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Case Report

Endobronchial tuberculosis mimicking malignancy: Lessons from a case report

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ABSTRACT

Endobronchial tuberculosis is characterized by the presence of tuberculous lesions within the bronchi, irrespective of the formation of pulmonary lesions. When these lesions are visible, their morphology often raises the differential diagnosis of malignancy. Diagnostic challenges arise as sputum smear tests—crucial for mycobacterial identification—may yield negative results in up to half of the cases. Here, we present a 66-year-old male who exhibited clinical and radiological findings suggestive of malignancy but was ultimately diagnosed with endobronchial tuberculosis through a combination of bronchoscopy, histopathology, and polymerase chain reaction testing. The patient responded favorably to anti-tuberculosis therapy. This case underscores the importance of comprehensive diagnostic strategies for endobronchial tuberculosis, particularly in distinguishing it from tracheal malignancies.

1. Introduction

Endobronchial tuberculosis (TB), a rare form of pulmonary TB, is defined as the involvement of the trachea and major bronchi by tuberculous lesions, irrespective of concurrent pulmonary parenchymal disease [1]. Historically, endobronchial TB has presented diagnostic challenges due to its diverse clinical manifestations and resemblance to other airway pathologies, particularly malignancies [2,3]. While TB incidence has declined in many low-prevalence countries, including Japan, the disease remains a significant global health concern. In 2021, the World Health Organization (WHO) estimated 10.6 million new TB cases worldwide, highlighting its ongoing public health impact [4,5]. Despite advancements in diagnostic modalities, endobronchial TB often remains elusive. The pathogenesis of endobronchial TB involves several potential mechanisms, including direct extension from pulmonary lesions, lymphatic spread, and hematogenous dissemination [1]. The disease's rarity further complicates timely diagnosis, as evidenced by recent reports indicating that endobronchial TB accounts for less than 1 % of all TB cases in developed nations [6]. Furthermore, the

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radiologic and endoscopic findings of endobronchial TB often closely resemble those of malignancies, requiring vigilant diagnostic discernment [7].

This case highlights the diagnostic challenges of endobronchial TB, focusing on its differentiation from tracheal malignancy. We review the clinical, radiological, and pathological features of this rare entity and discuss the importance of integrating molecular diagnostic techniques into routine practice to enhance diagnostic accuracy and patient outcomes.

2. Case report

A 66-year-old male presented with progressive hoarseness persisting for three months. He had no significant medical history but reported a 45-pack-year smoking history and regular alcohol consumption. He consumed 20 cigarettes daily and drank 350 ml of canned beer per day. Hoarseness had initially prompted a visit to a nearby clinic, where right recurrent laryngeal nerve paralysis was identified. Subsequently, the patient was referred to our otolaryngology department for further evaluation. On presentation, the patient's physical examination revealed a palpable, tender, and mobile subcutaneous nodule in the right supraclavicular fossa. Vital signs were stable, with a body temperature of 36.5 °C, pulse rate of 69 beats per minute, blood pressure of 156/92 mmHg, respiratory rate of 14 breaths per minute, and oxygen saturation of 97 % on room air. No abnormal breath sounds, heart murmurs, or clubbing of the fingers were observed. Laboratory investigations revealed a white blood cell count of 8390/μl with 69.7 % neutrophils, 17 % lymphocytes, and 4.3 % eosinophils. Biochemical and urine analyses were unremarkable. The T-SPOT® TB assay was positive, and HIV antibodies were negative.

Contrast-enhanced computed tomography (CT) of the chest demonstrated a 40 mm × 25 mm necrotic mass in the S1 region of the right upper lobe adjacent to the mediastinum (Fig. 1A). Enlarged mediastinal lymph nodes were noted, with the lesions appearing as a single confluent mass. Contrast enhancement revealed central necrosis, raising suspicion of malignancy and direct infiltration into the right tracheal wall (Fig. 1B and C). At this stage, while a primary lung malignancy and mediastinal lymph node metastasis were suspected, the positive T-SPOT test necessitated ruling out pulmonary tuberculosis and tuberculous lymphadenitis, prompting the decision to perform a bronchoscopy. Bronchoscopy revealed a broad-based elevated lesion in the right tracheal wall, characterized by thick white plaques and submucosal bleeding (Fig. 2A). The lesion disrupted the tracheal cartilage rings, compressed the longitudinal folds of the tracheal membranous portion, and was associated with bleeding from the submucosal vessels (Fig. 2B). No other mucosal abnormalities were observed. A biopsy of the endotracheal elevated lesion was performed (Fig. 2C), revealing granuloma formation without evidence of caseous necrosis (Fig. 3A and B). The presence of contrast enhancement in some regions of the intratracheal lesion targeted for biopsy may explain the absence of caseous necrosis in the pathological specimen. Acid-fast bacilli smear tests from bronchial lavage fluid and tracheal sputum were negative; however, a transcription-reverse transcription concerted reaction (TRC) study using the TRC Ready80 (TOSOH BIOSCIENCE, Tokyo, Japan) detected *Mycobacterium tuberculosis* [8]. Subsequent cultures of the bronchial lavage fluid confirmed the presence of *Mycobacterium tuberculosis*, solidifying the diagnosis.

The patient was initiated on a first-line anti-tuberculosis regimen comprising isoniazid (INH), rifampicin (RFP), ethambutol (EB),

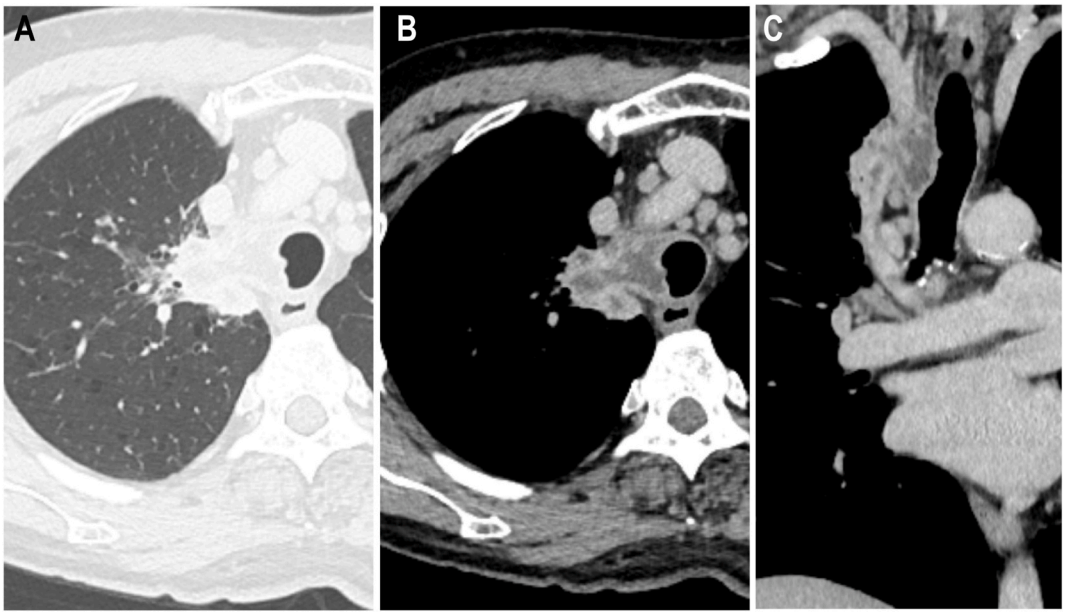

Fig. 1. Contrast-enhanced CT findings of the chest at the initial presentation. A. Axial view in the lung field window demonstrates a mass located on the mediastinal side of the right upper lobe. **B**. Axial view in the mediastinal window reveals extensive necrosis within the mass, with suspected invasion into the lumen of the right tracheal wall (indicated by the white arrow). **C**. Coronal view in the mediastinal window illustrates marked compression of the trachea, displacing it towards the left side.

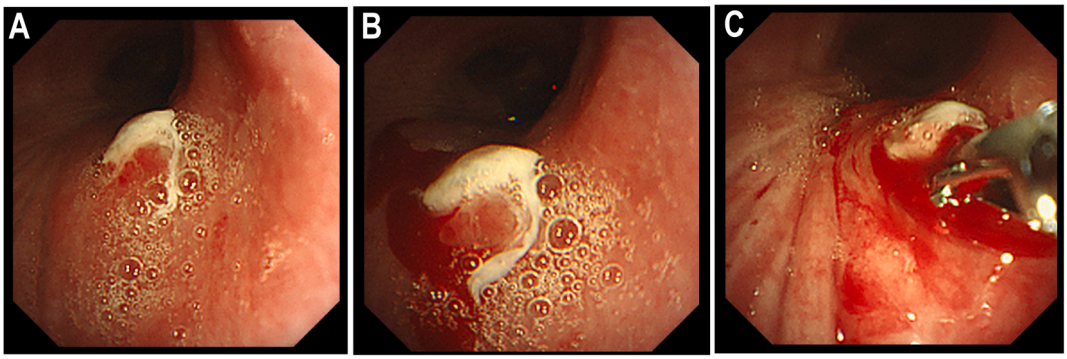

Fig. 2. Bronchoscopic findings. A. A broad-based elevated lesion is visible on the right wall of the trachea, causing compression and displacement of the longitudinal folds in the membranous portion. **B**. The mucosal surface of the lesion is covered with thick white necrotic material, with notable erythema and friability, rendering it prone to bleeding. **C**. A direct biopsy was performed under visual guidance from the elevated lesion within the tracheal lumen.

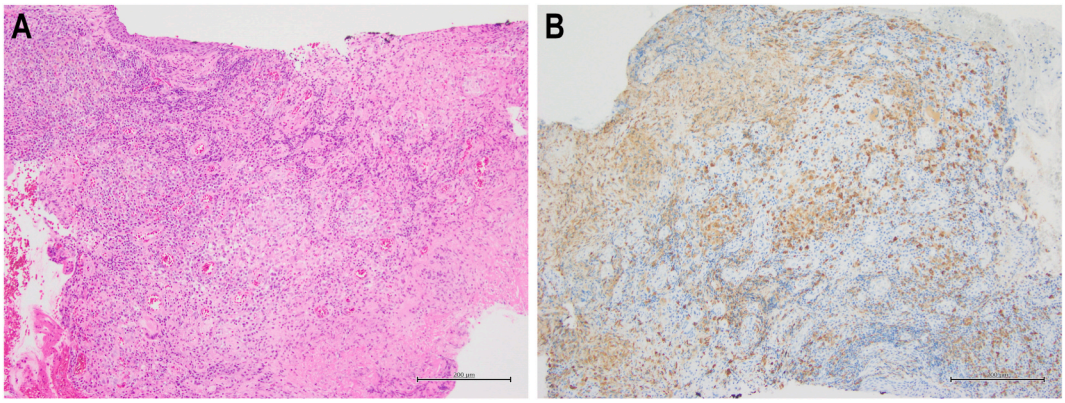

Fig. 3. Histopathological findings of the specimen. A. Hematoxylin and eosin staining. **B**. CD68 immunohistochemistry. A granuloma with prominent infiltration of inflammatory cells was observed within the stromal tissue. Notably, there was no evidence of caseous necrosis or the presence of Mycobacterium tuberculosis in the specimen.

and pyrazinamide (PZA). The treatment course was well-tolerated without adverse effects. One month after bronchoscopy, follow-up cultures of the bronchial lavage fluid reconfirmed *Mycobacterium tuberculosis*, and drug sensitivity testing revealed susceptibility to all four agents. Over six months of therapy, imaging demonstrated significant resolution of lung and tracheal lesions, as well as mediastinal lymphadenopathy (Fig. 4A, B, C). The patient remains asymptomatic and is under regular outpatient follow-up with no evidence of recurrence.

3. Discussion

In 2021, the number of newly registered TB cases in Japan was 11,519, corresponding to an incidence rate of 9.2 per 100,000 population, which meets the threshold for classification as a low TB prevalence country (incidence below 10.0 per 100,000) [9]. Updated data from 2023 indicate a further decline, with 10,096 new registrations and an incidence rate of 8.2 per 100,000 [9]. Despite these encouraging trends, there is growing concern that decreasing TB incidence may inadvertently delay diagnosis due to reduced clinical suspicion and frequency of consultations for suspected TB. Nonetheless, TB remains a critical public health concern requiring continued vigilance. Endobronchial TB was first described by Morlock et al., in 1939 using a rigid bronchoscope [10]. Endobronchial TB is defined by the presence of tuberculous lesions in the central bronchi proximal to the segmental bronchi, irrespective of coexisting pulmonary tuberculosis [11]. According to 2023 data, endobronchial TB accounted for only 58 cases (0.6 %) out of the total 10,096 new TB registrations in Japan, underscoring its rarity [9]. However, when TB lesions involve major bronchi, they pose significant risks of airway obstruction and respiratory failure, necessitating accurate diagnosis and prompt therapeutic intervention [1]. Clinical symptoms associated with endobronchial TB, such as cough and sputum production, are nonspecific and may overlap with other respiratory conditions [2,12]. Structural alterations in the bronchi, including stenosis or atelectasis, may occasionally produce abnormal chest auscultation findings, such as wheezing or diminished breath sounds [2,12]. However, these findings are relatively uncommon. In the present case these classical symptoms and physical signs were lacking.

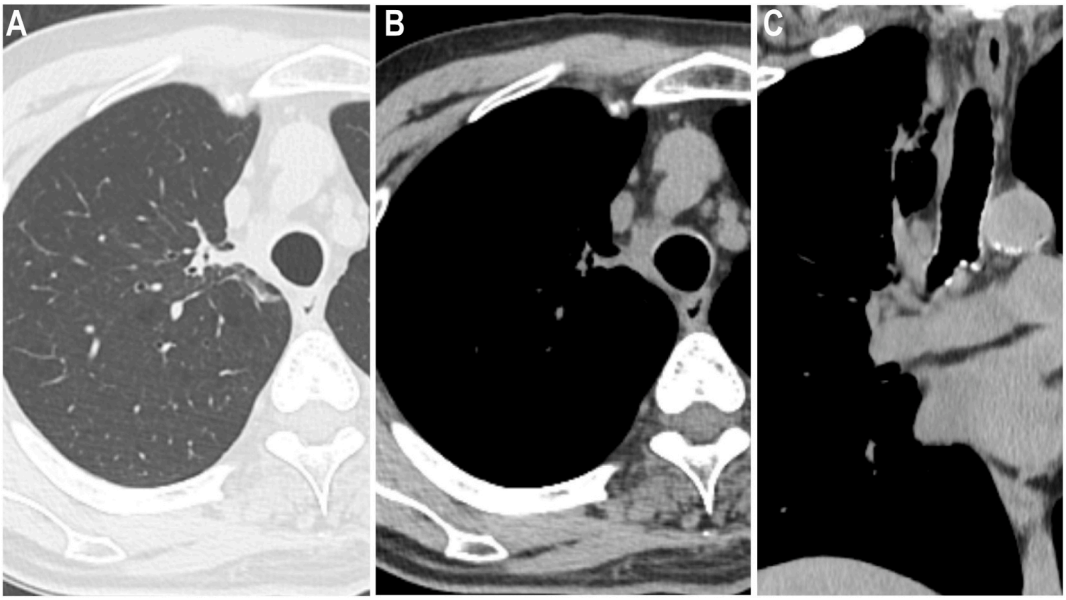

Fig. 4. CT findings following the completion of tuberculosis treatment. A. The mass shadow in the right upper lobe has resolved, leaving a residual shadow. B. In the mediastinal window, the mass demonstrates significant reduction in size. C. The coronal section reveals substantial improvement in the previously noted tracheal compression.

The pathophysiology of endobronchial TB is not fully elucidated. Primary endobronchial TB, in which *Mycobacterium tuberculosis* directly forms lesions in the bronchi, is rare. Potential pathways for bacterial dissemination to the bronchi include direct implantation from pulmonary parenchymal lesions, including cavitary lesions, direct invasion from intrathoracic lymph nodes, lymphatic progression to peribronchial areas, and hematogenous dissemination via bronchial arteries [13–16]. In the present case, bronchoscopy revealed a broad-based elevated lesion within the tracheal lumen, while external compression of the right tracheal wall by mediastinal lymphadenopathy was evident. Notably, there were no lesions observed in the segmental bronchi of the right upper lobe or the right main bronchus. This pattern suggests that the primary TB lesion originated in the right upper lobe and extended directly into the tracheal lumen via mediastinal lymph node invasion.

Sputum smear microscopy plays a pivotal role in diagnosing and monitoring mycobacterial infections. However, in endobronchial TB, the sensitivity of sputum smears is highly variable, with positive results reported in only about 50 % of cases [17–20]. Factors that may contribute to the low sensitivity of sputum smear include obstruction of mucus expectoration by granulation tissue, natural healing processes, and fibrotic stenosis [21]. In the present case, sputum samples were not available, despite the presence of a central bronchial lesion. Therefore, it is critical not to exclude endobronchial TB based solely on negative sputum smear results. Nucleic acid amplification tests, including real-time PCR, have demonstrated high diagnostic utility [17,21,22]. Hou et al. reported a diagnostic sensitivity of 89.2 % for PCR in bronchial specimens from endobronchial TB patients, significantly surpassing the sensitivity of sputum smear and bronchial brushing tests [21]. In this case, PCR testing of lavage fluid from the right upper lobe bronchus was instrumental in confirming the diagnosis. Clinicians should strongly consider nucleic acid amplification testing when evaluating patients with suspected endobronchial TB.

Bronchoscopy is a cornerstone diagnostic modality for endobronchial TB, enabling direct visualization and targeted biopsy of lesions within the tracheal lumen [23–26]. Several classification systems have been proposed to categorize bronchoscopic findings in endobronchial TB. Among these, Chung's classification is widely recognized and includes seven subtypes based on endoscopic appearance: i) active caseating, ii) edematous-hyperemic, iii) fibrostenotic, iv) tumorous, v) granular, vi) ulcerative, and vii) nonspecific types [23,24]. In the present case, the endobronchial TB manifested as an elevated lesion with a thick white coating, aligning with the tumorous type. This subtype poses considerable diagnostic and prognostic challenges, as it is associated with complications such as complete bronchial obstruction, anthracofibrosis, and the emergence of new mass lesions [13]. The prognosis for this subtype is complex and unpredictable, necessitating vigilant monitoring through serial bronchoscopy [13]. However, in this case, post-treatment bronchoscopy was not performed due to the patient's lack of consent. As an alternative, follow-up chest computed tomography (CT) imaging was conducted, revealing no evidence of bronchial stenosis or other sequelae, thereby confirming successful resolution of the disease.

Bronchial biopsy remains a definitive diagnostic tool for endobronchial TB when hallmark features such as caseous necrosis or acid-fast bacilli are identified [27]. However, the diagnostic yield of bronchial biopsy varies widely, ranging from 30 % to 84 % [18,20,28]. In this case, initial biopsies demonstrated granulomas without definitive evidence of caseous necrosis. Despite negative acid-fast bacilli smear tests from bronchial lavage fluid and sputum, subsequent polymerase chain reaction (PCR) testing confirmed the presence of *Mycobacterium tuberculosis*. Additionally, culture tests using bronchial lavage fluid later yielded positive results for TB bacteria,

solidifying the diagnosis of endobronchial TB.

This case underscores the critical importance of integrating multiple diagnostic modalities, including histopathology, microbiological testing, and advanced molecular techniques, to accurately diagnose endobronchial TB. The heterogeneity in test sensitivities highlights the need for a comprehensive and individualized diagnostic approach in clinical practice.

4. Conclusion

This case underscores the critical need for comprehensive diagnostic approaches in endobronchial TB, especially given the variability in test results and the potential severity of the disease. Despite the rarity of endobronchial TB, its significant impact on patient health necessitates vigilant monitoring and timely intervention. The integration of nucleic acid amplification tests, alongside traditional methods, enhances diagnostic accuracy and aids in early detection and treatment. Continuous evaluation and adaptation of diagnostic strategies are essential to effectively manage and mitigate the public health threat posed by tuberculosis.

CRediT authorship contribution statement

Tomohito Okano: Writing – original draft, Resources, Project administration. **Hajime Fujimoto:** Validation, Supervision, Resources. **Toshiyuki Ito:** Resources, Methodology, Data curation. **Atsushi Tomaru:** Supervision, Resources. **Haruko Saiki:** Validation, Resources. **Tatsuki Tsuruga:** Visualization, Resources. **Taro Yasuma:** Validation, Supervision. **Corina N. D'Alessandro-Gabazza:** Writing – review & editing, Supervision. **Esteban C. Gabazza:** Writing – review & editing, Validation, Supervision. **Tetsu Kobayashi:** Writing – review & editing, Supervision, Resources, Conceptualization.

Authors' contribution

Resources: T.O, H.F., T.I., A.T., T.K. Supervision: H.S., T.T., Visualization: T.Y., C.N.D-G., E.C.G, T.K. Writing original draft: T.O., H. F., C.N.D-G. Writing review editing: E.C.G., C.N.D-G., T.K.

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Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:Tetsu Kobayashi, Hajime Fujimoto reports a relationship with Chugai Pharmaceutical Co Ltd that includes: funding grants and speaking and lecture fees. Tetsu Kobayashi, Hajime Fujimoto reports a relationship with Pfizer Pharmaceuticals Ltd that includes: funding grants and speaking and lecture fees. Tetsu Kobayashi, Hajime Fujimoto reports a relationship with Ono Pharmaceutical Co Ltd that includes: funding grants and speaking and lecture fees. Tetsu Kobayashi, Hajime Fujimoto reports a relationship with Taiho Pharmaceutical Co Ltd that includes: funding grants. Tetsu Kobayashi, Hajime Fujimoto reports a relationship with Boehringer Ingelheim GmbH that includes: funding grants and speaking and lecture fees. Tetsu Kobayashi, Hajime Fujimoto reports a relationship with Eli Lilly and Company that includes: funding grants and speaking and lecture fees. If there are other authors, they declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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