



## Miliary Nodules Caused by Multi Drug Resistant *Mycobacterium tuberculosis* - Rare Presentation of Common Disease: Case Report

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### Abstract

"Tuberculosis" (TB) is a disease caused by the bacteria '*Mycobacterium tuberculosis*'. Miliary tuberculosis is a type of tuberculosis that occurs when there is hematogenous spread of the bacilli. It is a type of disseminated tuberculosis. There is presence of grossly visible tiny tubercles that resemble millet seeds in size and form. Which can be of different sizes as per the stage. It is usually seen with associated immunodeficiency states. It can be a fatal if it is not detected and treated early. Miliary Tb in itself is an arduous task to treat as it presents with multi system involvement and significant involvement of organs like Brain and Adrenal Glands can lead to disastrous results. If Miliary Tb is caused by a Drug Resistant *Mycobacterium tuberculosis* which in itself is a challenge to diagnose and treat, resulting in increase of the disease severity by multiple folds. A rare case of Multidrug Resistant Miliary Tuberculosis is presented here (MDR-TB).

**Keywords:** Miliary TB; Multidrug resistance; *Mycobacterium tuberculosis*

### Introduction

John Jacob Manget was the first to invent the word "Miliary TB" in the year 1700. It was named after the Latin word "miliarius" which means millet seeds. It is caused by a large lymphohematogenous spread from *Mycobacterium tuberculosis* infected foci [1]. If left untreated, the disease is fatal to say the least. Miliary TB remains a serious challenge for the physician to diagnose and treat. As it presents with varied clinical presentations various radiographic findings with involvement of almost all the Organs of the body leading to diagnostic difficulties. Characteristically Miliary TB presents with features of small Millet sized opacities seen on Radiography. Miliary TB accounts for not more than 2% of all TB cases and up to 20% of all Tb due to Extra-Pulmonary Involvement (EPTB) cases [2]. Despite efforts to minimize the global incidence of TB, it is seen that incidence of drug sensitive TB is on a decline but MDR-TB has risen as a serious illness globally in the last 20 years [3]. MDR TB in itself presents a serious challenge in timely diagnosis and treatment, with diagnoses requiring an array of tests which in itself require multiple expensive machinery, and some tests requiring a very long time (up to 8 weeks) for it to accurately give the results and all of this with multiple number of drugs to taken for an extended period of time, leading to poor patient compliance and ultimately leading to treatment default. As Miliary TB if not treated early can be fatal and delay in diagnoses of drug resistance pose a serious challenge in front of the treating physician. Here, we present a case of Miliary TB caused by Drug Resistant *Mycobacterium tuberculosis*".

### Case Presentation

A 35-year female presented to the chest outpatient area with complaints of shortness of breath and dry cough for 15 days. Shortness of breath was present on mild exertion. There were no complaints of fever or weight loss. She gave no family history of tuberculosis and also denied any contact with an active TB patient. Patient was non diabetic, non-hypertensive and had no history of any chronic illness or any long duration drug intake. On examination, her vital parameters were within normal limits. Oxygen saturation was 85% while breathing ambient air. Her blood parameters were within normal range. Patient was immunocompetent. Chest radiograph suggested of bilateral nodular opacities, which was followed up by a tomographic scan of the thorax (Figure 1) which revealed presence of bilateral multiple miliary nodules of a varied sizes diffusely present throughout the lung and presence of 'Tree in Bud' pattern suggestive of active infection. Patient underwent Bronchoscopy where mild endobronchial erythema was noted. Bronchoalveolar

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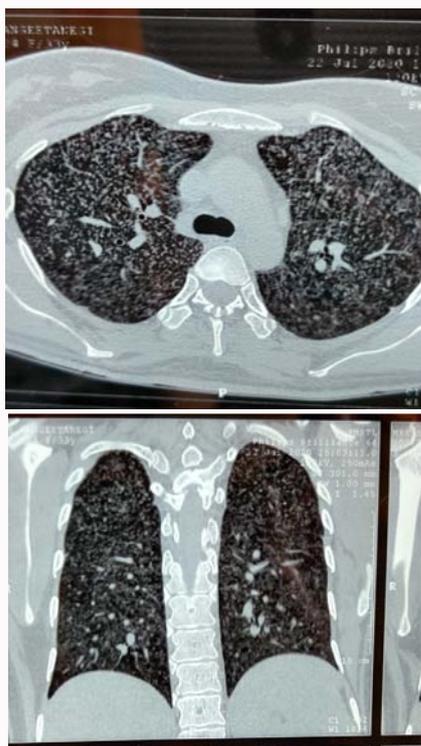


Figure 1: (a) and (b) shows bilateral extensive miliary nodules.

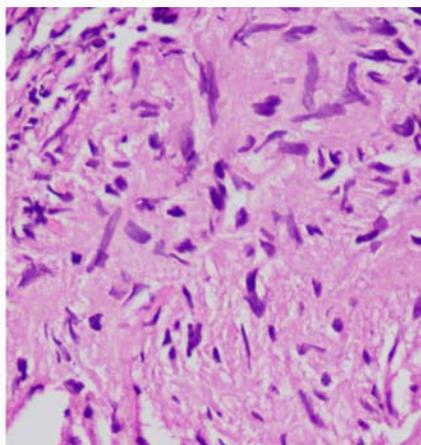


Figure 2: H&E stained section showing high power view of epitheloid granuloma (40x).

Lavage (BAL) was taken, Transbronchial lung biopsy was done. Histopathological examination was done (Figure 2) which was suggestive of tuberculosis. Patient was started on anti-tubercular fixed dose regimen while the BAL CBNAAT (cartridge based nucleic acid) report was awaited. BAL CBNAAT came out to be suggestive of Rifampicin Resistance, BAL LINE PROBE ASSAYS correlated with CBNAAT report. No Resistance to Isoniazid, Second line injectable agents or Fluroquinolones. Patient was then started on All Oral Bedaquiline containing regimen. Regular follow up was done. Patient showed improvement with decrease in symptoms and weight gain of 4 kg in the following few months. Patient has completed her anti-tubercular treatment. Her X-ray showed remarkable improvement (Figure 3).

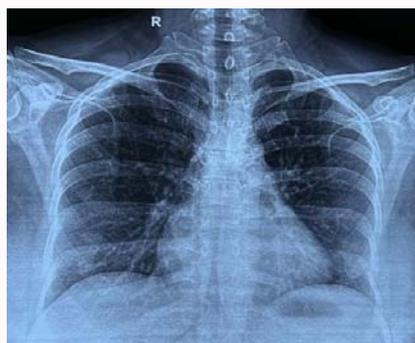


Figure 3: Chest X-ray of the patient after 1 year of treatment showing references.

## Discussion

Owing to the disease's increasing frequency and severity, Multidrug-Resistant TB (MDR) has become a global threat. Furthermore, due to a lack of equipment necessary to detect resistance, this condition goes misdiagnosed and hence unreported. Despite significant efforts in some countries, surveillance shows that the incidence of MDR-TB is increasing [4]. Multidrug-resistant Tuberculosis (TB), against which crucial first-line anti-tubercular drugs are less effective, poses serious issues for world health, with an estimated incidence of 490,000 cases in 2016. History of previous intake of anti-tuberculosis drugs, non-compliance, treatment defaulter, female gender, urban residence and high prevalence of drug resistance in the community, malnourishment, immunodeficient states are all important risk factors. MDR TB diagnosis is difficult because numerous investigations, such as cultures, take a long time to complete [5], and genotypic approaches require expensive equipment and qualified lab staff. Poor treatment outcomes, along with a large treatment gap between those who need and receive second-line therapy, highlight the urgent need for novel techniques to combat the pandemic of drug-resistant tuberculosis. MDR-TB can induce miliary TB, but due to the rarity of this extrapulmonary type of TB, the prevalence of MDR-TB in miliary TB infection remains unknown [6]. There are multiple reported cases of miliary TB due to a Drug resistant MTB in an immunocompromised host. It is known that in 30% to 65% of cases are diagnosed microbiologically on the basis of cultures grown from respiratory specimen [7]. Miliary TB accounts for around 1% of all TB cases. It results from massive lymphohematogenous dissemination of bacilli-laden focus. Characteristic finding on histopathological examination in cases of miliary TB is a tubercle (granuloma) that measures ~2 mm in  $\geq 2$  non-contiguous organs [8].

## Conclusion

Drug Resistance should therefore be considered in cases of miliary nodules; however, it is extremely rare. Multidrug-resistant TB is becoming a severe global health issue that must be addressed quickly. Early detection of instances can help with proper management and treatment, lowering the prevalence of the disease and improving public health.

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