Edelweiss Applied Science and Technology
ISSN: 2576-8484
Vol. 8, No. 6, 5082-5088
2024
Publisher: Learning Gate
DOI: 10.55214/25768484.v8i6.3114

An adolescent with disseminated tuberculosis with complicating bronchiectasis

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Abstract: Disseminated tuberculosis is a potentially fatal condition, and its identification is complicated due to its vague symptoms, together with the limited availability of testing options. Early detection is crucial for prompt diagnosis, as numerous reports indicate favorable responses to first-line anti-tuberculosis medications. Adolescence correlates with an elevated risk of developing tuberculosis, which is often infectious and can serve as a vector for transmission. This particular at-risk group frequently faces significant psychosocial obstacles and distinct issues regarding autonomy and treatment adherence. The case study focuses on an adolescent patient with disseminated tuberculosis complicated by bronchiectasis. It outlines the diagnostic process and treatment plan for a 17-year-old male who came to the pediatric department, primarily complaining of an unproductive cough lasting three weeks. The diagnosis was made based on clinical and radiologic findings. A considerable number of individuals may develop bronchiectasis as a complication of the illness, particularly in cases of pulmonary tuberculosis. These illnesses impose a substantial burden globally regarding morbidity, death, and financial impact on the affected populations. Both tuberculosis and bronchiectasis continue to be major public health concerns in developed and developing nations alike.

Keywords: *Adolescent, Bronchiectasis, Miliary tuberculosis, Tuberculosis.*

1. Introduction

Tuberculosis (TB) continues to be a significant cause of morbidity and mortality in children and adolescents [1,2]. A rare consequence of *Mycobacterium tuberculosis* infection, which is a disseminated TB, can result in severe complications, including meningitis, adrenal insufficiency, liver failure, pancreatic insufficiency, and enlarged spleen [3,4]. The symptoms of disseminated TB vary widely, often presenting as subacute or chronic systemic issues and diverse clinical manifestations [5,6]. Its identification is complicated due to its vague symptoms, and testing options are limited [7]. Adolescence correlates with an elevated risk of developing tuberculosis, which is often infectious and can serve as a vector for transmission. This particular at-risk group frequently faces significant psychosocial obstacles and distinct issues regarding autonomy and treatment adherence [8].

Annually, approximately 7.5 million children (0-14 years old) contract TB [9]. Tuberculosis claimed the lives of 183,000 children, 16% of the total deaths among human immunodeficiency virus (HIV)-negative people in 2022 [10], and 17% were estimated pediatric HIV infections deaths caused by TB worldwide [11]. In 2012, an estimated 721,000 adolescents (10-19 years old) developed TB [12]. The mortality rate for children with disseminated TB is roughly 15%-20%, often due to delayed diagnosis [4].

A considerable number of individuals may develop bronchiectasis as a complication of the illness, particularly in cases of pulmonary tuberculosis. These illnesses impose a substantial burden globally regarding morbidity, death, and financial impact on the affected populations. Both tuberculosis and bronchiectasis continue to be major public health concerns in developed and developing nations [13]. Bronchiectasis is marked by a productive cough that persists, an infection or inflammation in the lower

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airways, and abnormal bronchial dilation that can be seen on chest computed tomography (CT) scans. It is a heterogenous chronic lung disorder with multiple risk factors and etiologies [14,15]. Recent years have seen increased efforts to understand the airway inflammation associated with bronchiectasis [16]. Managing bronchiectasis requires a comprehensive strategy to alleviate symptoms, reduce exacerbations, preserve lung health, antibiotics, and methods for airway clearance [17]. The primary objectives of anti-tuberculosis treatment include curing the patient, preventing death from TB or its long-term effects, avoiding relapse, stopping the development and spread of drug-resistant TB, reducing TB transmission, and achieving these objectives with minimal toxicity [8]. The case report will likely focus on the unique challenges faced in diagnosing and treating disseminated tuberculosis in an adolescent patient, particularly given the non-specific symptoms and limited diagnostic tools available. It will likely emphasize the importance of early detection and appropriate management to prevent complications such as bronchiectasis, which can have long-term health implications.

2. Case Report

A teenage boy, aged 17, came to the pediatric department with a primary concern of a dry cough that had persisted for three weeks. The cough occurred spontaneously, without being provoked by allergens, physical activity, or environmental pollutants. The patient also reported experiencing fever for the same duration, particularly intense at night, with the peak temperature reaching 38.4 C. Night sweats were present. The patient did not exhibit a hoarse voice, difficulty breathing, chest discomfort, or heartburn. Additionally, he had been experiencing ear discharge for three weeks and had lost weight over the past month. There were no symptoms of nausea, vomiting, or diarrhea. The patient's vaccination record was complete, with a visible BCG vaccine scar on his right upper arm. His anthropometric measurement revealed moderate malnutrition.

Physical findings revealed fever and tachycardia. The examination noted anemia, absence of breathing difficulties, and no enlarged lymph nodes in the neck. Lung auscultation detected rhales in both lung fields. There was a perforated tympanic membrane with persistent drainage from the middle ear. Other physical examinations were within normal limits. Chest X-ray showed reticulonodular infiltrates in both lung fields, suggesting a miliary pattern, and localized consolidation in the left pulmonary hilum, suggesting a suspected bronchiectasis appearance. Laboratory tests yielded anemia, hypoalbuminemia, and an increase in C-reactive protein levels. The patient was hospitalized with preliminary diagnoses of miliary tuberculosis with suspected bronchiectasis, chronic suppurative otitis media, anemia, hypoalbuminemia, and moderate malnutrition.

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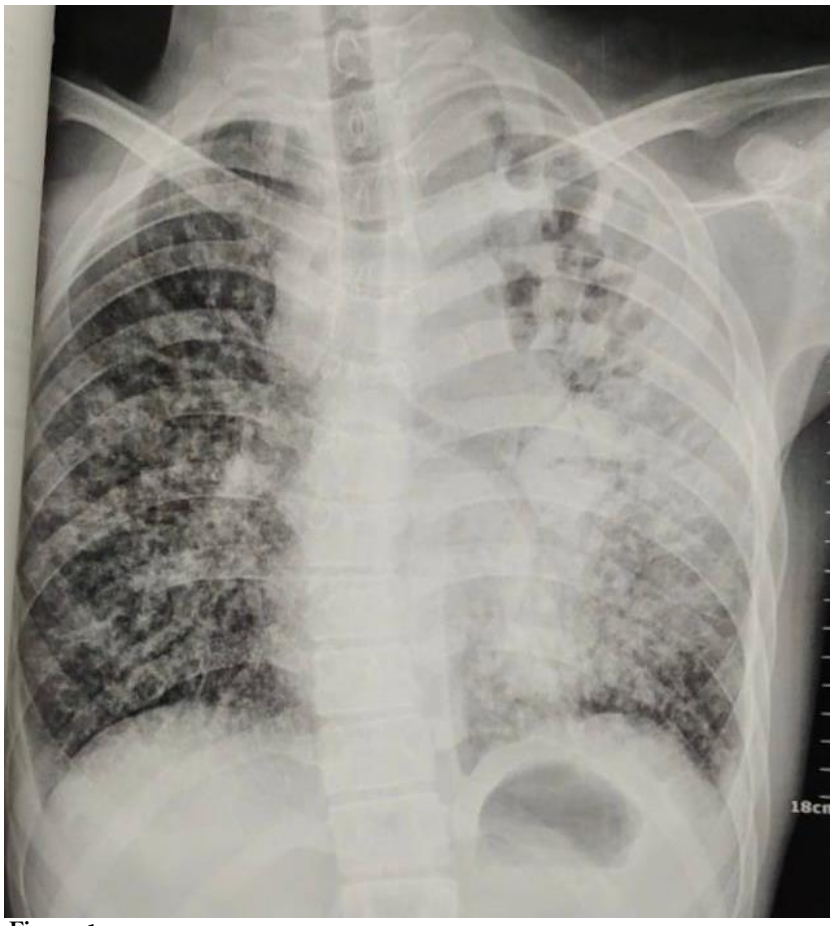

Figure 1.
The chest X-ray of the patient revealed a miliary pattern with a suspected bronchiectasis appearance.

Additional tests showed that the skin reaction to purified protein derivative tuberculin was anergic. The patient's transferrin saturation was 27%, indicating an iron deficiency anemia. The Xpert MTB/RIF analysis of the sputum sample detected medium levels of *Mycobacterium tuberculosis* and did not detect rifampicin resistance. Both sputum and ear discharge samples tested positive for acid-fast bacilli (AFB). The cerebrospinal fluid's Xpert MTB/RIF test yielded normal results.

A subsequent chest CT scan confirmed miliary TB with varicose bronchiectasis in the posterior bronchus of the left superior lobe and cylindric bronchiectasis in the superior lingula of the left superior lobe. Echocardiography revealed mild tricuspid valve regurgitation with a 66% ejection fraction. The diagnosis was determined to be disseminated tuberculosis with complicating bronchiectasis. Treatment began with standard fixed-dose combination (FDC) tablets containing four drugs of rifampicin-isoniazid-pyrazinamide-ethambutol (RHZE): R150/H75/Z400/E275. The initial phase lasted 2 months, followed by a 10-month continuation phase using two drugs of rifampicin-isoniazid (RH). The patient was also prescribed oral prednisone at 2 mg/kg/day, not exceeding 60 mg/day, for 4 weeks. After discharge, monthly evaluations were conducted in an outpatient setting.

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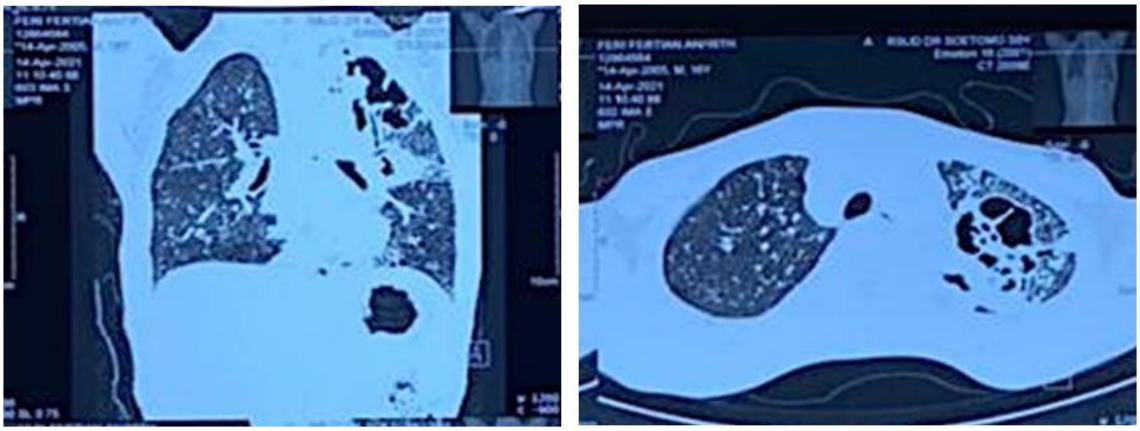

Figure 2.
A chest CT scan of the patient revealed miliary TB with varicose bronchiectasis in the posterior bronchus of the left superior lobe and cylindric bronchiectasis in the superior lingula of the left superior lobe.

3. Discussion

A teenage boy, aged 17, came to the pediatric department, reporting a persistent dry cough and fever lasting three weeks. This duration classified the cough as subacute (2-4 weeks), accompanied by an abnormal chest X-ray, leading to the implementation of assessing risk factors for bronchiectasis or recurrent pneumonia, aspiration, chronic or less common infections, interstitial lung disease, or cardiac problems. Echocardiography results showed mild tricuspid valve regurgitation with a 66% ejection fraction, ruling out pulmonary hypertension and cardiac edema, thus eliminating cardiac conditions as a probable cause. The patient's history lacked indicators of impaired consciousness, swallowing difficulties, or aspiration, excluding aspiration-related causes. For this patient, who was exhibiting a miliary pattern on a chest X-ray, additional tests were conducted. The purified protein derivative tuberculin skin test was anergic, but the Xpert MTB/RIF analysis of the sputum sample detected medium levels of *Mycobacterium tuberculosis*. Both sputum and ear discharge samples tested positive for AFB. However, the Xpert MTB/RIF test of cerebrospinal fluid showed normal results. From the result of the CT scan, the patient was then diagnosed with disseminated tuberculosis with complicating bronchiectasis.

Disseminated TB is a potentially fatal condition characterized by the involvement of two or more non-contiguous sites due to the hematogenous spread of *Mycobacterium tuberculosis*. Its clinical manifestation varies widely, commonly presenting with subacute or chronic systematic symptoms such as fever, weight loss, and night sweats. Presentations range from loss of appetite and fever of unknown origin to multi-organ failure, reflecting the affected organs [5,6]. Symptom duration before diagnosis can vary, with patients experiencing progressive symptoms over days, weeks, or occasionally months [5].

Blood abnormalities associated with disseminated TB include various types of anemia, pancytopenia, leukopenia (mainly lymphopenia), leukemic reaction, elevated erythrocyte sedimentation rate, disseminated intravascular coagulation, and infrequently, myelofibrosis [5,18]. The purified protein derivative tuberculin skin test is not diagnostically valuable, often yielding false negatives in confirmed disseminated TB cases [5]. Chest X-rays, being cost-effective and initial diagnostic tools, play a crucial role in early detection. The miliary pattern is observed in 90% of cases; however, it may be confused with other conditions, including histoplasmosis, sarcoidosis, pneumoconiosis, metastasis, bronchoalveolar carcinoma, and pulmonary siderosis [19,20]. Infrequent chest X-ray findings encompass consolidation, cavities, calcification, granulomas, and pleural effusion [5,19]. High-resolution CT scans can identify miliary nodules, ground-glass opacities, and interlobular septal thickening [19].

Identifying AFB through smear and culture of specimens is a valuable diagnostic method for disseminated TB, similar to other forms of TB. The AFB smear is a rapid, economical, and highly

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specific diagnostic method; however, its sensitivity differs among various specimens, and it is unable to detect drug-resistant strains [21,22]. Culture serves as the gold standard for diagnosis; however, traditional mycobacterial culture necessitates 4-6 weeks for results, whereas liquid culture requires a minimum of two weeks, potentially contributing to elevated mortality and morbidity [21-23]. Polymerase chain reaction-based nucleic acid amplification (NAA) tests provide a rapid diagnostic method for tuberculosis, enabling the detection of *Mycobacterium tuberculosis* complex in patient samples within two hours. The FDA-approved Xpert MTB/RIF test is an example of this type of NAA test, which can directly detect *Mycobacterium tuberculosis* complex from respiratory samples and give information on possible rifampicin resistance [22,24].

Bronchiectasis, a clinical syndrome characterized by irreversible bronchial dilation and destruction of bronchial wall components, presents with recurring lower airway infections and/or inflammation, productive cough, shortness of breath, occasional hemoptysis, and abnormal bronchial dilation visible on chest CT scans. Chronic airflow obstruction is also common [15]. This heterogeneous chronic pulmonary disorder has numerous risk factors and etiologies [14,15]. In many cases of bronchiectasis, the cause of pulmonary infections remains unknown, with some studies reporting over 50% of cases having no identified etiology. Conditions associated with this include cystic fibrosis, primary and secondary ciliary dyskinesia, immunodeficiency syndromes, and rheumatoid arthritis [13,17].

Managing bronchiectasis requires a multifaceted approach to address symptoms, minimize flare-ups, and maintain lung health. The cornerstone of treatment involves antibiotics and techniques for clearing airways, although pediatric guidelines are limited [17]. Antibiotic use, whether for acute episodes or as preventive measures, should be based on the severity of exacerbations, results from sputum or bronchoalveolar lavage cultures, and airway microbiology [17,25]. Due to TB being the etiology of the bronchiectasis, anti-tuberculosis treatment was administered to the patient. Anti-tuberculosis treatment includes isoniazid (7-15 mg/kg, maximum 300 mg/day), rifampicin (10-20 mg/kg, maximum 600 mg/day), pyrazinamide (30-40 mg/kg), and ethambutol (15-25 mg/kg). The regimen includes an initial phase lasting two months, succeeded by a continuation phase of four to ten weeks, irrespective of the type of TB [8]. Delayed diagnosis and treatment of sputum smear-positive pulmonary TB can result in ongoing transmission, especially to children, which may lead to latent TB or heightened mortality rates [26]. Another management of bronchiectasis is various airway clearance techniques, which are generally recommended for children, although evidence is limited. These methods include breathing exercises, drainage techniques, and physical activities. Mucolytic agents may be beneficial due to their ability to reduce mucus thickness, facilitating expectoration. For instance, recombinant human DNase works by breaking down DNA released by neutrophils at infection sites [17].

Research has shown that individuals with bronchiectasis often experience bronchial hyperresponsiveness and chronic airflow obstruction. Inhaled corticosteroid therapy may enhance inflammatory markers and clinical symptoms; however, elevated doses could heighten the risk of adverse effects. The combination of long-acting beta2-agonists and inhaled corticosteroids in a single device has shown a synergistic effect in decreasing bronchial inflammation [17]. Localized bronchiectasis with persistent symptoms and recurrent infections, despite optimal treatment, may warrant surgical interventions such as segmentectomy or lobectomy. Further research is necessary before endorsing surgery as a viable option for non-cystic fibrosis bronchiectasis. Contraindications for surgical resection may include non-cylindrical disease, persistent Pseudomonas infection, residual disease following resection, and non-localized disease [17,27,28].

Preventing bronchiectasis progression relies on accurate identification and treatment of underlying conditions. Improved drug therapies and early detection have reduced the need for surgical intervention. Most experts agree that aggressive drug treatment should precede surgical options [29]. Regular follow-up and monitoring are crucial for managing TB and bronchiectasis effectively. This includes periodic assessments of lung examination, sputum examination, and imaging studies to track disease progression and adjust treatment plans accordingly. Patient education plays a vital role in successful management, adherence to medication regimens, and lifestyle modifications to support overall lung health.

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4. Conclusions

Disseminated tuberculosis poses a significant threat to life, with diagnosis proving challenging due to its vague symptoms, together with the limited availability of testing options. A considerable number of individuals with pulmonary TB may subsequently develop bronchiectasis. Adolescence correlates with an elevated risk of developing tuberculosis, which is often infectious and can lead to transmission. This particular high-risk group faces unique challenges related to psychosocial factors, autonomy, treatment adherence, and the transition from pediatric to adult healthcare services.

Abbreviations:

TB- tuberculosis, HIV- human immunodeficiency virus, CT- computed tomography, C- celsius, BCG- Bacillus Calmette-Guérin, AFB- acid-fast bacilli, MTB- *Mycobacterium tuberculosis*, RIF- rifampicin, FDC- fixed-dose combination, RHZE- rifampicin-isoniazid-pyrazinamide-ethambutol, RH- rifampicin-isoniazid, mg- milligrams, kg- kilogram, NAA- nucleic acid amplification, FDA- Food and Drug Administration, DNase- deoxyribonuclease, DNA- deoxyribonucleic acid.

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Edelweiss Applied Science and Technology
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