



A Complex Interplay: Mycobacterium Tuberculosis co-infection complicated by Pulmonary Embolism—A case report

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ABSTRACT

Co-infections of Mycobacterium tuberculosis (MTB) and Mycobacterium leprae (ML) are exceedingly rare but can pose a diagnostic and management challenge. These co-infections can also be complicated by conditions like pulmonary embolism (PE). Although possessing distinct existence, Tuberculosis (TB) and leprosy share historical and epidemiological connections and often coexist in regions with high endemicity. Tuberculosis is primarily found to target the lungs followed by other organs, and leprosy predominantly targets the skin and peripheral nerves, with potential systemic involvement. Despite advancements in healthcare still, leprosy remains a concern in several regions globally, especially in areas where poverty, overcrowding, and inadequate healthcare infrastructure prevail. The clinical picture of both these infections overlap and both of them share a feature of drug resistance necessitating individualized therapeutic approaches.

Keywords: Leprosy; Pulmonary Tuberculosis; Peshawar

Introduction

Co-infections of *Mycobacterium tuberculosis* (MTB) and *Mycobacterium leprae* (ML) is an exceedingly rare scenario but can pose a diagnostic and management challenge.¹ These coinfections can also be complicated by conditions like pulmonary embolism (PE).² Although possessing distinct existence, Tuberculosis (TB) and leprosy share historical and epidemiological connections often coexisting in regions with high endemicity. Tuberculosis is primarily found to target the lungs followed by other organs, leprosy predominantly targets the skin and peripheral nerves, with potential systemic involvement. Despite advancements in health-care still leprosy remains a concern in several regions globally, especially in areas where poverty, overcrowding, and inadequate healthcare infrastructure prevail. The clinical picture of both these infections are overlapping and both of them share a feature of drug resistance necessitating individualized therapeutic approaches.^{3,4}

While the powerful drug thalidomide effectively controls type 2 leprosy reactions, its use demands caution due to potential side effects, particularly thromboembolic events. It requires consideration in patients who are already at increased risk of such complications. Pulmonary embolism is commonly seen in conditions like DVT and malignancies but cannot be ignored in infective and inflammatory conditions like COVID pneumonia or as drug side effect which is exceptionally rare but offers a diagnostic challenge. Recognizing PE early on in these cases is crucial to avoid potentially life-threatening complications.

This report brings a rare case of co-infection with MTB and ML complicated by pulmonary embolism in the background of thalidomide usage. Through this case, we aim to highlight the diagnostic dilemmas, therapeutic considerations, and clinical outcomes associated with this rare constellation of conditions. Because these cases are so rare and complicated, we should have heightened clinical suspicion and multidisciplinary collaboration to tailor individualized management strategies. This is the best way to ensure the best possible care and outcome in such difficult situations.

Case Report

A 52-year-old non-smoking laborer was newly diagnosed Hansen's disease and started on treatment including dapsone, rifampin, and clofazimine. After two months on his multi-drug therapy, patient developed symptoms including fever, and numerous painful, red nodular lesions across his face and torso. These symptoms were suggestive of lepromatous leprosy-type II reaction. To manage this, the patient was prescribed a regimen consisting of prednisolone and thalidomide in addition to his ongoing multibacillary therapy, which included dapsone, rifampin,

and clofazimine. On follow up the patient was assessed and he complained of on off chest pain with breathlessness. Upon examination, the patient had vital signs indicative of physiological distress, with a heart rate of 121 beats per minute, oxygen saturation (SpO₂) of 89% on room air, and a respiratory rate of 31 breaths per minute. The patient had skin lesions which he developed previously. The Respiratory system examination revealed the presence of crepitations in bilateral infra-axillary and infrascapular regions. The baseline investigations had elevated leukocyte count and inflammatory markers including ESR, CRP and D dimers. The cardiac enzymes were within the normal limits and other baselines including liver and renal functions were also inconclusive. Chest X-ray (CXR) findings showed bilateral blunting of the costophrenic angles and nonhomogeneous opacities in the bilateral lower zones. A high-resolution computed tomography (HRCT) scan of the chest was performed, revealing bilateral diffuse reticular pulmonary interstitial thickening along with multiple scattered ground-glass opacities and patchy parenchymal infiltrates involving the right middle lobe lingula and superior anterior and posterior basal segments of both lower lobes. These imaging findings suggested significant pulmonary involvement characterized by interstitial thickening, ground-glass opacities, and parenchymal infiltrates, indicative of an inflammatory process affecting the lungs. The presence of bilateral findings and the distribution pattern observed on HRCT necessitated further evaluation and management to address the underlying pulmonary pathology contributing to the patient's respiratory symptoms and clinical deterioration.

The patient was further planned for bronchoscopy to clear the Diagnostic ambiguity. Bronchial wash was taken for gene xpert, fungal and bacterial cultures. The gene xpert was detected positive with no RR resistance. The patient was started on antituberculosis therapy according to weight. Despite two weeks of treatment, the patient continued to experience persistent chest pain, and his oxygen saturation levels failed to improve. Further investigations were planned on follow up and they revealed an elevated D-dimer level of 13293 which was double of the previous value prompting. A computed tomography pulmonary angiography (CTPA) was ordered which confirmed the presence of segmental and subsegmental pulmonary artery emboli in the right lower lobe.

In response to the diagnosis of pulmonary embolism (PE), therapeutic anticoagulation was initiated with low-molecular-weight heparin during hospitalization. Subsequently, the patient was shifted to outpatient care and started on rivaroxaban, a novel oral anticoagulant (NOAC), for a duration of 3 months and advice of monthly follow-up. The patient showed symptomatic improvement, and his oxygen saturation levels returned to normal on room air. This positive response to anticoagulant therapy highlights the importance of timely diagnosis and

management of pulmonary embolism in patients with underlying medical conditions.

Discussion

Both tuberculosis and Leprosy are chronic bacterial infections but even in endemic regions, it is uncommon for one person to be infected with both at once. Intracellular Gram-positive aerobic acid-fast bacteria cause both tuberculosis and leprosy, which are granulomatous infections. On the other hand, having two infections has been linked to higher rates of morbidity (5.5%) and fatality (37.2%). Furthermore, lepromatous leprosy is more likely to be associated with tuberculosis.⁵

This case explores the impact of steroid treatment on type 2 leprosy reactions, specifically considering the potential role of immunosuppression in the development of pulmonary tuberculosis. In patients with multibacillary leprosy, erythema nodosum leprosum (ENL) can occur, which is a multisystem immune-mediated condition. ENL is primarily caused by hypersensitivity reactions mediated by type III immune complexes. It typically presents with several painful erythematous nodules along with symptoms such as fever, arthralgia, weight loss, malaise, and systemic manifestations. In severe cases, ENL may also manifest as bullous lesions as well.

Corticosteroids are the mainstay treatment for reducing the severity of this leprosy reaction. As is widely recognized, prolonged use of steroids can lead to various complications, including diabetes mellitus, hypertension, and increased susceptibility to infections such as gastrointestinal ulcers and osteoporosis. Thalidomide, initially introduced as a steroid-sparing agent, has shown efficacy in suppressing erythema nodosum leprosum (ENL) reactions. Its serendipitous discovery of remarkable effectiveness against the cutaneous manifestations of type 2 leprosy response or ENL occurred in 1964. Since then, no comparable medication has been found. Despite its well-documented teratogenic effects, thalidomide remains the preferred treatment for ENL. Its endorsement as the therapy of choice for moderate-to-severe ENL in both men and women of childbearing age was affirmed by the Fifth International Leprosy Congress in 1973 and subsequently by the World Health Organization in 1994.⁶

In the current case, thalidomide therapy was initiated for the patient's erythema nodosum leprosum (ENL). Thalidomide is believed to act through various mechanisms, including antiangiogenics, suppression of tumor necrosis factor-alpha, and immunological regulation. However, its use is associated with significant risks such as teratogenicity, hypothyroidism, drowsiness, constipation, and skin reactions, with rare but severe manifestations like Stevens–Johnson syndrome and toxic epidermal necrolysis. Notably, deep vein thrombosis and other thrombotic events have emerged as serious concerns with increasing thalidomide usage, posing intriguing challenges in clinical hematology. Previous literature suggests that thalidomide use may have contributed to thrombosis and pulmonary thromboembolism in our patient, although it's important to note that pulmonary tuberculosis (PTB) itself carries a risk of thrombotic events.

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Conclusion

Consideration of tuberculosis in patients with leprosy when they have respiratory symptoms not responding to usual management is very crucial. In the setting of two highly infectious diseases the complications like pulmonary embolism should be ruled out in time to avoid disastrous consequences.

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