

# Septic shock and multi-organ failure in a non-immunosuppressed patient – sepsis tuberculosa gravissima in intensive care: A case report

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## Abstract

It's well documented that patients on immunosuppressive therapy are at increased risk of developing Tuberculosis (TB). However, in particular regions, general population is highly exposed to contracting tuberculosis. In fact, TB is becoming a global epidemic. We report a 71-year-old male with lower limb pain with a trauma wound, who was admitted to the hospital due to fever, anemia, and moderate respiratory distress. Chest x-rays showed non-specific findings. A CT chest scan showed multiple miliary micronodular images diffusely distributed and mediastinal enlarged lymph nodes with central necrosis, suggestive of tuberculosis. Although the characteristics imaging of TB are very variable, in a significant proportion of cases these images can be very oriented concerning the presence of this disease.

Sputum smear sample shows acid-fast bacilli. Antituberculous treatment was started and discharged. He was readmitted in respiratory insufficiency and shock one week later and died. Mycobacteria were massively observed in the direct sputum sample. After her death cultures for Mycobacterium tuberculosis were informed as positive. The clinical picture of the patient is known as sepsis tuberculosis gravissima. The best treatment of pulmonary TB is early diagnosis and prompt initiation of tuberculosis drugs, as well as close monitoring to detect the development of severe forms.

## Key clinical message

Septic shock due to Mycobacterium tuberculosis is an uncommon but well recognized clinical syndrome, behaves similarly to bacterial septic shock. Early appropriate antimicrobial therapy appears to improve mortality, as in bacterial septic shock, the use of antifimics should not be delayed. Tuberculosis is becoming a global epidemic. Respiratory samples and images help the diagnosis.

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## Introduction

Tuberculosis (TB) is one of the most globally prevalent diseases, with some 2 billion patients affected worldwide and 9 million new cases reported in 2005 [1]. Likewise, TB was the world's second leading cause of death from a single infectious agent, after Coronavirus Disease (COVID-19), and caused almost twice as many deaths as HIV/AIDS. More than 10 million people continue to fall ill with TB every year. Urgent action is required to end the global TB epidemic by 2030 [2].

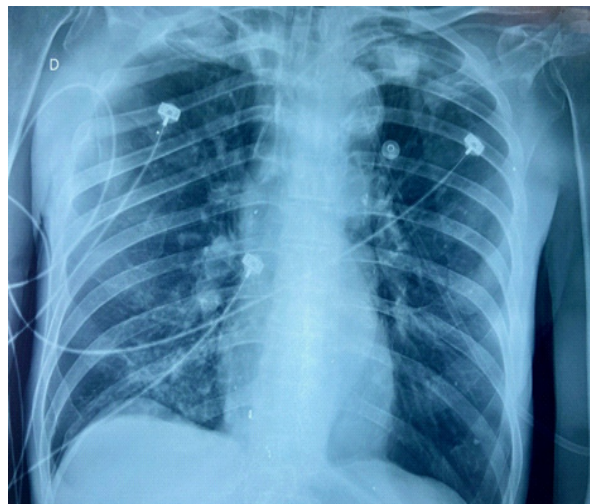
In the acute forms of presentation of pulmonary TB (symptoms <30 days) [3], the take with characteristics of miliary TB or bronchiolar dissemination, both of which can progress in severity and require management in units of intensive care between 1 and 3% of cases, presentation as sepsis or shock [4]. Pulmonary TB is most common among these conditions to require critical care, with a resultant hospital mortality of 25% to 33% [5]. Two well-defined entities exist at either end of the spectrum of miliary TB: acute miliary TB and nonreactive TB.

## Case presentation

A 71-year-old man presented with pain and functional impotence of the lower limb with a non-suppurating, red, and swollen wound. Febrile and tachycardic, his basic blood chemistry revealed that the white blood cell count was  $15.66 \times 10^9/L$ , the C-reactive protein concentration was more than 555.5 mg/L, with anemia. Respiratory discomfort presented 6 months ago. Arteriography shows occlusion of the anterior tibial artery with the presence of collateral circulation and severe diffuse disease in the posterior tibial artery as well as in the peroneal artery. A surgical procedure was performed with debridement of the lower limb wound, taking bone samples from the tibia and peroneal bone, with bone and skin and soft tissue cultures that were negative. In induced sputum, direct examination with the Ziehl Neelsen technique was positive for mycobacteria starting treatment with 4 antituberculous drugs, consisting of quadruple therapy, with isoniazid, rifampicin, pyrazinamide and ethambutol. Antibiotic treatment with trimethoprim sulfamethoxazole, ciprofloxacin and home isolation with prophylaxis is indicated for the family group.

One week later he was readmitted with insufficiency respiratory. Chest X-rays revealed faint interstitial infiltrate predominantly in the right lower lobe, with areas compatible with pulmonary nodules of different sizes in the same area with no pleural effusion (Figure 1). The CT scan revealed patchy areas with increased parenchymal attenuation in both upper lobes and in the right lower lobe, the larger areas have tracts that join them with the pleura. In the right lower lobe, areas of nodules with a tree-in-bud pattern are observed. (Figure 2) Bilateral mediastinal lymph nodes are present (Figures 2 and 3). Echocardiogram showed impaired LV relaxation without motility alterations, with preserved left ventricular systolic function.

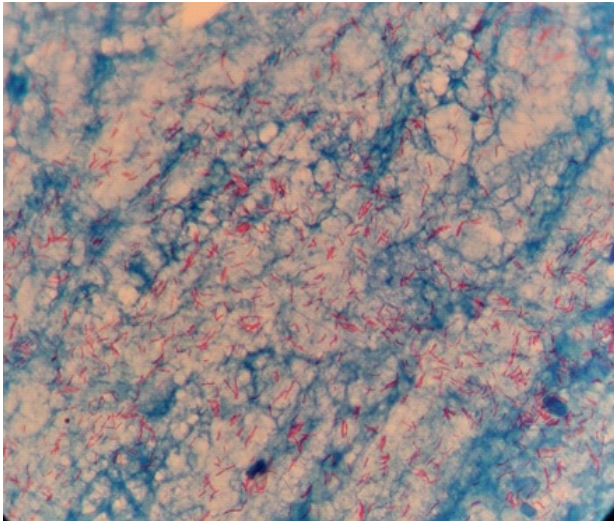
Patient, was intubated with mechanical ventilator, was followed up for 7 days. Tracheal aspirate shows massive covered field of bacilli acid-fast (Figure 4). Septic shock developed with norepinephrine vasopressin requirement, becoming refractory, with severe metabolic acidosis (bicarbonate <7) without response to bicarbonate infusion. blood cultures positive for mycobacteria, in this clinical picture, he suffers cardiac arrest and dies.



**Figure 1:** Chest X-rays showed faint interstitial infiltrate predominantly in the right lower lobe, with areas compatible with pulmonary nodules. Patient on mechanical ventilation.



**Figures 2 & 3: (pulmonary window) – 3 (mediastinum window):** Chest CT - parenchymal attenuation in both upper lobes and in the right lower lobe, the larger areas have tracts that join them with the pleura. In the right lower lobe, areas of nodules with a tree-in-bud pattern are observed.



**Figure 4:** Sputum smear sample. Sputum smears evaluated with Light-Emitting Diode (LED) microscopy at a magnification of 100 $\times$ . Acid-fast bacilli are identified, characterized by a bright red color on a blue background, rod-shaped and straight, slightly curved, small (between 1 and 4  $\mu$ m). Massively covered field.

### Discussion

This case report describes a baciliferous TB with septic shock who was receiving tuberculostatic drugs and antibiotic treatment.

Adult Respiratory Distress Syndrome (ARDS) is a infrequent complication of TB in both immunocompetent and immunocompromised population. Disseminated disease has been seen in up to 30% of patients with tuberculosis admitted to the intensive care unit and disseminated disease appears to predispose individuals to ARDS, perhaps to a greater degree than isolated pulmonary tuberculosis [6]. TB also can infrequently lead to sepsis and shock, which has been well described in the literature since the original report by Landouzy, called Landouzy Syndrome [7]. Hematogenous dissemination may occur with or without miliary disease, the latter known as Landouzy septicemia or sepsis tuberculosa acutissima. Disseminated TB from any cause might lead to septic shock with multiorgan failure, termed sepsis tuberculosa gravissima [8]. In cases of severe bacterial septic shock, microbially appropriate empirical antimicrobial therapy appears to improve mortality. Compared with bacterial septic shock, a substantially larger fraction of patients with TB septic shock received inappropriate initial antimicrobial therapy, receiving only antibiotic treatment and delaying the start of tuberculostatic drugs, which was associated with a significantly worse clinical outcome, including decreased ICU and hospital survival [9].

A significant finding in thorax CT is the so-called “tree-in-bud” images, which consist of multiple linear opacities that can represent, among other causes, the diffusion bronchogenic tuberculous infection. Are the images represent the foci of caseous necrosis. That affect the terminal and respiratory bronchioles, but are not pathognomonic of tuberculosis pulmonary and can be found in pathologies such as postviral bronchiolitis, due to inhalation of toxic gases and inorganic dusts [10] and, central lung cancer involving the peripheral airways [11]. Subsequently, metastatic diseases showing “tree-in-bud sign” caused by tumor cells in and around the intralobular pulmonary artery were also reported [12].

It has been documented that intralobar peribronchiolar nodules, observed in pathological anatomy of patients carrying pulmonary TB, are those that are evident as “tree-in-bud” opacities on CT, and this occurs because the tuberculous infection located around the bronchioles causing infectious bronchiolitis due to *Mycobacterium tuberculosis* [13].

Diagnosis of pulmonary tuberculosis requires three consecutive sputum samples, collected at 24-hour intervals, preferably with at least one being an early morning sample, to be sent for microscopy, culture, Ziehl–Neelsen stain, polymerase chain reaction analysis and sensitivity testing [14].

There is no evidence to suggest that treatment of patients with tuberculosis on the intensive care unit should differ from standard World Health Organization guidelines, consisting of quadruple therapy, with isoniazid, rifampicin, pyrazinamide and ethambutol. It is worth considering that some drugs (rifampicin specifically) may adhere to the nasogastric tube and be preferentially administered intravenously while the patient is on the intensive care unit.

Using corticosteroids to treat individuals admitted to the intensive care unit with acute respiratory distress syndrome secondary to miliary tuberculosis has been associated with a significant decrease in mortality in some reports [15]. Its routine use is not recommended and should be considered on a case-by-case basis.

### Conclusion

Most of the evidence to date is from retrospective cohorts and case series - more prospective research needs to be conducted in this area. Intensive care unit patients are ultimately a heterogeneous patient population and the complexity of tuberculosis pathogenesis exacerbates this. Treatment initiation should not be delayed for culture confirmation, since a delay is strongly associated with death. Chest X-rays and sputum direct examen and cultures are fundamental in the diagnosis. Chest CT is considered the most important technique for the detection on chest x-rays of occult disease; it can detect micro nodules, infiltrations, consolidations, lymph node enlargement, and cavities.

### Declarations

**Acknowledgement:** Roberto Villa thanks the patient family for their permission to publish this report. Written informed consent was obtained from the patient to publish this report in accordance with the journal’s patient consent policy.

He also thanks his family for the time he takes from them, and out of love, they forgive him.

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