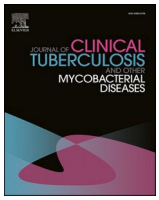
Journal of Clinical Tuberculosis and Other Mycobacterial Diseases 33 (2023) 100396

Contents lists available at ScienceDirect

Journal of Clinical Tuberculosis and Other Mycobacterial Diseases

journal homepage: www.elsevier.com/locate/jctube



Case Report

Pulmonary tuberculosis complicated by pneumothorax, and acute respiratory distress syndrome (ARDS) in the settings of advanced HIV disease: A case report

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ARTICLE INFO

Keywords:
Advanced HIV disease
Ethiopia
Spontaneous pneumothorax
Septic shock
TB related ARDS

ABSTRACT

Introduction: A large proportion of the global burden of HIV-associated TB occurs in sub-Saharan Africa; including 74% of new cases of TB and 79% of deaths occurs in this area. Spontaneous pneumothorax occurs more frequently in patients with AIDS than the general population with the estimated incidence to be about 2–5% of overall total cases. Tuberculosis ARDS and septic shock are rare but carries extremely poor prognosis.

Case summary: A 27 year old male with advanced HIV disease with very low CD4 count presented to Wolaita Sodo University comprehensive specialized hospital, Ethiopia on July 6, 2023. The patient diagnosed with spontaneous pneumothorax secondary to drug susceptible tuberculosis after positive urine LF-LAM and sputum gene expert. He was intubated after emergency tube thoracostomy, and subsequently treated with anti-TB, corticosteroid, broad-spectrum IV antibiotics and high dose cotrimoxazole. The patient developed ARDS due to possible tuberculosis related septic shock and died of multi-organ failure.

Discussion: Spontaneous pneumothorax in the setting of HIV raises concern for PCP, though in this case it could be secondary to TB. Tuberculosis related ARDS and septic shock are rare complication but carries poor prognosis especially in setting of AHD. We had limited experience and difficulties in the management of patient with persistent pneumothorax with the concomitant ARDS requiring lung protective management, and this part remain the future area of scientific research.

Conclusion: In patients with advanced HIV disease, who present with signs of respiratory failure, the likelihood of spontaneous pneumothorax, TB-ARDS and septic shock should be anticipated in the differential diagnosis and optimal management plan should be designed.

1. Introduction

The World Health Organization (WHO), estimated 9.9 million new Tuberculosis (TB) cases in 2020, 8 percent of whom were people living with HIV [1]. The WHO defines Advanced HIV disease (AHD) in adults, adolescents, and children older than five years as having a CD4 cell count <200 cells/mm. or stage 3 or 4, including both ART naïve individuals and those who interrupt treatment and return to care; all children younger than five years with HIV are considered as having AHD [2]. Among stage 3 or 4 defining opportunistic infections, undiagnosed TB is the commonest cause (up to 27%) of mortality of all acquired immunodeficiency syndrome (AIDS) related deaths globally [3]. A large proportion of the global burden of HIV-associated TB occurs in sub-Saharan Africa including 74% of new cases of TB and 79% of deaths occurs in this area [4]. According to the cross-sectional study conducted on Eastern Ethiopia, a significantly higher proportion of bacteriologically confirmed pulmonary TB patients (42%) were HIV co-infected [5]. A systematic review and meta-analysis in Ethiopia indicated that the odds of getting incident TB was 2.88 for patients with AHD with CD4 count of <200cells/dl as compared to patients with baseline CD4 cell count of greater than 200 cells/dl [6,7].

More importantly, patients with AHD are vulnerable to develop complicated TB than any other population. They are particularly prone to develop pneumothorax from several causes like sever necrotizing bacterial pneumonia, TB, Pneumocystis jiroveci pneumonia (PJP) and fungal infections [7]. Spontaneous pneumothorax occurs 450 times

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https://doi.org/10.1016/j.jctube.2023.100396

Available online 4 September 2023

more frequently in patients with AIDS than the general population [8]; with the estimated incidence to be about 2–5% of overall total cases [9]. Patients with HIV can also be at risk for iatrogenic pneumothorax as well as pneumothorax due to the presence of pneumatoceles (typically from old Staphylococcal or PJP infection [7,10]. Among ART naïve patients, the most common cause of bilateral pneumothorax was PJP (62.5%) whereas unilateral SP was most commonly associated with bacterial pneumonia (40.2%) [7].

Acute respiratory distress syndrome (ARDS) requiring mechanical ventilation as a presentation of TB is rarely reported in TB patients. Mortality rates range between 47 and 80 percent. Patients with Milliary or disseminated TB were significantly more likely to develop respiratory failure requiring mechanical ventilation despite the availability of effective antituberculous therapy [11]. Furthermore, TB can cause ARDS from sepsis and septic shock that behaves similarly to bacterial septic shock. Compared with patients with septic shock due to other pathogens, patients with septic shock due to TB have lower mean BMI (22 vs. 27), lower mean WBC (10.4 vs. 16.2), more often HIV infected (15 vs. 3%) and extremely high hospital mortality rate reaching to 79% [12].

Although WHO reports of 2020 [13], shows that the global treatment success rate of new cases of TB was as high as 85%, presentation to an ICU setting with multiorgan failure can carry an extremely poor prognosis. Delayed diagnosis and treatment initiation due to lack of recognition in low income countries are some of the chief contributors to this mortality. In ART naïve patients presenting with respiratory failure requiring mechanical ventilation, the differential diagnosis can range from fungal infections to community acquired bacterial infections, tuberculosis and secondary pneumothorax. Therefore, the novelty of this case presentation is that it describes the clinical prognosis and progression of a patient with HIV-associated tuberculosis TB complicated by both pneumothorax and ARDS. It also illustrates the rapid deterioration in a patient with undiagnosed HIV and TB, demonstrating that all the three conditions may present to the healthcare for the first time at once, and can be challenging to manage especially in resource limited setups like Ethiopia. Following the case, we also discuss the prognosis and current ICU management and challenges in identifying and managing a critically ill TB patient.

2. Case summary

This a 27 year old male patient presented to emergency unit of Wolaita Sodo University comprehensive specialized hospital, Ethiopia on July 6, 2023 with the complaint sudden onset of exacerbations of shortness of breath of 2hrs duration. He had shortness of breath, high grade fever and pleuritic chest pain for 1 week duration. The patient had the complaint of non-productive cough, appetite loss, drenching night sweats, weight loss, and easy fatigability for 1 month duration. He had sought treatment from local primary hospital 1 week prior to this presentation and treated for community acquired pneumonia. No history of smoking cigarette, and drinking alcohol. No history of significant past medical or surgical illness. His HIV test was turned positive in our hospital.

On presentation the patient was tachypnoeic and tachycardic, with a respiratory rate of 46 bpm, a heart rate of 168 bpm, and a temperature of 37˚C. His oxygen saturation was 60% on facemask oxygen at 15 L/min with a blood pressure of 110/82 mmHg. Crepitations were heard throughout left lung fields and there was no air entry on the right lung field. Hyper-resonant percussion note is heard on the right lung field. The remainder of the physical exam was normal with the patient noted to be alert and oriented. Urgent PA chest x-ray was taken and that showed right side pneumothorax and left lung multifocal pneumonic consolidation as depicted in the Fig. 1 below.

Laboratory results at this time were significant for leukocytosis with the (WBC, 25.4 × 109/L) with left shift and a normal platelet count and red blood cell count. Serum createnin and electrolytes were grossly normal. An HIV rapid test was performed, which was subsequently

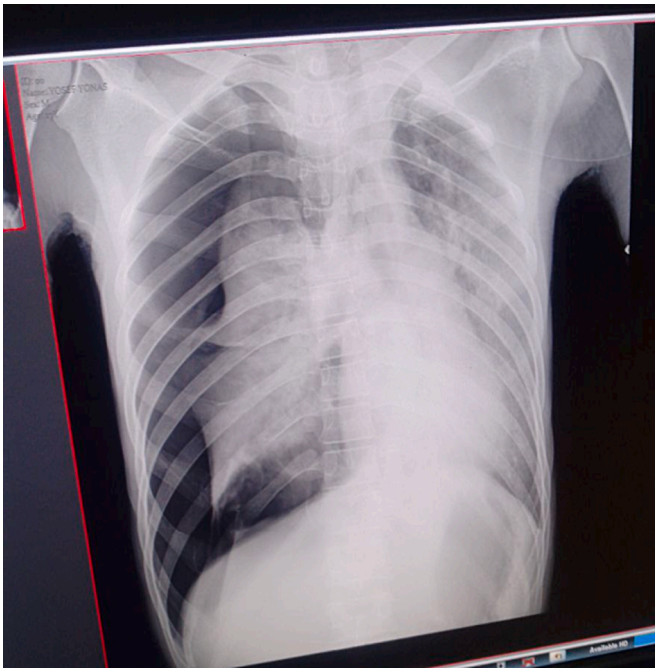

Fig. 1. Initial PA CXR: Right side pneumothorax and left side multifocal pneumonic consolidation.

reported as positive [Determine and UNIGOLD]. Mycobacterium Tuberculous (MTB) was detected on Urine LF-LAM (lateral flow urine lipoarabinomannan assay) and drug susceptibility was confirmed by sputum gene-expert. His CD4 count was very low (14 cells/mm^3) and LDH was 862 U/L. Differential diagnoses at this time included pneumocystis pneumonia, bacterial pneumonia, and tuberculosis as cause of hypoxemia and pneumothorax.

An emergency right side chest tube was inserted using a 28FG sized chest tube and gush of air was removed. He was started on broad-spectrum IV antibiotics consisting vancomycine 1 g IV bid, and ceftazidime 2 g IV TID. Anti-TB, therapeutic dose cotrimoxazole 1920 mg po bid and prednisolone were initiated 40 mg po bid. The patient continued to deteriorate despite above management. Then, he was transferred to ICU, intubated, and placed on mechanical ventilation. The patient was ventilated using a lung protective approach with a tidal volume of 330 ml (6 ml/kg), PEEP 6 and Fio2 100 pecent.

The patient continued persistent pyrexia, increased work of breathing, tachypnea and tachycardia. His oxygen demand was high until 4th day in the ICU. We escalated his PEEP to 10 and Fio2 100pecent was maintained. He had adequate urine output and kidney function was within normal range. On admission day 6, his urine amount significantly decreased (only 612 ml/24 h), and his createnin become 4 mg/dl. The patient was noted to be hypotensive with MAP <60 mmHg and persistently pyretic. Multiple crystalloid fluid boluses were given and a noradrenaline infusion was started.

As his condition continued to deteriorate, the noradrenaline dose increased to a max of 50ug/min and with added dopamine (started with 10 mg/kg/min escalated to 40 mg/kg/min). Hours later he developed refractory hypotension and despite two different vasopressors. Repeated Chest x-ray (Fig. 2) on the 6th day indicated as chest tube was in situ with bilateral extensive multifocal pneumonic consolidation.

He became pulseless shortly afterwards and advanced cardiac life support (ACLS) protocol was initiated. The patient remained in asystole throughout the arrest. Unfortunately, we were unable to achieve return of spontaneous circulation (ROSC) and the patient expired.

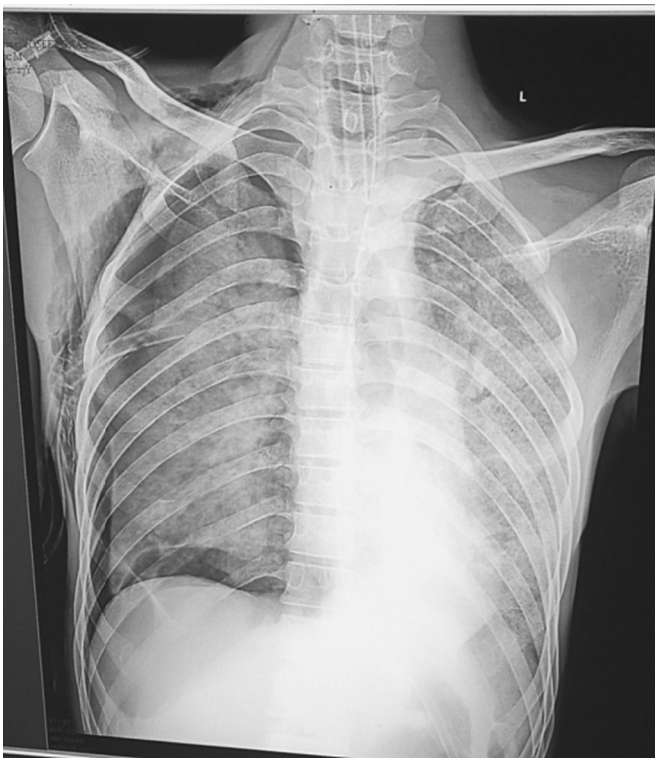

Fig. 2. Second CXR that show right side minimal pneumothorax, subcutaneous emphysema and bilateral multifocal consolidation.

3. Discussion

Spontaneous pneumothorax in the setting of HIV raises concern for PCP, though in this case it could be secondary to TB [14,15] or bacterial pneumonia [16]. In the era of antiretroviral therapy (ART), the frequency of pneumothorax complicating PCP is approximately 5 to 10 percent [17]. However this figure can be higher in ART naïve patient because of the fact that most cases occurring when the CD4 count drops below 200 cells/μL particularly a CD4 cell count percentage of <14 percent [18]. In places where diagnostic modalities are not available, the diagnosis of PCP is largely presumptive, putting together the symptoms, radiographic presentation, stage of HIV, ancillary laboratory features (e.g. LDH), and presence or absence of other etiologies. Empiric therapy for PCP should be initiated pending the results of the diagnostic evaluation if there is a high clinical suspicion for PCP (e.g., CD4 count <200 cells/μL, hypoxemia, interstitial infiltrates) [19].

Tuberculosis is the main cause of death in people living with HIV [20]. Previous studies on pulmonary TB in the ICU setting reported hospital mortality of 52.9%. Attributable factors include delay in diagnosis and ATT initiation, altered drug absorption in critically ill patients, comorbidities like HIV and TB related complications [21]. In TB/HIV co-infected patients, ICU related complications were also common, with nosocomial pneumonia in 67.2% patients, pneumothorax in 13.8%, ARDS in 12.1%, acute renal failure in 12.1% and multi-organ failure (MOF) in 3.4% [22]. The mortality for ARDS secondary due to TB has not changed significantly over time, despite advances in new treatment regimens and ventilatory strategies in ICU [11,21]. Canadian study found a significantly higher in-hospital mortality of 69% for patients requiring mechanical ventilation for TB in comparison to ARDS of any cause (56%) and nontuberculous pneumonia (36%) requiring mechanical ventilation [11].

It should be emphasized that advanced HIV disease has high morbidity and mortality especially when it get complicated by tuberculosis pneumothorax and ARDS and it is intuitive that individuals with HIV will be a significant proportion of the population with tuberculosis presenting in septic shock. A diagnosis of septic shock in this gentlemen was made after guideline directed fluid therapy was given [23]. The existing evidences and knowledge suggested that without prompt treatment, TB continues to spread both lymphatically and hematogenously causing a systemic response through activation of different inflammatory and proinflammatory mediators like cytokines, arachidonic acid and tumor necrosis factor-α (TNF-α) and activation of complement pathway [24,25]. In addition, the absence of bacterial growth in the standard blood and worse outcome despite timely initiation of appropriate antibiotics in our patient raises suspicion of TB immune reconstitution as a possible pathogenesis for TB septic shock.

We learnt that patients can present with all the three conditions simultaneously and their management become challenging. We had difficulty of using lung protective mechanical ventilation for the ARDS due to the secondary pneumothorax that persisted up to 4th day after the patient intubated. We also had limited experiences for managing HIV patients complicated with pulmonary tuberculosis-pneumothorax and ARDS all together at the same time.

4. Conclusion

Tuberculosis related ARDS and septic shock are rare complications of the disease but carries worst prognosis irrespective of advanced ICU care. And, in patients with advanced HIV disease who present with signs of respiratory failure, the likelihood of spontaneous pneumothorax should be anticipated in the differential diagnosis. Therefore, this case report highlights how in resource limited settings a diagnosis are made based on clinical judgment and underscores the need for better access diagnostics especially highly prevalent conditions like HIV, PJP, TB and associated conditions. This also calls for channeling further research in the field of diagnostics, and treatment among newly diagnosed HIV patients with very low CD4 cells and multiple opportunistic infections.

Informed consent

Consent to publish this case report was not obtained. The report does not contain any personal information that leads to the identification of the patient.

Funding

Not applicable.

Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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