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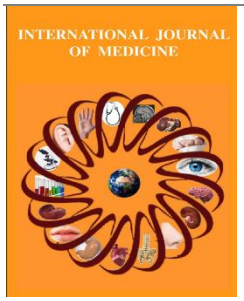

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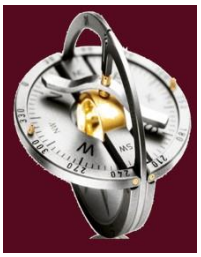

Review Article

Chronic Cavitary Pulmonary Aspergillosis Masquerading as Recurrent Tuberculosis: A Case Series from a Tertiary Care Hospital in Sikandrabad.

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Abstract

Background: Chronic Cavitary Pulmonary Aspergillosis (CCPA) is a progressive lung disease that commonly develops in patients with prior pulmonary tuberculosis. Because its symptoms closely resemble recurrent or smear-negative TB, CCPA is frequently misdiagnosed in resource-limited settings, leading to repeated ineffective anti-tuberculosis treatment and delayed antifungal therapy. ***Case Series Overview***: We report a series of patients with long-standing respiratory symptoms, progressive cavitary lung disease, and a prior history of treated tuberculosis, who were incorrectly managed as recurrent TB before presenting to our tertiary care centre in Sikandrabad. All patients had worsening cough, hemoptysis, fever, weight loss, and dyspnea over several months. Radiology showed evolving thick-walled cavities with intracavitary fungal balls and pericavitary infiltrates. Aspergillus IgG was positive in each case, confirming the diagnosis of CCPA. ***Management and Outcomes***: Patients were initiated on oral voriconazole with appropriate dose adjustments and monitoring. Symptomatic improvement was noted within weeks of therapy, and follow-up demonstrated stabilization of cavities and reduction in hemoptysis. ***Conclusion***: CCPA is frequently mistaken for recurrent TB in post-tuberculosis patients, especially where advanced diagnostics are limited. Early consideration of fungal etiology, timely CT imaging, and Aspergillus IgG testing are crucial to avoid misdiagnosis. Prompt antifungal therapy significantly improves outcomes and prevents progressive lung destruction.

Keywords: Chronic pulmonary aspergillosis; CCPA; post-tuberculosis sequelae; aspergilloma; recurrent TB mimic; voriconazole therapy.

Introduction:

Chronic Cavitary Pulmonary Aspergillosis (CCPA) is a slowly progressive, destructive fungal infection of the lung caused primarily by Aspergillus fumigatus, occurring most commonly in individuals with pre-existing structural lung disease [1]. Globally, the most important underlying condition associated with CCPA is healed or partially healed pulmonary tuberculosis, which leaves behind fibrotic cavities that create an ideal environment for fungal colonization and growth [2]. Because India accounts for the world's highest tuberculosis burden, the country consequently faces a substantial but under-recognized burden of CCPA.

Clinically, CCPA closely mimics recurrent or smear-negative pulmonary tuberculosis, with patients presenting with chronic cough, hemoptysis, weight loss, fever, and progressive dyspnea—symptoms that frequently lead clinicians to initiate or repeat anti-tubercular therapy, especially in peripheral settings [3]. Studies have shown that 15–20% of patients labeled as recurrent TB may actually have underlying chronic pulmonary aspergillosis rather than active mycobacterial infection [4]. This misdiagnosis results in delayed initiation of antifungal therapy, progressive lung destruction, and increased morbidity and mortality.

Diagnostic challenges are amplified in low-resource environments where access to advanced imaging and fungal serology is limited. Routine chest radiographs may not reliably distinguish healed TB cavities from CCPA, as both may present with chronic cavitary lesions [5]. High-resolution computed tomography (HRCT) plays a crucial role, revealing characteristic findings such as thick-walled cavities, intracavitary fungal balls (aspergilloma), and pericavitary infiltrates [6]. Serum Aspergillus-specific IgG antibody testing is the most sensitive non-invasive diagnostic tool for chronic aspergillosis and is considered the serological gold standard [7].

If untreated, CCPA is associated with significant morbidity and a 5-year mortality rate exceeding 50%, underscoring the need for timely diagnosis and therapeutic intervention [8]. Early initiation of long-term antifungal therapy—most commonly with itraconazole or voriconazole—improves symptoms, stabilizes cavitations, and reduces hemoptysis, thereby altering disease trajectory [9]. However, limited awareness among clinicians, together with inadequate diagnostic capacity in rural and semi-urban healthcare settings, often results in prolonged misdiagnosis as tuberculosis.

This case series highlights patients with progressive cavitary lung disease who were repeatedly treated for suspected tuberculosis before being correctly diagnosed with CCPA at a tertiary care hospital in Sikandrabad. Through detailed clinical, radiological, and serological evaluation, the report underscores the importance of maintaining a high index of suspicion for CCPA in post-tuberculosis patients with persistent or worsening respiratory symptoms

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Case 1

A 60-year-old male presented to the outpatient department with a 7–8-month history of intermittent fever, progressive dyspnea, significant weight loss, and worsening hemoptysis. He had been treated for pulmonary tuberculosis two years earlier with a 6-month regimen (2HRZE/4HR). He had no history of smoking, alcohol use, or other comorbidities.

Over the preceding months, the patient had been receiving anti-tubercular therapy (ATT) empirically from a local practitioner due to persistent symptoms, but his condition continued to worsen. On presentation, his vital signs showed a blood pressure of 140/90 mmHg, pulse 75 bpm,

respiratory rate 25/min, temperature 100°F, and oxygen saturation of 92% on room air. Chest auscultation revealed bilateral reduced air entry; heart sounds were normal.

Laboratory evaluation revealed leukocytosis (WBC 18.2 ×10³/µL) with neutrophilia, anemia (Hb 10.9 g/dL), and ESR of 90 mm/hr. Platelet count was 322 ×10³/µL. Renal function tests were normal, while liver function tests showed hyperbilirubinemia and elevated SGOT/SGPT. Hepatitis C serology was positive. Arterial blood gas analysis indicated uncompensated respiratory alkalosis. The patient tested negative for HIV and had no history of immunosuppressive therapy.

Comparison of current and prior chest radiographs revealed progression from poorly defined bilateral cavitations to multiple thick-walled cavities with dense pericavitary infiltrates. HRCT confirmed these findings, showing a static right-sided cavitary lesion with an intracavitary soft-tissue mass suggestive of aspergilloma, along with confluence of multiple adjacent cavities.

Given the radiological pattern and chronicity, fungal investigations were pursued. Serum Aspergillus IgG returned positive, confirming the diagnosis of Chronic Cavitary Pulmonary Aspergillosis (CCPA) in the context of post-tuberculosis lung disease.

The patient was initiated on voriconazole (150 mg BID on Day 1 followed by 100 mg BID), along with supportive measures. Over the subsequent week, the patient showed clinical improvement with reduction in fever, dyspnea, and hemoptysis. He was discharged on oral therapy with instructions for regular follow-up and liver function monitoring, and was advised review after 2 weeks.

Figure 1. High-Resolution CT Thorax Showing Multiple Thick-Walled Cavitary Lesions with Intracavitary Soft-Tissue Mass and Pericavitary Infiltrates Suggestive of Chronic Cavitary Pulmonary Aspergillosis

I.

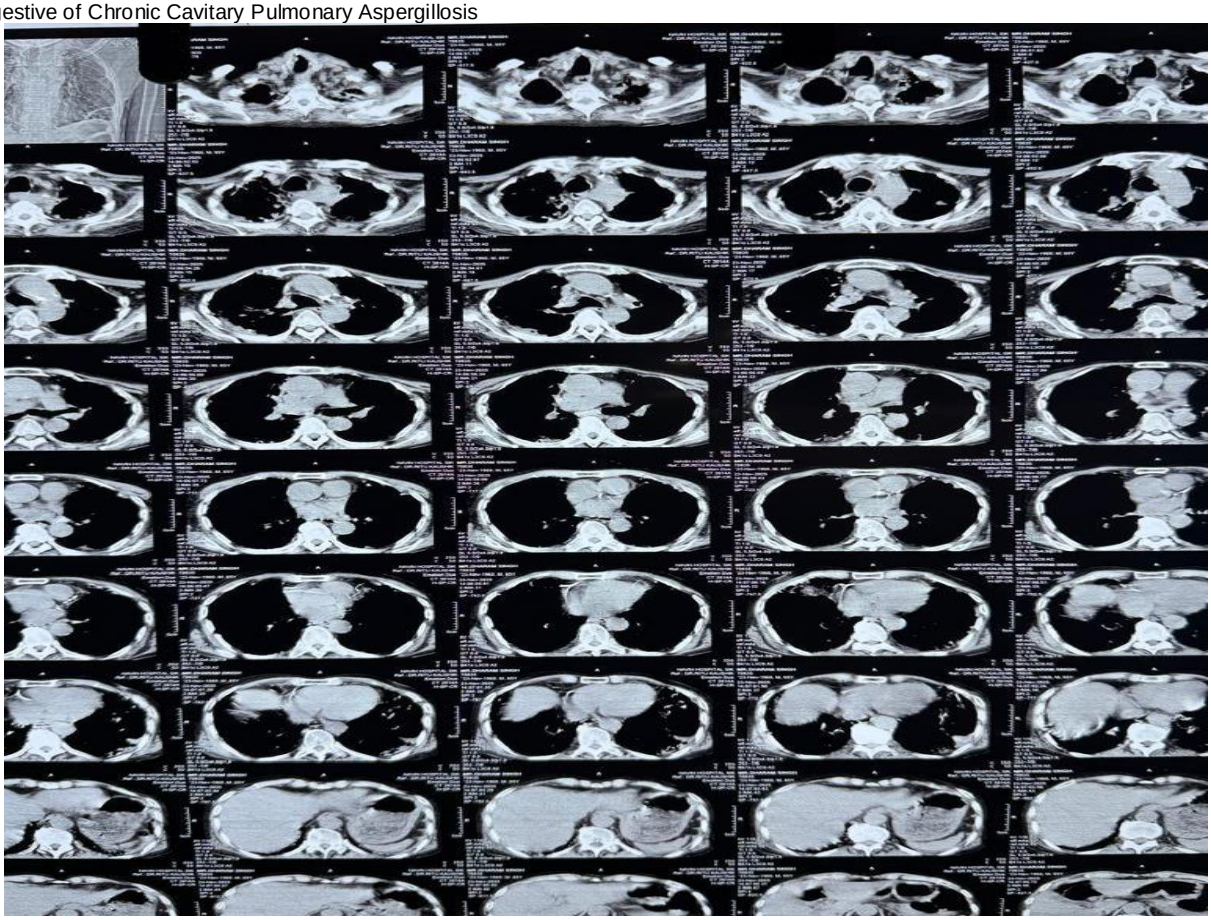
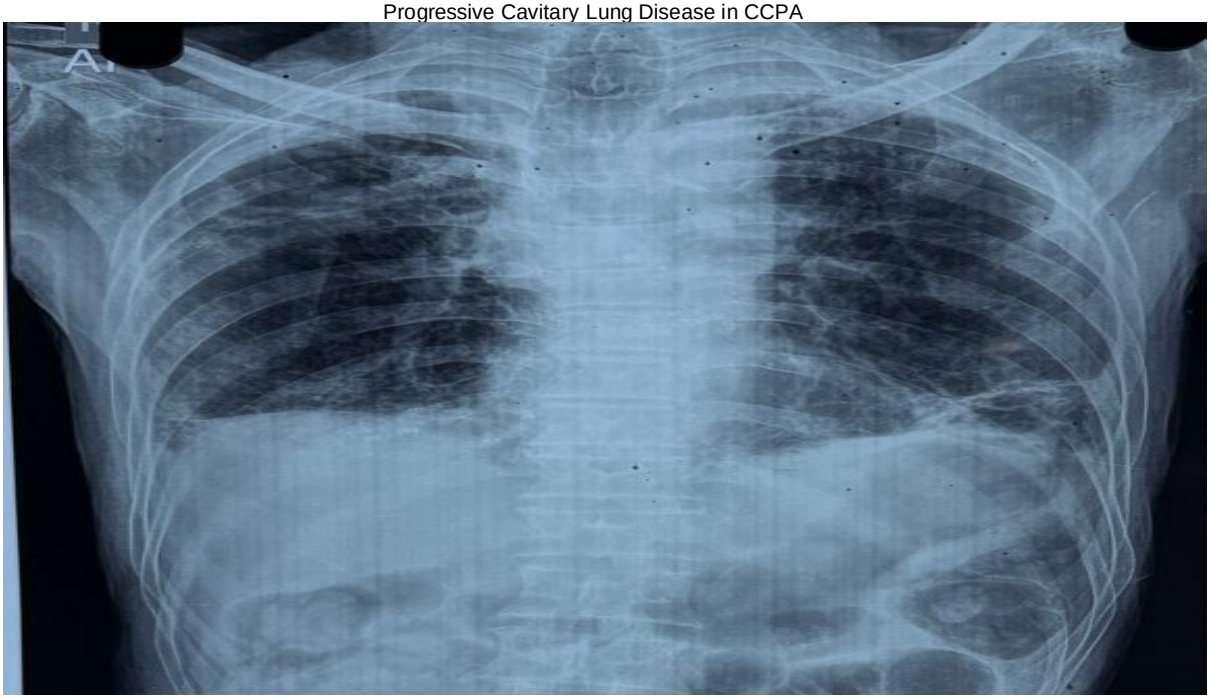


Figure 2. Chest X-ray (AP View) Demonstrating Bilateral Cavitary Lesions with Heterogeneous Opacities Consistent with Progressive Cavitary Lung Disease in CCPA

II.



Case 2

A 54-year-old male agricultural worker presented with a chronic history of cough, intermittent hemoptysis, fatigue, and progressive breathlessness for nearly 6 months. He had a significant history of pulmonary tuberculosis treated 3 years ago with a standard 6-month regimen (2HRZE/4HR). The patient had no history of smoking or diabetes but reported recurrent respiratory infections over the past year.

He had been empirically restarted on anti-tuberculosis therapy by a private practitioner 4 months prior due to persistent symptoms and an abnormal chest X-ray, but his clinical condition progressively deteriorated. At presentation, his vitals were stable except for mild tachypnea (RR 22/min). Oxygen saturation was 94% on room air. Chest examination revealed coarse crepitations over the right upper zone.

Investigations revealed mild leukocytosis (WBC 14.6 ×10³/µL), hemoglobin 11.2 g/dL, and ESR 72 mm/hr. Liver and kidney function tests were within normal limits. HIV and hepatitis serology were negative.

Chest radiography demonstrated a thick-walled cavity in the right upper lobe with associated pleural thickening. HRCT of the thorax showed a large, irregular-walled cavity with an intracavitary mobile soft-tissue mass showing an “air-crescent” sign, consistent with an aspergilloma. Adjacent parenchymal fibrosis and pericavitary infiltrates were noted. Comparison with previous CT imaging from 10 months earlier revealed interval enlargement of the cavity and development of new pericavitary nodularity.

Serum Aspergillus IgG antibody was strongly positive. Sputum fungal culture subsequently grew Aspergillus fumigatus, confirming Chronic Cavitary Pulmonary Aspergillosis.

The patient was started on oral itraconazole 200 mg twice daily along with bronchodilator therapy. Liver function tests were monitored weekly. Over the next 4 weeks, the patient showed marked reduction in hemoptysis and improvement in exercise tolerance. He remained clinically stable on follow-up and continued long-term antifungal therapy.

Case 3

A 48-year-old woman presented with complaints of chronic cough, persistent low-grade fever, chest discomfort, and significant weight loss for the past 5 months. She had been treated for sputum-positive pulmonary tuberculosis 5 years earlier. She denied smoking, diabetes, or immunosuppressive drug use.

Due to worsening symptoms and cavitary lesions seen on a previous X-ray, she had received two incomplete empirical courses of anti-tuberculosis therapy in the past year from local health providers. Despite this, her symptoms progressed, prompting referral to our tertiary centre.

On examination, she appeared pale and cachectic. Vitals showed RR 24/min and SpO_2 93% on room air. Chest auscultation revealed amphoric breath sounds over the left upper lung fields.

Laboratory tests demonstrated anemia (Hb 9.8 g/dL), elevated ESR (88 mm/hr), and mild leukocytosis. Renal and liver profiles were within normal limits. HIV, Hepatitis B, and Hepatitis C tests were negative.
A chest X-ray showed a large left upper-lobe cavity with heterogeneous internal opacities. HRCT confirmed multiple thick-walled cavities with an intracavitary fungal ball and extensive pericavitary fibrosis. Serial imaging comparison over 8 months demonstrated increasing cavity wall thickness and development of new adjacent cavitary lesions, indicating progressive disease.

Given the high suspicion for CCPA, serum Aspergillus IgG was performed and returned significantly positive. Sputum for fungal smear revealed hyaline septate hyphae consistent with Aspergillus species.

The patient was initiated on voriconazole with a loading dose followed by maintenance therapy, and was advised regular LFT monitoring. Symptomatic improvement was observed after 2 weeks, with reduction in cough and improved appetite. She was discharged with instructions for long-term antifungal therapy and close follow-up.

Table 1: Comparative Summary of Three CCPA Cases

Parameter	Case 1	Case 2	Case 3
Age / Sex	60-year-old male	54-year-old male	48-year-old female
Past TB History	Completed 2HRZE/4HR 2 years ago	Completed 2HRZE/4HR 3 years ago	Completed TB treatment 5 years ago
Duration of Symptoms	7–8 months	~6 months	~5 months
Key Symptoms	Fever, dyspnea, weight loss, worsening hemoptysis	Cough, hemoptysis, fatigue, dyspnea	Cough, fever, weight loss, chest discomfort
Empirical ATT Before Diagnosis	Yes (2 months)	Yes (4 months)	Yes (2 incomplete courses)
Vitals at Presentation	RR 25/min, SpO_2 92%	RR 22/min, SpO_2 94%	RR 24/min, SpO_2 93%
Lab Findings	WBC ↑, Hb 10.9, ESR 90; LFT deranged; Hep C +	WBC mildly ↑, Hb 11.2, ESR 72; LFT normal	Hb 9.8, ESR 88, mild leukocytosis
Radiology (X-ray)	Multiple bilateral cavitations with progression	Right upper-lobe thick-walled cavity with pleural thickening	Large left upper-lobe cavity with heterogeneous opacities
CT Findings	Multiple cavities + aspergilloma + pericavitary infiltrates	Large irregular cavity + “air-crescent” sign + fibrosis	Multiple cavities + aspergilloma + pericavitary fibrosis
Aspergillus IgG	Positive	Strongly positive	Significantly positive
Fungal Culture	Not done	Aspergillus fumigatus positive	Hyaline septate hyphae (Aspergillus) seen
Final Diagnosis	CCPA with post-TB cavities	CCPA with aspergilloma	CCPA with progressive cavitary disease
Treatment Given	Voriconazole	Itraconazole	Voriconazole
Response to Therapy	Symptomatic improvement; discharged	Improvement in hemoptysis& exercise tolerance	Improved cough, appetite, and stamina
Follow-up Advice	LFT monitoring; 2-week review	Long-term antifungal therapy; LFT monitoring	Long-term antifungal therapy; regular follow-up

DISCUSSION

Chronic Cavitary Pulmonary Aspergillosis (CCPA) commonly develops in individuals with prior structural lung damage, predominantly healed or partially treated tuberculosis, making countries with a high TB burden particularly vulnerable to missed or delayed diagnoses [10]. In all three cases in this series, patients had a documented history of pulmonary tuberculosis and developed progressively symptomatic cavitary lung disease over

several months, consistent with known global patterns of CCPA epidemiology.

A major challenge in clinical practice is that the symptom profile of CCPA—including persistent cough, hemoptysis, weight loss, fatigue, and dyspnea—overlaps significantly with that of recurrent or smear-negative pulmonary tuberculosis. This frequently results in repeated empirical courses of anti-tubercular therapy (ATT), particularly in low-resource settings where fungal diagnostics are limited [11]. Similar to reports from other Indian and Asian studies, all three patients in our series were initially misdiagnosed as having recurrent TB, leading to unnecessary ATT exposure and delayed antifungal therapy [12].

Radiological evaluation plays a central role in distinguishing CCPA from post-tuberculosis sequelae. Progressive thick-walled cavities, intracavitary fungal balls (aspergilloma), and pericavitary infiltrates are classic features of CCPA, especially when there is documented interval enlargement or development of new cavities on serial imaging [13]. These characteristic findings were consistently seen in all three patients. HRCT is considered the imaging modality of choice for diagnosis, as it reliably identifies aspergillomas, air-crescent signs, and fibrotic changes that are often missed on routine chest radiographs [14].

Serological testing for Aspergillus-specific IgG antibodies remains the most sensitive non-invasive diagnostic tool, with positivity rates exceeding 90% in most studies [15]. All three cases showed elevated Aspergillus IgG levels, confirming the role of serology in differentiating CCPA from bacterial or mycobacterial infections. Although direct fungal culture has low sensitivity, positive results—such as the Aspergillus fumigatus growth observed in Case 2—provide additional microbiologic confirmation [16].

Voriconazole and itraconazole remain the mainstay of therapy for CCPA, requiring prolonged treatment to stabilize cavitary lesions and reduce symptoms, particularly hemoptysis and dyspnea [17]. All patients in this series responded favorably to azole therapy, with notable clinical improvement during follow-up. However, antifungal therapy requires careful monitoring of liver function, as hepatotoxicity remains an important consideration, especially in patients with comorbid liver disease, such as the hepatitis C–positive patient in Case 1 [18].

Delayed recognition of CCPA is associated with significant morbidity and mortality. Untreated disease progresses to chronic fibrosing pulmonary aspergillosis, leading to respiratory failure and higher five-year mortality [19]. Early diagnosis, therefore, depends on heightened clinical suspicion, especially in patients with post-TB cavities who develop new or progressive respiratory symptoms. Educational interventions for clinicians, integration of fungal serology into routine evaluation of cavitary lung disease, and improved access to HRCT imaging have been identified as essential strategies to reduce diagnostic delay [20].

This case series emphasizes the importance of considering CCPA in patients previously treated for tuberculosis who present with persistent or worsening respiratory symptoms despite adequate ATT. The cases also highlight the critical need for improved diagnostic capacity in peripheral healthcare settings and for strengthening clinician awareness to prevent repeated misdiagnosis and delayed antifungal therapy.

Conclusion

Chronic Cavitary Pulmonary Aspergillosis (CCPA) is an important and frequently overlooked cause of chronic cavitary lung disease in patients with a history of pulmonary tuberculosis. As demonstrated in this case series, the clinical presentation of CCPA closely mimics recurrent or smear-negative TB, often resulting in repeated empirical anti-tubercular treatment and significant delays in correct diagnosis. Progressive cavitary changes on serial imaging, presence of intracavitary fungal balls, and strongly positive Aspergillus-specific IgG serve as key diagnostic indicators.

Early recognition of CCPA is essential to prevent irreversible lung damage, reduce hemoptysis, and improve long-term outcomes. Azole therapy—particularly voriconazole and itraconazole—remains effective when initiated promptly, provided appropriate monitoring is ensured. This series highlights the need for heightened clinical suspicion, wider availability of fungal serology, and improved access to HRCT in settings where tuberculosis is endemic. Strengthening diagnostic capacity and clinician awareness will help reduce misdiagnosis and enable timely antifungal treatment, ultimately improving patient survival.

Limitations

This case series is limited by its small number of patients and its retrospective descriptive nature, which restricts the ability to generalize findings to the larger population. Radiological comparisons were based on available prior imaging, which varied in quality and timing across patients. Fungal culture sensitivity was low, and diagnosis relied predominantly on serological and radiological criteria, which may introduce diagnostic variability. Additionally, long-term follow-up data were not available for all patients, limiting assessment of treatment response and disease progression. Despite these limitations, the series provides valuable insights into the diagnostic challenges of CCPA in post-tuberculosis patients in resource-constrained settings.

Recommendations

Clinicians should maintain a high index of suspicion for CCPA in patients with a history of treated tuberculosis who present with persistent respiratory symptoms or worsening cavitary lesions despite adequate anti-tubercular therapy. Wider availability of Aspergillus-specific IgG testing and increased access to HRCT imaging at peripheral health centres can significantly reduce diagnostic delays. Routine evaluation of post-TB cavitary disease should include fungal serology, especially in regions with high TB burden. Structured training programs to raise clinician awareness, along with standardized diagnostic algorithms, are essential to differentiate CCPA from recurrent TB. Long-term antifungal therapy should be initiated promptly, with appropriate monitoring of liver function. Strengthening diagnostic capacity, establishing referral pathways, and integrating CCPA awareness into national TB-control programs can improve early detection and patient outcomes

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