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Comprehensive management for miliary tuberculosis associated with schizoaffective disorder in an adolescent female: A case report

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Abstract: Adolescents are vulnerable to tuberculosis (TB), some with severe forms like miliary TB, due to biological, psychosocial, and environmental factors. Schizoaffective disorder, though rare, adds complexity to TB management, requiring a multidisciplinary approach. This report aims to describe the comprehensive management of a 17-year-old female with miliary TB, anti-tuberculosis drug-induced hepatotoxicity (ADIH), and schizoaffective disorder, emphasizing the interplay between infectious disease and mental health. A 17-year-old female presented with shortness of breath, chronic cough, prolonged fever, and weight loss. Diagnosed with miliary TB via GeneXpert MTB/RIF testing and imaging, she was treated with first-line anti-tuberculosis drugs. On day 12, the patient developed ADIH, necessitating temporary discontinuation of particular anti-tuberculosis drugs and gradual reintroduction of therapy. Concurrent psychological evaluations revealed schizoaffective disorder, managed with psychiatric medication and counseling. Over 12 months, the patient exhibited clinical and psychological improvements, supported by family involvement and environmental adjustments. Integrated medical and psychosocial strategies are required in managing complex TB cases. Addressing comorbid mental health conditions and fostering a supportive environment is crucial for optimizing outcomes. The findings highlight the comprehensive management of complex TB and schizoaffective disorder using pharmacological and psychological therapy.

Keywords: *Adolescents, Management, Schizoaffective, Tuberculosis.*

1. Introduction

Tuberculosis (TB) is an infectious disease caused by Mycobacterium tuberculosis (Mtb). Most TB primarily affects the lungs. In certain cases, it may develop into more severe forms, such as miliary TB, which results from the hematogenous spread of tubercle bacilli to the lungs and other organs [1]. Adolescents are particularly vulnerable to TB due to hormonal changes, shifts in social contact patterns, and behavioral changes that impact their immune response [2] [3]. Adolescents with pulmonary TB can serve as sources of transmission, as they often present with adult-type TB and engage in high levels of social interaction [2]. Additional challenges in managing adolescent TB include psychosocial factors such as stigma, treatment non-compliance, cognitive impairments, depression, comorbidities like Human Immunodeficiency Virus (HIV) infection, and risky behaviors such as smoking, alcohol consumption, and drug use [4, 5]. Mental health issues, including depression and anxiety, are frequently observed among adolescents with TB [6]. Some patients report psychosis-like experiences linked to past trauma, substance use, or suicidal behaviors [7]. Adolescents with TB are particularly susceptible to

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psychosocial distress, stigma, and reduced quality of life, with depression and anxiety rates twice as high as in non-TB groups [1, 8].

Globally, approximately 1.8 million adolescents and young adults are diagnosed with TB annually, accounting for 20% of global cases [2, 9]. Tuberculosis is a significant public health concern in South Asia, contributing to a substantial portion of the global TB burden [10]. In 2022, Indonesia reported 38,720 TB cases among individuals aged 15–19 years [11]. At Dr. Soetomo General Academic Hospital, Surabaya, Indonesia, adolescents constituted 27% of 149 TB cases. Adolescent girls face increased TB risk beginning at menarche, peaking in mid-adolescence [12]. Miliary TB is relatively rare, with a prevalence of 1.3–3.3% among pediatric TB cases, predominantly in children under five [4]. Mortality rates for pediatric TB are significant, with 20.8% of deaths attributed to miliary TB [13]. Studies in Indonesia have shown that adolescents with TB are more vulnerable to mental and emotional disorders. The primary mental health issues associated with TB are anxiety and depression [14, 15]. Individuals diagnosed with TB report psychosocial distress, pain, stigma, reduced physical capacity, and poor quality of life even after completing TB treatment [16]. To date, there are no large-scale studies on the epidemiology, incidence, and prevalence of schizoaffective disorders. Research indicates that 30% of schizoaffective cases occur between the ages of 25-35 years, with a higher prevalence among women, estimated at approximately 0.3% [17].

Tuberculosis diagnosis in adolescents follows the general approach for TB, including history-taking, physical examination, and diagnostic investigations. A persistent cough lasting more than two weeks is a common symptom. Adolescents often present with varied clinical features due to the transition from childhood to adult-type TB. Chest radiography may reveal intrathoracic findings such as infiltrates, cavities, or miliary patterns [18]. Mental health assessments are crucial in adolescent TB care to address stigma and psychosocial impacts [19]. Treatment follows adult TB guidelines, with drug-sensitive miliary TB managed using a regimen of antituberculosis drugs extended up to 12 months [4, 20]. Psychosocial interventions have improved treatment adherence and mental health outcomes [21].

Adolescence represents a critical period of biological, cognitive, and social development, with long-term implications for physical and mental health [6]. Studies have provided evidence supporting that psychosocial factors can influence immunity to infectious diseases and vaccinations, although through highly heterogeneous pathways [22]. Holistic management of TB requires a multidisciplinary approach to optimize outcomes [14, 22]. Considering these factors, this case aims to describe the comprehensive medical and psychosocial management strategies employed in the care of a 17-year-old adolescent diagnosed with miliary TB and schizoaffective disorder, emphasizing the association between infectious disease and mental health.

2. Case Illustration

RT, a 17-year-old female, was referred from a general hospital to the emergency room of Dr. Soetomo General Academic Hospital, with the chief complaint of shortness of breath. The patient had a persistent cough for nearly a month, fever for two weeks, and worsening shortness of breath for a week. Her family reported significant night sweats and a weight loss of 5 kg over two weeks. Her condition deteriorated with severe shortness of breath two days before admission. Upon arrival, the patient was admitted to the infectious resuscitation room due to impending respiratory failure. The patient had no history of severe illness or hospitalizations before this episode.

Based on the patient's birth history, RT was delivered at full term through cesarean section with a birth weight of 3,300 g and a birth length of 50 cm. She experienced neonatal jaundice that resolved spontaneously by day 5. Developmental milestones were achieved appropriately. The patient was exclusively breastfed until two years of age, received appropriate complementary foods, and completed all immunizations according to the schedule. She is currently a senior high school student with regular menstrual cycles since she was 12 years old. RT is the youngest of three siblings, living with her parents and siblings. Family screening at a local health facility revealed no TB cases among household

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members. The family resides in a small, densely populated neighborhood, where the home lacks optimal ventilation and sunlight.

On initial examination, the patient was fully conscious with a Glasgow Coma Scale (GCS) score of 15. Vital signs were a blood pressure of 100/60 mmHg, a pulse rate of 112 beats per minute, a respiratory rate of 32 times per minute, a temperature of 38.6°C, and an oxygen saturation of 98% on a non-rebreathing mask delivering 15 L/min oxygen. She appeared severely ill, with nasal flaring but no cyanosis. There was no lymphadenopathy. Examination of the chest revealed symmetrical thoracic movement with subcostal retractions and fine crackles at both lung bases. Breath sounds were diminished in the right lower lung zone without wheezing. Cardiovascular, abdominal, and neurological examinations were normal, with Tanner stage A5M5P5. Anthropometric assessment showed weight at <p5 (40 kg), height at p10 (155 cm), and a body mass index of 16.6 kg/m² (<p5).

Laboratory tests revealed slightly elevated liver enzymes (AST 129 IU/L, ALT 59 IU/L), hypoalbuminemia (albumin 2.73 g/dL), hypocalcemia (corrected calcium 8.3 mg/dL), and compensated respiratory acidosis (pH 7.39, pCO_2 58 mmHg, HCO_3^- 35.1 mmol/L). The PF ratio was 172.5. A chest X-ray (CXR) indicated miliary tuberculosis with right pleural effusion (Figure 1). Rapid molecular diagnostic using GeneXpert MTB/RIF confirmed rifampicin-sensitive *Mtb*.

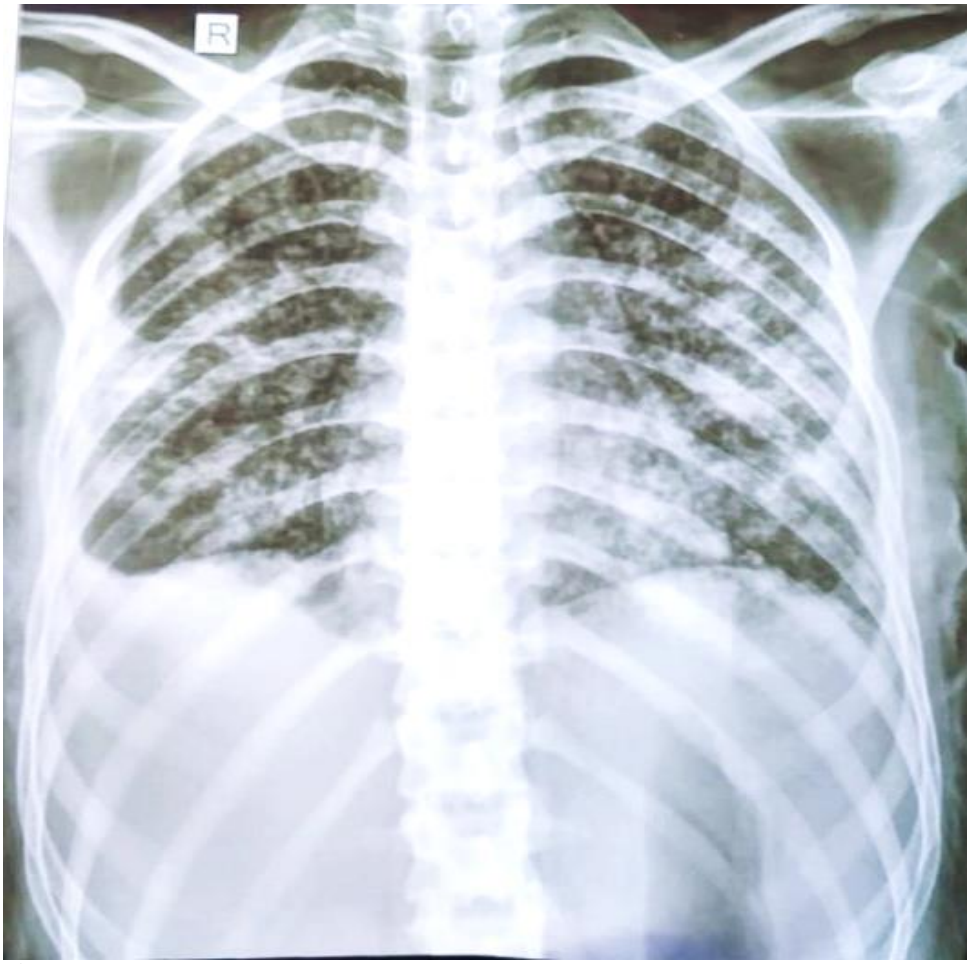

Figure 1.
Chest X-ray examination revealed miliary tuberculosis with right pleural effusion.

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The patient was managed with high-flow nasal cannula (HFNC), maintenance intravenous fluids, corticosteroids, and first-line anti-tuberculosis (anti-TB) drugs (isoniazid, rifampicin, pyrazinamide, and ethambutol). After two days in the infectious resuscitation unit, she was transferred to the high-care unit on 1 L/min nasal oxygen. The tuberculin skin test (TST) revealed no induration, HIV testing was non-reactive, and blood glucose and lumbar puncture results were normal. Subsequent blood gas analysis, serum electrolytes, and albumin evaluation were normalized.

On day 12 of hospitalization, the patient developed jaundice, with elevated liver enzymes (AST 119 IU/L, ALT 188 IU/L) and bilirubin (total bilirubin 5.1 mg/dL; direct bilirubin 3.1 mg/dL). Hepatitis screening was negative. Anti-tuberculosis drugs, except ethambutol, were temporarily discontinued. Symptoms and liver function normalized within three days (AST 33 IU/L, ALT 67 IU/L, bilirubin total 0.8 mg/dL). Rifampicin, isoniazid, and later pyrazinamide were reintroduced sequentially without recurrence of jaundice and increased liver enzymes. The patient was discharged after three weeks of hospitalization with an adult fixed-dose combination (FDC) and corticosteroid. A biweekly visit during the first 2 months was advised.

In the first month, the patient experienced mild nausea after taking anti-TB medications. She often avoids social interactions due to concerns about disease transmission, preferring to stay at home and engage in solitary activities such as reading, gaming, and watching videos. The school provides a supportive environment, allowing the patient to catch up on missed lessons after a month-long absence. However, psychological distress, including mild depression and anxiety, was noted. Psychological screening indicated a Beck Depression Inventory score of 8 (minimal depression) and a Beck Anxiety Inventory score of 15 (mild anxiety). The patient was referred to psychiatry, where she was diagnosed with adjustment disorder with depressive features and prescribed sertraline 50 mg daily. Anti-TB drugs were continued with tapering of corticosteroids. By the 2nd month, the patient reported reduced sadness about the illness but increased anxiety related to the upcoming national examination. The patient continued the prescribed medications with comprehensive education about the diagnosis and long-term treatment plans, along with psychological support. Evaluation after 2 months of anti-TB drugs showed a negative acid-fast bacilli (AFB) test and improvement on CXR (Figure 2); thus the anti-TB drug regimen was continued with FDC for the continuation phase.

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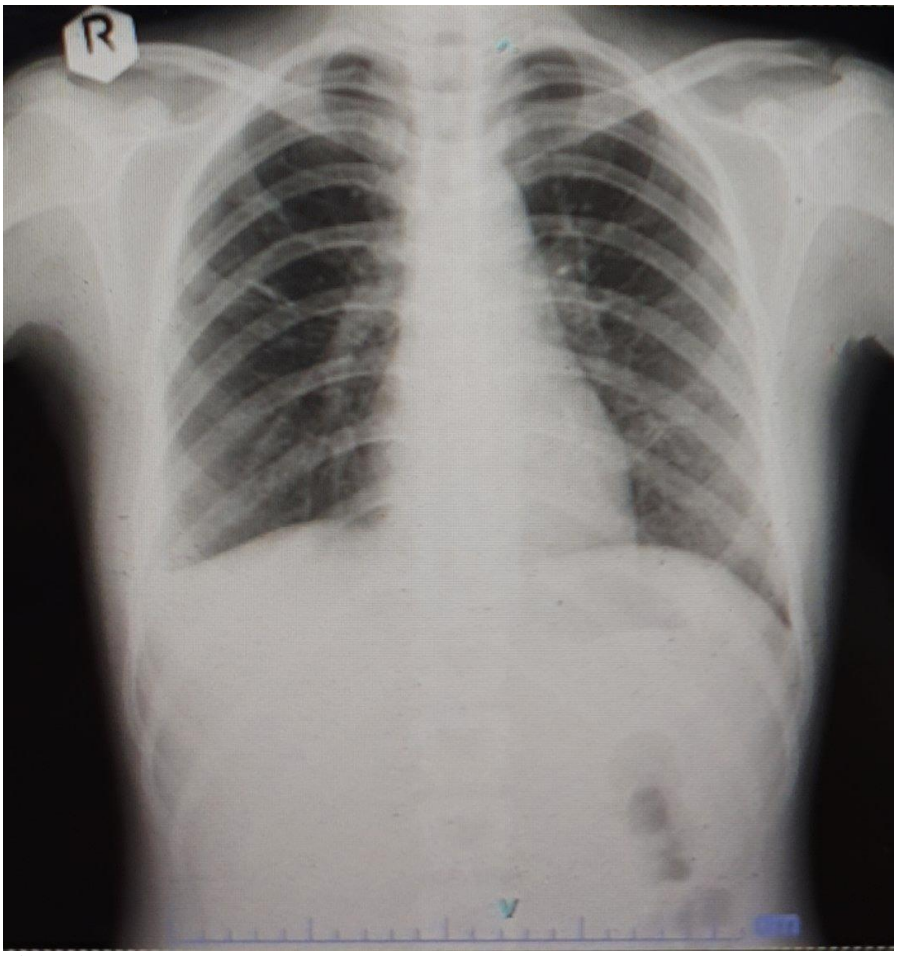

Figure 2.
Chest X-ray examination after 2 months of TB treatment showed significant improvement.

By the 3rd month, she reported worsening sadness after failing the university entrance test. The patient also experienced intermittent auditory hallucinations and feelings of being targeted by peers. These symptoms prompted reassessment at the psychiatry clinic, resulting in a diagnosis of schizoaffective disorder. Medication adjustments included the addition of lorazepam (1 mg qhs) and risperidone (1 mg qhs) alongside continued sertraline. Patient received enhanced non-pharmacological psychotherapy sessions.

By the 4th month, the psychological symptoms significantly improved with the medication adjustments. She no longer had auditory hallucinations. The patient actively participated in family activities, such as helping with an online bakery business. Clinical parameters were stable, and nausea was less frequent. Psychiatric medications were adjusted, with lorazepam as needed, sertraline 25 mg daily, and risperidone 1 mg daily. The patient reported better sleep even without taking lorazepam. This improvement continued through the 5th month, with the patient showing more positive emotions and greater participation in social activities. The patients continued further reduction in sertraline dosage to 12.5 mg daily along with continuation of risperidone. By the 6th month, the patient had improved psychological and clinical condition. She stated her desire to pursue future academic goals. Sertraline was discontinued, and other medications (risperidone and anti-TB drugs) were continued.

Throughout the remaining follow-up from the 7th-12th month, the patient had good physical and psychological conditions. The antipsychotic drug was tapered down monthly and eventually

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discontinued on the 10th month. During the 12 months of treatment and monitoring, the patient showed gradual improvement in both clinical and psychological aspects. Repeat AFB test and CXR after 12 months of anti-TB drugs revealed normal results.

3. Discussion

The patient is a 17-year-old adolescent who presented with the primary complaint of shortness of breath, which had progressively worsened over the past week, especially during the two days before hospitalization. The patient had been experiencing a cough for one month and developed a fever 2 weeks before admission. A significant weight loss occurred over the past two weeks. Studies showed that adolescents, particularly those aged 10-19 years, are considered at increased risk for tuberculosis, a disease more commonly seen in adults and capable of transmission to those around them. In Indonesia, 38,720 cases of pediatric TB were reported, with the majority occurring in those aged 15-19 years [4]. The vulnerability of adolescents to TB infection is thought to be related to hormonal changes, alterations in social behavior, and immune system alterations, as well as factors such as late-night activities, irregular eating habits, excessive physical activity, and emotional instability [2]. In females, the risk of TB increases after menarche, reaching its peak during mid-adolescence [12].

The clinical manifestations of TB in adolescents can vary due to the overlapping forms of the disease during this stage of life [19]. TB diagnosis, particularly pulmonary TB, is confirmed based on the patient's history, physical examination, and diagnostic tests [2]. Typical symptoms include a cough lasting more than 2 weeks, fever, weight loss, or malaise. In a study conducted in Brazil, 81% of TB cases in children and adolescents were pulmonary TB, with the most common symptoms being cough (38%), fever (31%), and shortness of breath (8%). A local study in Surabaya also found that the most frequent symptoms were cough (80%) and fever (72%) [11]. This patient presented with shortness of breath, a cough persisting for one month, and prolonged fever before hospitalization, suggesting pulmonary TB. Upon presentation, the patient exhibited significant respiratory distress despite receiving oxygen therapy via a non-rebreather mask at a flow rate of 15 liters per minute. The clinical findings included tachypnea with a respiratory rate of 32 breaths per minute and visible subcostal retractions, indicating severe respiratory compromise. Physical examination further revealed fine crackles and diminished breath sounds localized to the right lower lung field. Given the critical nature of the patient's condition and the signs of impending respiratory failure, immediate management was initiated, including oxygen supplementation via a high-flow nasal cannula (HFNC), administration of intravenous fluids, corticosteroids, and initiation of first-line anti-TB treatment.

The diagnostic workup provided crucial insights into the patient's condition. Laboratory findings indicated thrombocytopenia with a platelet count of 108,000/mcL and elevated liver enzymes <3 times upper limit normal (AST 129 IU/L, ALT 59 IU/L). Additionally, hypoalbuminemia (albumin 2.73 g/dL), hypocalcemia (serum calcium 7.7 mg/dL, corrected to 8.3 mg/dL), and evidence of compensated respiratory acidosis (pH 7.39, pCO2 58 mmHg, HCO3 35.1 mmol/L) were noted. The arterial blood gas analysis revealed a PF ratio of 172.5, indicative of moderate acute respiratory distress syndrome (ARDS). A sputum GeneXpert MTB/RIF test confirmed the presence of Mtb sensitive to rifampicin, establishing the diagnosis of TB. Chest radiography demonstrated a miliary pattern along with right-sided pleural effusion, which was consistent with the diagnosis of miliary TB. These findings underscored the severity of the systemic and respiratory involvement, necessitating a multidisciplinary approach to treatment and close monitoring.

Miliary TB is caused by the hematogenous and lymphatic dissemination of Mtb, affecting various organs, and accounts for 3-7% of total TB cases [23]. The prevalence of miliary TB among all pediatric TB cases ranges from 1.3% to 3.3%, primarily in young children. Miliary TB is often classified as pulmonary TB but can manifest extra-pulmonary signs, making it essential to evaluate for possible TB meningitis, especially in children under two years old, even in the absence of neurological symptoms. This patient did not show neurological deficits, and lumbar puncture was negative for TB meningitis. Although the general symptoms of TB are often non-specific, delayed diagnosis is common, and chest

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radiographs showing a miliary pattern are crucial for diagnosis [1, 4]. Tuberculin skin testing is often anergic in miliary TB compared to other forms of TB [24]. This patient also showed no induration on TST, despite receiving BCG vaccination, with a scar observed on the right shoulder. Studies indicate that BCG vaccination provides some protection against miliary TB, but the duration of this protection is not well documented [25, 26].

The treatment regimen for miliary TB depends on the severity of the disease, the patient's age, and the disease type. The recommended regimen for miliary TB with drug-susceptible strains is 2HRZE (2 months) followed by 10HR [20, 27]. Corticosteroids are used in TB with complications such as TB meningitis, obstructed airways from TB lymphadenitis, or pericarditis. In severe cases, prednisone is administered at doses of 2-4 mg/kg/day for up to 60 mg/day for 4 weeks, followed by gradual tapering over 2-4 weeks. Alternatively, dexamethasone can be used at 0.3-0.6 mg/kg/day with a similar tapering schedule [27]. This patient was given the standard adult TB regimen (4 tablets/day) along with prednisone at 20 mg three times a day, with plans to taper after one month of treatment according to guidelines.

Monitoring is crucial during anti-TB therapy, particularly for anti-tuberculosis drug-induced hepatotoxicity (ADIH). Rifampicin, isoniazid, and pyrazinamide are known to cause hepatotoxicity. Symptoms of liver dysfunction include nausea, vomiting, anorexia, jaundice, and hepatomegaly. The criteria for diagnosing ADIH include AST/ALT levels ≥5 times the normal limit without symptoms, or ≥3 times the normal limit with symptoms, or any increase in serum AST and/or ALT level above pretreatment values together with anorexia, nausea, vomiting, and jaundice, or total bilirubin level >1.5 mg/dL [27, 28]. In this case, the patient developed jaundice on day 12 of treatment, with laboratory results showing elevated liver enzymes and bilirubin (total bilirubin 5.1 mg/dL, direct bilirubin 3.1 mg/dL, AST 119 IU/L, ALT 188 IU/L). Rifampicin, isoniazid, and pyrazinamide were temporarily stopped. Ethambutol, a liver-friendly drug, was continued considering her severe form of TB. After 3 days, the jaundice resolved, and liver function normalized. Rifampicin and isoniazid were then reintroduced, followed by pyrazinamide.

Factors contributing to the development of miliary TB in this patient include both individual and environmental risk factors. The patient lives in a densely populated area with inadequate ventilation and lighting and malnutrition, a significant risk factor for TB, likely compromised immune function, making the patient more susceptible to infection [23]. The family has been educated on maintaining a healthy home environment according to Ministry of Health guidelines. Screening for close contacts within the household was performed, with results showing no TB members with TB. Adolescents with TB, especially infectious forms, are more likely to transmit the disease in their community due to their high mobility and broad social interactions. Studies suggest that household and school contact investigations should be prioritized [27, 29]. This patient returned to school after one month, consistently wearing a mask to minimize transmission risk.

Routine monitoring of patients on anti-TB treatment includes assessing symptom improvement, weight gain, side effects, medication adherence, and sputum examination for acid-fast bacilli (AFB) at two months and at the end of treatment. This patient showed clinical improvement with resolution of symptoms and weight gain after two months. Chest radiographs taken during follow-up showed signs of recovery, with plans for further evaluation at the 12-month mark.

Growth and development may be impaired in TB patients due to the chronic nature of the disease and late diagnosis. Malnutrition, which impairs cellular immune responses, increases susceptibility to TB, and weight gain is often used as an indicator of treatment success [30]. Children and adolescents with TB are particularly vulnerable to malnutrition, which exacerbates immune system deficiencies. In addition, TB can lead to further weight loss and muscle mass reduction due to decreased appetite and metabolic changes. The patient's nutritional status was closely monitored to ensure appropriate weight gain during treatment. The immunological status of adolescents, particularly during puberty, is linked to an increased risk of TB progression, with females being more susceptible to post-menarche [12].

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Therefore, ensuring adequate nutrition and immune function is essential in reducing the risk of TB progression and improving treatment outcomes.

The patient experienced anxiety and sadness shortly after starting TB treatment, driven by fears of mortality and doubts about recovery. These emotions disrupted her sleep and appetite. However, clinical improvements following anti-TB therapy led to a reduction in anxiety and sadness. The consultation to the Department of Psychiatry further alleviated her symptoms with medications and psychological support. By the 3rd month of treatment, the patient faced additional stressors, including long-term management of miliary TB and a personal setback—failing the university entrance test. During this time, she began hearing male voices without a visible source, which disrupted her sleep. She also believed that a friend was envious of her. Psychiatric reevaluation led to a diagnosis of schizoaffective disorder.

Schizoaffective disorder is reported in approximately 30% of cases between the ages of 25–35 years, with a higher prevalence in women at around 0.3% [16]. However, large-scale studies on the epidemiology, incidence, and prevalence of schizoaffective disorder remain limited. According to DSM-5 criteria, this disorder is characterized by an uninterrupted period of illness with major depressive episodes alongside symptoms meeting Criterion A for schizophrenia. Hallucinations or delusions must persist for at least two weeks in the absence of prominent mood symptoms. Additionally, mood episode symptoms should constitute a substantial portion of the active and residual phases of the illness, and the condition should not result from substance use or medical conditions [31].

Currently, no direct correlation has been established between TB or anti-TB drugs and schizoaffective disorder. However, neuropsychiatric side effects such as psychosis have been associated with certain antituberculosis drugs, particularly isoniazid and cycloserine. Baytunca et al. reported a case of isoniazid-induced psychosis with obsessive-compulsive features [32]. Isoniazid and cycloserine are the most commonly implicated antituberculosis drugs associated with neuropsychiatric adverse reactions, including psychosis [33]. In this patient, psychotic symptoms were also noted during middle school and resurfaced, triggered by the stress of the miliary TB itself and her academic failure. Extensive discussion between the teams regarding the mental health disruption during anti-TB treatment assumed the schizoaffective disorder's association with her miliary TB was still unclear. The possibility of drug-induced psychosis cannot be entirely ruled out, in which the team decided to continue the anti-TB drugs with the addition of psychiatric medications and psychological therapy. The idea of the illness and academic failure as the trigger to her mood and psychotic symptoms was also considered for the team's decision for holistic management.

The World Health Organization (WHO) advocates for patient-centered care to improve adherence by providing education, communication, and psychological support, particularly for adolescents undergoing TB treatment [34]. A systematic review by Farooq et al. highlighted the efficacy of psychosocial interventions in enhancing adherence and recovery rates in TB and drug-resistant TB and mental health outcomes [21]. The patient was managed with risperidone, sertraline, and lorazepam for her schizoaffective disorder, alongside psychological counseling. This comprehensive medical and psychosocial approach resulted in significant progress. She became consistent in her sleep and eating patterns and eventually secured employment. The patient expressed reduced fear about the future and developed concrete plans for it, marking a positive trajectory in her recovery journey.

4. Conclusion

This case highlights the challenges of managing miliary TB in adolescents with schizoaffective disorder. The long-term treatment required a holistic evaluation to ensure early identification of any problems encountered during therapy. Early identification enables proper management, thus leading to better outcomes. The patient's condition improved significantly with close monitoring, highlighting the importance of a multidisciplinary approach in managing complex cases of adolescent TB.

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Institutional Review Board Statement:
This study has been approved by the parents as the patient's guardian through written informed consent.

Conflict of Interest:
The authors declare that there is no conflict of interest regarding the publication of this manuscript.

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Transparency:
The authors confirm that the manuscript is an honest, accurate, and transparent account of the study; that no vital features of the study have been omitted; and that any discrepancies from the study as planned have been explained. This study followed all ethical practices during writing.

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Authors' Contributions:
All authors contributed to the diagnosis and management of the patient. All authors have read and agreed to the published version of the manuscript.

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