



MILIARY TUBERCULOSIS IN AN IMMUNOCOMPETENT PATIENT: CASE REPORT

TUBERCULOSIS MILIAR EN PACIENTE INMUNOCOMPETENTE: REPORTE DE CASO

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ABSTRACT

Miliar Tuberculosis (TB) is a presentation with a fatal outcome if it is not diagnosed or treated on time; although certain conditions are required to develop this presentation. **Clinical case:** In this article, the case of a 48-year-old man with no pathological history is studied, who started the disease with a time of six months with an initial diffuse gastrointestinal pain and later one month before admission presented progressive respiratory symptoms; he was admitted for emergencies where bilateral diffuse miliar compromise was evident in the chest computed tomography; upon admission, he was administered oxygen and support measures, an HIV test was obtained which was negative, and positive results were obtained in the sputum smear microscopy. His clinical evolution was stationary until the administration of antituberculosis therapy, observing slight clinical improvement, likewise, low doses of corticosteroids were administered after which a favorable evolution was demonstrated and he was discharged.

Keywords: Tuberculosis; Miliary; Respiratory insufficiency; Corticosteroids. (Source: MESH-NLM)

RESUMEN

La tuberculosis (TB) miliar es una presentación con un desenlace fatal de no ser diagnosticada ni tratada a tiempo; para desarrollar esta presentación se requieren de ciertas condicionantes. **Caso Clínico:** En este artículo, se estudia el caso de un varón de 48 años sin antecedentes patológicos, quien inició la enfermedad por un periodo de seis meses, con un cuadro gastrointestinal difuso inicial; un mes antes del ingreso presentó un cuadro respiratorio progresivo, por lo que fue ingresado a Emergencias, en donde se evidenció, en la tomografía computarizada de tórax, compromiso miliar difuso bilateral; se le administró oxígeno y medidas de soporte, se obtuvo prueba VIH, cuyo resultado fue negativo. Se obtuvieron resultados positivos en la baciloscopia de esputo. Su evolución fue estacionaria hasta la administración de la terapia antituberculosa y se observó leve mejoría clínica; así mismo, se le administraron dosis bajas de corticoide, luego de los cuales se evidenció una evolución favorable, por lo que se le dio de alta.

Palabras clave: Tuberculosis miliar; Insuficiencia respiratoria; Corticoesteroides. (Fuente: DeCS- BIREME)

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INTRODUCTION

Tuberculosis (TB) continues to be a significant global health concern, with the COVID-19 pandemic having a detrimental effect on access to diagnosis, treatment, and disease burden. In 2021, an estimated of 10.6 million people fell ill with TB, which represented a 4.5% increase from 2020. In the same year, 1.4 million deaths were reported among HIV-seronegative individuals⁽¹⁾. In Peru, the Directorate of Tuberculosis Prevention and Control (DPCTB, by its Spanish acronym) reported an incidence rate of 60.1 per 100,000 inhabitants in 2022⁽²⁾. Miliary TB is a lethal form of disseminated TB, resulting from massive lymphohematogenous dissemination of a Mycobacterium tuberculosis-laden focus⁽³⁾, occurring either during primary mycobacterial infection or upon reactivation of a latent infection⁽⁵⁾. The dissemination usually results from erosion into a blood vessel and the release of caseating material from any bodily focus. In an individual with low immunity, this leads to the seeding of small, often caseating granulomas resembling millet grains, that is why they are called miliary⁽⁴⁾. Various predisposing or associated conditions have been documented in miliary TB patients, including childhood infections, malnutrition, HIV/AIDS, alcoholism, chronic renal disease, dialysis, post-gastrectomy state, organ transplantation, use of immunosuppressive drugs, connective tissue disorders, pregnancy, postpartum period, underlying malignant tumors, and silicosis⁽⁶⁾.

CLINICAL CASE

The patient, a 48-year-old male mechanic in the mining industry with no significant medical history, presented six months before admission with diffuse abdominal pain,

progressive abdominal distension, and weight loss of approximately 10 kilograms. Therefore, he initially visited an outpatient Gastroenterology clinic, where he was diagnosed with ascites and was scheduled for a procedure, which he did not attend due to personal reasons. Two months later, he was re-evaluated by a specialist who informed him that the ascites had resolved. It is important to note that one month prior to hospital admission, the patient experienced sporadic dry cough associated with progressive dyspnea, and even with mild efforts. Additionally, he presented with febrile episodes and headache, which led him to consult a company doctor. There, an oxygen saturation of 70% was identified, prompting his transfer to the emergency clinic.

Upon physical examination at admission, the patient had an oxygen saturation of 95% at FiO₂ of 21%, generalized pallor, tachypnea, use of accessory muscles for breathing, and a slightly distended but non-painful abdomen; the rest of the physical examination was within normal ranges. Laboratory tests showed hemoglobin: 13.5 gr/dL, hematocrit: 43%, total leukocytes: 9.64, total proteins: 5.75 g/dL, alkaline phosphatase: 75, total bilirubin: 0.45, indirect bilirubin: 0.26, direct bilirubin: 0.19, with tumor markers: CA 21-1 and carcinoembryonic antigen negative and HIV negative. Imaging studies revealed a bilateral diffuse micronodular pattern in the chest X-ray upon admission (Figure 1); the same pattern was observed in the chest computed tomography at admission, with no evidence of pleural effusion or lymphadenopathy (Figure 2).

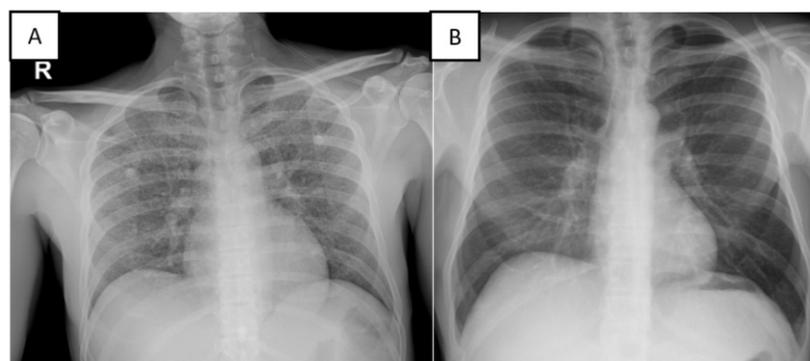


Figure 1. Chest X-ray: (A) Admission image showing bilateral diffuse micronodular pattern. (B) Control image after three months of treatment showing improvement of the initial lesions.

During his hospitalization, the patient showed poor clinical evolution and increased respiratory effort, leading to his transfer to the Intensive Care Unit, where he received oxygen support through a binasal cannula. After positive sputum smear microscopy results for *Mycobacterium tuberculosis*, specific treatment was initiated. Two weeks into the treatment, a slight improvement was noted compared to his condition upon admission, but there was a worsening in the control tomography (Figure 2), along with persistent tachypnea and oxygen supplementation.

Consequently, corticosteroid therapy was initiated, leading to significant improvement in the respiratory pattern within a week, and he was transferred to a non-critical patient hospitalization ward. Following the progressive weaning from mechanical ventilation and gradual reduction of corticosteroids, as well as tolerance to the antituberculosis treatment, the patient was discharged 21 days after hospitalization. Three months into the treatment, during a follow-up, he was in phase 2, showing evidence of improvement in the control tomography image.

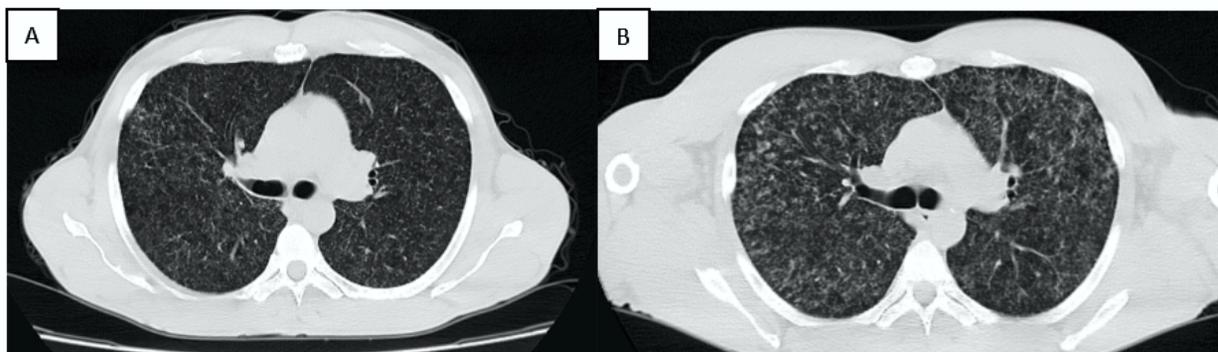


Figure 2. Tomografía computarizada de tórax sin contraste: (A) Imagen del ingreso con presencia de patrón micronodular de distribución simétrica en ambos hemitórax. (B) Imagen control, luego de dos semanas de inicio de tratamiento antituberculoso, en donde se evidencia mayor compromiso parenquimal

DISCUSSION

Miliary TB is a deadly form of TB resulting from massive lymphohematogenous dissemination of a *Mycobacterium tuberculosis*-laden focus. Radiologically, the miliary pattern has been defined as "a collection of tiny, discrete pulmonary opacities that are generally uniform in size and broadly distributed"; each one measures 2 mm or less in diameter⁽⁶⁾. This pattern involves the simultaneous compromise of multiple organs and is more common in extreme ages of life, in both infants, young children, and elderly individuals with debilitating conditions⁽⁴⁾. Organs with high blood flow, such as the spleen, liver, lungs, bone marrow, kidneys, and adrenal glands, are frequently affected. On macroscopic examination, the lesions are rounded, grey to reddish-brown, small, punctate, and more or less uniform in size. They can be observed in the lungs and several other organs. The "tubercle" is the histopathological hallmark of miliary tuberculosis. When miliary tuberculosis results from an acute massive hematogenous spread, lesions in all viscera

appear similar: "soft" or "exudative" tubercles; a clear caseous focus invading blood vessels is usually demonstrable, and the lesions often reveal acid-fast bacillus (AFB). This can develop at the time of primary infection or later, during the reactivation of a latent focus⁽³⁾. In the vast majority, the host's immune responses are capable of containing the primary infection, leading either to complete healing or persistence as a latent infection. However, in 10% of patients, the immune response is insufficient to contain the primary infection, resulting in dissemination⁽⁵⁾. Miliary tuberculosis is believed to result from inadequate effector T-cell (Teff) responses to contain the tuberculous bacillus; evidence suggests that selective chemokine-directed Th2 cell responses may play a critical role in the development of miliary TB. In a susceptible host, immune responses lean towards a protective inhibitory Th2 response, such as granuloma formation, and this inability to limit local disease activity favors dissemination. Miliary TB likely results from a Th2-biased response that occurs as a predetermined pathway⁽⁶⁾.



The predominant constitutional symptoms include anorexia, weight loss, and fever, the latter being the most common symptom. About 75-80% of patients experience an early morning peak in fever. Gradual onset of malaise and weight loss occurs in 60-65% of individuals; cough and difficulty breathing are seen in 50% of cases. Abdominal pain is the main symptom in about 7-14% of patients with miliary TB. Headache, observed in 10-15% of cases, suggests meningeal involvement⁽⁵⁾; night sweats are common, leaving a silhouette-like sweat mark on the bed, similar to a wet shadow (wet shadow sign)⁽⁶⁾. Some authors have discussed the concept of cryptic miliary TB^(6,8), defined as a form of disseminated TB with a non-miliary pattern or normal chest radiography, plus one of the following conditions: positive culture for *M. tuberculosis* from bone marrow, liver biopsy sample, or in two or more non-contiguous organs; and positive culture for *M. tuberculosis* from one organ and histopathological demonstration of caseating granulomas from another non-contiguous organ⁽⁷⁾.

Regarding pulmonary involvement evidenced in radiology, the predominant finding in miliary TB are diffuse nodules between 1-3 mm with random distribution⁽⁸⁾; Kim et al. showed that the number of small nodules and micronodules in HIV-positive patients was greater than in HIV-negative patients, and ground-glass attenuation was identified in 14 (93%) of 15 HIV-positive patients and nine (64%) of 14 HIV-negative patients. In our patient, diffuse micronodular lesions predominantly bibasal without secondary TB lesions were found. In the presence of clinical suspicion compatible with miliary TB, bacteriological confirmation should be performed, as there is a high incidence of this disease in our environment. Detection of mycobacterial isolates from a clinical sample provides a definitive diagnosis of disseminated tuberculosis. Examples of tissue samples include sputum, body fluids, tissue, and biopsy samples⁽¹⁶⁾; in our patient, a positive sputum smear confirmed

the diagnosis.

Similar case reports exist in other countries: Cueto et al. reported a case of a 38-year-old immunocompetent male patient with miliary TB and acute respiratory failure with a fatal outcome, who also required support with invasive mechanical ventilation⁽¹⁰⁾. Likewise, Agu et al. reported a case of a 67-year-old immunocompetent African American male with comorbidities such as hypertension, atrial fibrillation, and prostate cancer, who, after treatment, achieved complete remission of miliary TB⁽¹¹⁾; Echeverri-Fernandez et al. reported the case of a 24-year-old woman without comorbidities, who, after six months of gastrointestinal and constitutional symptoms, was diagnosed with peritoneal TB, received treatment, and was discharged after 15 days of hospitalization⁽¹²⁾.

Regarding the treatment of miliary TB, it is uniformly fatal if untreated. Standard antituberculosis treatment is the cornerstone of management. There is no consensus on the optimal duration of treatment in patients with miliary TB. In many parts of the world, patients with miliary TB are treated under the National Tuberculosis Control Program with observed short-duration chemotherapy⁽³⁾.

In general, corticosteroids lead to a clinically significant reduction in mortality, regardless of the affected organ group. The overall mortality reduction from steroid use is 17%⁽¹⁴⁾; the benefit of using corticosteroids has been demonstrated, as corticosteroids like dexamethasone inhibit the death of necrotic cells infected with *Mycobacterium tuberculosis* (*Mtb*) and facilitate mitogen-activated protein kinase phosphatase 1 (MKP-1) dependent dephosphorylation of p38 MAPK⁽¹³⁾; evidence has been published supporting the use of pulse corticosteroids in patients affected by miliary tuberculosis associated with respiratory distress syndrome, with favorable results for this therapy⁽¹⁵⁾.

CONCLUSIÓN

Miliary tuberculosis is a lethal presentation if not identified and treated in time, and diagnostic suspicion is the main tool: clinical follow-up and imaging support are important for its final diagnosis. While it occurs more frequently in extreme ages of life and in people with predisposing factors, it can also present in those outside these age ranges and without any risk factors. Prompt initiation of antituberculosis treatment and support

measures are the cornerstone of managing this unique pathological presentation; the use of corticosteroids in this presentation is debatable, but in our case, faced with poor clinical evolution, the response resulted in notable improvement, and the patient was successfully weaned off mechanical ventilation, leading to discharge.

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