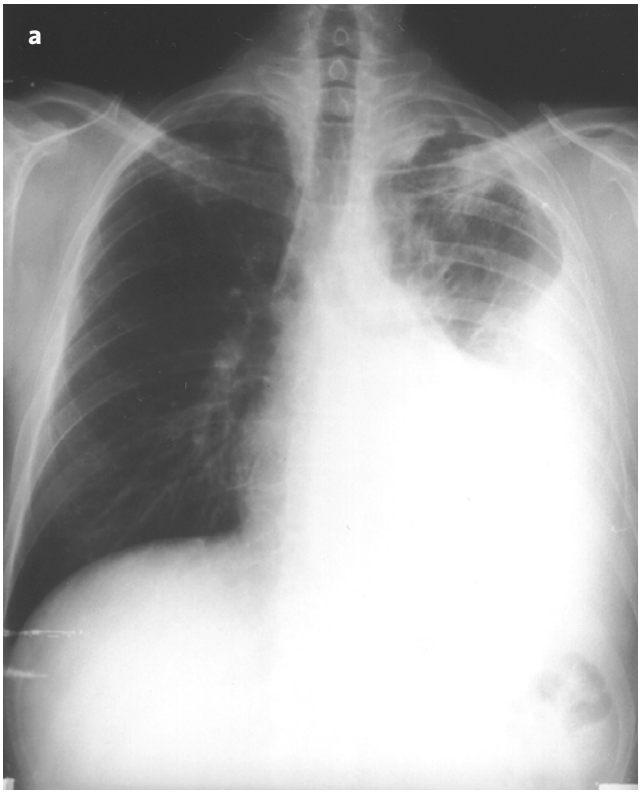
Discussion

There are two types of skin lesions associated with TB [3]: (1) direct lesions where the bacillus is present, produced by three different mechanisms (inoculation from an exogenous source; cutaneous myobacteriosis from an endogenous source, either by contiguous spread or by autoinoculation and third, those arising from hematogenous spread, such as lupus vulgaris, acute hematogenous dissemination and nodules or abscesses), and (2) hypersensivity vasculitis, where the microorganism has never been found and the proposed pathogenic mechanism is the deposit (in the walls of small vessels) of immune complexes formed by antibodies against *M. tuberculosis* proteins.

Table 1
Causes of hypersensitivity vasculitis.

Exogenous stimuli proved or suspected
Schönlein-Henoch purpura
Serum sickness and serum sickness-like reactions
Other drug-induced vasculitis
Penicillin
Sulfamides
Streptomycin
Barbiturates
Phenytoin
Vasculitis associated with infectious diseases
Streptococci
Staphylococci
Escherichia coli
Mycobacteria
Hepatitis B virus
Endogenous antigens likely involved
Vasculitis associated with neoplasms
Carcinoma
Lymphoma
Myeloma
Vasculitis associated with connective tissue diseases
Rheumatoid arthritis
Sjögren syndrome
Dermatomyositis
Vasculitis associated with other underlying diseases
Vasculitis associated with congenital deficiencies of the complement system
C1r
C2
C3
Selective deficiency of IgA

Source: Harrison: Principles of Internal Medicine, 14th ed., 1998, chapter 319 (modified)



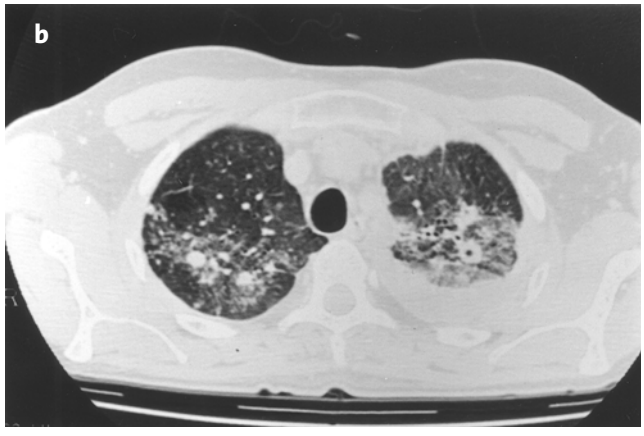


Figure 2
Chest x-ray (a) and thorax CT scan (b) showing a massive left pleural effusion, small pre-vascular lymphadenopathy in mediastinum and multiple nodular lesions on both pulmonary upper lobes.

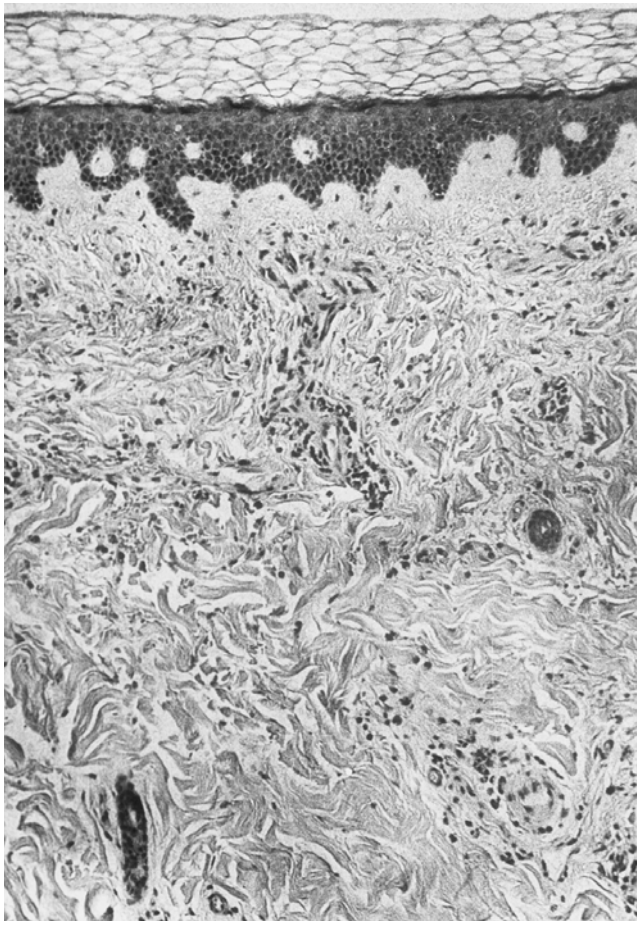


Figure 3
Microscopic view of the skin biopsy, showing the characteristic features of leukocytoclastic vasculitis: perivascular polymorphonuclear infiltrate in upper dermis together with abundant nuclear dust (leukocytoclasia) (hematoxylin and eosin, × 40).

The existence of circulating immune complexes in TB has been clearly demonstrated and their levels are related to the activity of the disease but unrelated to its site [4, 5]. However, there are only a few cases reported of vasculitis associated with TB: one of Schönlein-Henoch purpura [6] and leukocytoclastic vasculitis in the rest [7–11].

Vasculitis may either represent the first symptom of TB or appear after the diagnosis. Cases of vasculitis associated with initial treatment with rifampicin have also been reported [8, 12]. Some authors propose that the underlying mechanism is the production of antibodies against rifampicin [13], but the increase in immune complexes determined by the treatment itself in the first weeks [4] could also play a role in the pathogenesis.

According to the published cases of vasculitis associated with TB, this complication occurs more often in young patients with a normal immunity and chronic, untreated TB. No differences between the sexes have been reported. The treatment of vasculitis is that of the underlying infection (i.e., *M. tuberculosis*). In a few exceptional cases – those with systemic vasculitis and global repercussion – it may be necessary to use steroids [6], although this question is far from being clearly defined. In vasculitis associated with the use or rifampicin, authors recommend to stop the drug until the lesions subside and re-introduce it slowly: lesions do not reappear [8].

In summary: hypersensitivity vasculitis associated with TB is not frequent; the underlying mechanism is the deposit of immune complexes and not the bacillus itself. Patients are usually young people with a chronic, untreated infection by *M. tuberculosis*. The most frequent site is small vessels of the lower extremities, since patients lead normal, active lives and the deposit is affected by gravity. The treatment of choice is standard anti-TB therapy, although steroids might be necessary in selected cases.

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