Scientific Research Publishing

Journal of Tuberculosis Research, 2025, 13(3), 110-121
https://www.scirp.org/journal/jtr
ISSN Online: 2329-8448
ISSN Print: 2329-843X

Tuberculosis Presenting as Incidental Pulmonary Nodules: A Clinical Case Series and Review

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How to cite this paper: Han, W., Saggar, S.K. and Han, P.S. (2025) Tuberculosis Presenting as Incidental Pulmonary Nodules: A Clinical Case Series and Review. *Journal of Tuberculosis Research*, **13**, 110-121.
https://doi.org/10.4236/jtr.2025.133011

Received: August 2, 2025
Accepted: August 26, 2025
Published: August 29, 2025

Abstract

Background: The increasing use of diagnostic imaging, particularly low-dose CT (LDCT) for lung cancer screening, has led to an increase in the detection of solitary pulmonary nodules. While these nodules are often evaluated for malignancy, infectious causes, such as tuberculosis (TB), may be under-recognized, particularly in asymptomatic individuals. **Methods:** We present a case series of five patients diagnosed with tuberculosis during the evaluation of lung nodules in a community-based pulmonary practice in the United States between June 2024 and May 2025. All patients were asymptomatic, and lung nodules were found incidentally or during LDCT screening. Each patient underwent biopsy, either via CT-guided or robot-assisted bronchoscopy, for tissue diagnosis due to concern for malignancy. All patients were smear-negative and had no respiratory or systemic symptoms suggestive of TB. **Results:** Biopsy in all five cases revealed necrotizing granulomatous inflammation, and subsequent culture or biopsy results confirmed *Mycobacterium tuberculosis*. One patient was found to have multidrug-resistant TB. Four of the five patients were immigrants from TB-endemic regions. The imaging findings varied, demonstrating cavitation, airway obstruction, or satellite nodules. In all cases, sputum samples remained negative for AFB, and contact investigations, including those among healthcare workers, revealed no evidence of transmission. **Conclusion:** This series highlights the emerging phenomenon of incidental pulmonary tuberculosis, which is asymptomatic, sputum-negative, biopsy-proven TB discovered during malignancy workup. These cases suggest that such presentations may represent a less infectious form of TB, raising important questions regarding transmission risk, infection control, and diagnostic strategy. As imaging and biopsy tools continue to improve, clinicians should maintain a broader differential diagnosis when evaluating solitary pulmonary nodules, particularly in patients from high-

risk populations.

Keywords

Pulmonary Tuberculosis, Solitary Pulmonary Nodules, Contact Tracing

1. Introduction

Each year in the United States, over 1.5 million patients have an lung nodule [1]. An estimated 120 thousand lung nodules are found in low-dose CT screening chests [2] [3]. As the number of diagnostic imaging tests becomes more frequent in practice, the number of lung nodules that are found continues to increase.

Previous studies on lung nodules have focused on malignancy evaluation [4] [5]. Approximately 10% of lung nodules between 0.8 and 3 cm in size found on screening are malignant [6]. Most lung nodules discovered either incidentally or through screening are benign. However, because of the attention given to cancer diagnosis, the possibility of tuberculosis is often overlooked and underappreciated.

We present a series of cases in which pulmonary tuberculosis was unexpectedly diagnosed during the evaluation of lung nodules found on screening for lung cancer or in otherwise asymptomatic patients. We consider these cases to be examples of incidental pulmonary tuberculosis because the diagnosis was discovered in asymptomatic patients, with negative sputum cultures, via biopsy of a pulmonary nodule for other indications. These cases represent a pattern of tuberculosis with both a low disease burden and low infectiousness.

2. Case 1

A 76-year-old male with a history of smoking, chronic obstructive pulmonary disease (COPD) with fibrosis (normal FEV1), and latent tuberculosis infection (previously treated with rifampin) was found to have a 2 cm cavitary nodule in the right upper lobe on low-dose CT (LDCT) performed for lung cancer screening (see **Figure 1**). He was followed up for COPD with fibrosis, although his pulmonary function tests demonstrated a normal FEV1, and he did not require treatment with inhalers or other pulmonary medications. The Mayo Clinic model calculated 94% probability of malignancy. Owing to the patient's underlying lung disease, a decision was made to obtain a tissue diagnosis prior to surgical resection.

CT-guided lung biopsy revealed necrotizing granulomas with acid-fast bacilli (AFB) on staining. However, cultures from the biopsy specimens did not yield any organisms. Sputum AFB studies were negative, and HIV testing was non-reactive. The contact investigation was also negative. The patient was empirically started on RIPE therapy (rifampin, isoniazid, pyrazinamide, and ethambutol). Follow-up CT imaging demonstrated resolution of the nodule, with residual cavitary and bullous changes.

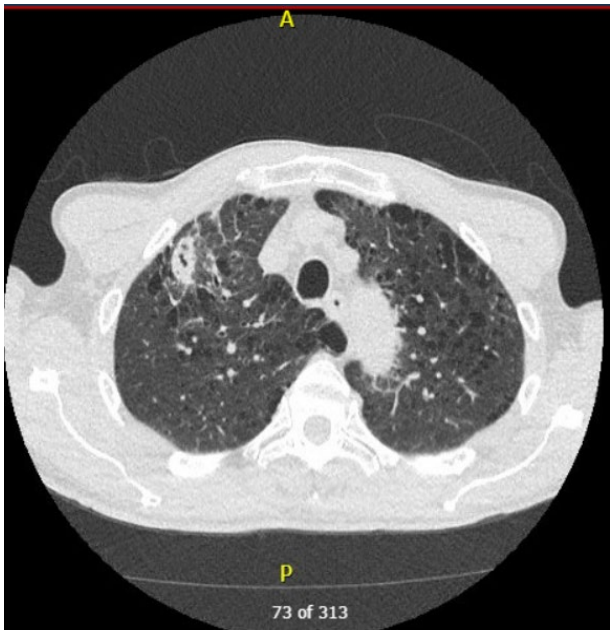

Figure 1. Low-dose screening CT chest shows a 2 cm right apical nodule with cavitation, with a background of emphysema and mild fibrosis.

3. Case 2

A 58-year-old Asian male with a history of chronic lower back pain and long-standing tobacco use underwent low-dose computed tomography (CT) for lung cancer screening. Imaging revealed an irregular right upper lobe (RUL) nodule with a satellite lesion and a 1 cm RUL endobronchial lesion, raising concern for neoplasm versus mucoid impaction (see **Figure 2**). The patient denied any systemic or respiratory symptoms, including fever, chills, cough, or sputum production. The patient was unable to produce sputum for analysis. Pulmonary function testing was normal, and laboratory workup revealed a positive interferon-gamma release assay (IGRA).

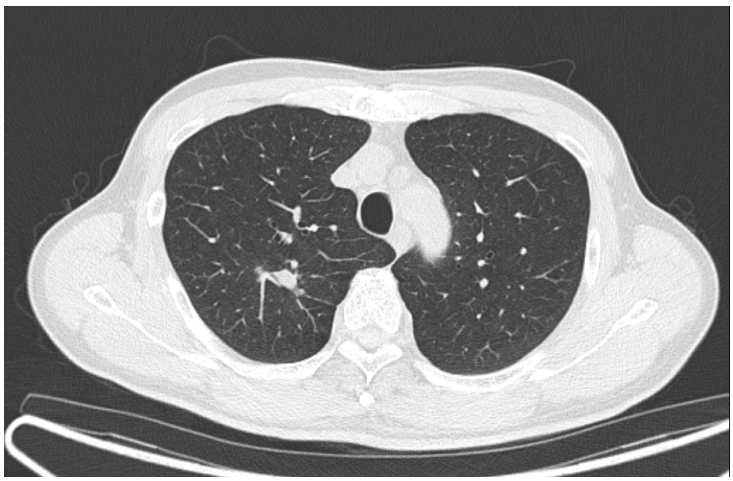

Figure 2. 58 yo smoker with RUL 1 cm nodule, possibly representing an impacted airway, found on screening CT chest.

The patient underwent a robot-assisted bronchoscopy. Biopsy of the endobronchial lesion revealed necrotizing granuloma. Bronchoalveolar lavage (BAL) smear was positive for acid-fast bacilli (AFB). HIV testing and contact investigations were negative. Empiric therapy with RIPE (rifampin, isoniazid, pyrazinamide, and ethambutol) was initiated. Subsequently, the sputum samples collected remained negative for AFB. After eight weeks of RIPE therapy, bronchoscopic cultures returned positive results for multidrug-resistant *Mycobacterium tuberculosis*. Repeat sputum AFB testing was negative. The patient was transferred to a BPaL regimen (bedaquiline, pretomanid, and linezolid).

4. Case 3

A 71-year-old Asian man with gastric cancer was referred to our hospital for endoluminal obstruction. He had previously been treated for tuberculosis in his twenties and had mild bronchiectasis of the right middle lobe. He had been diagnosed with Stage IV gastric adenocarcinoma (peritoneal metastases) two years earlier and had undergone palliative gastrectomy. He continued treatment with a combination of FOLFOX chemotherapy and nivolumab immunotherapy (now in cycle 30), with complete radiographic response. During recent routine follow-up, a surveillance CT of the chest, abdomen, and pelvis revealed worsening right middle lobe (RML) airway obstruction in the setting of previously known bronchiectasis (see Figure 3). The patient was asymptomatic from a pulmonary standpoint; however, intermittent fatigue was reported. Bronchoscopy with bronchoalveolar lavage (BAL) was performed. Cytology was negative for malignancy, and initial AFB smears were negative.

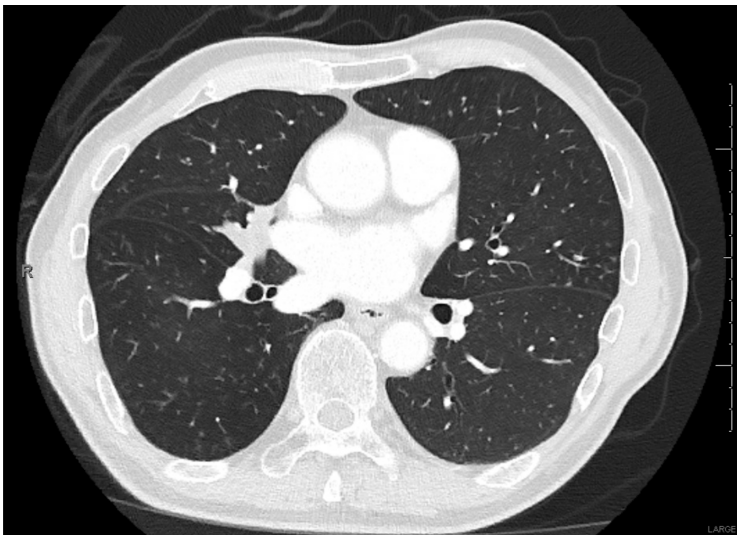

Figure 3. 71 yo gentleman with partial obstruction of proximal right middle lobe airways, in an area of previous bronchiectasis.

Approximately three weeks later, the patient presented to the emergency department with abdominal pain, anorexia, nausea, and vomiting, associated with a

six-pound weight loss. A repeat CT of the abdomen/pelvis demonstrated wall thickening and luminal narrowing at the rectosigmoid junction, along with lymphadenopathy and hepatic and splenic nodules. Colonoscopy revealed a rectal mass, and a biopsy confirmed a new diagnosis of colorectal adenocarcinoma.

Following hospital discharge, BAL cultures were positive for *Mycobacterium tuberculosis*. The patient began receiving RIPE therapy (rifampin, isoniazid, pyrazinamide, and ethambutol). An extensive contact investigation, including healthcare and community contact, revealed no evidence of IGRA conversion. Shortly thereafter, the patient was readmitted with worsening anorexia and weight loss. Owing to functional decline, he was transitioned to comfort care and transferred to an inpatient hospice.

5. Case 4

A 48-year-old Asian woman with a history of thyroid cancer (thyroidectomy) presented with an enlarged right upper lobe (RUL) lung nodule. Approximately three years prior, a preoperative chest radiograph obtained before hysterectomy for uterine fibroids and adenomyosis incidentally noted RUL nodularity. Subsequent CT imaging at an outside hospital revealed a 1.7 cm nodule that remained stable on repeat imaging six months later. The patient remains asymptomatic. A repeat chest CT scan at 18 months showed interval growth of the RUL nodule to approximately 2 cm (see **Figure 4**). She tested positive for interferon-gamma release assay (IGRA), but was unable to produce sputum. Robot-assisted bronchoscopy with navigational guidance was performed. Biopsy of the nodule revealed necrotizing granulomas, and bronchoscopic AFB smears were negative.

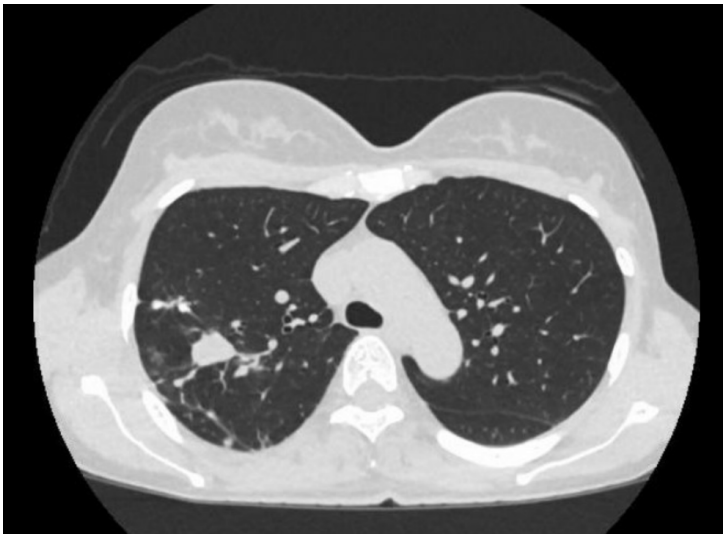

Figure 4. Enlarging 2 cm RUL nodule with small satellite nodules.

Given the increased nodule size and high clinical suspicion, empirical RIPE therapy (rifampin, isoniazid, pyrazinamide, and ethambutol) was initiated. Sputum samples collected from the Department of Health on three separate occasions were

negative for AFB. HIV testing was non-reactive, and the contact investigation was negative. Bronchoscopic cultures ultimately showed pan-sensitive *Mycobacterium tuberculosis*.

6. Case 5

A 76-year-old woman with a medical history of diabetes mellitus, hypertension, hyperlipidemia, and no history of smoking was initially hospitalized for syncope evaluation. During admission, cardiac evaluation was unremarkable. As part of the workup, a CTA of the chest was performed, which was negative for pulmonary embolism but revealed a right upper lobe (RUL) bronchocele measuring 1.2 × 2.5 cm (see Figure 5). On further examination, the patient had a chronic dry cough that had persisted for several years. Pulmonary function testing showed normal lung function. A follow-up CT chest after three months demonstrated mild enlargement of the RUL lesion. PET/CT showed moderately increased activity.

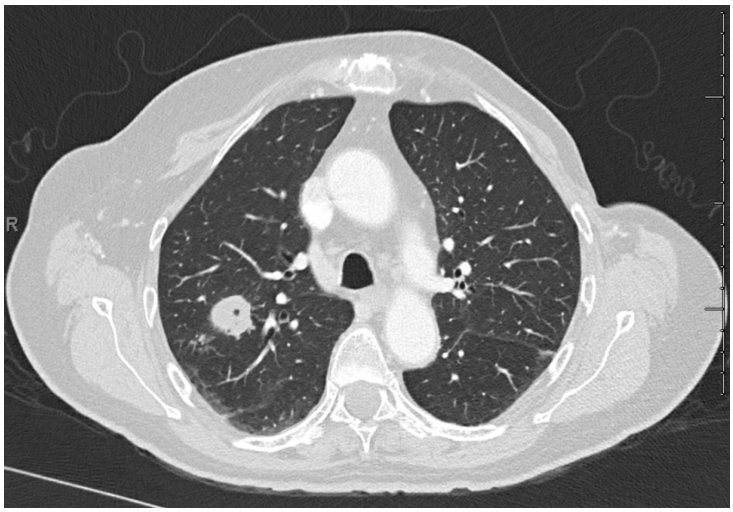

Figure 5. 76 yo woman with 2 cm RUL nodule found on CT chest angiogram. This finding was described as a possible bronchocele.

The patient underwent a robot-assisted bronchoscopy. A biopsy revealed necrotizing granulomatous inflammation. The sputum samples collected on three separate occasions were negative for acid-fast bacilli (AFB). HIV testing and contact investigations also yielded negative results. Given the radiographic progression and biopsy findings, she was empirically treated on RIPE therapy (rifampin, isoniazid, pyrazinamide, and ethambutol) for presumed pulmonary tuberculosis. After four weeks, AFB culture showed pan-sensitive *Mycobacterium tuberculosis*.

7. Discussion

The five cases presented here represent scenarios in which tuberculosis was unexpectedly found. In all five cases, the patients presented without any systemic or pulmonary symptoms of tuberculosis. All cases presented for evaluation of lung nodules found on chest CT in asymptomatic patients, either as part of screening for lung

cancer or incidentally (see Table 1). Evaluation was undertaken specifically because of the suspicion of a possible malignancy.

Table 1. Summary of cases.

	Demographics	Comorbidities	Clinical presentation	Radiographic findings	Biopsy route	Diagnosis
Case 1	76 yo male	Former smoker, COPD, h/o LTBI, previously completed prophylaxis	Asymptomatic, low-dose screening CT chest	2 cm irregular RUL cavitary nodule, background emphysema with fibrosis	Transthoracic needle aspiration	Biopsy with necrotizing granuloma. Nodule improved with RIPE
Case 2	58 yo male	Current smoker, h/o chronic low back pain	Asymptomatic, low-dose screening CT chest.	1 cm RUL nodule, endobronchial, with satellite nodule	Robot-assisted navigational bronchoscopy	Biopsy with necrotizing granuloma. Culture positive
Case 3	71 yo male	H/o previous TB, gastric cancer, on chemotherapy	Asymptomatic, on surveillance CT C/A/P	Bronchiectasis with RML endobronchial occlusion	Bronchoscopy with BAL	Culture positive
Case 4	58 yo woman	H/o thyroid CA, uterine fibroids	Asymptomatic. Pre-op CXR	RUL nodule with satellite nodules	Robot-assisted navigational bronchoscopy	Biopsy with necrotizing granuloma. Culture positive
Case 5	76 yo woman	DM, HTN, HLD, non-smoker	Chronic cough, with abnormal admission CXR (hospitalization for syncope)	RUL cavitary nodule, with possible airway obstruction	Robot-assisted navigational bronchoscopy	Biopsy with necrotizing granuloma. Culture positive

Note: All cases had negative sputum AFB.

In the past two decades, lung nodules have become increasingly more common [1]. In 2021, the USPSTF expanded recommendations for annual low-dose screening CT to include men and women aged 50 - 80 years with a twenty pack-year history of smoking [7]. The American Cancer Society has adopted the same guidelines [8]. The first two cases were initially found on low-dose chest CT. However, most lung nodules are found on CT scans performed for other reasons [1]. Incidentalomas in the chest have become increasingly common [9] [10]. The latter three cases were initially discovered using imaging performed for different indications.

The diagnostic tools that can be used to evaluate lung nodules have also improved. Nodule calculators are recommended to help stratify risk of lung cancer [5] [6]. Serum biomarkers have shown promise in guiding the decision to continue observation or proceed with biopsy [11]. For intermediate-to high-risk nodules, biopsies can be performed with increased safety and accuracy, regardless of size and location, owing to advances in biopsy techniques. Transthoracic lung biopsies can be supplemented with hydrogel plugs to reduce the risk of pneumothorax [12]. Navigational robotic systems improve the reach of bronchoscopy even into the apex of the right upper lobe, a notoriously hard-to-reach area [13]. These advances have helped to identify lung cancers at an earlier stage, which can improve treatment and survival [14]. The same may be true for infection. The first case in our series was diagnosed using CT guidance, the third case was diagnosed

using conventional bronchoscopy, and the remaining three cases were biopsied using navigational bronchoscopy.

A limited number of case reports of tuberculosis mimicking lung cancer have been published, primarily from endemic areas [15] [16]. The incidence of pulmonary tuberculosis among asymptomatic lung nodules remains unknown. Two cases of microbiologically proven pulmonary TB were included in a five-year retrospective analysis of caseating granulomas found during VATS for solitary pulmonary nodules at Tokyo University Hospital [17], although the total number of lung nodules evaluated was not reported. Similarly, a single case of microbiologically proven TB was identified in a retrospective six-year review of lung biopsies (either via CT guidance, bronchoscopy, or surgery) performed at an academic hospital [18]. We present five cases of incidental pulmonary tuberculosis that were diagnosed within a 12-month period (June 2024 to May 2025) in a community-based general pulmonary practice. During this period, we performed 118 diagnostic procedures for lung abnormalities (including 10 CT-guided lung biopsies and 108 bronchoscopies). In this period, the majority of biopsies proved to be malignant, but approximately one in 20 biopsies were diagnosed as tuberculosis. The incidence of tuberculosis in lung biopsies likely depends on various demographic factors.

The paradigm of tuberculosis has shifted, with some authors emphasizing the continuum of disease rather than dividing tuberculosis into latent and active disease states [19]. Likewise, although pulmonary tuberculosis has been described as a disease causing high mortality and contagion, the manifestations can be protean. In endemic areas, screening programs using chest radiographs can identify minimally symptomatic patients with subclinical tuberculosis. In these populations, the prevalence of subclinical tuberculosis can be high (although the reported prevalence varies, partly depending on the threshold for defining symptoms [20]-[22]. The current WHO treatment recommendations do not distinguish between asymptomatic and symptomatic cases of tuberculosis. However, asymptomatic TB has recently been featured as a condition that needs to be recognized and defined [23]. The WHO is currently reviewing its guidance in these cases for programmatic action [23].

Our cases were similar to those described as having subclinical tuberculosis in the screening studies cited above. However, subclinical TB was previously considered infectious [22], with cases confirmed with sputum testing, whereas our patients did not have positive sputum tests, and contact investigation conducted per CDC guidelines [24] did not show any evidence that they had been contagious. A more recent framework included a separate category for subclinical TB that is non-infectious; however, cases were discovered with sputum testing [25] [26]. In the cases described here, because sputum testing was negative (after induction), a diagnosis of pulmonary tuberculosis could only be made with invasive testing. Other studies have described similar cases of incipient TB, suggesting that the disease is early in the course of becoming active [27]. Although this may have been the scenario described in Case 4, the natural course of sputum-negative, asymptomatic tubercu-

losis without treatment is unknown (WHO). Incidental tuberculosis may be closer to latent tuberculosis on the tuberculosis continuum. Some cases may behave like low-grade infections and/or become dormant again, as in cases of nontuberculous mycobacteria.

In our series, we considered TB to be incidental because of the manner in which these cases presented themselves and were identified. Unlike subclinical or asymptomatic TB that has been detected through screening programs in endemic areas, these cases were unsuspected and only came to light because of imaging performed for entirely different indications. Incidental TB may be closer on the spectrum to latent TB infectious rather than active TB.

This series highlights several issues that have become increasingly important. During the evaluation of incidental lung nodules, which risk factors make TB more important to consider? Although our cases were all diagnosed in the United States, four were found in immigrants from areas where TB is common. Consideration of TB as a cause of solitary pulmonary nodules has been well described in endemic areas and in susceptible populations, such as those with active HIV infection [28] [29]. Our practice has been to check IGRAs in any patient from an endemic area with any lung abnormality. Thus, two patients were found to have positive IGRAs results as part of their initial evaluation. In addition, Case 1 had previously received prophylactic treatment for LTBI and Case 3 had already been treated for tuberculosis. In Case 2, the culture eventually showed multidrug-resistant TB, although he had no history of previous treatment.

Some CT findings might also provide clues to possible TB. In Cases 3 and 4, the nodules occurred in areas of underlying bronchiectasis, and in both cases, as well as in Case 5, the nodules were described as occluding the airway. In Cases 1 and 5, small areas of cavitation were observed. In Cases 2, 3, and 4, small areas of satellite nodularity were noted. Interestingly, all cases were found in the right upper or middle lobes. However, the usefulness of these findings in differentiating malignancy from TB remains unknown. Certainly, most CT findings of TB can mimic malignancy [30].

Older studies have demonstrated that patients with negative smears have significant transmission [31]. Dinkele *et al.* recently demonstrated that TB can spread without the presence of a cough [32]. However, previous studies performed in endemic areas did not report the actual incidence of subclinical TB transmission. In endemic areas, isolation to prevent transmission might not be viable or rational but is important for the control of tuberculosis in the United States [33].

Most guidelines do not include precautions against tuberculosis during evaluation of lung nodules [5] [29]. Isolating asymptomatic patients without confirmation of TB seems unreasonable. In our series, the patients were isolated only after diagnosis was confirmed and treatment was initiated until AFB smears were negative × 3, as has been the standard practice in all cases of active tuberculosis [33]. However, during the evaluation, many contacts (including healthcare workers) were potentially exposed. Contact investigation, conducted according to state guidelines,

suggested that none of the patients had been contagious. Cases one and five lived alone, and Cases 2, 3 and 4, each had a single household contact. In Case 4, the contact investigation included 135 healthcare workers who had been exposed during hospitalization before culture showed tuberculosis. Similarly, in all these cases, the proceduralists, anesthesiologists, and nurses involved in their biopsies remained negative. In cases two and five, the patients underwent PFTs, and the respiratory therapists who performed the PFTs remained negative on IGRA. As reported above, all five patients had negative smears at the time of diagnosis. These cases suggest that incidental tuberculosis may not be contagious.

8. Conclusion

As the number of lung nodules found on imaging continues to rise and diagnostic tools improve, incidental tuberculosis may become a more common finding. Our series suggests that incidental pulmonary tuberculosis may be less contagious than typical presentations, a reassuring finding for community and healthcare contacts. Larger studies of incidental pulmonary TB may be helpful in guiding diagnostic strategies and policies for similar cases.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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