A case of pulmonary tuberculosis mimicking as diffuse alveolar haemorrhage

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CASE REPORT
A Case of Pulmonary Tuberculosis Mimicking as Diffuse Alveolar Hemorrhage: A Case Report

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Abstract:
Background: Pulmonary tuberculosis (TB) and diffuse alveolar hemorrhage (DAH) have some commonalities in several parts of the world. However, acute hemoptysis with diffuse alveolar shadows while a patient is on anticoagulant and antiplatelet therapy for a specific reason suggests DAH over TB.

Case Presentation: In this case, a patient was presented with acute respiratory symptoms with hypoxia and bilateral alveolar shadows. He was treated for DAH at the initial encounter. However, on follow-up, he was confirmed having active pulmonary TB based on sputum acid-fast-bacilli culture.

Conclusion: He was successfully treated with standard first-line anti-tubercular therapy and was subsequently declared cured. Pulmonary DAH with TB, in the absence of an underlying autoimmune disorder, is rare.

Keywords: Pulmonary tuberculosis, Hemoptysis, Diffuse alveolar hemorrhage, Pulmonary artery stenosis, Clopidogrel, Rivaroxaban.

1. INTRODUCTION

Tuberculosis (TB) is a common infectious disease worldwide, and around one-quarter of the world population is estimated to be infected with Mycobacterium tuberculosis [1]. In 2018, approximately 10 million individuals were infected with TB, and 1.5 million died [1].

Since pulmonary TB and alveolar hemorrhage share some clinical features, the patient was misdiagnosed. The sputum smear was negative, and the presentation was masked by the CT chest findings and a history of antithrombotic therapy. Among the varied causes of diffuse alveolar hemorrhage (DAH), autoimmune disorders are the most common. DAH can be life-threatening due to hemoptysis, anemia, and hypoxia. Therefore, it is essential to differentiate it from the other causes of hemoptysis, and it is imperative to rule out an infection such as TB. The diagnosis of DAH can be made based on the accumulation of red blood cells, fibrin, or hemosiderin-laden macrophages in the alveolar space upon pathologic biopsy [2]. It was not possible to perform a bronchoscopy or biopsy as the patient was deteriorating rapidly. Therefore, he was started on empirical steroid therapy. The sputum AFB culture, in this case, was the vital step in clinching the diagnosis amid his deteriorating condition.

2. CASE PRESENTATION

A 48-year-old non-smoking Asian male, presented with an eight-day history of fever, cough, and dyspnoea. He was known to have bilateral pulmonary artery stenosis, for which he had undergone vascular stenting two months earlier. He was on clopidogrel and rivaroxaban therapy to prevent stent thrombosis. Upon examination, he was tachypneic with bilateral basal crackles, and his unventilated oxygen saturation was 94%.

His chest X-ray revealed ill-defined non-homogenous areas of airspace opacification within the left mid- and lower-lung zones. Non-homogenous opacification was also noted in the left retrocardiac region, with air bronchograms obscuring the...
left hemidiaphragm (Fig. 1). Blood analysis showed hemoglobin 13 gm%, white blood cells $5.43 \times 10^3$mcL, platelet count $275 \times 10^3$mcL, CRP 29.90 mg/L, and procalcitonin 0.76 ng/ml. His kidney function test showed normal urea (3.80 mmol/L) and raised creatinine (113.00 mmol/L) levels.

He was given antibiotics (ceftriaxone and clarithromycin) and oxygen therapy. His sputum culture grew pan-sensitive Klebsiella pneumonia, and his sputum generated a negative AFB smear. His condition deteriorated within four days. A follow-up chest X-ray also showed progression of the left-lung shadows (Fig. 2); therefore, his antibiotics were changed to piperacillin plus tazobactam and levofloxacin. Despite this, his oxygen saturation dropped to 89%. He started coughing up blood, and his hemoglobin dropped to 9.0 gm%.

Two days later, his oxygen saturation fell to 60%, and his chest CT (Fig. 3 a & b) showed areas of ground-glass attenuation with superimposed intralobular and interlobular septal thickening and air bronchogram involving the bilateral upper, right-middle, and lingular segments. These findings could represent bronchiolitis obliterans organizing pneumonia or DAH. His antiplatelet (clopidogrel) and anticoagulant (rivaroxaban) agents were discontinued, and he was kept on high flow oxygen and started on IV methylprednisolone 40 mg every eight hours.

His oxygen saturation gradually improved to 93%, and finally, he was discharged on antibiotics and prednisolone for ten days. However, he returned with worsening hypoxia (SpO$_2$-86%) and increased bilateral shadows on the chest X-ray. His Quantiferon TB GOLD test was positive, but repeat sputum AFB smears were negative. He was deemed unfit for a scheduled bronchoscopy due to hypoxia. He continued antibiotic treatment and a tapering dose of prednisolone. On follow-up, his sputum AFB culture report turned out to be positive for the Mycobacterium tuberculosis complex. He initiated standard ATT (isoniazid, rifampicin, ethambutol, and pyrazinamide) treatment and resumed his antithrombotic regimen after the initial stabilization. After six months of ATT, he showed significant clinical improvement, and his chest X-ray showed (Fig. 4) complete resolution of the bilateral shadows.
3. DISCUSSION

Tuberculosis is the leading infectious cause of death [3], making it one of the top ten causes of mortality worldwide. The bulk of TB cases occur in developing countries with the highest rates in sub-Saharan Africa, India, and the islands of Southeast Asia and Micronesia, followed by China, Central and South America, Eastern Europe, and northern Africa. Though total case numbers are higher in Southeast Asia, the proportion of TB cases among people with HIV infection in Africa (27%) is higher than in Southeast Asia (3%) [4]. Rifampicin-resistant (RR) and multidrug-resistant (MDR) TB is a major issue in Europe, where the majority of all cases are RR or MDR TB [4]. Although our case is from a high-prevalence area, his diagnosis was initially unrecognized due to the uncommon symptoms and rapid deterioration.

Pulmonary TB usually presents with cough, fever, weight loss, night sweats, and sometimes hemoptysis. Around 8% of patients with pulmonary TB usually experience hemoptysis during their lives [5, 6]; however, major or life-threatening hemoptysis is usually seen in post-TB sequelae or complications such as bronchiectasis, cavitation, mycetoma, and the rupture of a Rasmussen's aneurysm [7]. In 90% of cases with massive hemoptysis, the source is the high-pressure bronchial artery network [8]. Pulmonary TB infection can involve the vessels directly and cause mycobacterium-induced necrotizing granulomatous vasculitis, resulting in inflammation and aneurysmal changes in the broncho-pulmonary and arterio-venous connections [9]. Not only pulmonary TB infection, but other bacteria (e.g., Staphylococcus aureus, Pseudomonas aeruginosa), viruses (e.g., influenza), and fungi (e.g., Aspergillus species) are also common infectious causes of hemoptysis and can confound the diagnosis of pulmonary TB. In primary pulmonary TB, without any radiological evidence of cavitation and bronchiectasis, hemoptysis is rare. DAH as acute presentation could be life-threatening and may be related to autoimmune diseases, infections, and, rarely, drug or chemical exposure [10]. The diagnosis of DAH is based on clinical suspicion, chest imaging, laboratory findings, and the analysis of bronchoalveolar lavage fluid [10].

Autoimmune disease in the form of vasculitis is the most common cause of alveolar hemorrhage. While it has also been reported with mycoplasma, legionella, or viral infections [11], DAH is rarely seen in pulmonary TB [12]. A case of DAH in pulmonary TB was recently reported in a patient with an underlying, long-standing stable autoimmune disease (ankylosing spondylitis) and negative vasculitis markers, except a weakly positive c-ANCA [13]. Two other cases with similar presentations have been reported. One was after an autologous stem cell transplantation for diffuse large B-cell lymphoma [12]. The other was reported in a patient with anticardiolipin antibodies who did not meet the diagnostic criteria for antiphospholipid syndrome [11].

Clopidogrel is a potent antiplatelet agent commonly used in acute coronary syndrome to prevent stent thrombosis after coronary interventions. In our case, clopidogrel and rivaroxaban were used to obviate thrombosis from pulmonary artery stents. There are few case reports of DAH associated with clopidogrel therapy available in the literature [14, 15].

Some case reports of alveolar hemorrhage associated with rivaroxaban therapy have been reported in the literature; nevertheless, all of these cases include underlying chronic lung disease or autoimmune disease (i.e., bronchiectasis, interstitial lung disease, SLE, adenocarcinoma of the lung, LAM, and myelodysplastic syndrome) [16 - 18]. Our patient did not have any chronic parenchyma lung disease or autoimmune disease, except pulmonary artery stenosis, which was corrected with stents.

The treatment of DAH depends on the underlying etiology, and the principal regimen is corticosteroids and immunosuppressive agents [19, 20]. However, this treatment course is potentially harmful if the DAH has an infectious etiology [21].

Our case presented with bilateral diffuse alveolar shadows with a crazy-paving pattern without any evidence of cavities and bronchiectasis. The atypical radiological findings in our case were misleading, so the diagnosis was delayed, but at the same time, it could be a good reference for future case discussion of atypical syndromes of Pulmonary TB. In the context of a negative sputum AFB smear, the scenario favored a DAH diagnosis. The patient also showed partial improvement with steroid therapy and after the withdrawal of antithrombotic agents. The follow-up sputum AFB culture was the clue for the diagnosis of pulmonary TB, and upon commencing the appropriate therapy, he did not deteriorate further.

CONCLUSION

Localized pulmonary hemorrhage or hemoptysis is not uncommon in pulmonary TB; however, DAH with initially negative sputum AFB smears is rarely reported in the literature. Our patient's diagnosis was challenging because of the negative sputum AFB smears, history of antithrombotic therapy, initial positive responses to steroid therapy and the withdrawal of antithrombotic agents.

Atypical syndrome of TB presented as diffuse alveolar...
hemorrhage is not common, but a patient from a high endemic TB area presenting with DAH of unknown etiology needs careful monitoring and work up for the TB diagnosis.

We advocate for pulmonary TB being considered an important differential diagnosis for DAH unless proven otherwise, to avoid delayed treatment and unnecessary complications.

**LIST OF ABBREVIATIONS**

- PTB = Pulmonary Tuberculosis
- DAH = Diffuse Alveolar Hemorrhage
- AFB = Acid Fast Bacilli
- ATT = Anti-Tubercular Therapy
- MDR = Multi-Drug Resistant
- SLE = Systemic Lupus Erythematosus
- LAM = Lymphangioleiomyomatosis

**ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

The ethical approval was taken from the ethical committee of Burjeel Hospital, Najda street, Abu Dhabi, UAE.

**HUMAN AND ANIMAL RIGHTS**

Not applicable.

**STANDARDS OF REPORTING**

CARE guidelines have been followed for this case report.

**CONSENT FOR PUBLICATION**

The patient gave written consent to publish their case in a medical journal.

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**CONFLICT OF INTEREST**

The authors declare no conflict of interest, financial or otherwise.

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Declared none.

**REFERENCES**