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CASE REPORT

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Leukocytoclastic Vasculitis Associated with Pleural Tuberculosis. Case Report

Vasculitis leucocitoclástica asociada a tuberculosis pleural. Reporte de caso

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ABSTRACT

Tuberculosis remains a common disease in our setting and may involve various organs, including the pleura and, rarely, the skin. Leukocytoclastic vasculitis is an uncommon cutaneous manifestation that may represent an immune response secondary to infections such as tuberculosis. Although pleural tuberculosis is one of the most common extrapulmonary forms, it can be difficult to diagnose in the absence of direct bacteriological confirmation. We report the case of a 21-year-old immunocompetent male with no significant medical history who presented with exertional dyspnea, intermittent fever, and right-sided chest pain. Imaging studies revealed moderate right pleural effusion. The physicochemical analysis of the pleural fluid showed exudative characteristics with a predominance of lymphocytes and elevated levels of adenosine deaminase (ADA).

During the course of the illness, the patient developed rapidly progressive painful and pruritic skin lesions on the extremities. Skin biopsy confirmed leukocytoclastic vasculitis. Antituberculous therapy combined with tapering corticosteroid treatment was initiated, resulting in a favorable clinical evolution.

Although uncommon, the association between pleural tuberculosis and leukocytoclastic vasculitis has been reported as an immune-mediated manifestation secondary to tuberculosis infection. Early recognition of this association allows appropriate therapeutic management and may prevent complications.

Key words: pleural tuberculosis | leukocytoclastic vasculitis | adenosine deaminase | skin manifestations

RESUMEN

La tuberculosis continúa siendo una enfermedad frecuente en nuestro medio y puede comprometer diversos órganos, incluyendo la pleura y, en raras ocasiones, la piel. La vasculitis leucocitoclástica es una manifestación cutánea poco común, que puede representar

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una respuesta inmunológica secundaria a infecciones, entre ellas la tuberculosis. Si bien la tuberculosis pleural es una de las formas extrapulmonares más frecuentes su diagnóstico puede dificultarse en ausencia de confirmación bacteriológica directa.
Se presenta el caso de un paciente masculino de 21 años, inmunocompetente y sin antecedentes patológicos, que consultó por disnea de esfuerzo, fiebre intermitente y dolor torácico en el lado derecho. Los estudios por imágenes evidenciaron derrame pleural en el lado derecho de grado moderado. El análisis físico químico del líquido pleural arrojó características de exudado con predominio linfocitario y niveles elevados de adenosina deaminasa (ADA).
Durante la evolución, el paciente desarrolló lesiones cutáneas dolorosas y pruriginosas de rápida aparición en extremidades. La biopsia cutánea confirmó el diagnóstico de vasculitis leucocitoclástica. Se inició tratamiento antifímico asociado a corticoterapia en dosis descendentes, con evolución clínica favorable.
La asociación entre tuberculosis pleural y vasculitis leucocitoclástica es infrecuente, pero ha sido descrita en la bibliografía como una manifestación inmunológica secundaria a la infección tuberculosa. El reconocimiento precoz de esta relación permite ajustar la conducta terapéutica y evitar complicaciones.

Palabras clave: Tuberculosis pleural | vasculitis leucocitoclástica | adenosina deaminasa | manifestaciones cutáneas

INTRODUCTION

Tuberculosis is an infectious and contagious disease, known as the "great imitator," and caused by *Mycobacterium tuberculosis*. It is considered one of the leading causes of infectious morbidity worldwide. Although the pulmonary form is the most common presentation, extrapulmonary involvement accounts for approximately 20% of cases; pleural tuberculosis is one of the most frequent forms.

The pleural form results from the spread of *Mycobacterium tuberculosis* to the pleural space, either due to rupture of a subpleural focus or via hematogenous dissemination. It typically presents as a unilateral pleural effusion with exudative characteristics and a predominance of lymphocytes. In many cases, direct microbiological confirmation is not obtained, and so the diagnosis is based on the integration of clinical, epidemiological, radiological, and biochemical findings, including the measurement of adenosine deaminase in pleural fluid, as well as molecular tests of the fluid or pleural biopsy. Early diagnosis is essential to prevent long-term sequelae.

On the other hand, leukocytoclastic vasculitis (LCV) is a histopathological entity characterized by the inflammation of small vessels with neutrophilic infiltrate, red blood cell extravasation, and leukocytolysis. Clinically, it presents with purpuric lesions, some raised and palpable, on the lower extremities, and may be triggered by infections, drugs, neoplasms, or autoimmune diseases. Leukocytoclastic vasculitis draws attention because it is often regarded as an isolated problem, or interpreted as a reaction of unknown cause, or in any case related to the use of medications (drug eruption).

Inflammation of small-caliber vessels may be associated with chronic diseases or persistent infections, such as tuberculosis, which induce immune system responses that are difficult to regulate. In this clinical context, immune complexes are formed and deposited, and as they accumulate, they generate tissue damage. In the presence of vasculitis with purpuric lesions, especially if accompanied by respiratory symptoms or pathological findings in complementary studies, it is essential to consider differential diagnoses.

At the same time, the diagnostic approach to pleural tuberculosis is strengthened by the use

of biomarkers such as ADA, which have proven useful in complex clinical contexts where conventional microbiology does not always provide conclusive results.

In this context, the objective of the present study is to describe a case report of pleural tuberculosis in a young patient whose associated manifestation was biopsy-confirmed leukocytoclastic vasculitis, a rare association. Likewise, it intends to highlight the importance of maintaining a comprehensive clinical perspective, epidemiologically contextualized and supported by appropriate diagnostic tools, in order to identify unconventional presentations of this respiratory disease.

CASE REPORT

A 21-year-old male patient was admitted in January 2025 to the Internal Medicine Department due to exertional dyspnea, intermittent fever of 38°C, right-sided pleuritic chest pain, and radiological findings consistent with moderate-to-severe right pleural effusion, with no significant past medical history. He was an immunocompetent patient; HIV serology was negative, and had no history of immunosuppression or use of immunosuppressive drugs.

During hospitalization, a diagnostic thoracentesis was performed. The fluid obtained had a cloudy yellow appearance and became clear after centrifugation. The analysis showed: glucose 63 mg/dL, LDH (lactate dehydrogenase) 401 U/L, and total protein 5.5 g/dL.

Pleural fluid cytology showed predominance of lymphocytes.

It was interpreted as an uncomplicated exudate. Pleural fluid cultures were negative for tuberculosis, fungal infections, parasites, and common bacteria. Given these findings, empirical antibiotic treatment was started with amoxicillin/clavulanic acid for six days, followed by piperacillin/tazobactam for another six days. The patient was subsequently discharged from the hospital.

Seven days after discharge, he attended a follow-up visit at the pulmonology outpatient clinic due to persistent fever associated with dyspnea. He reported close contact with a coworker who had been diagnosed with smear-positive pulmonary tuberculosis, establishing a positive epidemiological link. Close contact history had not been disclosed during hospitalization. On physical examination, the patient was afebrile, hemodynamically stable, alert, with good ventilatory mechanics, and oxygen saturation of 98% while breathing room air. Auscultation revealed hypoventilation at the right lung base.

Chest X-ray showed a homogeneous opacity in the lower third of the right hemithorax with blunting of the costophrenic angle; chest CT scan revealed loculated pleural effusion with underlying partial lung collapse and pleural thickening (Figure 1).

Given the imaging findings, persistence of symptoms, and confirmation of the epidemiological link, pleural puncture was repeated for ADA determination, which yielded a value of 39 U/L.

Based on the integration of the clinical, epidemiological, and biochemical findings, it was decided to start empirical antituberculous treatment (there was no bacteriological confirmation from the pleural fluid) with a four-drug regimen consisting of isoniazid (300 mg/day), rifampin (600 mg/day), pyrazinamide (1500 mg/day), and ethambutol (1200 mg/day).

The patient also reported the appearance of rapidly progressive pruritic and painful skin lesions on the upper and lower limbs, with distal-to-proximal distribution.

Physical examination revealed erythematous papules with a pale halo purpuric pattern, many of which were confluent, forming annular lesions (Figure 2). The patient had not yet started antituberculosis treatment.

A skin biopsy of the lesions with direct immunofluorescence was performed. At the same time, treatment with oral prednisone 20 mg/day was started, with a tapering regimen and weekly follow-up.

The histopathology report showed preserved epidermis, mixed perivascular infiltrate with neutrophils, eosinophils, and lymphocytes, fibrinoid necrosis in the wall of small-caliber vessels, and red blood cell extravasation. Direct immunofluorescence was negative. The definitive diagnosis was leukocytoclastic vasculitis.

After ten days of combined treatment with antituberculosis drugs and corticosteroids, clear improvement in the skin lesions was observed, with reduction of erythema, disappearance of the purpuric halo, and progressive clearing of the skin (Figure 3).

DISCUSSION

We present the clinical case of a young patient with no significant medical history who developed pleural tuberculosis associated with a rare dermatological manifestation. The clinical presentation began with nonspecific symptoms, fever, and dyspnea, accompanied by imaging findings consistent with right pleural effusion and characteris-

Figure 1. Chest CT scan. Right pleural effusion with loculations and pleural thickening.

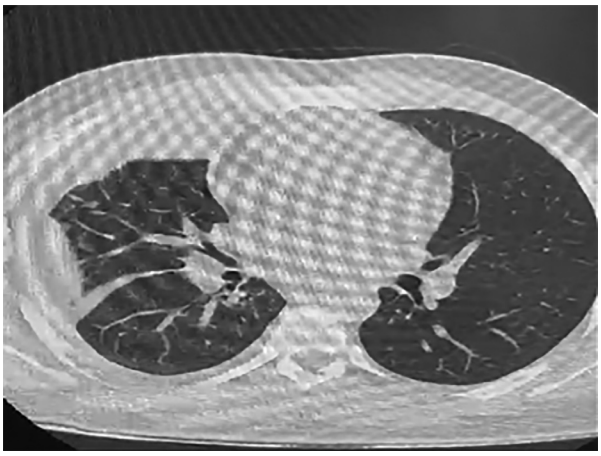
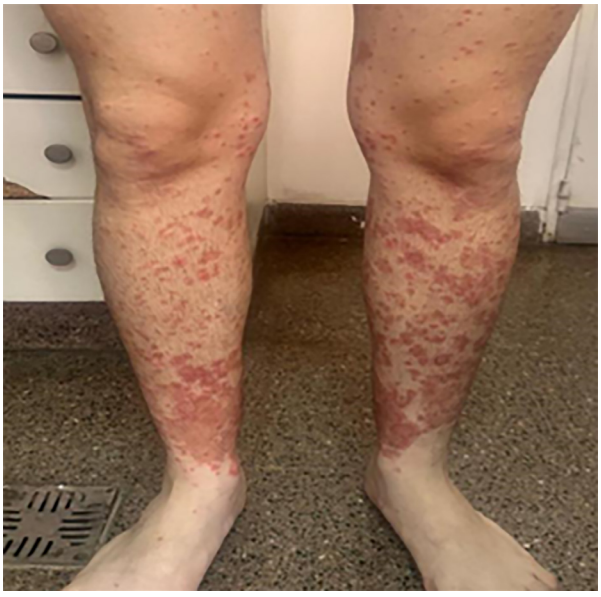


Figure 2. Active skin lesions (acute phase of vasculitis).



tic pleural fluid. Although the pleural fluid culture did not yield positive results, it showed parameters compatible with an uncomplicated exudate. This led to the inclusion of ADA measurement as an auxiliary diagnostic tool. With a value of 39 U/L (cutoff point 20 U/L), it was well above the threshold generally accepted in the medical literature for suspecting tuberculosis in lymphocytic effusions. This finding was interpreted together with

Figure 3. Skin lesions in clinical resolution.

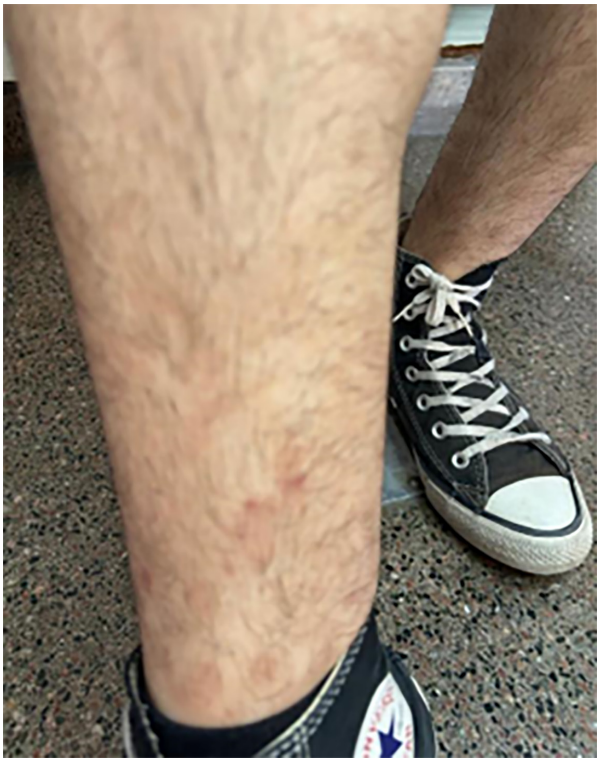


Table 1. Clinical course of the case

Moment	Clinical event
Days 1-3	Hospitalization due to dyspnea, fever and chest pain Moderate right pleural effusion Thoracentesis: lymphocytic exudate
Days 4-10	Amoxicillin/clavulanic acid
Days 11-16	Piperacillin/tazobactam
7 days after discharge	Persistence of symptoms and imaging findings consistent with pleural effusion Epidemiological link to tuberculosis; ADA testing is requested
14 days after discharge	Presents with ADA result of 39 U/L. Initiation of antituberculosis treatment was decided (not yet started) Appearance of skin lesions Dermatologic evaluation
15 days after discharge	Biopsy: leukocytoclastic vasculitis
Treatment	Prednisone + antituberculosis treatment
Disease course	Progressive resolution of lesions

the rest of the symptoms to justify the decision to initiate antituberculous treatment, as mentioned by Zhang[1] and Porcel.[2]

The usefulness of ADA is further reinforced by the persistence of symptoms and the presence of a positive epidemiological link. For this reason, several authors emphasize that cases with compatible symptoms, elevated ADA levels, and known exposure can be treated even in the absence of confirmatory bacteriological tests, according to statements by Garzón et al[3] and Carabalí-Isajar.[4]

As the patient's clinical course progressed, an unexpected, highly clinically relevant finding emerged: painful, pruritic, rapidly progressive skin lesions developed on the upper and lower limbs. Following clinical evaluation and a biopsy, leukocytoclastic vasculitis was diagnosed. It is a type of vascular inflammation that affects the small vessels of the dermis and in many cases is associated with hypersensitivity reactions mediated by immune complexes. These complexes form and deposit in the vascular walls triggering an acute inflammatory response, a mechanism that has been described in both drug-related settings and chronic infectious conditions, as explained by Hernández-López.[5]

Specifically, the association between tuberculosis and cutaneous vasculitis has been documented in case reports and clinical reviews that identify *Mycobacterium tuberculosis* as an agent capable of generating persistent antigenic stimuli that trigger sustained activation of the immune system, involving T lymphocytes, macrophages, and cytokines such as TNF-α and IFN-γ. These mediators not only contribute to tissue damage at the primary site of disease, such as the pleura in this case, but may also provoke inflammation at distant sites, as reflected in the vasculitic skin lesions. Some authors consider this phenomenon an indirect manifestation of the systemic activity of the disease, as indicated by Arsanios[6] and Herrera.[7]

The favorable clinical response observed after the administration of antituberculosis treatment, together with the use of corticosteroids (tapering doses are always used to avoid secondary adrenal insufficiency), suggests that the vasculitis had a secondary origin linked to the active disease and did not correspond to a primary autoimmune or idiopathic entity.

Recent studies explain how the resolution of the disease often leads to spontaneous or accelerated remission of dermatological manifestations when accompanied by appropriately adjusted immunomodulatory treatment, as seen in this patient, who showed progressive improvement both in respiratory symptoms and in the appearance and sensitivity of the skin lesions, as demonstrated by Corrêa.[8]

The beta-lactam antibiotics initially administered (amoxicillin/clavulanic acid and piperacillin/tazobactam) have been reported as potential triggers of hypersensitivity-induced leukocytoclastic vasculitis. Therefore, their role in the development of the skin lesions cannot be completely ruled out. However, the persistence of the lesions after discontinuation of these antibiotics, together with their subsequent resolution after initiation of antituberculosis treatment, more strongly suggests an immunological mechanism secondary to active pleural tuberculosis.

Diagnosis of pleural tuberculosis

The diagnosis of pleural tuberculosis can be established through microbiological or histological confirmation; however, in a considerable number of cases, direct demonstration of *Mycobacterium tuberculosis* in pleural fluid is not possible. In these scenarios, the diagnosis may be supported by the integration of clinical, epidemiological, radiological, and pleural fluid biochemical criteria, which are widely described in the literature.

Among the most suggestive findings are the presence of unilateral pleural effusion, pleural fluid with exudative characteristics and lymphocytic predominance, elevated ADA levels, compatible constitutional symptoms, and the existence of an epidemiological link with active tuberculosis.

In this case, the patient exhibited several of these diagnostic criteria: intermittent fever, exertional dyspnea, and pleuritic chest pain; right-sided unilateral pleural effusion with pleural thickening on imaging studies; pleural fluid with exudative characteristics and lymphocytic predominance; an ADA value of 39 U/L; and a history of close contact with a case of smear-positive pulmonary tuberculosis.

The integration of these clinical, epidemiological, and biochemical findings made the diagnosis of pleural tuberculosis highly probable, prompting the initiation of empirical antituberculous treatment even in the absence of direct bacteriological confirmation. This diagnostic approach has

been supported by several studies that highlight the value of ADA in pleural fluid as a complementary tool in lymphocytic pleural effusions, particularly when interpreted together with the patient's clinical and epidemiological context.

Leukocytoclastic vasculitis

Leukocytoclastic vasculitis is a small-vessel vasculitis histopathologically characterized by neutrophilic infiltrate, leukocytoclasia, fibrinoid necrosis, and red blood cell extravasation. It typically manifests clinically as palpable purpura, erythematous papules, or purpuric lesions, predominantly on the limbs, though presentations can vary.

In this case, the patient developed rapidly progressive pruritic and painful skin lesions on the upper and lower limbs. Skin biopsy showed preserved epidermis, mixed perivascular infiltrate with neutrophils, eosinophils, and lymphocytes, fibrinoid necrosis of small-caliber vessels, and red blood cell extravasation, all consistent with leukocytoclastic vasculitis. Direct immunofluorescence was negative, which does not exclude the diagnosis, since it was established based on clinicopathological correlation.

The beta-lactam antibiotics initially administered (amoxicillin/clavulanic acid and piperacillin/tazobactam) have been reported as potential triggers of hypersensitivity-induced leukocytoclastic vasculitis. Therefore, their role in the development of the skin lesions cannot be completely ruled out. However, the persistence of the lesions after discontinuation of these antibiotics, together with their subsequent resolution after initiation of antituberculosis treatment, more strongly suggests an immunological mechanism secondary to active pleural tuberculosis.

Immunological mechanisms

The association between tuberculosis and cutaneous vasculitis is uncommon, but it has been described in the literature. It has been proposed that tuberculous infection may act as a persistent antigenic stimulus capable of inducing the formation and deposition of immune complexes in the walls of small vessels, with complement activation and neutrophil recruitment, thereby triggering the vascular damage characteristic of leukocytoclastic vasculitis.

In addition, the immune response to *Mycobacterium tuberculos*is involves activation of T lymphocytes, macrophages, and the release of proinflammatory cytokines, including TNF-α and IFN-γ, which may contribute not only to infection control but also to distant inflammatory phenomena. In this context, the cutaneous manifestations may be interpreted as a secondary immunological expression of the active disease and not necessarily as the result of direct dissemination of the microorganism to the skin.

Therapeutic response

The patient's clinical course was favorable following initiation of antituberculous therapy associated with oral corticosteroid treatment in tapering doses. After ten days of combined treatment, a clear improvement in the skin lesions was observed, with reduction of erythema, disappearance of the purpuric halo, and progressive clearing of the skin.

Treatment response is a clinically relevant element in the interpretation of the case. Although it does not by itself prove causality, the improvement of the lesions in parallel with the treatment of pleural tuberculosis supports the hypothesis of leukocytoclastic vasculitis secondary to the underlying infectious process. The concomitant use of corticosteroids likely contributed to more rapid control of the cutaneous inflammation.

Comparison with the literature

The association between pleural tuberculosis and leukocytoclastic vasculitis is uncommon. Most available reports describe cutaneous vasculitis associated with pulmonary or extrapulmonary tuberculosis, interpreted as secondary immunological phenomena. In this regard, this case is consistent with previously published reports by demonstrating a vasculitic manifestation in the setting of active tuberculosis, without evidence of systemic autoimmune disease and with favorable evolution after specific treatment.

This case is of additional interest because it involves a young immunocompetent patient with highly probable pleural tuberculosis from a clinical, epidemiological, and biochemical standpoint, associated with histologically confirmed leukocytoclastic vasculitis. The coexistence of both entities requires consideration not only of

infectious and pharmacological diagnoses, but also of the possibility of uncommon immunological manifestations of tuberculosis.

CONCLUSION

In this case, leukocytoclastic vasculitis was interpreted as an immune manifestation secondary to pleural tuberculosis.

Early recognition of this association enables timely diagnosis and initiation of appropriate antituberculosis treatment, potentially leading to a favorable clinical course.

Conflict of interest

The authors have no conflict of interest to declare.

Ethical considerations

The project was approved by the Ethics Committee of each institution, and the participant provided informed consent to take part in the study.

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