




Pulmonary Tuberculosis in Immunocompromised Patients: A Review

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Abstract

Tuberculosis (TB) remains a leading cause of morbidity and mortality worldwide and in India. Immunocompromised individuals, including those with human immunodeficiency virus (HIV)/acquired immunodeficiency syndrome (AIDS), cancer, diabetes, or those undergoing immunosuppressive therapy, are at a heightened risk of developing TB, often presenting with atypical symptoms, imaging features, and more severe disease outcomes. This review highlights the atypical radiological pattern of TB in these states. It is well recognized that there is considerable overlap of imaging findings across a variety of pulmonary infections and noninfectious processes. The presence or absence of specific indicators and consideration of clinical factors can help narrow the differential diagnoses. Thereby, it is crucial for radiologists to identify the imaging features that not only are characteristic of pulmonary TB but also interpret the atypical findings and corroborate with appropriate clinical history, especially concerning the immune status of the patient, to provide crucial information while minimizing radiation exposure and patient expenditures for the best possible care.

Keywords

- ▶ immunocompromised
- ▶ tuberculosis
- ▶ pulmonary infections

Introduction

Tuberculosis (TB) is a bacterial infection caused by *Mycobacterium tuberculosis*, most commonly affecting the lungs. Every year, over 10 million people fall ill with TB, and India accounts for 27% of the total TB cases in the world, according to the Global TB Report 2023 by the World Health Organization. Despite being a preventable and curable disease, about 1.7 million deaths were attributed to TB, with more than 167,000 of these occurring among people living with human immunodeficiency virus (PLHIV).¹

Pulmonary TB is conventionally divided into primary and postprimary (or reactivation) TB. ▶**Fig. 1** depicts the

natural history and a few of the common radiological features of TB.²

Primary TB: The manifestations after the first exposure of the host to *Mycobacterium* can lead to primary TB. Following this, depending on the individual's immunity, the infection might resolve or progress as primary progressive TB or enter a state of latency known as tuberculous infection (TBI; previously termed latent TB infection [LTBI]). The WHO defines TBI as a state of persistent immune response to stimulation by *M. tuberculosis* antigens without overt clinical manifestations of active TB.^{1,3}

Postprimary TB, also known as reactivation TB or secondary TB, results from either the reactivation of latent

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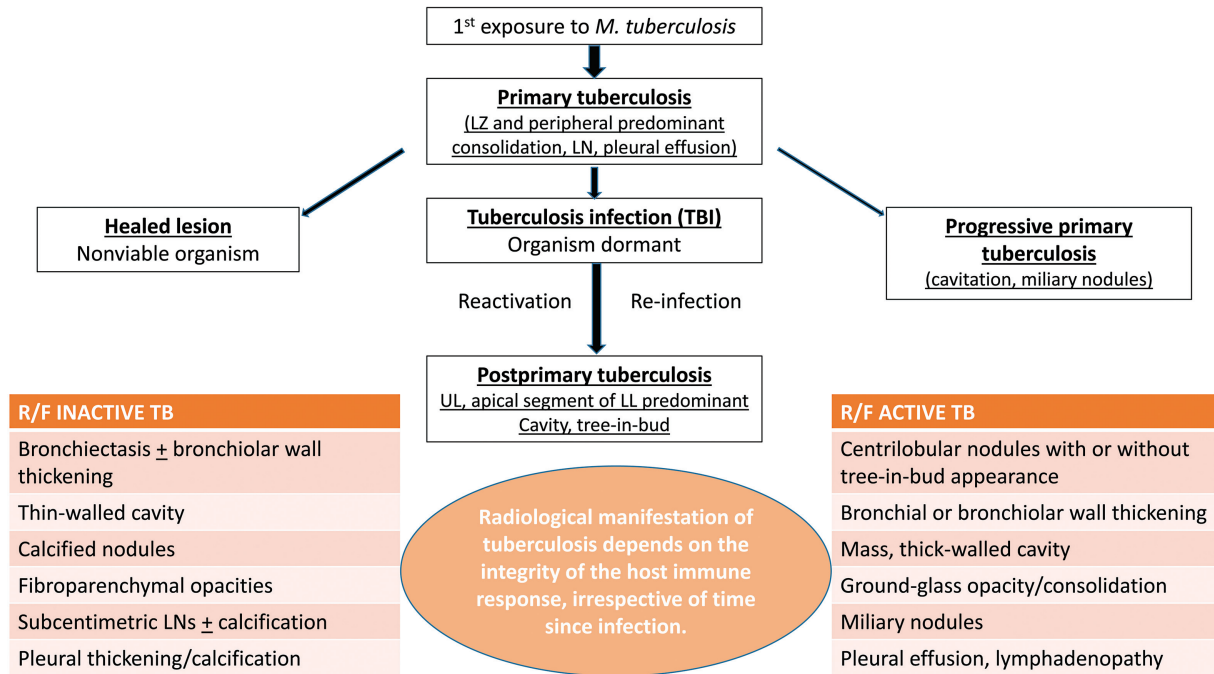


Fig. 1 Natural history and common radiological features of tuberculosis (LL, lower lobe; LN, lymph node; LZ, lower zone; R/F, radiological features; UL, upper lobe).

primary infection or, less commonly, repeat infection of a previously sensitized host.⁴

The classical teaching of the radiological appearance of primary, progressive primary, and postprimary (reactivation or secondary) TB is challenged, and a growing body of evidence suggests that the radiological manifestation of TB depends on the integrity of the host immune response, irrespective of time since infection.⁴

The clinical manifestations and radiologic features of pulmonary TB are affected by various factors, especially the host's immune response to *M. tuberculosis*. Immunocompromised patients, such as those with HIV/acquired immunodeficiency syndrome (AIDS), cancer, diabetes, or those taking immunosuppressive drugs, have a greater risk of developing TB and are likely to experience more severe disease outcomes.^{5,6} The clinical findings of immunocompromised patients with pulmonary TB differ from those of nonimmunocompromised patients. The differences include an increase in respiratory symptoms during the follow-up period of underlying diseases, undernourishment, negative response to the tuberculin skin test, atypical radiological findings, an increase in the number of patients who are misdiagnosed with pneumonia upon admission, and an increase in mortality rate.⁷ Therefore, radiologists need to identify the imaging features that not only are characteristic of pulmonary TB but also interpret the atypical findings while screening and imaging symptomatic immunocompromised patients and differentiate them from other opportunistic infections or neoplasms that these individuals are prone to.

Immunocompromised patients are more susceptible to TB and prone to the following^{8,9}:

- An increased risk of progression from TBI to active TB than in the healthy population.
- Developing disseminated TB.
- Increased risk of progression of co-morbid conditions.

Diagnosis of TB in immunocompromised patients can be challenging due to atypical symptoms and difficulty in obtaining adequate sputum samples for testing, even though nucleic acid amplification tests (NAATs), such as polymerase chain reaction (PCR), can rapidly detect the presence of *M. tuberculosis* DNA in clinical samples. Imaging studies in these states, such as chest X-rays (CXRs) and computed tomography (CT) scans, help guide early diagnosis and management.⁶ In this article, we review the radiological patterns of pulmonary TB in immunocompromised patients.

Pulmonary Tuberculosis and Human Immunodeficiency Virus

HIV is a retrovirus that attacks immune cells expressing the cluster of differentiation 4-cell surface glycoprotein (CD4+ cells), eventually leading to the death of these cells and progressive failure of the immune system and to the development of AIDS.¹⁰ Reduced CD4+ cells and dysfunction of humoral immune response by HIV result in a higher risk of developing active disease among those infected with *M. tuberculosis*.¹¹

TB is the leading cause of death of people with HIV and is also a significant contributor to antimicrobial resistance. TB continues to be the most common opportunistic infection in PLHIV, those who are antiretroviral therapy (ART) naive, as well as those who are on treatment. PLHIV have a 21-fold higher risk of developing TB.¹² TB slows CD4 count recovery

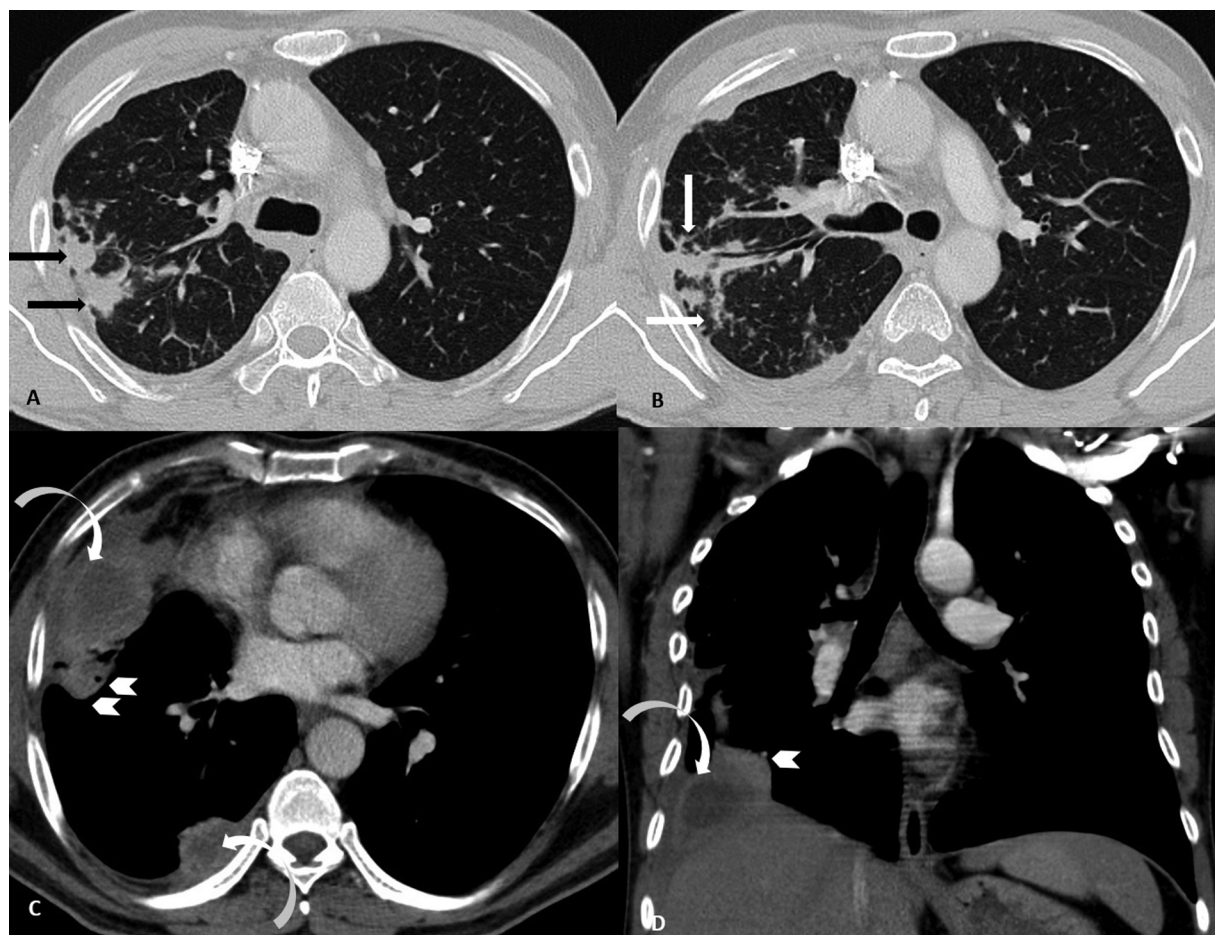


Fig. 2 Tuberculosis in a 48-year-old people living with human immunodeficiency virus (PLHIV) with fever and cough, antiretroviral therapy (ART) naïve, and CD4 count of 309 cells/ μ L. (A, B) Axial computed tomography (CT) images (lung window) at and just below the level of carina show consolidations (black arrows) with clusters of nodules (white arrows) in the right upper lobe. (C) Axial and (D) coronal reformatted CT thorax images (mediastinal window) reveal right-sided loculated empyema (curved white arrows) with adjacent subsegmental collapse consolidation (white arrowheads).

and hastens the progression to AIDS and death in the PLHIV.¹³ Also, HIV and TB coinfecting patients have weaker immune systems and lower bacterial load in sputum, making the detection of TB harder through conventional methods.^{14,15}

The prevalence of TB in newly diagnosed HIV patients was 17.8% in a study from Gujarat¹⁶ and 29.6% in a survey from Telangana.¹⁷

Pulmonary TB can occur at all stages of HIV infection. In developing countries where TB is endemic, latent TB is present in the majority of adults, which will present as postprimary TB and reactivation TB in the early stages of HIV, similar to immunocompetent individuals, as there is a reserved cell-mediated response.¹⁸ The imaging features include nodules, tree-in-bud opacities, thick-walled cavities with or without consolidation, and pleural effusion with pleural enhancement (**Fig. 2**).

However, in advanced HIV disease, when the CD4 count falls below 200 cells/ μ L, pulmonary TB reactivation and reinfection resemble primary TB and features such as adenopathy and interstitial or noncavitary consolidation with mid or lower lobe predilection develop (**Fig. 3**). When CD4 counts fall even further, disseminated TB dominates (**Fig. 4**). Diffuse bilateral reticulonodular opacities are also

seen (**Fig. 5**). Pleural effusion, though seen in early stages, could also be seen in advanced stages. The presence of adenopathy is a predictor of low CD4 count.¹⁹

Immune reconstitution inflammatory syndrome (IRIS) is due to the excessive immune response to *M. tuberculosis* that may occur in HIV-infected patients during or after the completion of anti-TB therapy. This is manifested by paradoxical worsening or recurring of preexisting tuberculous lesions or the development of new lesions on starting ART. This immunological response could be seen in patients with low CD4 counts (<100 cells/ μ L). However, it may also occur in those with CD4 counts above 200 cells/ μ L. Reducing viral load and improving the immunological response to ART will favor IRIS. However, drug-resistant infection, superadded bacterial infection, drug intolerance or other adverse drug reactions, patient noncompliance, or other causes that can reduce the drug levels should be excluded.²⁰

Pulmonary Tuberculosis and Diabetes

The global rise in type 2 diabetes mellitus (DM) poses a challenge to TB control. The prevalence of DM is increasing faster where TB

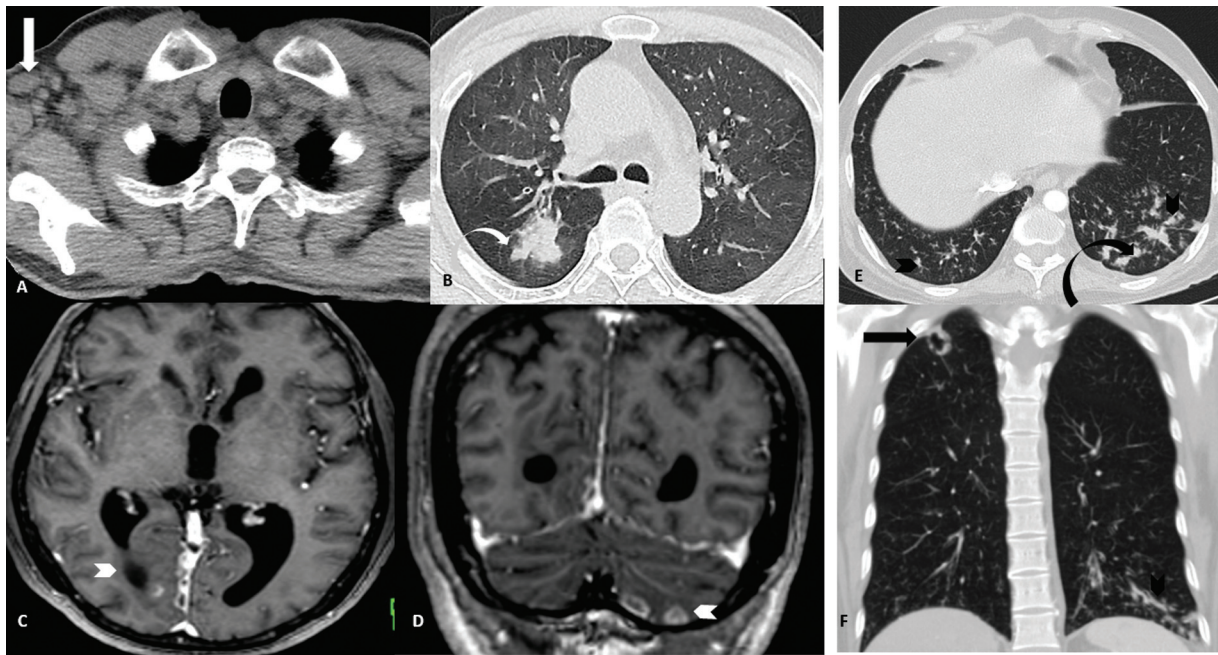


Fig. 3 Tuberculosis in people living with human immunodeficiency virus (PLHIV) with CD4 less than 200 cells/ μ L (different patients). A 63-year-old PLHIV on antiretroviral therapy (ART) for 4 years with clinical and immunological failure, having a CD4 count of 52 cells/ μ L, presented with a holocranial headache. (A) Axial thorax image (mediastinal window) reveals right axillary nodes with absent fatty hilum (white arrow). (B) The axial image (lung window) shows a patchy consolidation in the right lung (curved white arrow), suggestive of active pulmonary tuberculosis. (C, D) Gadolinium-enhanced axial and coronal magnetic resonance imaging (MRI) of the brain in the same patient show nodular and ring-enhancing lesions (white arrowheads) in the right occipital parafalcine region and left cerebellum with meningeal enhancement. Overall imaging features suggestive of disseminated tuberculosis. (E) Axial computed tomography (CT) image (lung window) of a 42-year-old man, newly diagnosed with HIV, shows branching nodules (black arrowheads) and peribronchial consolidations (black curved arrows) in both the lower lobes. (F) The coronal reformatted high-resolution CT (HRCT) image shows a thick-walled cavity (black arrow) in the right upper lobe.

is already endemic, and this has earned them the names “the converging epidemics” and “double burden” due to their epidemic proportions. Prolonged hyperglycemia can have detrimental effects on both innate and adaptive immunity, leading to weakened cell-mediated immunity, cytokine response, and the defense of alveolar macrophages. Altered pulmonary microvasculature and micronutrient deficiency can create a favorable environment for TB invasion, increasing the risk of infection and higher bacilli load in affected individuals.²¹

Various studies have demonstrated that due to underlying DM, there is an increased frequency of atypical pulmonary findings, including lower lobe involvement, increased lung lesions, multiple lung cavities (→ Fig. 6) and extensive parenchymal involvement. These studies also suggested a correlation between radiological manifestations and glycemic control.^{22–24} Patients with HbA1c > 9% are more likely to have more cavities in the lower lung field and more lobe involvement in the chest CT.^{23,25}

Cavitation is a more severe manifestation of pulmonary TB (→ Fig. 7) and is associated with an increased risk of disease transmission, poor disease control, relapse, and development of drug resistance.²⁶

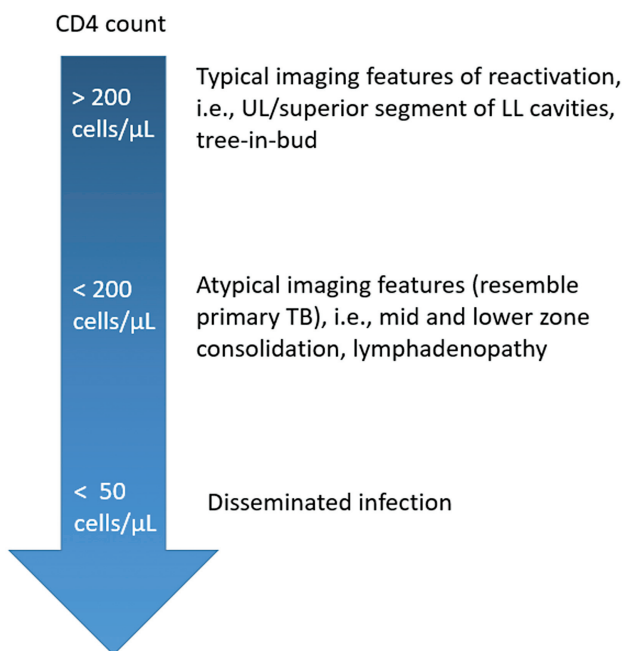


Fig. 4 Imaging features of tuberculosis in relation to the CD4 count (LL, lower lobe; UL, upper lobe).

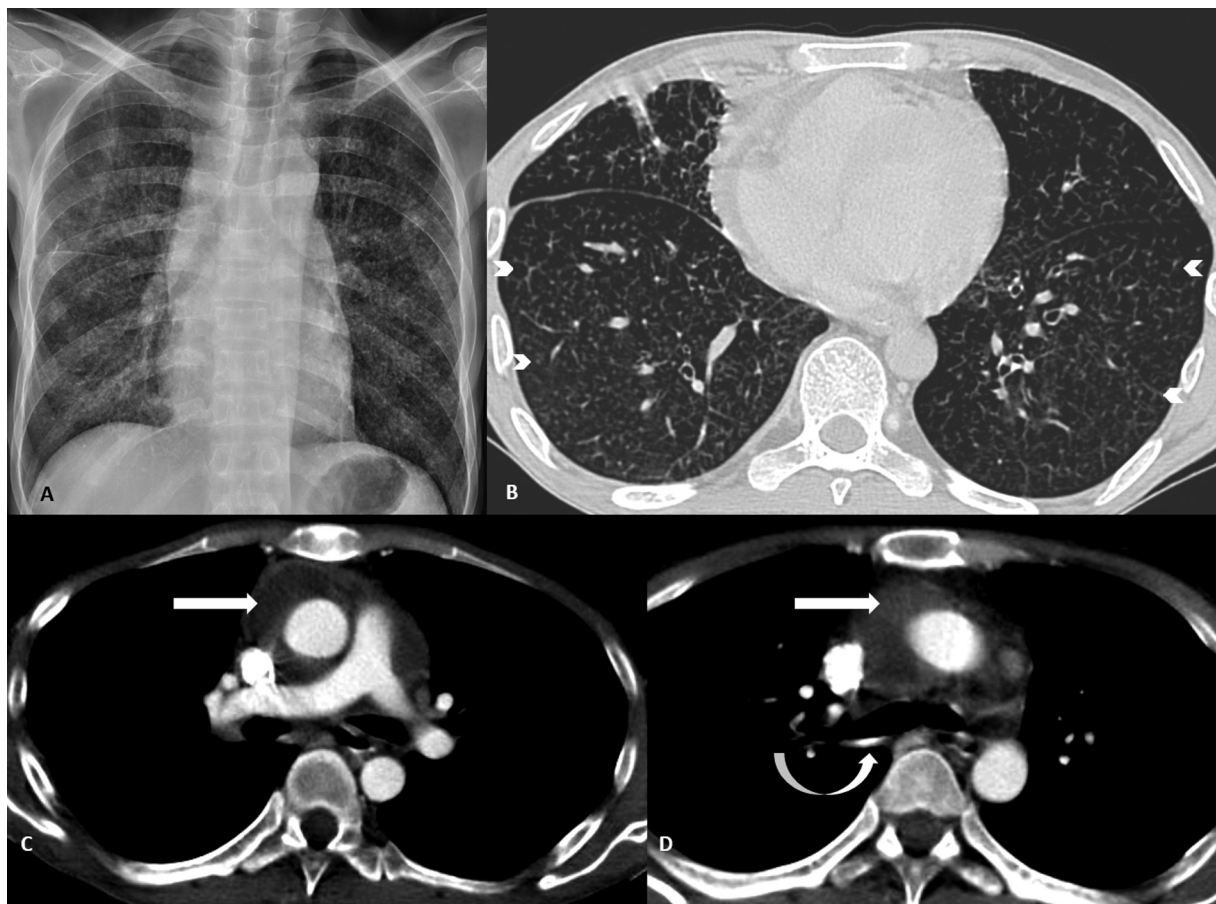


Fig. 5 Tuberculosis in people living with human immunodeficiency virus (PLHIV). (A) Posteroanterior (PA) radiograph of a 43-year-old with dysphagia and a CD4 count of 80 cells/ μ L shows bilateral multiple miliary nodules. (B) Computed tomography (CT) axial image of the thorax (lung window) shows multiple miliary nodules in both lower lobes (*white arrowheads*). (C) The axial image (mediastinal window) shows multiple confluent necrotic nodes (*white arrows*). (D) Oral contrast opacifies the right main bronchus (*white curved arrow*), indicating esophagobronchial fistulous communication.

Pulmonary Tuberculosis and Chronic Kidney Disease

Like DM, chronic kidney disease (CKD) has also emerged as one of the leading causes of morbidity and mortality,

affecting 8 to 16% of the general population worldwide.²⁷ Reduced immunity in patients with CKD is multifactorial, increasing susceptibility to infectious complications, with pneumonia being the leading cause of mortality in CKD and end-stage renal disease (ESRD) receiving dialysis.^{28,29}

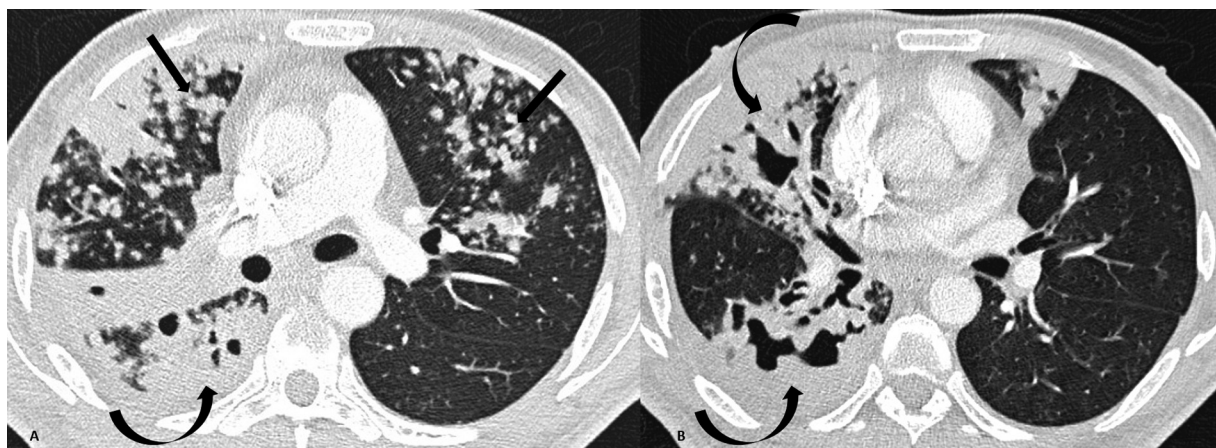


Fig. 6 A 53-year-old diabetic with cough and expectoration, loss of weight, and appetite. (A) The axial image of the thorax (lung window) shows multiple nodules (*black arrows*) in both upper lobes and (B) consolidation with cavitation in the right middle and lower lobes (*black curved arrows*).



Fig. 7 A 54-year-old diabetic with a history of cough with mucoid expectoration for 2 months. He was diagnosed with pulmonary tuberculosis 3 years back, took anti-tuberculosis treatment (ATT) for 4 months and stopped. Axial images of the thorax computed tomography (CT) in the lung window show (A) consolidation with cavitation (*black arrow*) in the right upper lobe and (B) numerous nodules (*white arrow*) involving both lungs, more in the right lower lobe and also a few other cavities (*white arrowheads*) in the left lung. He was diagnosed with rifampicin susceptible Xpert positive tuberculosis on bronchoalveolar lavage (BAL) and transbronchial lung biopsy (TBLB) specimens.

The risk of active TB in CKD is 6.9- to 52.5-fold higher than in the general population, resulting from either the progression of recent exposure to *M. tuberculosis* infection or secondary to reactivation of latent TB infection (► **Fig. 8**).^{29,30} This particularly applies to high TB burden

countries like India and China, which also account for a vast majority of CKD patients worldwide. The risk of developing TB increases with the stage of CKD and is also seen in patients on hemodialysis and renal transplant recipients.

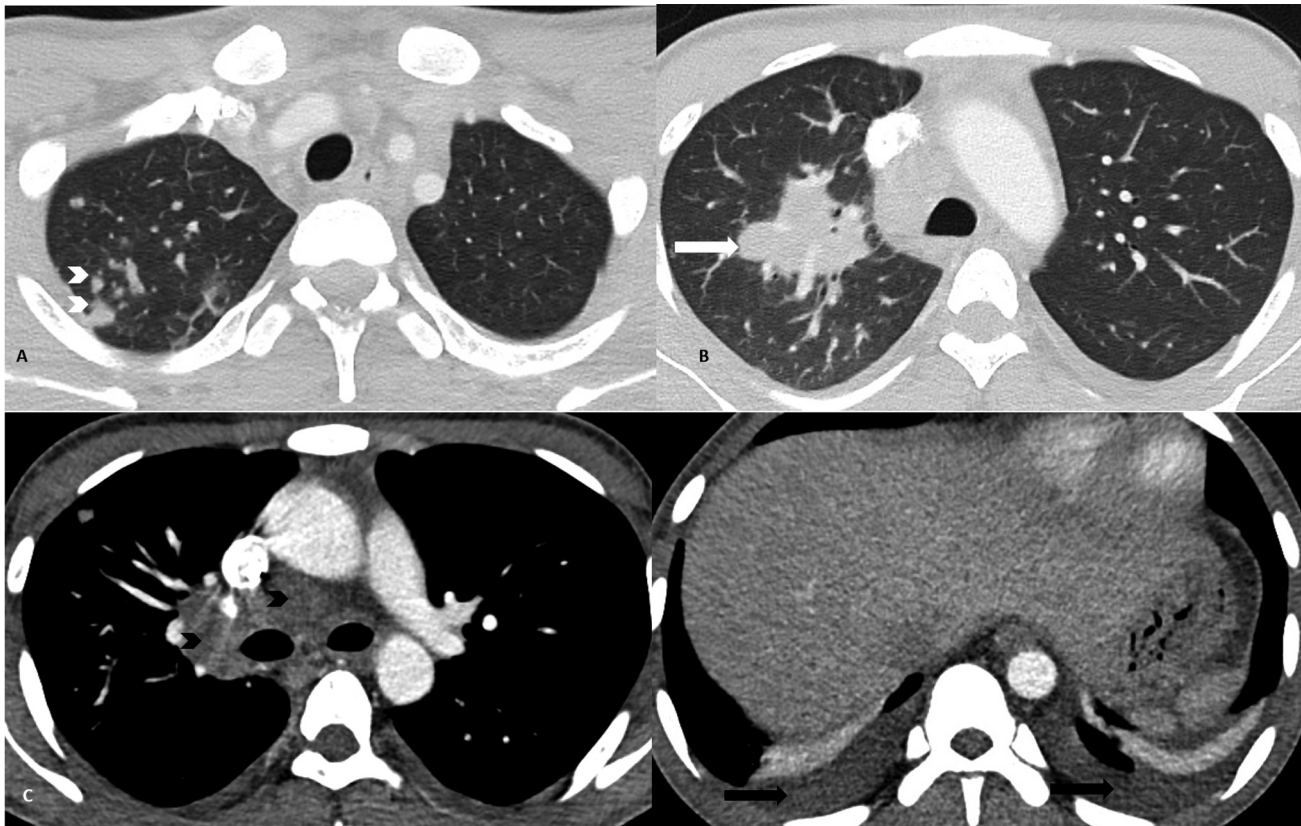


Fig. 8 Tuberculosis in chronic kidney disease (CKD). A 19-year-old boy with CKD stage 5D—diffuse global glomerulosclerosis presented with a fever for 2 weeks and loss of appetite for 1 month. Thorax computed tomography (CT) axial images in the lung window show (A, B) patchy consolidation (*white arrow*) in the right upper lobe and surrounding scattered nodules (*white arrowhead*). The mediastinal window images show (C) right hilar and mediastinal lymphadenopathy (*black arrowhead*) and (D) bilateral small pleural effusion (*black arrow*). He was started on weight-based and renal-adjusted doses of anti-TB therapy (ATT), after which the fever subsided.

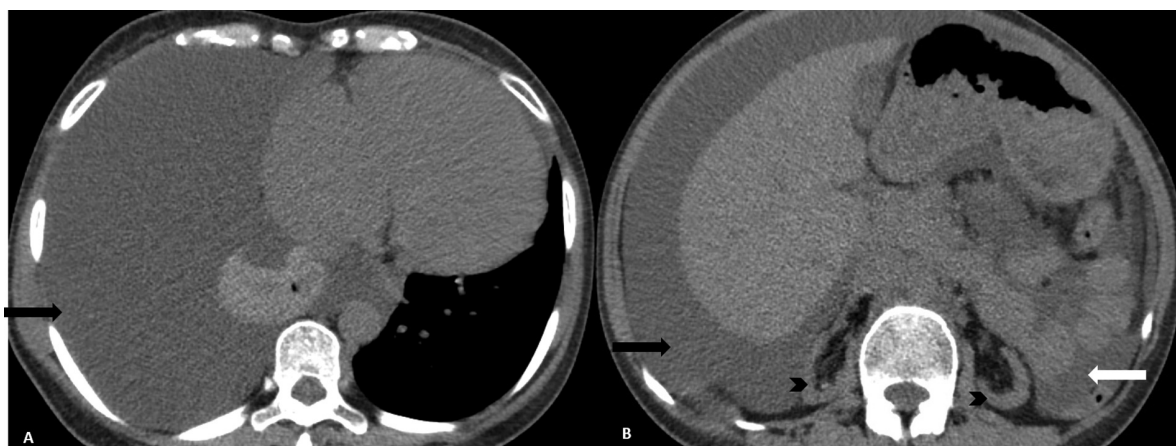


Fig. 9 A 37-year-old lady with stage V chronic kidney disease (CKD) on maintenance hemodialysis, axial noncontrast images showed (A) right-sided pleural effusion (black arrow), which was exudative in nature on thoracentesis and positive for *Mycobacterium tuberculosis* on polymerase chain reaction (PCR). (B) Also, note the bilateral shrunken kidneys (black arrowheads) and ascites (white arrow).

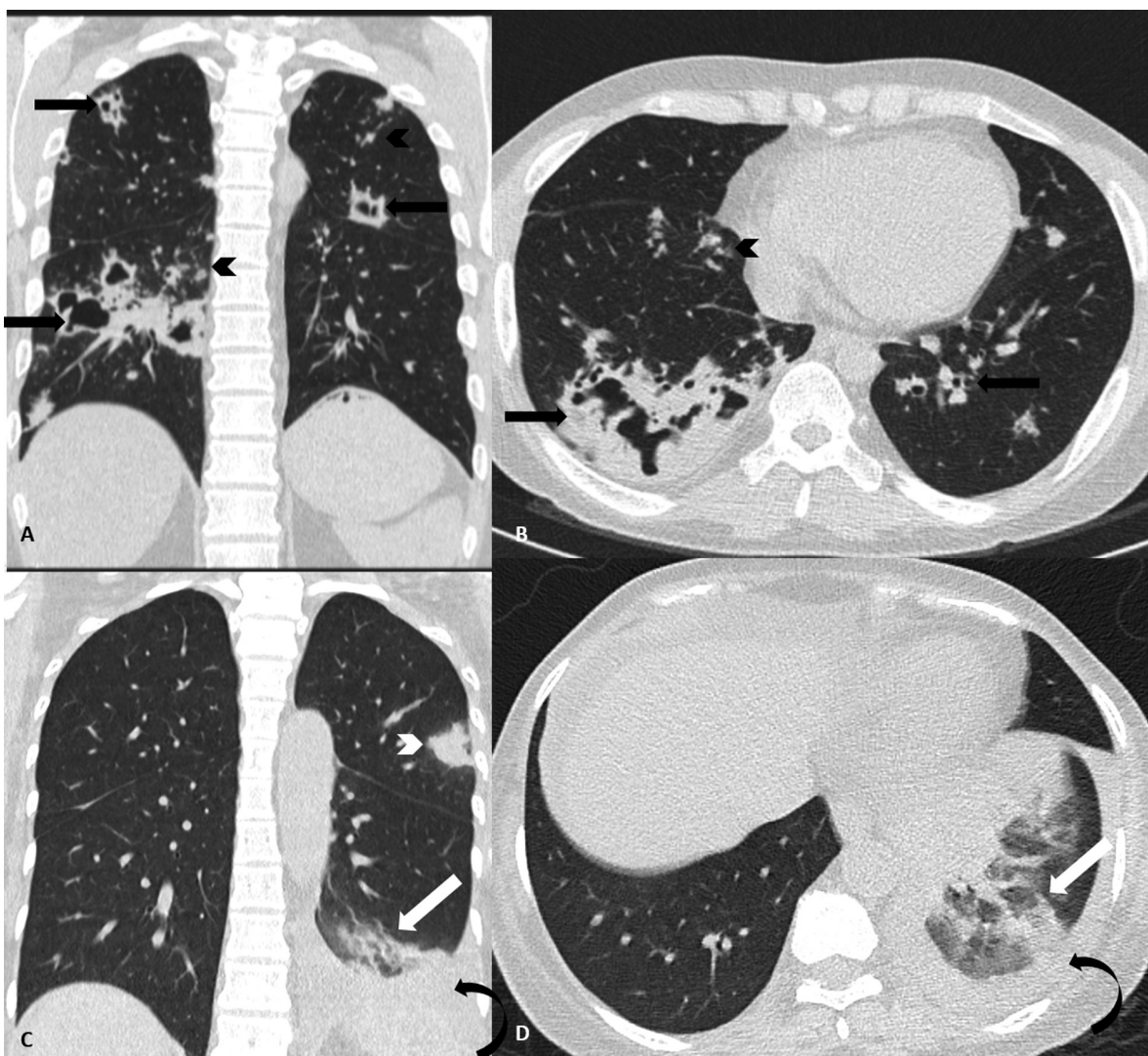


Fig. 10 Tuberculosis in transplant recipients (different patients) thorax computed tomography (CT) images in the lung window of a renal allograft transplant and on triple immunosuppression (prednisolone, cephalosporin, and MMF) shows (A, B) multiple cavitating lesions (black arrows) in both the lungs with surrounding nodules (black arrowheads). (C) Coronal reformatted image of the thorax CT of a 35-year-old gentleman with renal allograft transplant, on immunosuppression, shows consolidation (white arrowhead) in the left upper lobe and patchy consolidation with ground glass opacities (white arrow) in the left lower lobe and left pleural effusion (black curved arrow). (D) The axial images in the lung window show patchy consolidation and GGOs (white arrow) in the left lower lobe and left pleural effusion (black curved arrow). MMF, mycophenolate mofetil.

TB in CKD can have an atypical and insidious clinical presentation, mimicking uremia, resulting in delayed diagnosis and treatment. Extrapulmonary and disseminated disease is more common and accounts for 60 to 80% of cases along with miliary TB.³¹ The most common extrapulmonary presentation includes TB lymphadenitis and peritonitis.

The thoracic findings in CKD like the following make it difficult to differentiate CKD from TB: pulmonary edema with central batwing appearance and absence of cardiomegaly; bacterial or fungal pneumonia with multifocal patchy consolidations and ground-glass opacities; metastatic calcium deposition predominantly of the vessels of the chest wall, myocardium, multiple diffuse or focal nodules, superior vena cava and bronchial walls; uremic pleuropericarditis with sterile pleural and pericardial effusions; and diffuse alveolar hemorrhage.

Uremia and fluid overload can also mimic TB. In a known case of CKD, persistent unilateral loculated pleural effusion with internal septation and associated pleural thickening in the absence of lung findings can be observed in both uremia and TB (→Fig. 9). Although pleural aspirate in both these

cases is exudative, uremic pleural culture is sterile. Pleural nodularity on thoracoscopy is more specific for TB pleural effusion.

Diagnosing mediastinal nodal TB can again be challenging in patients with CKD, especially on noncontrast CT examinations, and lymph nodes may also enlarge due to fluid overload. However, accurate diagnosis is achievable with careful evaluation and testing.³² Magnetic resonance imaging (MRI) has also proven useful in the assessment and follow-up of lymphadenopathy and could be helpful in situations when intravenous (IV) contrast cannot be administered.³³

Pulmonary Tuberculosis in Solid Organ Transplant Recipients

Solid organ transplant recipients are more prone to develop TB in the first year posttransplant when they are more heavily immunosuppressed.³⁴

Liver and lung transplant patients who develop TB more often (nearly two-thirds of the time) show typical patterns of TB on imaging with cavities and tree-in-bud-like

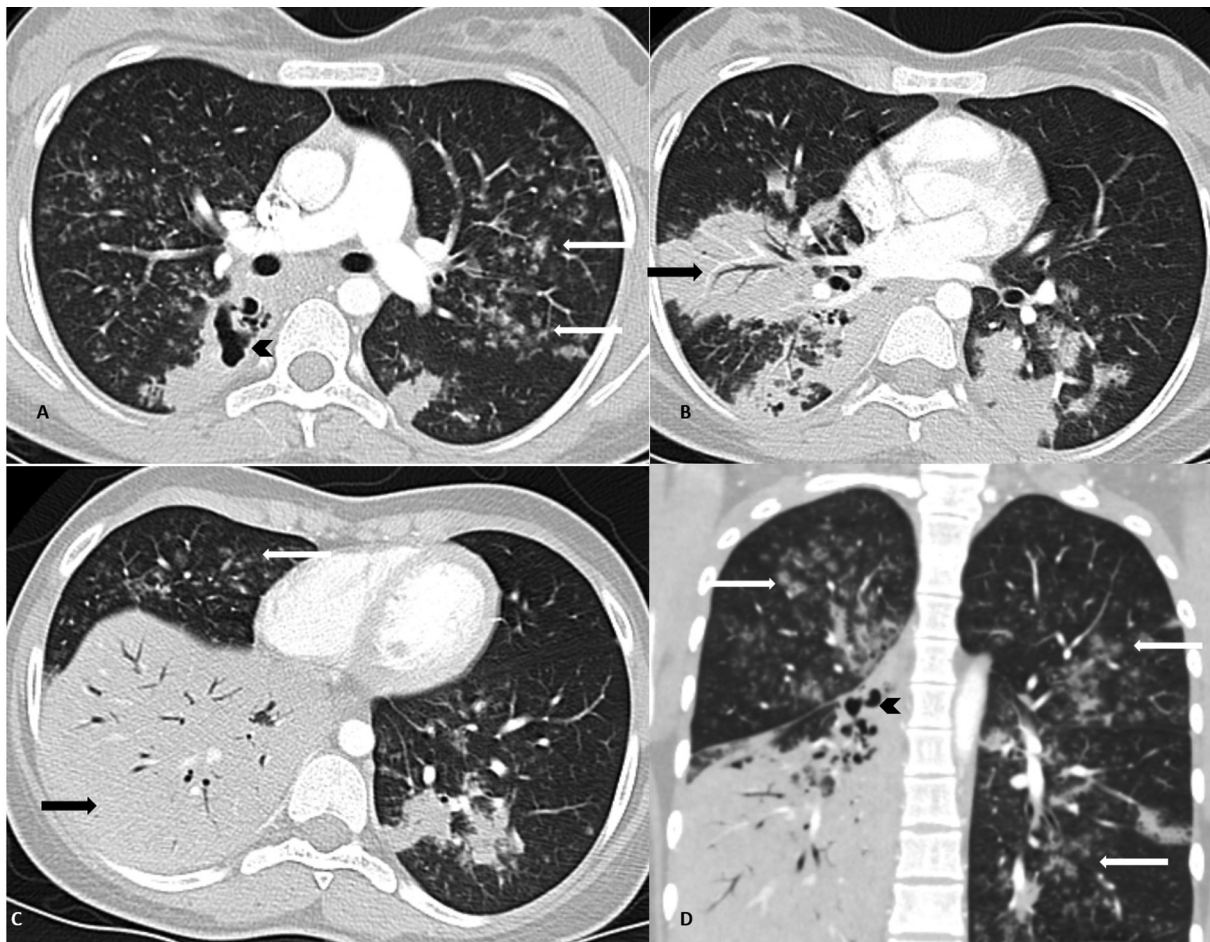


Fig. 11 A 15-year-old girl presented with complaints of cough and fever for 2 months. She was diagnosed with COVID-19 illness and was on oral steroids. Her fever increased over the following 2 weeks, so a thorax computed tomography (CT) was done. (A–D) Lung window images of the CT show multifocal patchy and confluent consolidation (black arrow), some with cavitation (black arrowhead), branching, and nodular opacities (white arrow) in both lungs. Her sputum tested positive for tuberculosis, and she started on anti-TB therapy (ATT), following which her symptoms subsided.

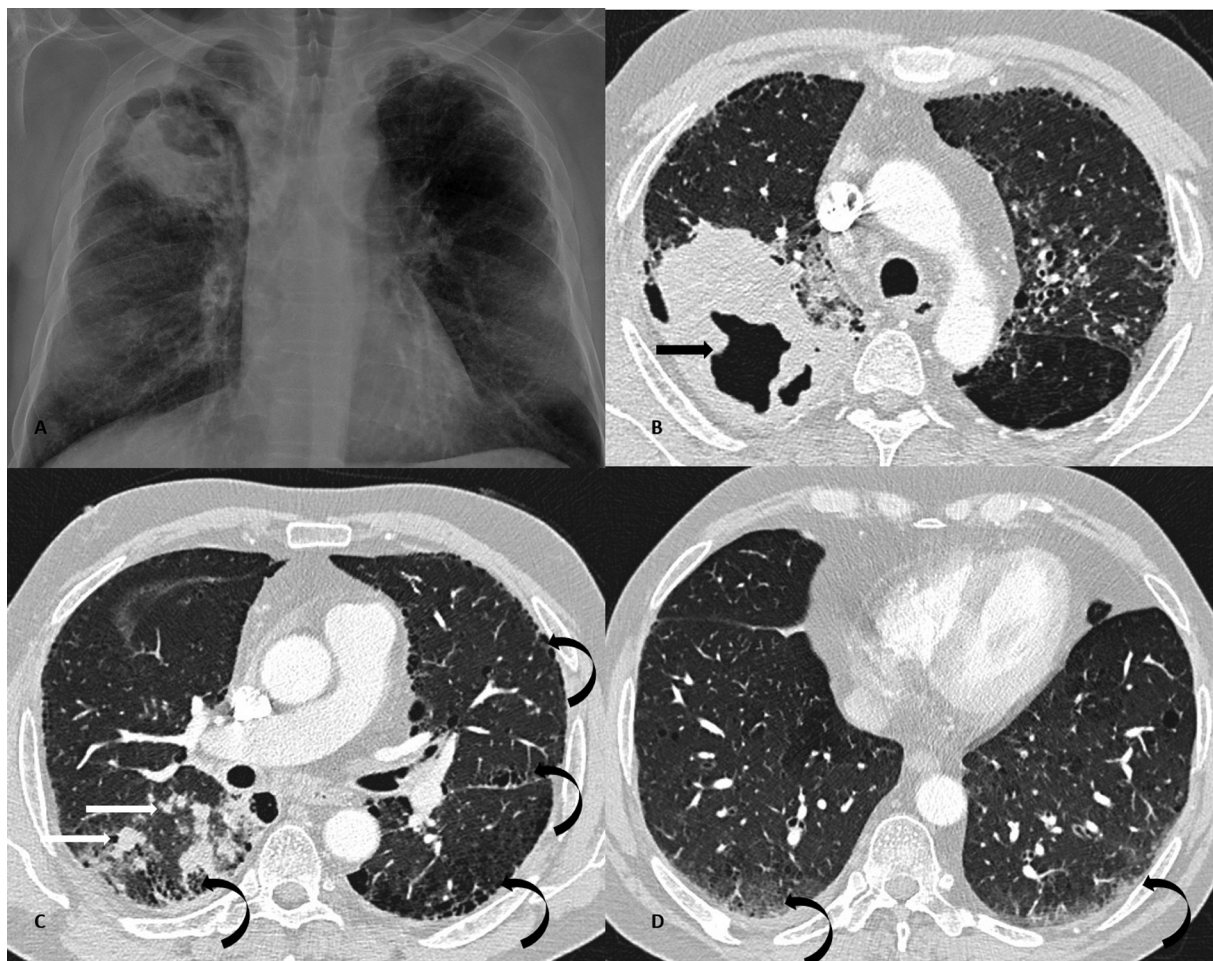


Fig. 12 A 52-year-old gentleman with a 3-year history of polyarthritis lost to follow-up and was on steroids. He presented for pain and swelling in small and large joints. (A) Posteroanterior (PA) radiograph shows a cavitary lesion in the right upper zone. (B) The axial image of the computed tomography (CT) thorax (lung window) shows masslike consolidation with cavitation (*black arrow*) in the right upper lobe. (C) Multiple nodules in clusters are seen in the right lower lobe. (C, D) Subpleural ground-glass opacities, reticulations, and a few cysts in both lungs (*black curved arrows*) suggest interstitial lung disease – fibrotic nonspecific interstitial pneumonia (NSIP) pattern. His sputum was found to be Xpert positive and he was started on anti-tuberculosis treatment (ATT).

appearance. In contrast, renal transplant recipients more often show lymphadenopathy, effusions, and miliary disease (akin to TB in HIV) and less often show cavities (►Fig. 10).³⁵

Pulmonary Tuberculosis in Allogenic Hematopoietic Stem Cell Transplant Recipients

TB is rare in hematopoietic stem cell transplant (HSCT), and when it occurs, it is typically seen in the late engraftment period (>100 days after transplant). Consolidation, nodules with bilateral and multilobar distribution, and lymphadenopathy are often seen than cavitation or tree-in-bud-like opacities.³⁶

Pulmonary Tuberculosis and Cancers, Chemotherapy, and Other Immunosuppressive Medications

The immunocompromised state induced by chronic steroid use complicates the diagnosis and treatment of TB, often

leading to atypical presentations of the disease and a higher risk of treatment failure and mortality (►Figs. 11 and 12). Inhaled corticosteroids also mildly increase the risk of TB.³⁷

Many chemotherapeutic and immunosuppressive agents, including tumor necrosis factor-alpha (TNF-alpha) inhibitors and immune checkpoint inhibitors, can predispose an individual to develop TB (►Fig. 13).³⁸

Tuberculosis Complications and Other Coinfections

In immunocompromised individuals, TB poses a significantly heightened risk of severe complications due to the compromised state of the immune system. The vulnerability of immunocompromised patients to coinfections and the presence of concurrent illnesses further complicate the TB disease course.

Tubercular and bacterial and viral and fungal coinfections are uncommon in individuals with intact immunity but noted in immunocompromised patients, such as those with HIV/AIDS.³⁹

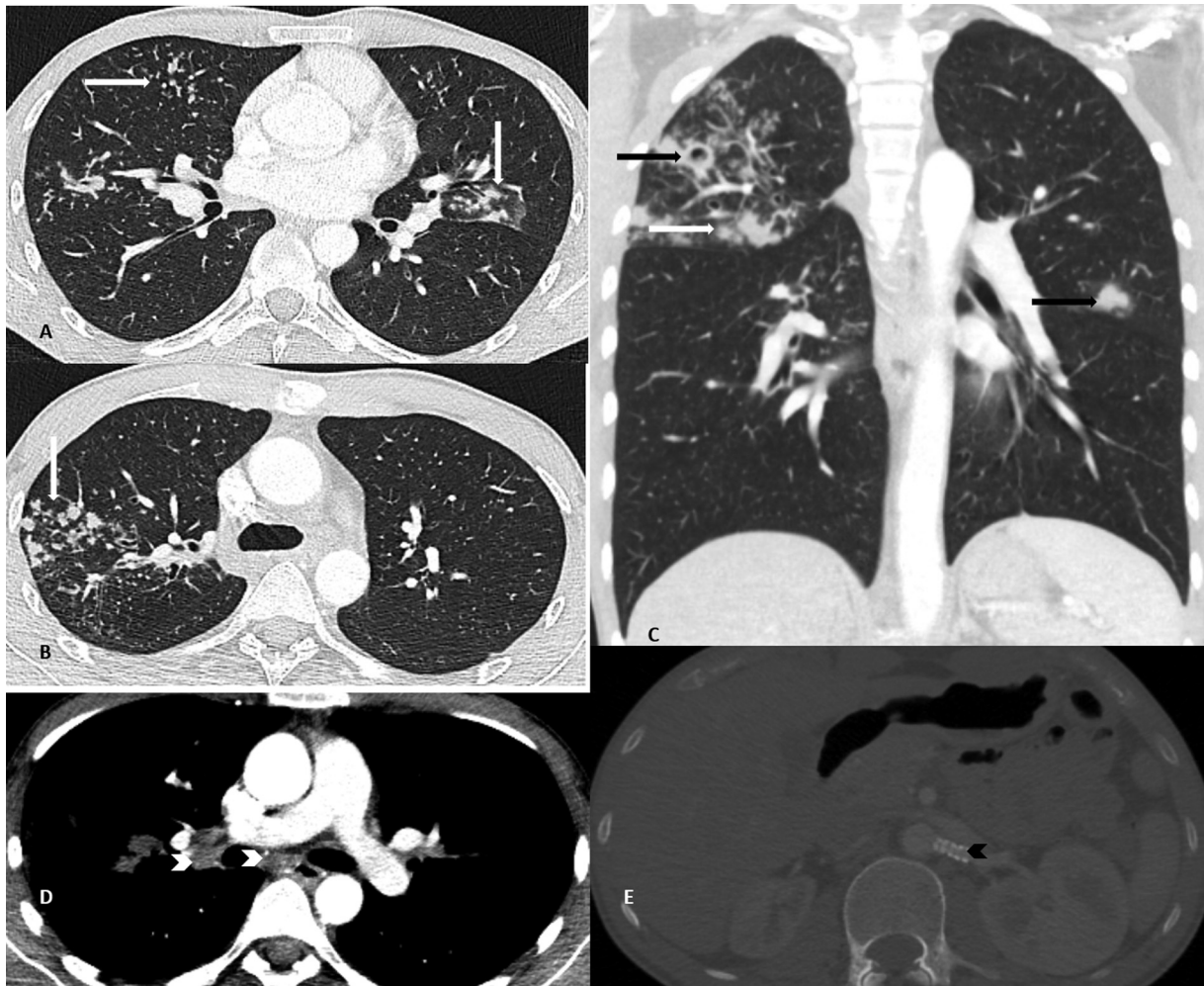


Fig. 13 A 21-year-old gentleman on immunosuppression for Takayasu arteritis presented with complaints of cough for 1 week. (A-C) Thorax computed tomography (CT) shows multifocal clusters of nodules with a tree-in-bud-like appearance (white arrow) and a patchy area of consolidation with cavitation in both lungs (black arrow). (D) Enlarged right hilar and mediastinal lymph nodes (white arrowhead) and (E) stent in situ in the left renal artery (black arrowhead). Sputum Xpert confirmed the presence of *Mycobacterium tuberculosis* and was started on antituberculosis treatment.

Complications like aspergilloma colonization in preexisting tuberculous cavities, destructive lung changes, scar carcinoma, and tracheobronchial and esophageal involvement (►Fig. 5) are more common and severe in immunocompromised individuals with TB. It is crucial to assess immunocompromised patients with TB for vascular, pleural, mediastinal, and extrapulmonary complications (►Fig. 3). These may manifest as pseudoaneurysms (►Fig. 14), hypertrophied bronchial arteries (►Fig. 15), systemic collaterals, chronic empyema, fibrothorax, bronchopleural fistula, pneumothorax, mediastinal fibrosis, pericarditis, and spondylodiskitis.

Imaging Differentials for TB in Immunocompromised Hosts

Immunocompromised hosts are susceptible to various infections, coinfections, and neoplasms like lymphoma. Knowledge of the host immunity status (e.g., the CD4 counts [►Fig. 4], days after transplant, neutropenia), along with the radiological pattern, will aid in arriving at a diagnosis. For

instance, in advanced HIV disease with CD4 counts below 50 cells/ μ L, patients are susceptible to *Pneumocystis jirovecii* (PJP) and cytomegalovirus (CMV) infections (►Figs. 16–17). Consolidation with or without cavitation with associated ground-glass opacities, bronchial wall thickening, and consolidation are common characteristics of bacterial pneumonia (►Fig. 18). Bronchopneumonia patterns are typically observed in infections caused by *Pseudomonas aeruginosa* (►Fig. 19) and *Staphylococcus aureus*. In contrast, lobar pneumonia patterns are commonly seen in *Streptococcus pneumoniae* and *Klebsiella pneumoniae* infections. When nodules, centrilobular or miliary, are seen along with surrounding ground-glass opacities that give a halo appearance, the possibility of fungal infection should be considered. A fungal ball or invasive fungal infection should be suspected when a cavitating mass with a mobile or immobile component is present (►Figs. 20–22). Pleural effusion with pleural enhancement can also be seen in infections like *S. aureus* and *Nocardia*.^{40,41} Differentials based on predominant imaging patterns are discussed in ►Table 1.

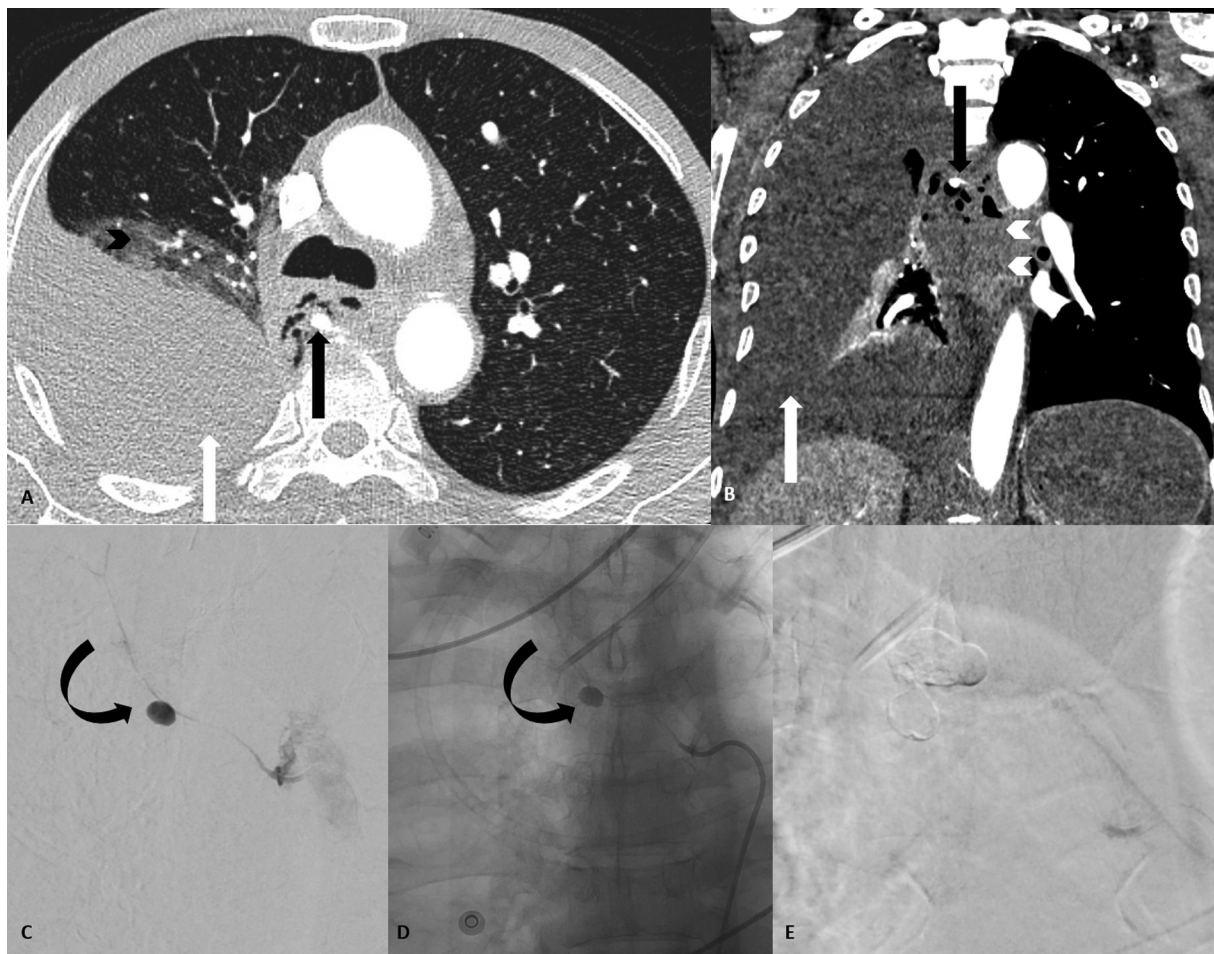


Fig. 14 Complications and coinfections in tuberculosis and immunocompromised. A 65-year-old gentleman with peripheral T-cell lymphoma, bulky mid-thoracic, posterior mediastinal, prevertebral and retroperitoneal mass on chemotherapy presented with blood in sputum four to five episodes since 2 days and low-grade fever since 1 month. (A, B) Computed tomography (CT) pulmonary angiography shows a pseudoaneurysm of the right intercostal artery anterior to the vertebral column (*black arrow*) and a large right pleural effusion (*white arrow*) with ground-glass opacities in the lower lobe (*black arrowhead*). The posterior mediastinal paravertebral mass (*white arrowhead*) is also noted. (C, D) The right intercostobronchial trunk was cannulated, and an angiogram was done, which revealed a pseudoaneurysm (*black arrowhead*). (E) Glue embolization was done.

Role of Imaging in Screening for TB in Immunocompromised Hosts

The idea of screening is for the following purposes:

- To detect active TB in patients with no or atypical symptoms in order to minimize patient morbidity and the spread of TB to others.
- To detect TBI and initiate preventive treatment.

Screening for TB in most scenarios employs clinical assessment for typical TB symptoms (fever, cough, night sweats, and weight loss) and immune assays (like tuberculin skin testing and interferon-gamma release assays).

Among others, screening for TBI is recommended in immunocompromised people, including PLHIV, transplant patients, those on immunosuppressive medications like TNF-alpha inhibitors and steroids, those with renal failure, diabetes, leukemia, and lymphoma, lung, or head and neck malignancy, and when TBI is discovered on screening, they are usually treated.

In PLHIV, CXR can be used as a screening tool in addition to four-symptom screening to increase the sensitivity or pretest probability of detecting TBI. WHO recommends annual CXRs in PLHIV and comparison with baseline.³

In other groups, if symptom screen or immune assays are positive, CXR is performed, along with sputum testing, to rule out active TB disease.

According to the American College of Radiology, CXR is appropriate in a clinical setting of suspected TB or if immune assays are positive. CT scans can be done when CXR findings are equivocal.⁴² MRI or ultrasound is not usually appropriate but may be used in individualized situations.

Quality of clinical practice guidelines for screening and management of TB infection in immunosuppressed patients is essential. According to a systematic review study of 38 published guidelines for screening and management of TBI in immunosuppressed patients conducted by Hasan et al, the quality and scope of clinical practice guidelines on TBI varied. While treatment recommendations were broadly consistent, screening recommendations varied across different

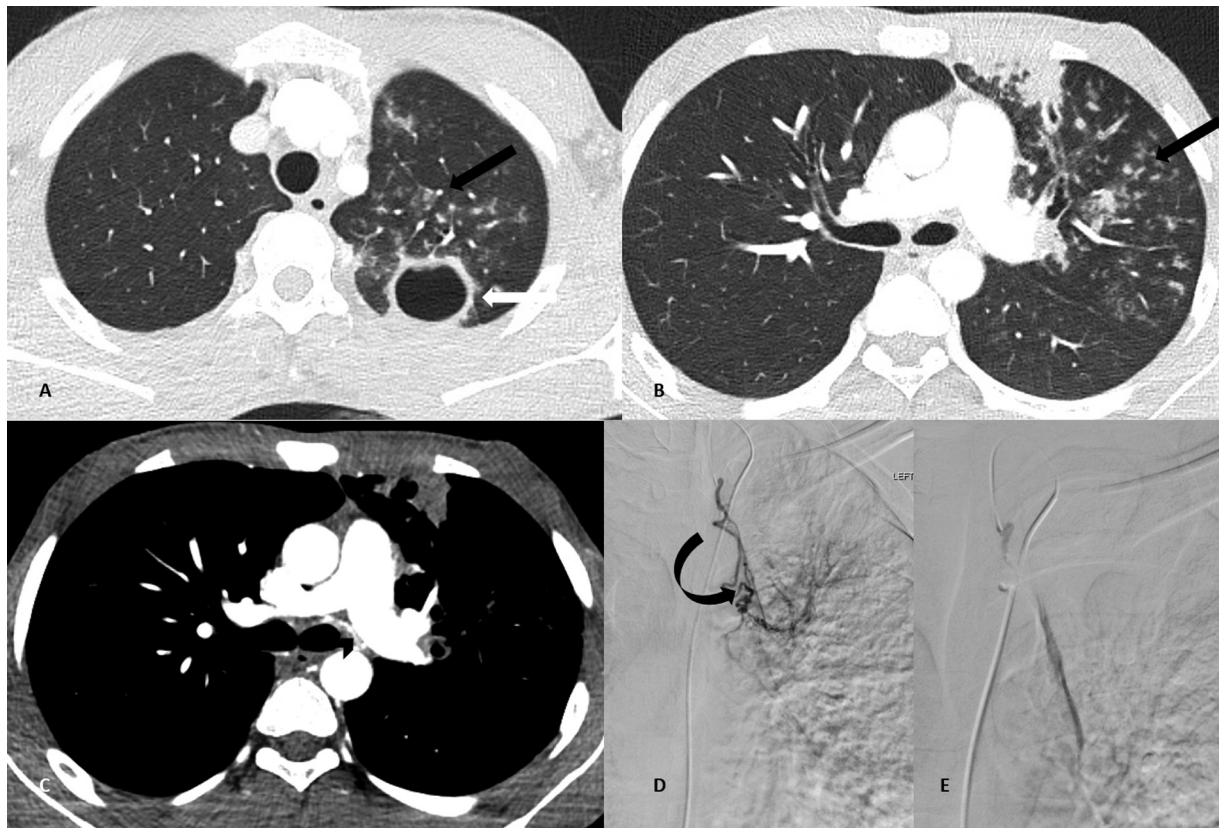


Fig. 15 A 16-year-old presented with cough and fever for 20 days and hemoptysis for 5 days. Computed tomography (CT) pulmonary angiogram shows (A) a cavity with surrounding consolidation in the left upper lobe (white arrow), (B) numerous centrilobular nodules in the left lung (black arrow), and (C) hypertrophied bronchial artery (black arrowhead). (D) The hypertrophied intercostobronchial trunk on the right side was cannulated. The Progreat was selectively taken into the bronchial artery (black curved arrow), (E) followed by embolization with PVA (polyvinyl alcohol) particles until stasis was achieved. *Mycobacterium tuberculosis* growth was noted on culture.

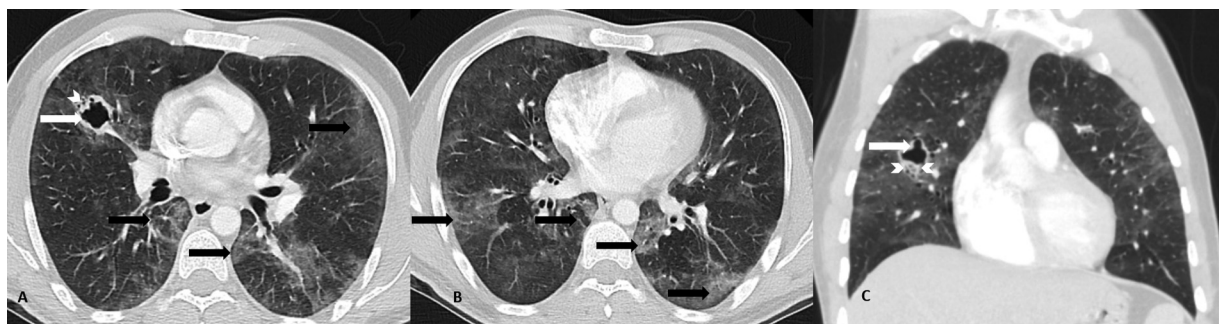


Fig. 16 A 27-year-old person living with human immunodeficiency virus (PLHIV) with a CD4 count of 13 cells/ μ L presented with breathlessness, cough, and fever for 4 months. (A) An axial image of the thorax (lung window) shows a cavity (white arrow) in the right upper lobe with a cluster of small cysts surrounding it (white arrowhead). (B) An axial image of the thorax (lung window) shows extensive patchy, ill-defined ground-glass opacities with peripheral and central regions involvement (black arrow). His sputum was negative for acid-fast bacillus (AFB) and Xpert. His *Pneumocystis jirovecii* pneumonia (PJP) antigen test was positive in bronchoalveolar lavage (BAL) analysis.

guidelines. To ensure better patient care, improving the consistency and quality of these guidelines is imperative.⁴³

Summary

In conclusion, the interplay between TB and immunocompromised states, such as HIV/AIDS, diabetes, or the use of

immunosuppressive medications, presents unique challenges, including a heightened risk of progression from latent to active TB and higher susceptibility to disseminated TB. The clinical and radiological manifestations of TB in immunocompromised hosts often deviate from the classical presentations observed in immunocompetent individuals. Rapid molecular tests like *M. tuberculosis* PCR and Xpert



Fig. 17 A 49-year-old man with human immunodeficiency virus (HIV) and bilateral chest infiltrates, with CD4 count of 44 cells/ μ L. Axial images of the computed tomography (CT) of the thorax in the lung window at the upper (A), middle (B), and lower (C) thoracic level show nodular and confluent ground-glass opacities, predominantly involving the upper lobes (white arrows), consolidation with cavitation (black arrow), and cylindrical bronchiectasis with peribronchial wall thickening (white arrowheads) in the lower lobes. Bronchoalveolar lavage (BAL) fluid was positive for cytomegalovirus (CMV) by polymerase chain reaction (PCR). He was treated for the same and also started on anti-TB therapy (ATT). The patient was symptomatically better, and follow-up CT after 12 months—(D) axial image in lung window—showed resolution of the nodular opacities in the upper lobe.

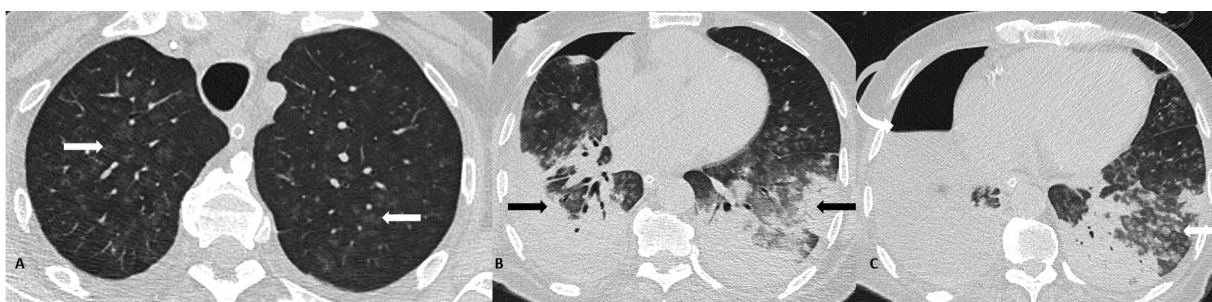


Fig. 18 A 71-year-old man with chronic kidney disease stage 5 presented with altered sensorium, low-grade fever on and off, and cough and expectoration. Axial images of the computed tomography (CT) of the thorax (in lung window) show (A) multifocal nodular ground-glass opacities (white arrow) in both lungs, (B) confluent areas of consolidation (black arrows) in both the lower lobes, and (C) right hydro-pneumothorax (white curved arrow). The patient succumbed to death. Sputum culture grew *Acinetobacter baumannii*.

TB/rifampin (RIF) are more sensitive for diagnosing pulmonary TB, but they still have limited sensitivity in paucibacillary pulmonary TB patients. Given the escalating global incidence of DM and CKD, alongside an increase in the utilization of immunosuppressive therapy, radiologists must adopt a nuanced approach to identify both standard and atypical imaging signs of TB, considering the patient's immunological status to provide timely information that can

help avoid unnecessary delay, minimize radiation exposure, and reduce patient expenses for the best possible care. The vulnerability of immunocompromised patients to coinfections and the presence of concurrent illnesses further complicate the TB disease course. Again, radiology plays an important role, along with laboratory investigations, in arriving at an appropriate diagnosis (–Table 2). Despite advancements in diagnostic tools like molecular tests and

Table 1 Radiological patterns and associated common etiologies in a few of the immunocompromised states

	HIV/AIDS	Solid organ transplant	HSCT	Diabetics
Air space consolidation	<ul style="list-style-type: none"> Bacterial Fungal Mycobacterium tuberculosis (lower CD4 counts present with consolidation and LN) Noninfectious (Kaposi's sarcoma or lymphoma) 	<ul style="list-style-type: none"> Bacterial (<i>Staphylococcus aureus</i>, GNB like <i>Pseudomonas</i>, <i>Klebsiella</i>, <i>Enterobacter</i>) Fungal Posttransplant lymphoproliferative disease (PTLD; nodular pattern is more common) 	<ul style="list-style-type: none"> In neutropenic phase: <ul style="list-style-type: none"> Bacterial Fungal (peripheral wedge-shaped consolidation due to angioinvasion and hemorrhagic infarction) In late phase: <ul style="list-style-type: none"> Organizing pneumonia (bronchocentric/subpleural) 	<ul style="list-style-type: none"> Bacterial Fungal <i>M. tuberculosis</i> (low attenuation necrotic areas, associated tree-in-bud opacities favor TB over bacterial)
Nodules or masses	<ul style="list-style-type: none"> Fungal: <ul style="list-style-type: none"> Cryptococcosis when CD4 count < 200/mm³ Invasive pulmonary aspergillosis when CD4 count < 50/mm³ Bacterial <ul style="list-style-type: none"> Septic emboli Nocardiosis Viral: usually micronodules Noninfectious <ul style="list-style-type: none"> Kaposi's sarcoma (CD4 < 200/mm²) Peribronchovascular irregular nodules Lymphoma 	<ul style="list-style-type: none"> Fungal Bacterial: <ul style="list-style-type: none"> Septic emboli Nocardiosis Viral: usually micronodules Noninfectious <ul style="list-style-type: none"> PTLD (randomly distributed nodules) 	<ul style="list-style-type: none"> In neutropenic phase: <ul style="list-style-type: none"> Fungal (<i>Aspergillus</i>, <i>Mucor</i>, <i>Candida</i>, <i>Cryptococcus</i>) CT halo sign in invasive pulmonary aspergillosis and reverse halo in <i>Mucor</i> Other infections (<i>Nocardia</i>, viral, septic emboli) Bacterial: <ul style="list-style-type: none"> Septic emboli Nocardiosis Viral: usually micronodules Noninfectious <ul style="list-style-type: none"> PTLD (randomly distributed nodules) 	<ul style="list-style-type: none"> Bacterial Fungal
Micronodules	<ul style="list-style-type: none"> Miliary TB Histoplasmosis NTM Noninfectious: miliary hematogenous metastases 	<ul style="list-style-type: none"> Miliary TB Viral Candida Noninfectious: miliary hematogenous metastases 	<ul style="list-style-type: none"> Miliary TB Viral Candida Noninfectious: miliary hematogenous metastases 	<ul style="list-style-type: none"> Miliary TB Histoplasmosis Noninfectious: miliary hematogenous metastases
Cavity	<ul style="list-style-type: none"> TB Nontuberculous Mycobacterial (NTM) Fungal <ul style="list-style-type: none"> Histoplasmosis Aspergillus Mucor Cryptococcosis <i>Nocardia</i> (cavitation in up to 1/3) Bacterial: GNB 	<ul style="list-style-type: none"> TB Nontuberculous Mycobacterial (NTM) Fungal <ul style="list-style-type: none"> Histoplasmosis Aspergillus Mucor Cryptococcosis <i>Nocardia</i> (cavitation in up to 1/3) Bacterial: GNB PTLD 	<ul style="list-style-type: none"> TB Nontuberculous Mycobacterial (NTM) Fungal <ul style="list-style-type: none"> Histoplasmosis Aspergillus Mucor Cryptococcosis <i>Nocardia</i> (cavitation in up to 1/3) Bacterial: GNB 	<ul style="list-style-type: none"> TB Nontuberculous Mycobacterial (NTM) Fungal <ul style="list-style-type: none"> Histoplasmosis Aspergillus Mucor Cryptococcosis <i>Nocardia</i> (cavitation in up to 1/3) Bacterial: GNB

Abbreviations: AIDS, acquired immunodeficiency syndrome; GNB, gram-negative bacilli; HIV, human immunodeficiency virus; HSCT, hematopoietic stem cell transplant; LN, lymphadenopathy.

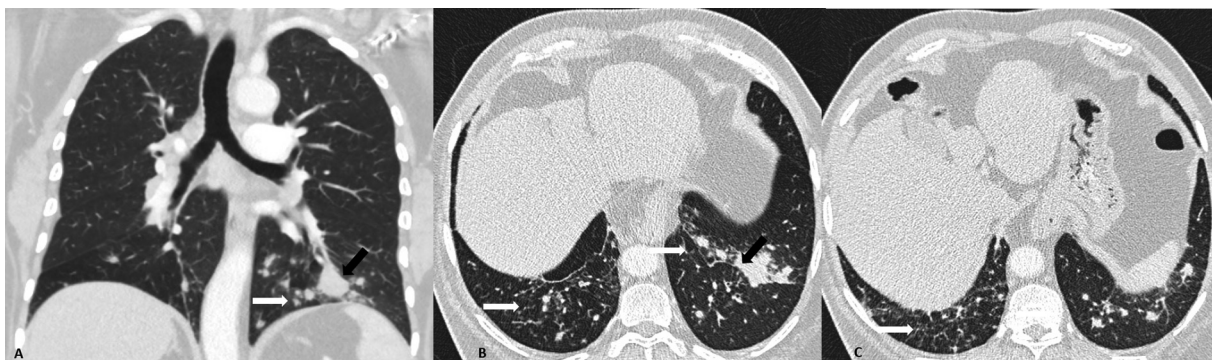


Fig. 19 A 65-year-old man presented with a dry cough and loss of weight for three months and a low-grade fever for ten days. (A) Coronal reformation and (B & C) axial images of the Computed tomography (CT) thorax show patchy consolidation (black arrow) in the left lower lobe and multiple nodules (white arrow) in both lower lobes. Sputum culture grew *Pseudomonas*.

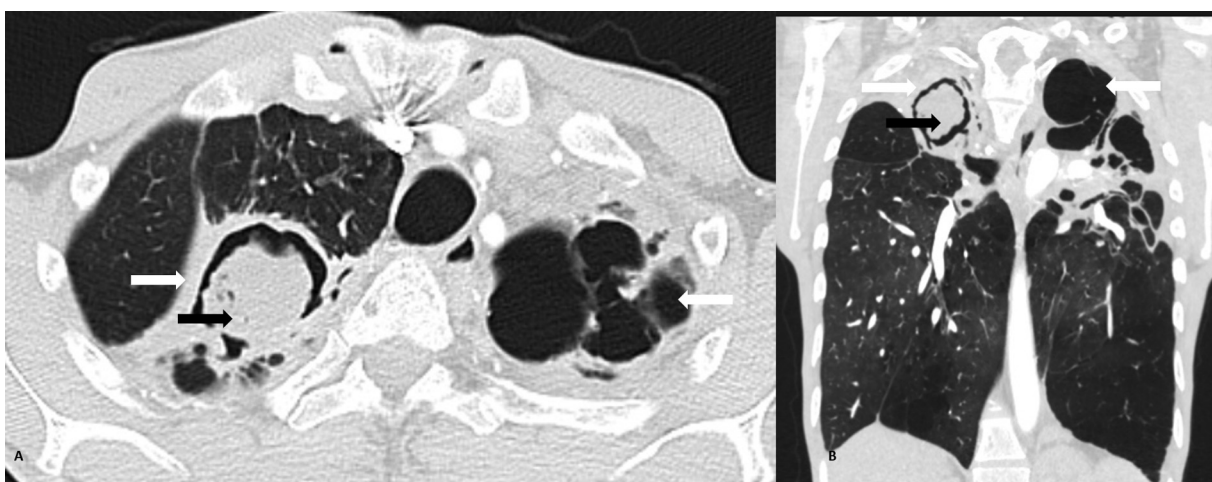


Fig. 20 A 40-year-old man with diabetes presented with cough, breathlessness, and weight loss with active streaky hemoptysis. The (A) axial image and (B) coronal reformatted image of the computed tomography (CT) of the thorax (in lung window) show fibrocavitary changes in both the upper lobes (white arrows) with an intracavitary soft-tissue density (black arrow) in one of the cavities in the right upper lobe suggestive of aspergilloma, which was proven microbiologically on sputum and bronchoalveolar lavage (BAL) analysis. He also had a history of pulmonary tuberculosis (PTB) 20 years ago and had completed treatment.

Table 2 Common radiological features of tuberculosis (TB) in a few of the immunocompromised states

Immunocompromised state	Common radiological features in TB
HIV: early stages (CD4 count > 200 cells/ μ L)	<ul style="list-style-type: none"> • Centrilobular nodules with or without tree-in-bud appearance • Thick-walled cavities with or without consolidation • Pleural effusion with pleural enhancement
HIV: late stages (CD4 count < 200 cells/ μ L)	<ul style="list-style-type: none"> • Lymphadenopathy • Noncavitary consolidation with mid/lower lobe predilection • Miliary TB, disseminated TB
DM (two- to threefold higher risk of developing TB)	<ul style="list-style-type: none"> • Multiple cavities • Nonsegmental distribution • Multilobar involvement with lower lobe predilection
CKD (risk of active TB in CKD is 6.9- to 52.5-fold higher)	<ul style="list-style-type: none"> • Consolidation, centrilobular nodules • Pleural effusion, pleural nodularity, adenopathy • Other lung findings in CKD can mimic TB

Abbreviations: CKD, chronic kidney disease; DM, diabetes mellitus; HIV, human immunodeficiency virus.

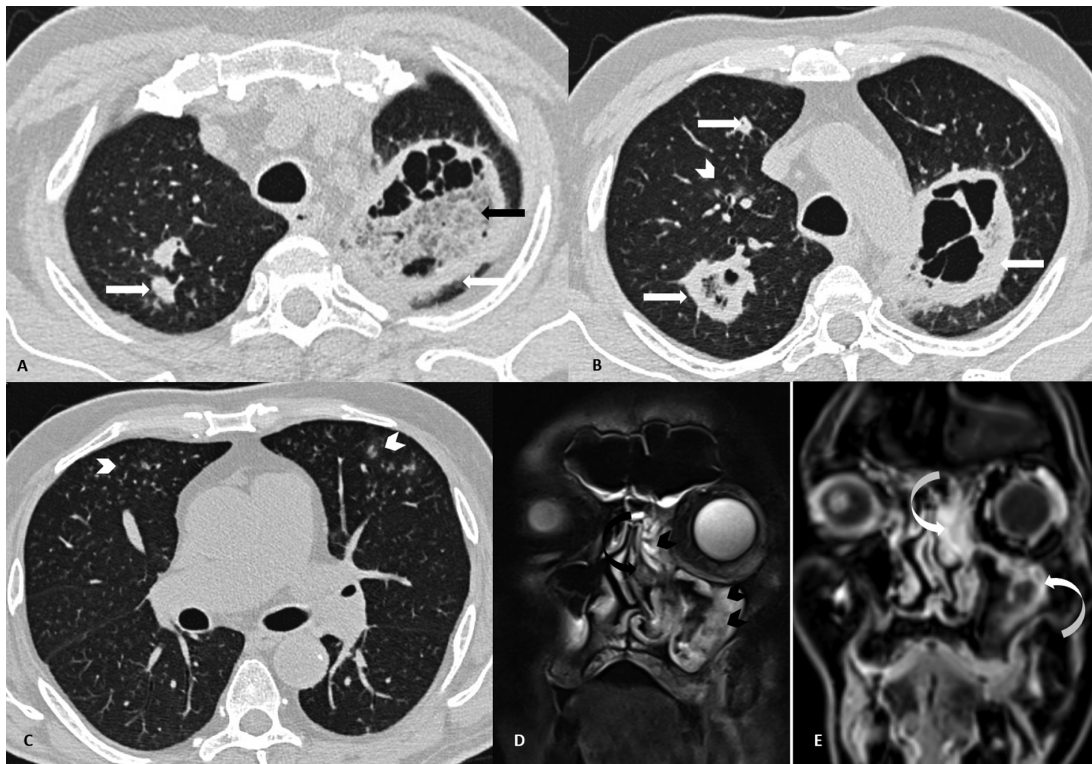


Fig. 21 A 65-year-old man with uncontrolled diabetes and HbA1c of 10.9% presented with high-grade intermittent fever and left-side cheek swelling for 3 weeks. (A–C) The axial computed tomography (CT) images of the thorax (in lung window) show thick-walled cavities (*white arrow*) in both the upper lobe. The cavity in the left upper lobe gives a typical bird's nest appearance (*black arrow*), suggestive of pulmonary mucormycosis. Branching nodules are seen in the upper lobes and the right middle lobe (*white arrowhead*). T2 coronal image (D) through the face shows near complete opacification of the left maxillary and ethmoid sinuses (*black arrowhead*) and mild hypointensity in the left middle turbinate (*black curved arrow*). T1 postgadolinium coronal image (E) shows enhancing polypoidal soft-tissue mass (*white curved arrow*) in the left maxillary and ethmoid sinuses. He underwent endoscopic sinonasal debridement and, on histopathology, was confirmed to be an acute invasive mucormycosis.

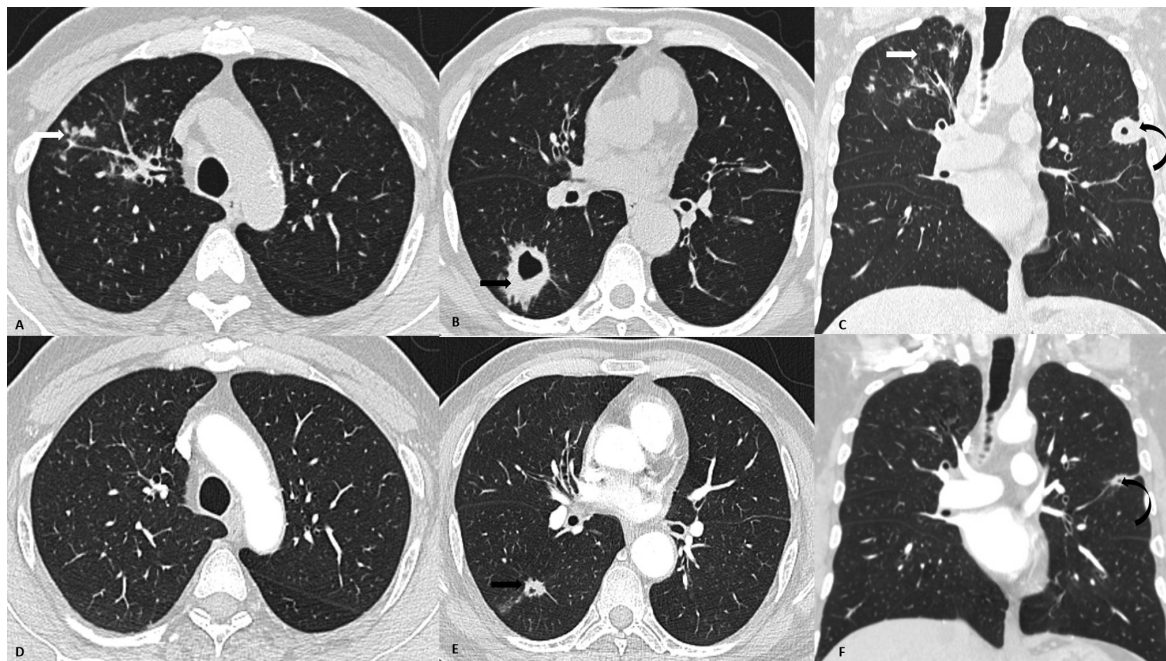


Fig. 22 A 56-year-old man presented with cough and intermittent fever for 2 weeks on a background of uncontrolled diabetes mellitus with an HbA1C of 12.5. The axial image of the thorax computed tomography (CT) in the lung window shows (A) a small peri-bronchial consolidation in the right upper lobe (*white arrow*) and (B) a thick-walled cavity in the right lower lobe (*black arrow*). The coronal reformatted image shows (C) a small peribronchial consolidation (*white arrow*) in the right upper lobe and another thick-walled cavity in the lingula (*curved black arrow*). He underwent a CT-guided biopsy of the right lung cavity consolidation, and histopathology showed invasive mucormycosis. He was initiated on lipid emulsion amphotericin B. Follow-up CT 6 months later showed resolution of the consolidation and nodules in the right upper lobe and reduction in the size of the thick-walled cavities in the right lower lobe (*black arrow*) and lingula (*black curved arrow*).

high-resolution CT scans, there remain gaps in their sensitivity and integration of these technologies into guidelines for managing TB in immunocompromised patients. This calls for establishing committees that include a wide range of experts to regularly review and update guidelines for TB management in immunocompromised patients at the policy-making level, and emphasize the importance of interdisciplinary collaboration among health care professionals in diagnosing and managing TB in immunocompromised patients.

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Conflict of Interest

None declared.

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