

Incidental diagnosis of pulmonary tuberculosis in patients referred for diagnostic bronchoscopy or clinical follow-up due to malignant tumor disease: a cross-sectional study

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Abstract

Introduction: Incidental pulmonary tuberculosis is unexpectedly diagnosed in patients without prior clinical suspicion, usually during investigations of other diseases. Few studies have been conducted on this type of diagnosis. Here, we describe the general characteristics of incidental pulmonary tuberculosis diagnosis in patients undergoing bronchoscopy for neoplastic diseases.

Materials and Methods: A cross-sectional study was conducted on patients with an incidental diagnosis of pulmonary tuberculosis identified during diagnostic bronchoscopy performed on individuals suspected of having cancer or undergoing cancer surveillance. tuberculosis diagnosis was diagnosed using GeneXpert MTB/RIF.

Results: Eighteen patients were included, with a mean age of 50.3 years (SD: 20.4) and a predominance of females (55%;10/18). The most frequent comorbidities were diabetes mellitus (44%; 8/18) and systemic hypertension (44%;8/18). Seventeen% (3/18) of the patients had previously received oncological treatments. The most common symptom associated with the procedure indication was involuntary weight loss (61.1%, 11/18). Seventeen% (3/18) had a positive tuberculin test result, while none had a positive sputum smear result. Chest computed tomography revealed alveolar/interstitial infiltrates in 50% (9/18) of patients, masses in 28% (5/18), nodules in 22% (4/18), and lymphadenopathies in 28% (5/18).

Discussion: Incidental pulmonary tuberculosis occurs in patients with suspected cancer or those under oncological follow-up. It is crucial to consider differential diagnosis in bronchoscopic studies.

Keywords: tuberculosis; diagnosis; incidental; cancer.

Diagnóstico incidental de tuberculosis pulmonar en pacientes remitidos para broncoscopia diagnóstica o seguimiento clínico por enfermedad tumoral maligna: un estudio transversal

Resumen

Introducción: La tuberculosis pulmonar incidental se diagnostica inesperadamente en pacientes sin sospecha clínica previa, generalmente durante estudios por otras enfermedades. Existen pocos estudios sobre este tipo de diagnóstico. Describimos las características generales sobre el diagnóstico incidental de tuberculosis pulmonar en pacientes sometidos a broncoscopia por enfermedad neoplásica.

Materiales y Métodos: Se llevó a cabo un estudio transversal en pacientes con diagnóstico incidental de tuberculosis pulmonar, identificado durante broncoscopias diagnósticas realizadas a personas con sospecha de cáncer o en seguimiento oncológico. El diagnóstico de tuberculosis se realizó utilizando la técnica GeneXpert MTB/RIF.

Resultados: Se incluyó un total de 18 pacientes, con una edad promedio de 50,3 años (DE: 20,4) y predominio de mujeres (55%; 10/18). Las comorbilidades más frecuentes fueron la diabetes mellitus (44%; 8/18) y la hipertensión arterial sistémica (44%; 8/18). El 17% (3/18) de los pacientes había recibido tratamientos oncológicos previos. Los síntomas más comunes asociados a la indicación del procedimiento fueron la pérdida de peso involuntaria (61,1%; 11/18). El 17% (3/18) presentó una prueba de tuberculina positiva, mientras que ninguno mostró baciloscopia positiva. Las tomografías de tórax revelaron infiltrados alveolares/intersticiales en el 50% (9/18), masas en el 28% (5/18), nódulos en el 22% (4/18) y adenopatías en el 28% (5/18).

Discusión: La tuberculosis incidental ocurre en pacientes con sospecha de cáncer o en seguimiento oncológico. Es crucial considerar su diagnóstico diferencial en los estudios de broncoscopia.

Palabras clave: tuberculosis; diagnóstico; incidental; cáncer.

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Introduction

Tuberculosis (TB) remains a global infectious disease. Pulmonary TB accounts for 85% of all TB cases. In 2019, TB caused 1.4 million deaths and 10 million cases, making it one of the leading infectious causes of death¹⁻³. Despite advancements, no region of the World Health Organization has met the targets of reducing incidence by 90% and mortality by 95% by 2035^{1,2}. Barriers include HIV-associated TB, drug resistance, broader case diagnosis, and socioeconomic factors that worsen the disease^{1,3,4}.

Bronchoscopy is a low-morbidity diagnostic method that allows for the collection of a larger amount of material for analysis in patients with suspected TB not confirmed by sputum smear, significantly increasing the chances of diagnosis^{5,6}. This study highlights its usefulness not only in detecting TB, but also as an incidental diagnostic tool in patients undergoing bronchoscopy for suspected neoplastic diseases, emphasizing its importance in complex clinical settings⁷⁻⁹. Despite advancements in diagnostic techniques and global efforts to control TB, its incidental detection in patients investigated for malignant tumor pathology remains largely understudied^{9,10}.

The coexistence of pulmonary TB and cancer may be mediated by chronic inflammation and fibrosis, which are common in cancer patients, and can impair immune function and promote the reactivation of latent TB⁷⁻¹⁰. Additionally, chemotherapy or immunotherapy can predispose patients to respiratory infections, highlighting the importance of thorough monitoring⁹⁻¹¹. In this context, bronchoscopy has the potential to play a key role, especially in patients in whom infection is not initially suspected^{10,11}. However, scientific evidence evaluating its systematic usefulness in this population is limited⁹⁻¹¹. This knowledge gap restricts our understanding of the true burden of TB in patients suspected of having neoplasms, and underscores the need for further research to optimize the diagnostic approach in these cases. The objective of this study was to describe the clinical characteristics of patients with an incidental diagnosis of pulmonary TB who underwent bronchoscopy for the diagnosis or clinical follow-up of neoplastic disease.

Materials and Methods

Study Design

This cross-sectional study included patients with an incidental diagnosis of TB between January 2023 and August 2024 following the STROBE guidelines¹². This study aimed to characterize the clinical, laboratory, and imaging variables of patients who underwent diagnostic bronchoscopy for neoplastic disease.

Population and Setting

Patients over 18 years of age were included, all of whom underwent diagnostic bronchoscopy due to abnormal findings on imaging studies suggestive of malignant tumor disease or had a prior diagnosis of cancer with clinical follow-up. The-

se patients had no prior clinical suspicion of TB and were asymptomatic with respect to mycobacterial infections. All patients were adults with clinical indications for diagnostic bronchoscopy and were incidentally diagnosed with pulmonary TB, confirmed through the molecular biology test GeneXpert MTB/RIF¹³.

Data Collection

Sociodemographic, clinical, laboratory, and imaging data were collected from electronic medical records. The variables included age, sex, comorbidities, the Charlson comorbidity index, anthropometric characteristics (height, weight, and body mass index), indications for bronchoscopy, and laboratory and imaging findings. Indications for the procedure, associated symptoms, and disease stage according to the TNM staging system were also assessed. The tuberculin skin test (PPD; Purified Protein Derivative) is based on a delayed hypersensitivity reaction that follows the intradermal injection of *Mycobacterium tuberculosis* (MT) antigens into the anterior surface of the forearm, with the resulting induration measured 48-72 hours after the injection. Laboratory results included blood count, erythrocyte sedimentation rate, C-reactive protein levels, and liver biochemical parameters. Additionally, the findings from diagnostic imaging were analyzed using both chest X-rays and computed tomography.

To quantify MT genetic material, the Cycle Threshold (CT) parameter obtained through the Xpert MTB/RIF test was used (14,15). This value allowed for the estimation of bacterial load in the analyzed samples and was classified into three categories: low CT (<20-25), indicative of a high bacterial load and suggestive of active infection; intermediate CT (25-35), associated with a moderate or low bacterial load, where infection might be present in a smaller quantity; and high CT (>35-40), which could reflect a very low bacterial load, latent infection, or a possible false-positive result.

Statistical Analysis

Data were processed using statistical software. Continuous variables are summarized as means with standard deviations (SD) and categorical variables as absolute frequencies and proportions (%)¹⁶. Given the descriptive design of this study, no hypothesis testing or inferential analysis was performed.

Results

Eighteen patients were included in the study, all with an incidental diagnosis of pulmonary TB confirmed by molecular biology using the GeneXpert MTB/RIF technique. Among the cultures performed as the reference test for TB diagnosis, 78% (14/18) were positive for MT. The average age was 50.3 years (SD: 20.4), with a predominance of females (55%; 10/18). The mean Charlson comorbidity index was 4.2 (SD: 2.4). The most common comorbidities were diabetes mellitus (44%; 8/18) and systemic arterial hypertension (44%; 8/18). The general characteristics of the study population are summarized in Table 1.

The main indications for the procedure were a pulmonary mass (33%, 6/18) and interstitial/alveolar infiltrate (39%, 7/18) (Table 2). Seventeen percent (3/18) of the patients had previously received oncological treatments. The most common symptom associated with the procedure indications was unintentional weight loss (61.1%; 11/18).

Seventeen percent (3/18) tested positive in the tuberculin skin test, while none had a positive sputum smear (Table 3). Twenty-two percent (4/18) had leukopenia ($<4,000/\text{mm}^3$), 6% (1/18) had leukocytosis ($>10,000/\text{mm}^3$) and neutrophilia ($>7,500/\text{mm}^3$), and 11% (2/18) had thrombocytosis ($>450,000/\text{mm}^3$) and thrombocytopenia ($<150,000/\text{mm}^3$). The average erythrocyte sedimentation rate was 30.5 mm/h (SD: 7.9), and the average C-reactive protein level was 44.8 mg/L (SD: 29.4).

In the evaluation of bacterial load using the CT parameter from the Xpert MTB/RIF test, 61% (11/18) of the patients had a low CT, 33% (6/18) had an intermediate CT, and 6% (1/18) had a high CT. However, upon repeating the test, the result showed an intermediate CT. Additionally, this patient had a positive MT culture, confirming an infection.

Chest X-rays showed interstitial/alveolar infiltrate in 56% (10/18) and pulmonary masses in 28% (5/18) (Table 4). Regarding chest computed tomography scans, alveolar/interstitial infiltrate was identified in 50% (9/18), masses in 28% (5/18), nodules in 22% (4/18), and adenopathy in 28% (5/18). 100% (18/18) of the patients received anti-TB treatment.

Discussion

In this study, which included patients undergoing diagnosis or follow-up for malignant neoplastic disease who were incidentally diagnosed with confirmed pulmonary TB during diagnostic bronchoscopy, various clinical, laboratory, and imaging variables were characterized, reflecting the complexity of the disease. Most patients had significant comorbidities such as hypertension and diabetes mellitus, highlighting the high burden of chronic diseases in this population. Clinically, the most common symptoms associated with the procedure were unintentional weight loss and chronic cough. Laboratory findings, such as leukopenia in one-fifth of cases and elevated C-reactive protein levels, underscore the systemic inflammation characteristic of the disease. In diagnostic imaging, chest X-ray and computed tomography identified patterns such as alveolar/interstitial infiltrates and adenopathy, emphasizing their relevance for initial evaluation and diagnostic planning. All 18 cases were MT-sensitive to treatment, with no rifampicin resistance. The patients received standard short-course therapy with isoniazid, rifampicin, ethambutol, and pyrazinamide, ensuring adherence and treatment completion. These results provide a comprehensive view of the clinical and paraclinical manifestations of TB, in the context of advanced diagnostic procedures.

Table 1. General characteristics of the population.

Total population, n(%)	18 (100)
Age years, m(SD)	50.3 (20.4)
Woman, n(%)	10 (55)
Size centimeters, m(SD)	161.7 (10.8)
Weight kilograms, m(SD)	60.1 (11.9)
BMI kg/m ² , m(SD)	23.3 (5.6)
Charlson index, m(SD)	4.2 (2.4)
Comorbidities, n(%)	
Obesity	4 (22)
Obstructive lung disease	5 (28)
Diabetes	8 (44)
Heart failure	3 (17)
Systemic arterial hypertension	8 (44)
Liver disease	1 (6)
Leukemia or lymphoma	5 (28)
Smoking	8 (44)
Package year index, m(SD)	32.6 (13.5)

Notes: n: number; %: percentage; m: average; SD: standard deviation; BMI: body mass index.

Table 2. Clinical variables related to the indications for diagnostic bronchoscopy.

Total population, n(%)	18 (100)
Indication for diagnostic bronchoscopy, n(%)	
Lung mass	6 (33)
Interstitial/alveolar infiltrate	7 (39)
Lung nodules	3 (17)
Consolidation	2 (11)
Oncological treatments, n(%)	3 (17)
Stadium	
IIA-IIIB-IIIC	4 (22)
IIIA-IIIB-IIIC	13 (72)
IV	1 (6)
Symptoms associated with the indication of the procedure, n(%)	
Fever, n(%)	4 (22)
Diaphoresis, n(%)	4 (22)
Involuntary weight loss, n(%)	11 (61)
Chronic cough, n(%)	6 (33)
Fatigue, n(%)	3 (17)
Chest pain, n(%)	2 (11)

Notes: n: numero; %: porcentaje.

Pulmonary TB and cancer, primarily lung cancer, can be diagnosed simultaneously due to a potential causal relationship, such as chronic inflammation, genomic changes, and fibrosis, which may promote carcinogenesis¹⁷⁻¹⁹. Moreover, cancer treatment can reactivate latent TB¹⁷⁻¹⁹. Given that TB is a chronic disease that may take weeks or months to manifest clinically, it is crucial to investigate more effective active detection methods in the community, especially in patients with immunosuppression due to cancer or cancer-related treatments¹⁷⁻²⁰. We believe that the routine implementation of bronchoscopy in patients with suspected malignant neo-

plasmas, cancer diagnosis, or nonspecific findings on chest imaging could facilitate timely diagnosis of TB and significantly improve clinical outcomes.

Pulmonary TB should be suspected in patients with persistent respiratory symptoms lasting more than 2 to 3 weeks, especially in immunocompetent individuals, whose presentation can vary^{2,3,5}. Diagnosis requires at least three representative samples for sputum smear and culture in liquid media, complemented by genetic amplification tests in cases of moderate or high suspicion^{3,5}. On the other hand, the standard test for diagnosing TB infection is the tuberculin test, which uses an extract from the filtrate of MT cultures^{1-3,8,11}. In our population, the most common symptoms were chronic cough and weight loss, which may have raised the suspicion of active infection. However, the patients were subjected to diagnostic bronchoscopy for malignant neoplastic diseases, which may bias, confuse, and decrease the likelihood of associating these symptoms with pulmonary TB.

The request for TB diagnostic tests (sputum smear microscopy, tuberculin skin test, and GeneXpert) in oncology patients without prior clinical suspicion was based on suggestive imaging findings identified during the staging evaluation of neoplastic disease⁸⁻¹¹. Given that cancer patients, especially those requiring immunosuppressive treatment, have a higher risk of reactivated latent TB or asymptomatic primary infection, a systematic assessment of pulmonary abnormalities is crucial before initiating oncologic therapy^{3,12,13,17}. Additionally, in regions with high TB burden, the possibility of subclinical infection in immunocompromised populations justifies a proactive diagnostic approach. Incidental detection of TB in these patients not only prevents delays in oncologic treatment, but also helps reduce nosocomial transmission and improve clinical outcomes.

Despite the valuable contribution of diagnostic imaging, such as chest X-rays and computed tomography, in identifying parenchymal lung lesions, these tools allow for the establishment of diagnostic probabilities and differential diagnoses based on observed findings²¹⁻²⁴. However, they did not guarantee absolute certainty regarding the final diagnosis. In our population, the imaging findings were not specific to TB, and in some cases, the cancer diagnosis further complicated the clinician's ability to associate these findings with TB and suspect infectious disease. Therefore, in this group of patients who are in the process of ruling out neoplastic disease or undergoing follow-up bronchoscopy for cancer and in whom pulmonary TB is not suspected, it would be advisable to conduct a simultaneous microbiological analysis of the material obtained from the lesion, as chest imaging can show similarities between cancer and TB²¹⁻²⁴.

Undiagnosed TB cases in the presence of other comorbidities, such as cancer, require greater effort for timely diagnosis, particularly in low- and middle-income countries where pulmonary TB has a high prevalence and incidence²⁵⁻²⁷.

Mucheleng et al.²⁸ identified pulmonary TB as the definitive cause of death in cases where the disease had not been previously suspected. The diagnosis was only made during forensic autopsies performed on individuals who died from other causes. In Colombia, a middle-income country with a high TB prevalence, incidental diagnosis of the disease is particularly relevant as an opportunity to address barriers that limit early detection and treatment.

The diagnosis of TB in cancer patients is challenging due to the overlapping symptoms, such as weight loss and chronic cough, which are common to both conditions^{4-6,10,11}. To improve early detection, we recommend a more systematic diagnostic approach, including routine microbiological analysis of samples obtained during bronchoscopy^{4-6,10,11}. This should be done even in the absence of clinical suspicion of TB, utilizing methods such as GeneXpert MTB/RIF to identify incidental cases and prevent missed diagnoses^{5,6,11,14,15}. Finally, bronchoscopy has proven to be a valuable tool for assessing the degree of involvement and airway obstruction in thoracic diseases, solidifying its role as a useful diagnostic procedure for both pulmonary TB and other thoracic diseases such as

Table 3. Laboratory tests.

Total population, n(%)	18 (100)
Positive PPD, n(%)	3 (17)
Bacilloscopy, n(%)	0 (0)
Leukopenia <4,000/mm ³ , n(%)	4 (22)
Leukocytosis >10,000/mm ³ , n(%)	1 (6)
Neutrophilia >7,500/mm ³ , n(%)	1 (6)
Thrombocytosis >450,000/mm ³ , n(%)	2 (11)
Thrombocytopenia <150,000/mm ³ , n(%)	2 (11)
ESR mm/h, n(%)	30,5 (7,9)
C-reactive protein mg/L, n(%)	44,8 (29,4)
AST U/L, n(%)	41,3 (27,3)
ALT U/L, n(%)	48,9 (41,7)
Alkaline phosphatase U/L, n(%)	111,9 (48,3)

Notes: n: number; %: percentage; PPD: Purified Protein Derivative; mm³: cubic millimeter; ESR: Erythrocyte Sedimentation Rate; mm/h: millimeters per hour; AST: Aspartate Aminotransferase; U/L: units per liter; ALT: Alanine Aminotransferase.

Table 4. Diagnostic images.

Total population, n(%)	18 (100)
Chest x-ray, n(%)	
Alveolar/interstitial infiltrate	10 (56)
Mass	5 (28)
Nodule	3 (17)
Widening of mediastinum or pulmonary hilia	4 (22)
Chest tomography, n(%)	
Alveolar/interstitial infiltrate	9 (50)
Mass	5 (28)
Nodule	4 (22)
lymphadenopathy	5 (28)

Notes: n: number; %: percentage.

cancer^{29,30}. This study highlights the importance of strengthening the skills of interventional pulmonologists in diagnosing infectious diseases, particularly in patients with cancer.

Limitations and Strengths

Our study has significant limitations, including the relatively small sample size (18 patients), which may restrict the generalizability of the results. Furthermore, as this was an observational study, certain factors that could have influenced the findings, such as oncological treatment received or the presence of comorbidities, were not controlled. However, efforts have been made to reduce the risk of bias, such as training the staff responsible for collecting medical data and constructing the manuscript based on the STROBE checklist for cohort studies¹². Finally, because patients were selected from a population with specific clinical indications for bronchoscopy, the results may not be representative of the general population, especially in areas with a higher prevalence of TB. Larger studies are required to confirm these findings and to explore their applicability in diverse contexts.

In conclusion, this study highlights the complexity of incidentally diagnosed PTB through bronchoscopy in patients undergoing evaluation for potential neoplastic disease or cancer follow-up. Laboratory findings and diagnostic imaging emphasize the importance of an integrated approach that combines advanced tools to improve the timely detection and management of the disease in populations with a high burden of comorbidities such as cancer.

Ethical considerations

Protection of persons. This study was conducted in accordance with the principles established by the World Medical Association in the Declaration of Helsinki (2013) and in compliance with national regulations stipulated in Resolution 8430 of 1993 by the Ministry of Health regarding Health Research, where it is considered minimal risk. Prior to the start of the study, the protocol was submitted for evaluation by the ethics and research committee of Oncólogos del Occidente, with which endorsement was accepted by the participating IPS. The study commenced only once approval was obtained.

Protection of vulnerable populations. Not applicable.

Confidentiality. During the collection and analysis of the data, the protocols established by the participating institution were followed, ensuring the privacy of the patients.

Privacy. Not applicable.

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