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ORIGINAL RESEARCH

CT-Occult Primary Benign Tracheobronchial Neoplasms: A Single-Center 40-Case Clinicopathologic Series

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Background: Primary benign tracheobronchial neoplasms are rare and often misdiagnosed due to non-specific presentation.

Objective: To describe the clinical, bronchoscopic, histopathologic and immunohistochemical features of these tumors in a TB-enriched population.

Methods: We retrospectively identified 40 patients with primary benign tracheobronchial tumors diagnosed by bronchoscopic biopsy in a single TB center over a period of 7 years (2017–2024) and summarized clinical data, bronchoscopic characteristics, pathology, and immunophenotype.

Results: Patients were predominantly middle-aged and older men. None of the tumors were detected by CT of the chest. The most common clinical symptoms were cough, sputum production, fever, hemoptysis, chest tightness and wheezing, The median symptom duration was 30 days (IQR, 7–135). The tumors were primarily located in segmental bronchi. Seventy-five percent of tumors were polypoid with wide base while 20% displayed columnar growth patterns and 5% cases had pedunculated morphology. Pathology was consistent with leiomyomas (40.0%), hamartomas (20.0%), peripheral nerve sheath tumors (22.5%) and squamous papillomas (7.5%). Rarer tumor types occupied 10.0% of all cases. Immunohistochemical analysis was consistent with pathology.

Conclusion: Primary benign tracheobronchial neoplasms are commonly small and undetectable by CT of the chest. Coupled with nonspecific symptoms this demands a high index of suspicion including in patients with coexisting conditions such as TB. Definitive diagnosis required bronchoscopy with histologic assessment.

Keywords: primary benign tracheobronchial neoplasms, pathology, immunohistochemical analysis, bronchoscopy

Introduction

Primary benign tracheobronchial neoplasms are exceedingly rare in clinical practice, comprising less than 0.5% of lung tumors.[1] These tumors primarily originate from the mucosal epithelium, salivary glands, and mesenchymal tissues. Among tracheobronchial benign tumors, common histological types include leiomyoma, hamartoma, papilloma, peripheral nerve sheath tumor, chondroma, lipoma, pleomorphic adenoma, and hemangioma, among others.[2] Diagnosis of these tumors typically relies on histopathological examination following lesion resection, supplemented by relatively specific immunohistochemical markers. Commonly used characteristic immunohistochemical markers include: SMA positivity in leiomyomas, S-100 positivity in schwannomas, and TTF-1 positivity in full-thickness cells with p40 and p63 positivity in basal cells in papillomas.

Common characteristics of many benign tumors include a size of less than 2 cm, submucosal location, intact epithelium, and well-defined borders.[3] They often present with an insidious onset characterized by polypoid growth within the bronchial lumen. This growth may lead to nonspecific respiratory symptoms, including cough, hemoptysis, or secondary atelectasis. Due to their typically indolent nature, some benign lesions may remain unrecognized

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for extended periods until the airway lumen becomes significantly compromised or they are discovered incidentally during chest imaging or bronchoscopy conducted for unrelated conditions, such as tuberculosis.[4]

Compared with surgical surgery, bronchoscopic biopsy combined with pathological examination can not only clarify the pathological type of the tumor, but also achieve complete tumor resection, thereby maximizing the preservation of the patient's lung function,[5] so it has become the main method for the diagnosis and treatment of benign tracheobronchial tumors. Although imaging examination (especially chest CT) is the preferred non-invasive method for evaluating non-specific respiratory symptoms, due to the usually small size of such tumors, atypical symptoms, and the fact that imaging physicians mostly focus on peripheral lung lesions, its detection sensitivity is generally low,[4] and there is currently a lack of large-scale imaging studies to confirm its true sensitivity. Virtual bronchoscopy technology based on CT three-dimensional reconstruction can stereoscopically and intuitively display airway lesions[6,] but it requires more experienced imaging physicians, is more expensive, and requires more clinical attention to lesions in the tracheobronchial tree to avoid missed diagnosis of airway lesions. It should be emphasized that even if CT detects bronchial tumors, bronchoscopy and/or surgical intervention is still required in the end.

To enhance the understanding and treatment capabilities regarding this unique entity, we conducted a retrospective analysis of the clinical data from patients with primary benign tracheobronchial neoplasms that were incidentally discovered through bronchoscopy. Among these patients, the majority were ultimately diagnosed with concurrent pulmonary tuberculosis. We summarized their clinicopathological and immunohistochemical characteristics, which provide a foundation for early detection, treatment, and prevention of secondary respiratory tract lesions.

Methods

Study Design

This was a retrospective observational study on the visits of patients with Primary benign tracheobronchial neoplasms diagnosed by bronchoscopic biopsy in Wuhan Pulmonary Hospital. This study was conducted in accordance with the Declaration of Helsinki and received approval from the medical ethics committee of Wuhan Pulmonary Hospital (approval number No. 2022(14)).

Participants and Data Collection

A total of 40 tumor patients underwent fibrobronchoscopic biopsy and received a pathological diagnosis at Wuhan Pulmonary Hospital from January 1, 2017, to November 1, 2024. Among these patients, 34 were male and 6 were female. All histopathological slides were retrospectively reviewed and subjected to a re-evaluation to ensure consistency and accuracy in diagnosis. Clinical data, bronchoscopic findings, pathological morphology, and immunohistochemical phenotypes were extracted from the patients' medical records maintained at Wuhan Pulmonary Hospital.

Imaging Examination

Chest non-enhanced CT scans were performed using an Optima 660 64-slice spiral CT scanner from General Electric (GE) Medical Systems, USA. The scans were conducted in helical mode with the following parameters: tube voltage 120 kV, tube current 80–150 mA, pitch 1.0, and both slice thickness and reconstruction interval set at 0.625 mm. No conventional three-dimensional airway reconstruction was performed in any of the examinations.

Bronchoscopy

All patients routinely underwent bronchoscopy, which was performed by specialized endoscopists with extensive experience. The terminology used to describe the bronchoscopic morphology of the tumors was standardized with reference to relevant literature[7] and the observed morphological features, and was specifically categorized into the following three types: wide-based polypoid (base width / longest nodule diameter $\geq$ 1/3), narrow-based pedunculated polypoid (connected to the bronchial wall via a slender stalk), and columnar (elongated, worm-like, or tortuous vascular-like). Given the high prevalence of pulmonary tuberculosis in the study population, all patients underwent simultaneous bronchoalveolar lavage during bronchoscopy. The lavage fluid was routinely tested for Mycobacterium tuberculosis (including fluorescent PCR, GeneXpert/RIF, smear, and culture) and for fungi (direct smear microscopy and culture).

HE Staining and Immunohistochemical Staining

All pathological tissues were fixed in 10% neutral formalin solution, and paraffin-embedded sections were subjected to hematoxylin and eosin (HE) staining. Immunohistochemical detection was performed on a Leica automated immunohistochemistry staining system using the EnVision two-step method. The primary antibodies included SMA (clone 1A4), S-100 (clone 15E2E2), CK (clone AE1/AE3), TTF-1 (clone 8G7G3/1), CK7 (clone OV-TL 12/30), Ki-67 (clone MIB-1), p40 (clone BC28), CK5/6 (clone D5/16 B4), and Napsin A (clone TMU-Ad02), all of which were purchased from Zhongshan Golden Bridge Biotechnology Co., Ltd. (Beijing, China). Positive staining for TTF-1, p40, and Ki-67 was localized to the nucleus, while S-100 was expressed in both the cytoplasm and nucleus. For the remaining antibodies, positive signals were localized to the cytoplasm. The primary antibody was incubated at room temperature for 1 hour, followed by secondary antibody incubation for 30 minutes, DAB development, and finally hematoxylin counterstaining, dehydration, clearing, and mounting. Both positive and negative controls yielded appropriate results for each stain.

Statistical Analysis

Continuous variables were described as medians with interquartile range (IQRs) and categorical variables were expressed as frequency (n) and percentage (%).

Results

Patient Characteristics

Clinical data are presented in Table 1. A total of 40 patients were included in the study, with a median age of 60.7 years (IQR, 55–68), ranging from 37 to 73 years. Among the patients, 34 (85.0%) were male and 6 (15.0%) were female.

Table 1 Baseline Clinical Characteristics of 40 Patients

Variables	No. (%) or Median (IQR)
Age (yr), median (Q1,Q3)	60.7 (55–68)
Sex, n (%)	
Male	34 (85.0)
Female	6 (15.0)
Signs and symptoms, n (%)	
Cough and sputum	14 (35.0)
Hemoptysis	6 (15.0)
Chest tightness	6 (15.0)
Fever	5 (12.5)
Wheezing	5 (12.5)
Night sweat	2 (5.0)
Asymptomatic	11 (27.5)
Associated lung diseases, n (%)	
Pulmonary tuberculosis	23 (57.5)
Pneumonia	7 (17.5)
Pulmonary atelectasis	2 (5.0)
Pulmonary aspergillosis	2 (5.0)
Lung squamous cell carcinoma	2 (5.0)
Pneumoconiosis	2 (5.0)
Unknown	3 (7.5)
Smoking history, n (%)	
Never	18 (45.0)
Former	5 (12.5)
Present	17 (42.5)
Course of disease (d), median (Q1,Q3)	30 (7–135)

33 were admitted due to suspected tuberculosis based on clinical symptoms and chest CT findings, while 2 patient was suspected of having lung cancer, 1 patient was suspected of intestinal tuberculosis, 1 patient was suspected of tuberculosis of lymph node, 1 patient was suspected of adrenal tuberculosis, 1 patient was suspected of bronchiectasis, and 1 patient was suspected of having a bronchial tumor secondary to atelectasis. The common clinical manifestations included cough and sputum (14 [35.0%]), hemoptysis (6 [15.0%]), chest tightness (6 [15.0%]),fever (5 [12.5%]), wheezing (5 [12.5%]), and night sweats (2 [5.0%]). The remaining 11 cases presented with lung lesions discovered during physical examinations or CT scans for other diseases, without obvious respiratory symptoms. Among the 40 cases, 23 were complicated with pulmonary tuberculosis, 7 with pneumonia, 2 with pulmonary atelectasis, 2 with pulmonary aspergillosis, 2 with lung squamous cell carcinoma, and 2 with pneumoconiosis, while 3 remained unknown. The total number of complications (41) exceeded the number of cases (40) because one patient had both pulmonary tuberculosis and pulmonary aspergillosis and was therefore counted in both categories. 22 (55.0%) patients had a history of smoking. The median duration of the disease was 30 days (IQR, 7–135), ranging from 2 days to 2 years. All patients underwent bronchoscopy after admission, which confirmed the presence of benign tumors in the bronchial lumen.

Imaging Findings

A common chest CT examination was conducted on all 40 patients, revealing segmental atelectasis in 2 patients with intrabronchial stenosis, distortion, or partial occlusion (Figure 1), which suggests the presence of intrabronchial neoplastic lesions. The remaining 38 patients showed patent tracheobronchial trees on CT scans; among them, 25 cases presented mixed imaging changes including pulmonary patches, nodules, fibrous streaks, and cavities, and were suspected as pulmonary tuberculosis by CT. Through pathogenic detection of bronchoalveolar lavage fluid (fluorescence PCR, GeneXpert MTB/RIF, and culture), 23 cases were diagnosed with concurrent pulmonary tuberculosis. No tumors within the bronchial lumens were observed in the examination results of these 38 patients.

Bronchoscopic Findings

The bronchoscopic tumors presented as confined raised nodules within the lumen of the bronchus, ranging in size from approximately 3 mm to 16 mm. The bronchoscopic characteristics in our cohort were summarized in Table 2. Tumors were located on the right side of the bronchus in 26 (65.0%) patients, on the left side in 13 (32.5%) patients, and in the trach in 1 (2.5%) patient. Specifically, tumors were found in the main bronchus in 4 (10.0%) case, in the upper lobe segmental bronchus in 11 (27.5%) cases, in the middle segmental bronchus in 7 (17.5%) patients, and in the lower lobe segmental bronchus in 17 (42.5%) patients. A total of 30 (75.0%) cases exhibited bronchoscopically manifested wide-base polypoid tumors (Figure 2A). Additionally, 8 (20.0%) cases displayed a striated columnar growth (Figure 2B), while

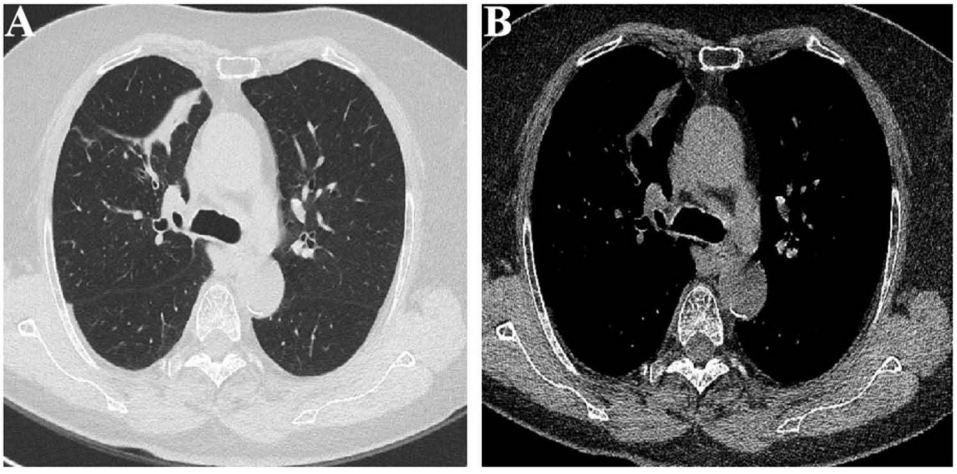

Figure 1 Segmental atelectasis of the right upper lung secondary to glandular papilloma of the right upper bronchus. (**A**) CT plain image in lung window; (**B**) CT plain image in soft-tissue window.

Table 2 Bronchoscopic Characteristics of 40 Patients

Variables	Total (N = 40)	Leiomyoma (N = 16)	Hamartoma (N = 8)	Peripheral Nerve Sheath Tumor (N = 9)	Lipoma (N = 1)	Sialolipoma (N = 1)	Papilloma (N = 5)
Location, n (%)							
Trachea	1 (2.5)	0	0	1 (11.1)	0	0	0
Main bronchus	4 (10.0)	1 (6.3)	1 (12.5)	1 (11.1)	0	1	0
Upper lobe segmental bronchus	11 (27.5)	4 (25.0)	1 (12.5)	3 (33.3)	0	0	3 (60.0)
Middle segmental bronchus	7 (17.5)	2 (12.5)	3 (37.5)	2 (22.2)	0	0	0
Lower lobe segmental bronchus	17 (42.5)	9 (56.2)	3 (37.5)	2 (22.2)	1 (100)	0	2 (40.0)
Morphology, n (%)							
Wide-based polypoid	30 (75.0)	11 (68.8)	7 (87.5)	6 (66.7)	1 (100)	1	4 (80.0)
Columnar	8 (20.0)	5 (31.2)	1 (12.5)	1 (11.1)	0	0	1 (20.0)
Narrow-based pedunculated polypoid	2 (5.0)	0	0	2 (22.2)	0	0	0

2 (5.0%) cases had a narrow-base pedunculated polypoid morphology (Figure 2C). The surfaces of the tumors were predominantly smooth, although cauliflower-like growth was observed in 2 (5.0%) cases (Figure 2D) and lobulated surfaces in another 2 (5.0%) cases (Figure 2E).

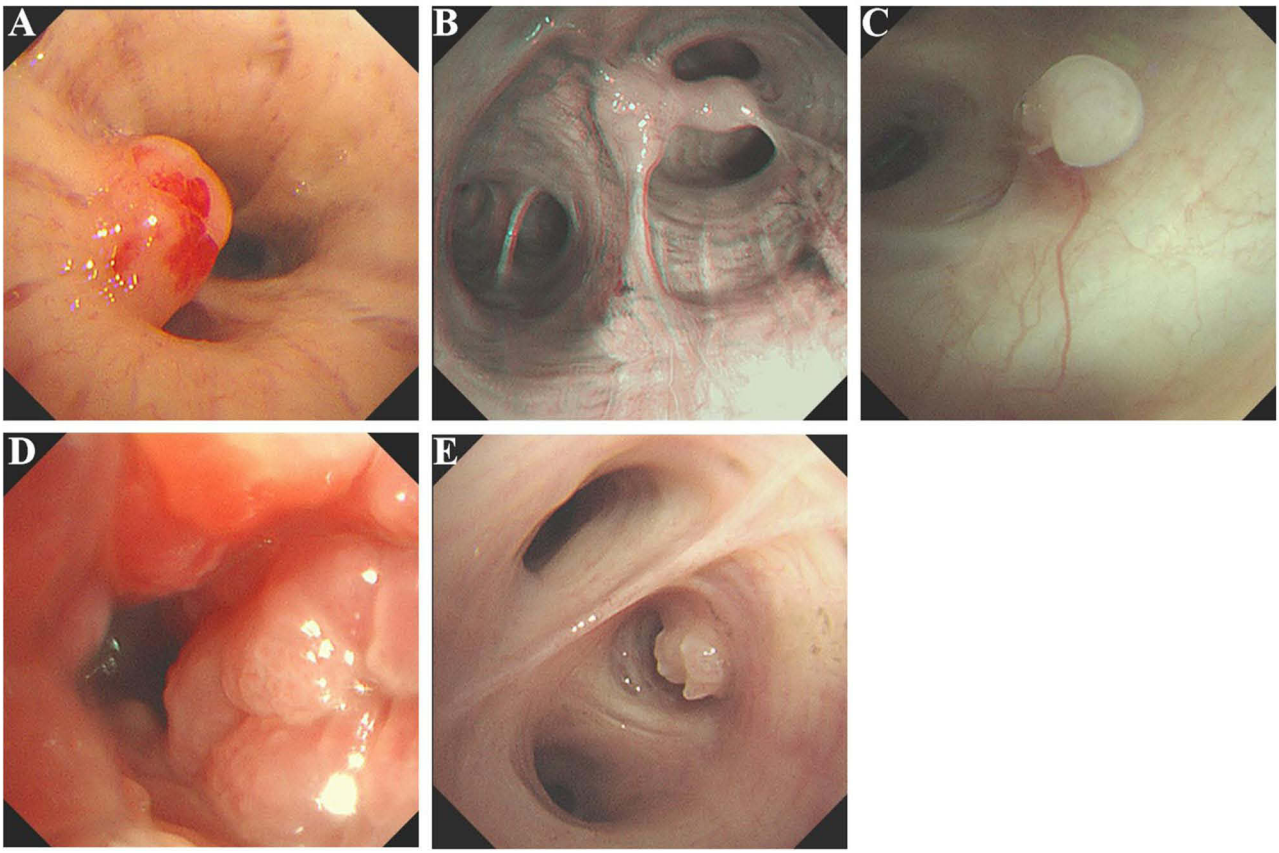

Figure 2 Bronchoscopic results of primary benign tracheobronchial neoplasms. (**A**) Wide-based polypoid nodules in the left lower lobe segmental bronchus, characterized by a lobed surface (Lipoma). (**B**) Columnar nodules in the right upper lobe segmental bronchus (Leiomyoma). (**C**) Narrow-based pedunculated polypoid nodules in the left upper lobe segmental bronchus (Peripheral nerve sheath tumor). (**D**) Cauliflower-like nodules in the right upper lobe segmental bronchus (Squamous epithelial papilloma). (**E**) Lobulated nodules in the left lower lobe segmental bronchus (Hamartoma).

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Histopathological Characteristics

The pathological diagnostic results of the 40 cases of benign tracheobronchial tumors were as follows: leiomyoma (16 cases), peripheral nerve sheath tumor (9 cases), hamartoma (8 cases), papilloma (5 cases, including 3 cases of squamous papilloma, 1 case of adenomatous papilloma, and 1 case of mixed squamous and glandular papilloma), and one case each of lipoma and sialolipoma. Among these cases, mesenchymal tumors accounted for 35 cases, while epithelial tumors accounted for 5 cases. The following sections will elaborate based on this classification of tissue origin.

Epithelial Tumors

1. Squamous epithelial papilloma: The tumor tissues exhibited papillary structures of varying sizes, characterized by fibrous axes rich in blood vessels. The surface of the papilla was covered with differentiated, non-keratinized stratified squamous epithelium (Figure 3A). 2. Glandular papilloma: The tumor tissue displayed an exophytic papillary growth pattern, with visible micropapillary clusters. Its axis comprised fibrous tissue containing a limited number of blood vessels, and signs of hyaline degeneration were evident. The surface of the papilla was lined with well-differentiated stratified or pseudostratified columnar epithelium, which may contain a few goblet cells and ciliated cells, along with a continuous basal layer of cells (Figure 3B). 3. Mixed squamous cell and glandular papilloma: The tumor tissue presented papillary formations covered by well-differentiated pseudostratified ciliated columnar epithelium and mature non-keratinized stratified squamous epithelium, with the glandular component comprising more than one-third of the total tissue.

Mesenchymal Tumors

1. Leiomyoma: The tumor was located in the submucosa and exhibited nodular growth with well-defined boundaries. Microscopically, the tumor consisted of bundles of spindle-shaped smooth muscle cells that were interwoven, demonstrating well differentiation, with cytoplasm that was red-stained (Figure 3C). 2. Peripheral nerve sheath tumor: This tumor was also located in the submucosa and presented with nodular growth and well-defined boundaries. The main pathological types include schwannoma and neurofibroma. Microscopically, the tumor cells appeared slender and fusiform, with some nuclei demonstrating wavy or comma-shaped configurations, arranged in tightly packed bundles, palisades, and whorled

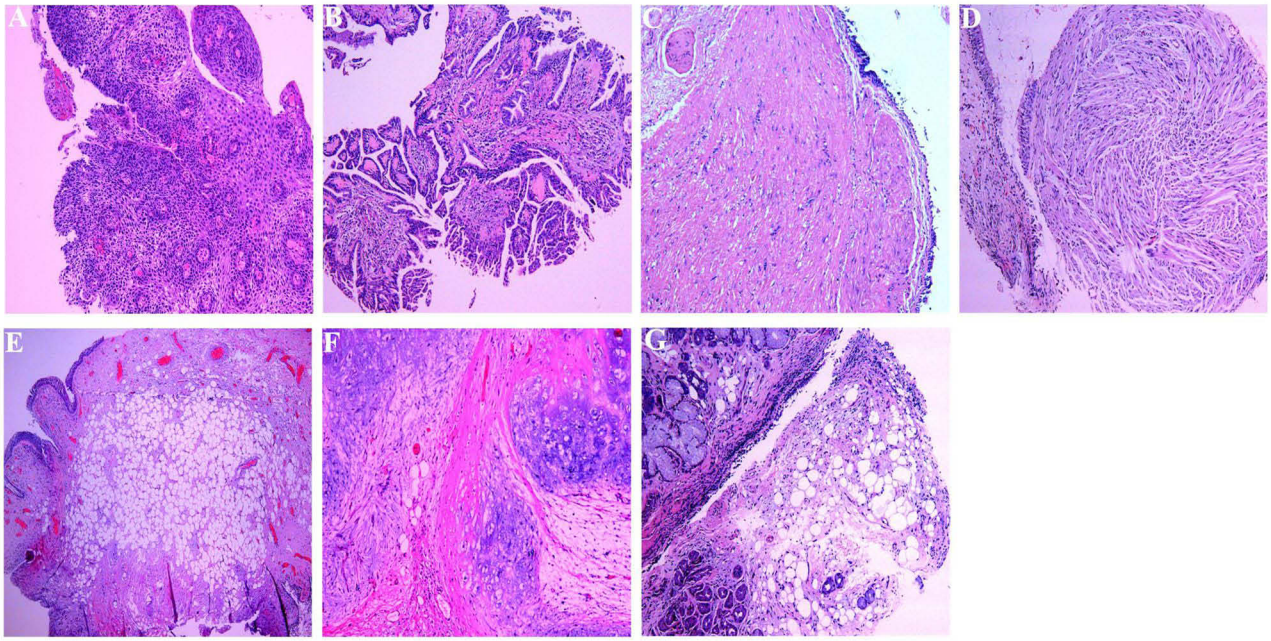

Figure 3 Histopathological characteristics of primary benign tracheobronchial neoplasms (HEx100). (**A**) Squamous epithelial papilloma: covered by well-differentiated stratified squamous epithelium. (**B**) Adenoid papilloma: covered by pseudostratified columnar epithelium and interstitial hyaline transformation. (**C**) Leiomyoma: spindle smooth muscle cells arranged in bundles and braided formations. (**D**) Peripheral nerve sheath tumor: elongated tumor cells organized in a spiral and palisade pattern. (**E**) Lipoma: situated in the submucosa, with indistinct boundaries, and composed of mature adipocytes. (**F**) Hamartoma: composed of a loose mucoid matrix, lobulated mature cartilage tissue, mature fat and smooth muscle tissue. (**G**) Sialolipoma: salivary gland parenchyma interspersed with mature adipose tissue.

patterns. (Figure 3D). 3. Lipoma: The tumor was found in the submucosa but exhibited unclear boundaries. Microscopically, it was primarily composed of mature adipocytes without any cartilage tissue (Figure 3E). 4. Hamartoma: This tumor was composed of various mesenchymal components, including lobulated mature cartilage tissue, a loose mucoid matrix, adipose tissue and smooth muscle tissue (Figure 3F). 5. Sialolipoma: The tumor consisted of mature adipocytes mixed with epithelial ducts and acini of salivary glands (Figure 3G).

Immunohistochemical Phenotype

Mixed and glandular papillomas exhibited strong expression of CK7 and TTF-1 in both the columnar epithelial layer and the basal layer (Figure 4A), while P40 expression was confined to the basal layer (Figure 4B). Napsin A was not detected in either the epithelial or basal layers (Figure 4C). Squamous epithelial papilloma exhibited strong expression of CK5/6, P63 and P40 (Figure 4D). Smooth muscle actin (SMA) demonstrated positivity in leiomyoma cells (Figure 4E), and S-100 was positive in peripheral nerve sheath tumors (Figure 4F). The proliferation index, as indicated by Ki-67, was less than 5%. The remaining tumors were diagnosed based on their pathomorphological characteristics.

Treatment and Prognosis

In this study, most tumors were small in size. Among the 40 patients, complete resection was achieved bronchoscopically in all except one case of squamous cell papilloma, which required surgical intervention due to its multinodular lobulated morphology. The remaining patients underwent successful resection using bronchoscopic biopsy forceps, high-frequency electrocautery (snare), or a combination of both. During follow-up, recurrence occurred in one patient with glandular papilloma at one year post-

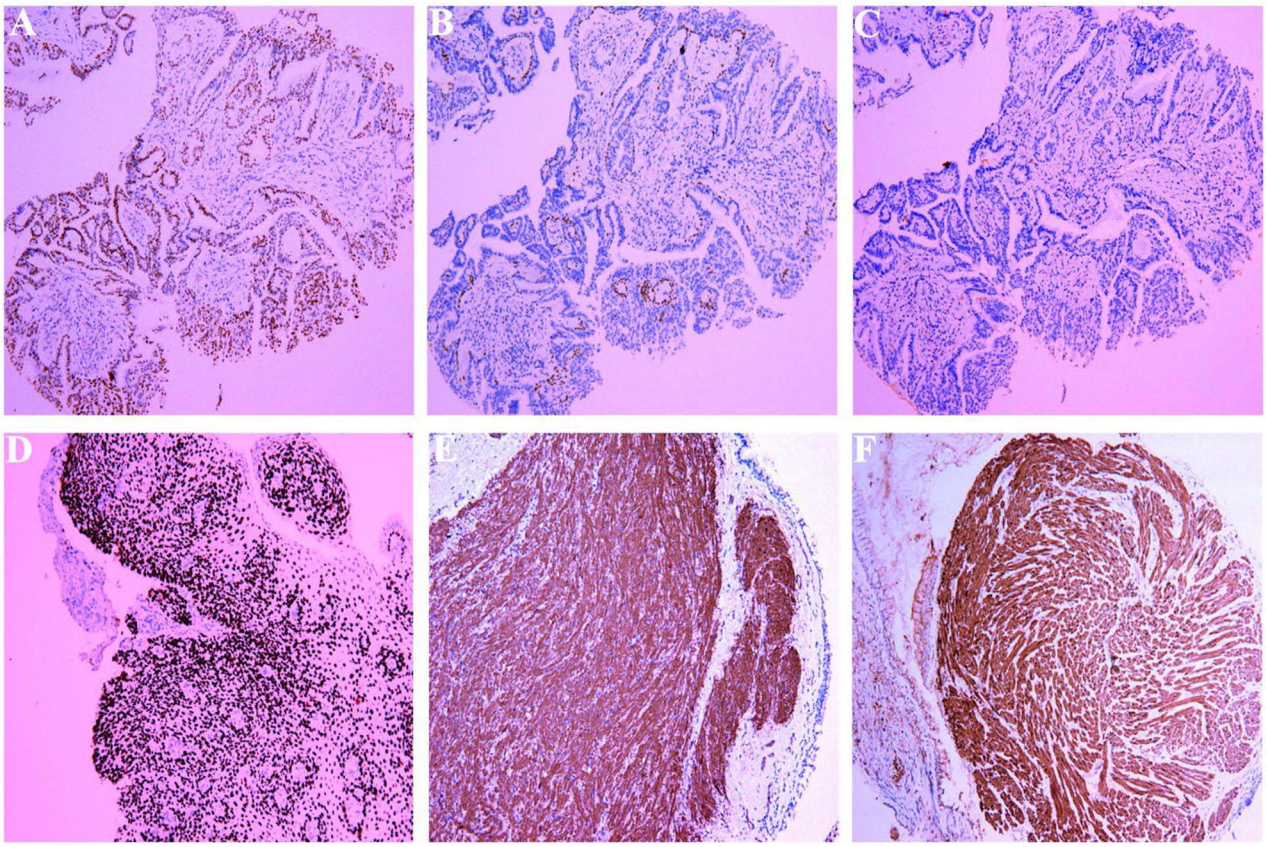

Figure 4 Immunohistochemical phenotype of primary benign tracheobronchial neoplasms (IHCx100). (**A**) Glandular papilloma: TTF-1 was expressed in glandular epithelium and basal layer. (**B**) Glandular papilloma: P40 was expressed in the basal layer. (**C**) Glandular papilloma: Napsin A was negatively expressed in tumor cells. (**D**) Squamous epithelial papilloma: P40 was expressed strongly in tumor cells. (**E**) Leiomyoma: SMA was positive in tumor cells. (**F**) Peripheral nerve sheath tumor: S-100 was positive in tumor cells.

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resection, which was subsequently managed with a repeat bronchoscopic excision. No further recurrence has been observed in this case after 1.5 years. None of the other patients experienced recurrence during the follow-up period.

Discussion

Rare and uncommon benign lesions of the tracheobronchial tract include non-neoplastic diseases such as tracheobronchopathia osteochondroplastica,[8] amyloidosis, and neoplastic lesions, all of which frequently present with intraluminal nodular growth patterns. This study systematically classified eight pathological types of benign tumors originating from the tracheobronchial region, including mesenchymal tumors and epithelial tumors. Unlike previous reports that focused on individual cases, our study integrates multiple pathological subtypes of primary tracheobronchial benign tumors, thereby providing valuable insights for a more comprehensive and in-depth understanding of these rare benign lesions.

Primary benign tracheobronchial neoplasms are rare, with the majority arising from mesenchymal tissue, while malignant tumors predominantly originate from epithelial sources.[3,9] In this study, 35 of the 40 cases were derived from mesenchymal tissue, aligning with existing literature. Primary benign tracheobronchial neoplasms encompass a wide spectrum and can originate from various dermal layers: ectodermal tumors include papilloma and adenoma, whereas mesodermal tumors comprise leiomyoma, peripheral nerve sheath tumors, hamartomas, lipoma, sialolipoma, hemangiomas, and others. The types and frequencies of tumors across different dermal layers vary among studies.[10,11] This study identified eight pathological types, with leiomyoma being the most prevalent, followed by peripheral nerve sheath tumors and hamartoma. A predominance of middle-aged and elderly men was observed, with an median age of 60.7 years, indicating a specific age and gender trend consistent with some literature reports.[2,12,13] Twenty-two cases had a history of smoking, suggesting a potential link between tobacco use and the pathogenesis of these tumors. Additionally, there were 23 patients with tuberculosis, and the relationship between tuberculosis and tumorigenesis has not been reported, indicating a need for further investigation.

This type of tumor grows slowly within the tracheobronchial lumen and is typically small in diameter, making it prone to misdiagnosis and missed diagnosis. In this study, most patients were admitted to the hospital with a suspicion of pulmonary tuberculosis, experiencing various misdiagnoses over time until a definitive diagnosis was made through bronchoscopy biopsy. The duration from the onset of symptoms to diagnosis ranged from 2 days to 2 years. Clinical manifestations vary according to the tumor's size, location, and degree of airway obstruction, including cough, sputum, hemoptysis, chest tightness, dyspnea, wheezing, and secondary complications such as pneumonia and atelectasis. Symptoms often emerge only when the tumor occludes more than 50–75% of the lumen or when the diameter is less than 1 cm.

In this study, a total of 23 patients with primary benign tracheobronchial neoplasms were found to have coexisting active pulmonary tuberculosis (confirmed by bronchoalveolar lavage fluid testing). It should be clarified that since *Mycobacterium tuberculosis* (*MTB*) was not directly detected in the tumor tissues, this study cannot confirm a direct etiological role of *MTB* infection in these benign tumors. Although the co-occurrence may be coincidental, it is important to note that chronic inflammation has been widely recognized as a significant driver of tumorigenesis[14.] *MTB* infection can induce persistent granulomatous inflammation and abnormal tissue repair responses. This process may alter the local microenvironment and indirectly promote the activation and proliferation of myofibroblasts, thereby contributing to the formation of benign tumors.[15,16] The proposed "infection–inflammation–hyperplasia" hypothesis provides a theoretical framework for understanding the potential association between the two. Future studies should employ more sensitive methods-such as *MTB*-specific PCR or 16S rRNA sequencing targeting tumor tissues-to further validate this potential mechanism.

CT examination has limited diagnostic value for benign bronchial tumors; in this study, 38 cases were missed by CT, and only 2 cases revealed segmental atelectasis secondary to stenosis, distortion, or partial occlusion of the bronchial lumen, indicating intrabronchial lesions. One contributing factor may be the small size of the tumors, as common CT resolution may be inadequate for detecting intraluminal lesions. Additionally, the imaging diagnostician's lack of familiarity with this rare disease may hinder appropriate diagnostic awareness. Bronchoscopy remains the most crucial method for definitive diagnosis and treatment. The bronchoscopic findings in this group included localized convex nodules within the lumen, typically small in diameter, most of which were polypoid with a broad base, smooth surface, uniform color, and without wall thickening, consistent with the growth characteristics of benign tumors. The right bronchus is more frequently affected than the left, with the upper and lower bronchi being more common sites of involvement compared to the main bronchus, which is less frequently affected.

Bronchoscopic, pathomorphological features and differential diagnosis: 1. Papilloma: Bronchoscopic appearance of the less common solitary form typically presents as a whitish polypoid lesion characterized by a distinctive "cauliflower" surface and a lack of surface vascularity.[17] Histologically, these lesions exhibit exogenous papillary growth, with the interstitium of the papilla being rich in fibrous vessels and the surface lined by compound epithelial cells. Based on the varying epithelial composition, papillomas can be classified into squamous papilloma (laminated squamous epithelium), glandular papilloma (pseudolaminated columnar epithelium), and mixed squamous and glandular papilloma (mixed laminated squamous epithelium and pseudolaminated columnar epithelium). Morphological assessment generally allows for diagnosis, and immunohistochemical analysis reveals that the squamous epithelium expresses CK5/6, P40, and P63. It is crucial to differentiate these lesions from squamous cell carcinoma, which is characterized by immature cell differentiation, disordered polarization, and cellular polymorphism, along with easily identifiable mitotic figures. Furthermore, squamous cell carcinoma often invades the walls of the trachea or bronchi. In contrast, the glandular epithelium of adenopapilloma expresses TTF-1 and exhibits continuous basal cell layers that also express P40 and P63.It is essential to differentiate adenocarcinoma, which lacks a basal cell layer and invades the bronchial wall or adjacent lung tissue, thereby promoting a connective tissue response. This implies that unless the lesion is completely excised, achieving a definitive pathological diagnosis of these tumors may be challenging.[1,17] Mixed papilloma must be differentiated from mucoepidermoid carcinoma, the latter of which typically presents as a solid growth lacking an apparent papillary growth pattern and is characterized by genetic features indicative of MAML2 gene rearrangement.[18] 2. Leiomyoma: Bronchoscopic descriptions typically reveal a wide-based, polyp-like or columnar morphology; pinkish to gray coloration; a smooth surface; and surface vascularity.[5] The morphological characteristics are akin to leiomyoma found in other tissues, comprising well-differentiated bundles of smooth muscle cells interwoven with one another. These tumors express markers such as Vimentin and SMA, and the diagnosis of bronchial leiomyoma should first exclude pulmonary metastases from other leiomyoma sites.[19] 3. Peripheral nerve sheath tumors: Bronchoscopic appearances are variable, presenting as whitish or pink coloration with broad-based or polypoid morphology and a smooth surface.[20] The morphological changes mirror those observed in other tissues. The main pathological types include schwannoma, neurofibroma, among which neurofibroma is more common.[8] Schwannoma tumor cells are spindle-shaped or oval with indistinct cell boundaries, and may exhibit growth patterns such as fascicular, palisaded, or whorled arrangements. Cellular-rich areas (Antoni type A), hypocellular areas (Antoni type B), and the formation of Verocay bodies can be observed. In contrast, neurofibroma cells are slender and spindle-shaped with wavy or comma-shaped nuclei, and scattered collagen fiber bundles may be seen. They lack Antoni A areas, though sometimes resemble the Antoni B areas of schwannomas. It is noteworthy that biopsy samples have inherent limitations and may not fully display typical diagnostic features for differentiation. Moreover, since both tumors express S-100 protein and share the same treatment approach, they are currently often uniformly classified as peripheral nerve sheath tumors in pathological diagnosis. These tumors are both positive for S-100, which helps to distinguish them from leiomyoma, and others. 4. Hamartoma: Some literature[3,10] reports that hamartoma is the most common type of benign bronchial tumor. Bronchoscopic findings are variable, with descriptions including white, gray, or pinkish coloration; rounded or broad-based polypoid morphology; a smooth or occasionally rough or gritty surface; and a hard or elastic consistency.[5] Histologically, hamartomas consist of multiple mesenchymal components, including lobulated mature cartilage tissue, a loose mucinous matrix, adipose tissue, sparse smooth muscle tissue, and invaginated respiratory epithelium. It is essential to differentiate between ossifying tracheobronchial disease, pleomorphic adenoma, and other conditions. 5. Lipoma: Bronchoscopic findings typically reveal a pale yellow to pinkish coloration, along with a smooth, lobulated, pedunculated, or polypoid morphology, occasionally exhibiting surface vascularity.[21] The morphological changes observed are consistent with those in other tissues, and the tumor is primarily composed of mature adipocytes, lacking cartilage tissue. 6. Sialolipoma: it is a remarkably rare salivary gland lesion characterized by benign salivary gland parenchyma interspersed with mature adipose tissue.[22] Bronchoscopic findings typically reveal a round-shaped, smooth-surfaced, solid, whitish-pink tumor. In terms of differential diagnosis, bronchial lipomas, hamartomas, carcinomas, and other tumors must be considered. A diagnosis of sialolipoma is confirmed by the presence of mature adipose cells intermixed with acinar, ductal, basal, and myoepithelial cells.

Pleomorphic adenoma is a tumor derived from the submucosal glands of the bronchus, frequently occurring in the trachea and main bronchi, with slow growth. Its histological morphology resembles that of pleomorphic adenoma in the

major salivary glands, manifesting as ductal structures, solid nests, and mucinous or chondroid stromal formations composed of epithelial and myoepithelial cells. It requires differentiation from hamartoma and squamous cell carcinoma. Mucinous adenoma and hemangioma are relatively rare: the former is mostly found in the main bronchus, characterized by multicystic mucinous structures and mild atypical epithelium, and needs to be distinguished from adenocarcinoma; the latter is commonly seen in children, presenting as a polypoid bright red mass, predominantly cavernous hemangioma, with positive immunohistochemical markers such as CD31 and CD34.

Treatment and prognosis: Resection, removal of obstruction, and reconstruction of the airway should be performed as promptly as possible to prevent irreversible damage to the distal bronchus and lung tissue. Bronchoscopic resection techniques include snare cauterization, Nd:YAG laser therapy, and microwave ablation.[10] In cases where the tumor has a broad base and is large, surgical intervention becomes necessary, particularly for patients with a history of endoscopic resection and recurrence. Thus, follow-up care is essential, especially in the case of pleomorphic adenomas, due to the potential for malignancy.[23] In this study, except for one case of squamous cell papilloma that was not completely resected via bronchoscopy, all other patients underwent complete tumor removal by bronchoscopy, and the overall prognosis was excellent.

This study retrospectively analyzed the clinical characteristics of patients with primary benign tracheobronchial neoplasms. Given the rarity of disease and the limited sample size, the analysis was conducted without statistical evaluation. Therefore, expanding the sample size is essential for future research. A larger sample size is anticipated to facilitate statistical analysis, ultimately aiming to enhance the early diagnosis rate of primary benign tracheobronchial neoplasms.

Conclusions

In summary, primary benign tracheobronchial neoplasms are relatively rare and present with insidious and nonspecific early clinical manifestations. They are often discovered incidentally during examinations for respiratory diseases, such as pulmonary tuberculosis. Due to their slow growth and small size, these tumors can be easily overlooked in CT scans, making bronchoscopy the primary method for both diagnosis and treatment. During bronchoscopy, tumors typically appear as localized polypoid growths within the bronchial lumen and exhibit a variety of pathological types. Leiomyomas are the most common, and accurate diagnosis requires morphological assessment along with necessary immunohistochemical examinations. Increasing awareness of this type of disease can facilitate early detection, treatment, and prevention of secondary respiratory conditions.

Ethical Statement

This study was conducted in accordance with the Declaration of Helsinki and received approval from the medical ethics committee of Wuhan Pulmonary Hospital (approval number No. 2022(14)). Patient consent was waived due to the retrospective nature of the study. The authors did not have access to any information that could identify individual participants during or after the data collection process.

Author Contributions

All authors made a significant contribution to the work reported, whether that is in the conception, study design, execution, acquisition of data, analysis and interpretation, or in all these areas; took part in drafting, revising or critically reviewing the article; gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

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Disclosure

The authors have no conflicts of interest to declare for this work.

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