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Epidemiological, Clinical, Radiological, Therapeutic and Outcome Aspects of Miliary Tuberculosis: A Study of 45 Cases in Morocco

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Abstract

Introduction: Miliary tuberculosis represents one of the most severe and life-threatening forms of tuberculosis. It is characterized by widespread hematogenous dissemination of *Mycobacterium tuberculosis* and is associated with significant morbidity and mortality. The present study aimed to describe the clinical, epidemiological, therapeutic, and outcome characteristics of miliary tuberculosis. ***Methods:*** We conducted a retrospective descriptive and analytical study over a two-year period, from January 1, 2022 to December 31, 2023. Medical records of patients hospitalized for miliary tuberculosis in the Department of Pneumology and Phthisiology at Moulay Youssef University Hospital, Rabat, Morocco, were reviewed and analyzed. ***Results:*** The mean age of patients was 43 years, with a male predominance (64%). A history of tuberculosis was found in 2 patients, and recent close contact with a tuberculosis case was identified in 5 patients. Four cases of miliary tuberculosis occurred following immunosuppressive therapy, including 3 patients who had previously received preventive anti-tuberculosis treatment. The clinical presentation was dominated by fever, night sweats, general condition deterioration, dyspnea, and cough. Extra-respiratory manifestations were observed in 17% of cases. Typical radiological findings were present in 91% of patients, while sputum smear microscopy was positive in 15%. Anti-tuberculosis treatment based on a four-drug regimen (ERIPK4) was initiated urgently in most cases. Complications occurred in 11 patients, including disease-related and treatment-related complications. The in-hospital case fatality rate was 17.7%. ***Conclusion:*** Miliary tuberculosis remains a severe and potentially life-threatening condition. Early diagnosis and prompt initiation of appropriate anti-tuberculosis therapy are essential to improve patient outcomes.

Keywords: Miliary tuberculosis, Hematogenous dissemination, Mycobacterium tuberculosis, Moulay Youssef University Hospital, Clinical presentation.

INTRODUCTION

Miliary tuberculosis is a severe and potentially life-threatening form of tuberculosis resulting from hematogenous dissemination of Mycobacterium tuberculosis [1,2]. Although relatively rare, it remains a major public health concern in high-burden countries such as Morocco [1,3]. The clinical presentation is often non-specific, leading to delayed diagnosis and increased morbidity and mortality [4]. Radiological findings, particularly diffuse micronodular patterns on chest imaging, play a key role in raising suspicion, although bacteriological confirmation remains challenging due to the paucibacillary nature of the disease [5].

Despite advances in diagnostic tools and treatment, miliary tuberculosis continues to be associated with significant complications and mortality [4,2]. The aim of this study was to describe the epidemiological, clinical, biological, radiological, therapeutic, and outcome characteristics of patients with miliary tuberculosis in our setting.

MATERIALS & METHODS

Study Design and Setting

This was a retrospective descriptive study conducted in the Department of Pneumo-phthisiology at Moulay Youssef Hospital, Rabat, Morocco, from January 1, 2022 to December 31, 2023.

Inclusion Criteria

We included all patients aged ≥15 years hospitalized with a diagnosis of miliary tuberculosis based on clinical, radiological, and/or bacteriological findings.

Exclusion Criteria

Patients with incomplete medical records were excluded.

Data Collection

Data were collected retrospectively from medical records using a standardized data collection form.

Statistical Analysis

Data were analyzed using Microsoft Excel. Quantitative variables were expressed as means, and qualitative variables as percentages.

RESULTS

Sociodemographic Characteristics

During the study period, 45 patients diagnosed with miliary tuberculosis were included in the analysis. The study population showed a male predominance, with 29 men (64%) and 16 women (36%), corresponding to a male-to-female ratio of approximately 1.8.

The mean age of the patients was 43 years. Miliary tuberculosis mainly affected young and middle-aged adults in our cohort, reflecting the involvement of an active-age population during the study period. (Table 1)

Table 1: Sociodemographic characteristics of patients with miliary tuberculosis

Characteristics	Number (n = 45)	Proportion (%)
Age (mean, years)	43	—
Sex		
Male	29	64
Female	16	36
History of tuberculosis	2	4.4
Recent close contact with a tuberculosis case	5	11
Immunosuppressive conditions	12	26.6
Delay before consultation (mean)	3 months	—

Past Medical History and Predisposing Factors

Among the included patients, a previous history of tuberculosis was reported in 2 patients. A history of recent close contact with a tuberculosis case was identified in 5 patients, highlighting the role of household or close-contact transmission. Several predisposing factors were identified in our cohort. Twelve patients developed miliary tuberculosis in the context of immunosuppression, related to underlying conditions or immunosuppressive therapies. Among these cases, four patients developed miliary tuberculosis following the initiation of immunosuppressive treatment, including three patients despite having received previous preventive anti-tuberculosis therapy.

Clinical Features

The interval between symptom onset and diagnosis of miliary tuberculosis ranged from 1 to 12 months, with a mean delay of 3.69 months.

Clinically, fever was present in 44 patients (97.8%), while deterioration of general condition was observed in all patients (100%); deterioration of general condition was defined as weight loss, asthenia, and/or anorexia.

Respiratory manifestations were frequent, dominated by cough, reported in all patients (100%), and dyspnea, observed in 44 patients (97.8%). Chest pain was noted in 2 patients (4.4%), whereas hemoptysis was reported in 7 patients (15.6%). Extra-respiratory manifestations were observed in 8 patients (17.8%), reflecting the systemic nature of miliary tuberculosis. (Table 2)

Table 2: Clinical manifestations of miliary tuberculosis (N = 45)

Clinical manifestation	Percentage (%)
Cough	100
Fever	100
General condition deterioration	100
Dyspnea	97.8
Extra-respiratory manifestations	17.8
Hemoptysis	15.6
Chest pain	4.4

On physical examination, signs of respiratory distress were frequently observed, including tachypnea and oxygen desaturation on room air. Lung auscultation commonly revealed bilateral crackles, consistent with diffuse pulmonary parenchymal involvement.

Paraclinical Findings

Chest radiography was performed in all patients and revealed a typical miliary pattern in all cases (100%, n=45) (Figure *1*). Associated findings included pulmonary cavitations, pleural effusion, and pericardial involvement. Chest computed tomography (CT) was performed in 21 patients and confirmed the miliary pattern (Figure *2*), with additional findings such as mediastinal lymphadenopathy, pulmonary embolism, and osteoarticular involvement consistent with spondylodiscitis.

Sputum smear microscopy was positive in 7 patients (15%, n=7), while no cases of multidrug-resistant tuberculosis were identified. The Xpert MTB/RIF assay was performed in 6 patients and was positive in 1 case. In several patients, the diagnosis was established based on a combination of clinical, biological, and radiological findings in the absence of bacteriological confirmation.

Biological abnormalities were frequent, including anemia (60.0%, n=27), lymphopenia (80.0%, n=36), and leukocytosis (22.2%, n=10). Elevated C-reactive protein levels were observed in 64.4% of patients (n=29), while 35.6% (n=16) had normal CRP levels.

Therapeutic Management and Outcomes

All patients received anti-tuberculosis therapy, mainly based on a standard four-drug regimen combining rifampicin, isoniazid, ethambutol, and pyrazinamide. In patients with hepatic involvement, an initial non-hepatotoxic regimen including levofloxacin and ethambutol, with or without additional agents, was used, followed by introduction of the standard regimen after normalization of liver function tests.

Supportive treatments were frequently required. Oxygen therapy was administered in 18 patients, and systemic corticosteroids were prescribed in selected cases, with gradual tapering over a mean duration of 45 days. The mean length of hospital stay was 45 days.

Complications

Complications occurred in 11 patients. Disease-related complications included pulmonary embolism (n=2), diabetic ketoacidosis (n=1), and hydropneumothorax (n=1). In addition, treatment-related adverse events were observed in 7 patients, mainly cytolytic hepatitis (n=4), as well as cutaneous hypersensitivity reactions, hematological disorders, and digestive intolerance. The in-hospital case fatality rate was 17.7%.

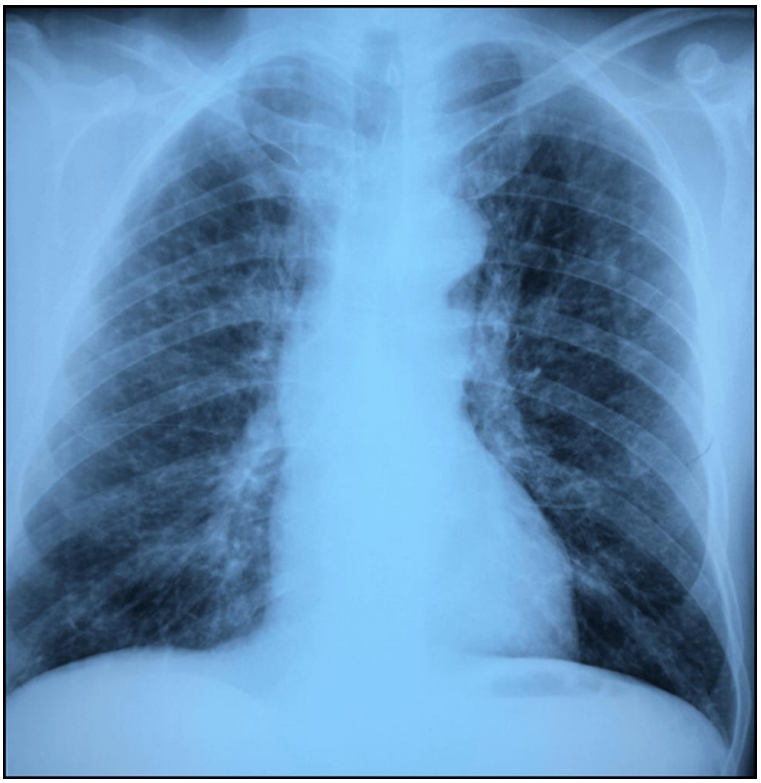

Figure 1: Frontal chest radiograph showing diffuse bilateral micronodular opacities

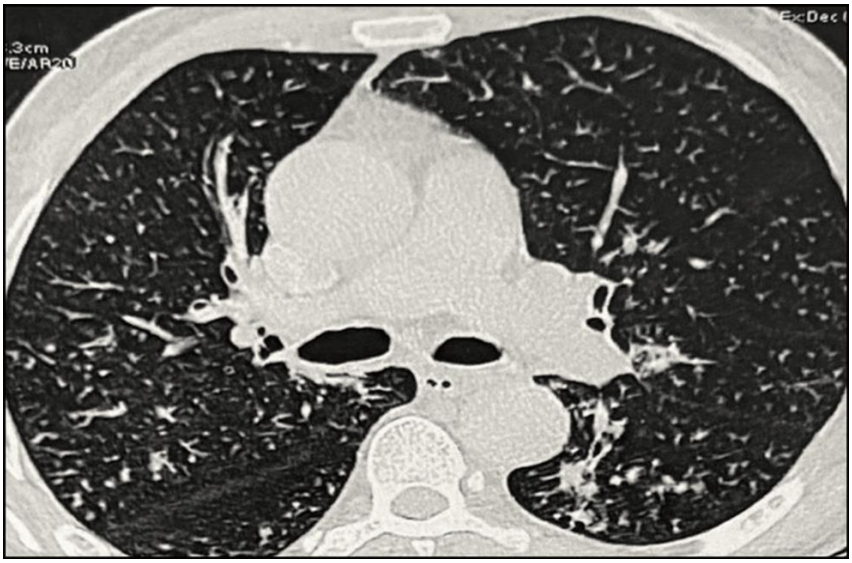

Figure 2: Axial chest computed tomography scan (lung window) showing diffuse bilateral pulmonary micronodules

DISCUSSION

Miliary tuberculosis is a severe and potentially life-threatening form of tuberculosis, with a frequency that varies widely across countries [1]. While it has become rare in developed countries, it remains a significant clinical entity in regions with high tuberculosis endemicity [2]. In our series, miliary tuberculosis predominantly affected young adults, with a clear male predominance, findings that are consistent with most published studies [6,7]. However, some authors, such as Ait Ahmed. [8], have reported a slight female predominance, highlighting the variability of demographic characteristics across different populations.

A history of close contact with a tuberculosis case should be systematically investigated, as reported rates in the literature range from 15% to 35% [9]. In our study, recent close contact was identified in 11% of cases, a lower rate that may reflect underreporting or difficulties in accurately tracing exposure in our setting. Several predisposing factors have been associated with the development of miliary tuberculosis. In our series, as in the literature, immunosuppressive conditions were the most frequently encountered, including diabetes mellitus and prolonged corticosteroid therapy [10,11]. These conditions may promote hematogenous dissemination of Mycobacterium tuberculosis and contribute to disease severity [5].

Delayed diagnosis remains a recurrent challenge in miliary tuberculosis, largely due to its nonspecific clinical presentation [9]. Several studies have reported consultation delays exceeding two months. In our series, the mean delay before consultation was approximately three months, which may partly explain the severity of clinical manifestations and the occurrence of complications. Clinically, miliary tuberculosis is often revealed by persistent general and respiratory symptoms. Fever, cough, night sweats, and deterioration of general condition are the most frequently reported manifestations in the literature, in accordance with our findings [6,7]. Extra-respiratory manifestations, although less frequent, should not be overlooked, as they may contribute to diagnostic delay [5].

Radiological imaging plays a key role in raising suspicion of miliary tuberculosis. In our series, as in most published reports, chest radiography revealed typical diffuse bilateral micronodular opacities in the majority of cases [12]. These micronodules are usually uniform in size, measuring less than 3 mm in diameter, and are diffusely distributed throughout both lung fields [12]. However, atypical radiological presentations may coexist, including nodular or macronodular lesions, cavitary lesions, and pleural effusion, which can further complicate the diagnostic process [12].

Bacteriological confirmation of miliary tuberculosis remains difficult to achieve. According to the literature, confirmation rates range from 24% to 36% [7]. In our series, direct sputum smear microscopy was positive in only 15% of cases, reflecting the paucibacillary nature of this form of tuberculosis and the difficulty in microbiological confirmation [13]. In high-endemicity settings, the presence of a suggestive clinical and radiological presentation may therefore be sufficient to retain the diagnosis and justify the urgent initiation of anti-tuberculosis therapy, even in the absence of bacteriological confirmation [2]. Standard first-line treatment using four major anti-tuberculosis drugs-rifampicin, isoniazid, pyrazinamide, and ethambutol-remains the cornerstone of management [2].

Adjunctive corticosteroid therapy was used in a proportion of patients in our series, particularly in

specific clinical situations such as severe dyspneic miliary tuberculosis, tuberculous meningitis, and tuberculous pericarditis. The benefit of corticosteroids in these conditions has been reported in several studies, mainly through the reduction of inflammatory complications and improved outcomes in selected patients [14,15].

Several complications may occur during the course of miliary tuberculosis. Some are directly related to the disease itself, including acute respiratory failure and pulmonary embolism [16], while others are related to anti-tuberculosis treatment, such as cytolytic hepatitis and digestive intolerance [17]. Close clinical and biological monitoring is therefore essential throughout treatment.

Despite advances in anti-tuberculosis therapy, the prognosis of miliary tuberculosis remains serious. Reported case fatality rates range from 12% to 52% in the literature [18]. In our series, the case fatality rate was 17.7%, highlighting the persistent severity of this condition and the importance of early recognition and prompt management.

Limitations

This study has several limitations, including its retrospective design, relatively small sample size, and the absence of advanced statistical analysis. In addition, some data were incomplete, which may have introduced bias.

CONCLUSIONS

Miliary tuberculosis remains a severe and potentially life-threatening condition, particularly in high tuberculosis burden settings. Delayed diagnosis and the presence of comorbidities contribute to poor outcomes. Early recognition based on clinical and radiological findings, along with prompt initiation of anti-tuberculosis therapy, is essential to improve prognosis and reduce mortality. Strengthening clinician awareness and improving diagnostic strategies are crucial to optimizing patient outcomes.

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