Original Article

Clinical and Radiological Manifestations of Primary Tracheobronchial Tumours: A Single Centre Experience

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Abstract

Introduction: Tracheobronchial tumours usually cause an airway obstruction and secondary pulmonary infections. Although rare, they are an important differential diagnosis as they may mimic other conditions and diseases. This paper aims to analyse clinical, radiological and histological characteristics of the patients with tracheobronchial tumours diagnosed for a period of 7 years. Materials and Methods: In this retrospective, observational study, we carefully reviewed 65 patients who were diagnosed with tracheal and endobronchial tumours, and performed statistical analysis on the results. Results: Among these 65 patients (36 men and 29 women) with a mean age of 48.8 years (range, 15 to 75), 50 had malignant tumours while 15 had benign ones. The most common symptoms were cough, chest pain and haemoptysis. Cough was a more frequent symptom in patients with benign tumours (P <0.0014). Only 2 patients were asymptomatic. Tumours were predominantly localised in the large airways (46 in large bronchi and 2 in trachea). The most common radiological manifestation of malignant tumours was tumour mass (46%) followed by atelectasis. One third benign tumour caused atelectasis, while tumour mass and consolidation were found in 3 patients each. Computerised tomography revealed endoluminal tumour mass in 29.2% of the cases, which was more frequently found in benign than malignant tumours (47% vs 24%, respectively). On bronchoscopy, tumours were visible in 73% and 70% benign and malignant cases respectively. Conclusion: Tracheobronchial tumours should be ruled as a possible diagnosis in patients with cough, haemoptysis, dyspnoea and chest pain. The imaging techniques and histological examination of the tissue would subsequently lead to correct diagnosis and proper treatment can be administered.

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Key words: Bronchus, Computerised tomography, Trachea, Tumour, X-ray

Introduction

Tracheobronchial tumours can occur in the form of a variety of benign or low- and high-grade malignant tumours. The symptoms of an endobronchial tumour depend on mechanical factors rather than its pathological characteristics. Clinically, these tumours usually cause an airway obstruction and secondary pulmonary infections, though the characteristics are non-specific. The patient usually seeks treatment because of cough and haemoptysis, chest pain, dyspnoea on exertion, localised wheezing, recurrent pneumonia or atelectasis due to the obstruction of airway. If there is no obstruction, the patient may be asymptomatic.[1,2] Delays in diagnosis of tracheal or endobronchial tumours commonly occur due to negative chest x-ray findings and non-specific symptoms.

In the early stages, both benign and malignant endobronchial tumours have similar signs and symptoms. The radiological findings may include a normal chest radiograph, a solitary pulmonary nodule, or bronchial obstruction with distal atelectasis or consolidation.[1-4] Computerised tomography (CT) provides precise information about the extent of a tumour, which is important for planning a surgical resection. More importantly, CT findings can exclude contiguous mediastinal and parenchymal lung involvement. Accurate diagnosis of benign endobronchial tumours is important

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because bronchoscopic tumour removal may be sufficient as radical treatment.[2-4] We retrospectively reviewed 65 cases of primary tracheobronchial tumours that have been diagnosed at our institution. Clinical characteristics, radiological and histological features of these rare tumours are described.

Materials and Methods

From 1 January 2002 to 31 December 2008, 10,995 patients with primary pulmonary tumours were diagnosed and treated at the Institute of Lung Diseases and Tuberculosis of the Clinical Centre of Serbia in Belgrade, Serbia. The series included 65 patients with tracheobronchial tumours (2 tracheal and 63 endobronchial) whom we have carefully reviewed for clinical, radiological and histological features.

The chest radiographs were obtained by using a standard posteroanterior and lateral projection. The majority of CT scans were obtained by Somatom 4 Plus scanner (Siemens Medical Systems, Erlangen, Germany). The helical technique (5 to 10 mm collimation) was used and covered the area from the lung apices to the middle portion of both kidneys. Additional thin-section (1.0 mm collimation) scans were obtained when the lesion was a solitary nodule.

In 2 patients, multi-detector CT with 1.2 mm images of the thorax was made for 3-dimensional (3D) reconstruction and virtual bronchoscopy (VB). We used bolus injections of intravenous contrast medium as indicated to clarify hilar vascular anatomy. The chest radiographs and CT scans were analysed simultaneously. The analysis of the chest radiographs included location of the main tumour and examination for the presence of post-obstructive pneumonia or atelectasis. When there was no evidence of associated post obstructive pneumonia or atelectasis, the lesion was regarded as a solitary nodule (less than 3 cm in diameter) or as a mass (3 cm or more in diameter). The CT analysis included determination of the airway location, shape, and size and determination of the attenuation coefficient of the tumour. By their location, tumours were subcategorised to tracheal and bronchial, and the latter one to main, lobar, segmental, or subsegmental tumour. All tumours were histologically diagnosed on tissue samples obtained by bronchoscopy, transthoracic biopsy or surgery.

Histological diagnosis was made routinely on haematoxylin-eosin paraffin block sections. When necessary, imunohistochemistry was performed to define the histological type of the tumour, which has been determined according to the World Health Organization classification of the lung tumours 2004.[5]

Statistical Package for the Social Sciences (SPSS) for Windows version 16.0 was used to perform statistical analysis. The mean values were compared by variance analysis. We evaluated qualitative features by contingency table analysis and the non-parametric χ^2 test. A P value of less than or equal to 0.05 was considered to indicate a statistically significant difference. Odds ratios, estimated with univariate logistic regression, were used to summarise the association of patients' symptoms and radiological manifestation of endobronchial tumours and whether the probability of some radiological findings is the same in benign and malignant tumours.

Results

During the observed 7-year period, a total of 10,955 patients were diagnosed with primary pulmonary tumours and in 65 cases (0.6%) they were primary tracheobronchial tumours. The latter have been an interest for analysis. Patients' characteristics and clinical profiles of the study group with slight female predominance (55.4%) are showed in the Table 1.

Clinical Characteristics

The patients' mean age was 48.8 years (range, 15 to 75 years). We reviewed 50 patients with malignant tumours and 15 with benign tumours accounting for 0.45% and 0.13%, respectively of all lung tumours diagnosed over the same period. Pathological analysis revealed 10 different histological types (Table 2). Carcinoid tumour was the most common type of malignant tumours (Fig.1). Seven out of 15 benign tumours were lipoma. Tracheobronhial

Table 1. Patients' Characteristics and Clinical Presentation of Malignant and Benign Tracheobronchial Tumours

Characteristic	Type of Tumour		*P* value
	Malignant	Benign	
Age in years (range)	46 (15 to 75)	58 (46 to 70)	*P* <0.004
Sex	N (%)	N (%)	
Male	22 (44)	7 (46.7)	
Female	28 (56)	8 (53.2)	
Patients with symptoms	50 (98)	14 (93.3)	
Patients without symptoms	1 (2.0)	1 (6.6)	
Symptoms			
Cough	25 (50)	13 (86.7)	*P* <0.014
Haemoptysis	14 (28)	5 (33.3)	
Pain	21 (42)	9 (60)	
Dyspnoea	13 (26)	4 (26.7)	
Fever	14 (28)	4 (26.7)	
Wheezing	7 (14)	3 (20)	
Symptoms' duration in months	13.71 ± 15.42 (2 to 60)	19.28 ± 25.1 (1 to 84)	*P* >0.05

Table 2. Tracheobronchial Tumours by Histological Type

Type of Tumuor	Number	%
Malignant	**50**	**76.9**
Carcinoid	42	64.7
Squamous cell carcinoma	2	3.1
Adenocarcinoma	1	1.5
Small cell carcinoma	1	1.5
Mucoepidermoid carcinoma	2	3
Adenoid cystic carcinoma of trachea	2	3
Benign	**15**	**23**
Lipoma	7	10.8
Hamartoma	4	6.2
Papilloma	1	1.5
Mucous gland adenoma	1	1.5
Leiomyoma	1	1.5
Myofibroblastic tumour	1	1.5
Total	**65**	**100**

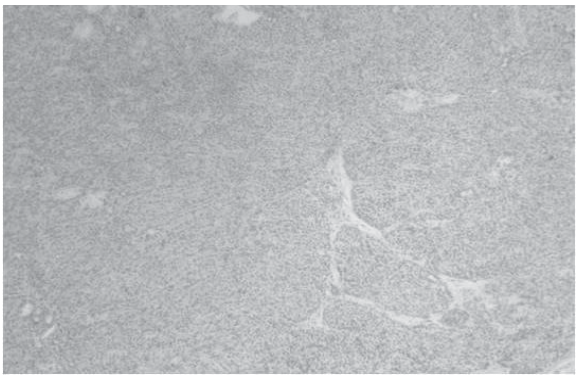

Fig. 1. Microphotograph of carcinoid tumour covered by respiratory epithelium, Staining H&E, magnification x20. Morphology of carcinoid: organoid and trabecular, rarely acinar pattern of uniform, cuboidal cells without nuclear polimorfism and prominenet nucleoli. Fibrovascular septa are present between groups of carcinoid tumour cells. There is no necrosis.

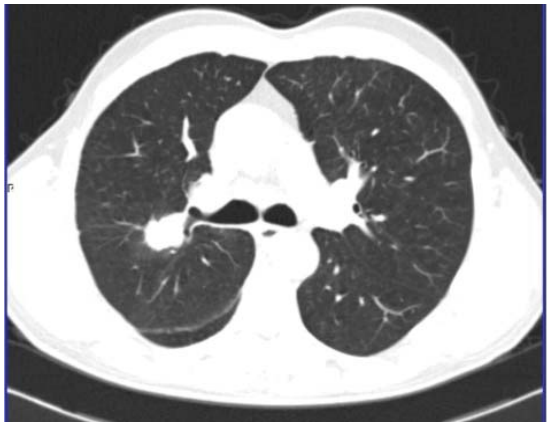

Fig. 2. Chest computed tomography (CT) in lung window setting shows oval, slightly lobulated mass close to the posterior segmental bronchus of the right upper lobe.

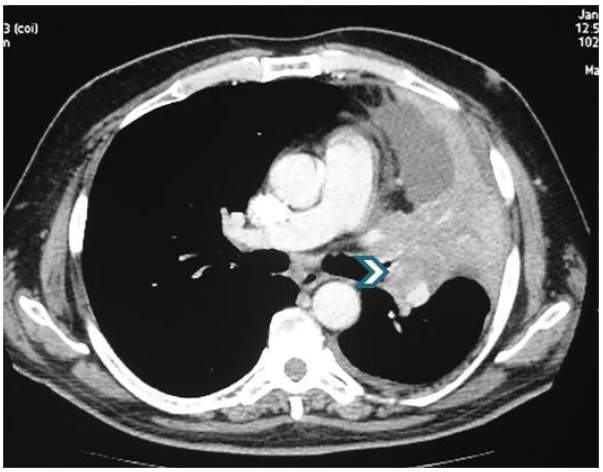

Fig. 3. Atelectasis of the left lung in patient with carcinoid tumour. Contrast-enhanced CT scan shows endobronchial mass (arrowhead) obstructing left upper lobe bronchus.

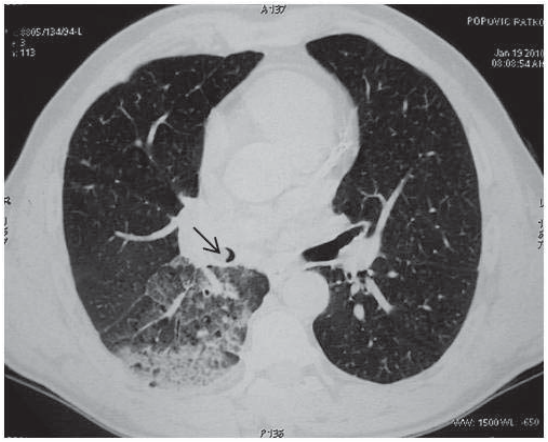

Fig. 4A. Chest CT in a patient with lipoma shows round tumour in bronchus intermedius and signs of inflammation.

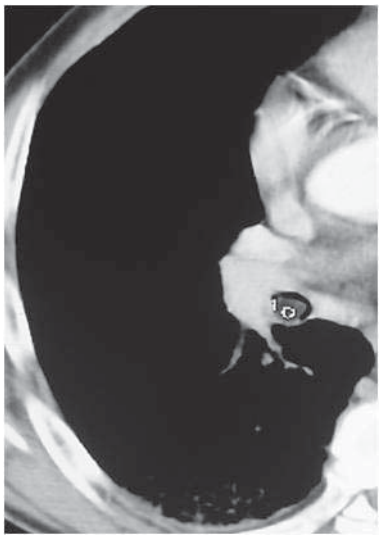

Fig. 4B. Image of the same patient in soft tissue setting shows endobronchial mass of fat density (circle).

Table 3. Chest X-ray Findings of Tracheobronchial Tumours by Type

Findings	Tumour type	
	Malignant	Benign
Normal	2 (4%)	1 (6.7%)
Atelectasis	9 (18%)	5 (33.3%)
Mass	23 (46%)	3 (20.0%)
Nodule	7 (14%)	2 (13.3%)
Consolidation	5 (10%)	3 (20.0%)
Pleural effusion	3 (6%)	0
Hyperlucency	1 (2%)	1 (6.7%)
Total	**50 (100%)**	**15 (100%)**

tumours were localised in large airways predominantly on the left side (41/63). The location was as follows: right main bronchus 1, right upper lobe 4, right middle bronchus 7, right lower lobe 10, left main bronchus 8, left lower lobe bronchus 22, left upper lobe bronchus 11, trachea 2.

Symptoms were present in all the patients but 1 with malignant tumour and 1 with benign tumour (Table 1). For these 2 patients, the tumours were revealed incidentally through abnormal chest x-ray finding. Cough, chest pain and haemoptysis were the most common symptoms in both groups. Cough was more frequent in patients with benign tumours (P <0.014) especially in those with atelectasis. The presence of atelectasis in patients with cough was 1.6 times more suggestive of benign tumour than malignant one (OR: 1.603).

Radiological Characteristics

Most commonly, malignant tumours have been presented as tumour mass on chest x-ray and thoracic CT in 46% (Fig. 2), followed by atelectasis in 18% (Fig. 3). One third of the benign tumours have been presented as atelectasis followed by tumour mass and consolidation (3 each) (Figs. 4A and 4B, Table 3). The presence of tumour mass increased the likelihood of its malignancy by about 3.5 times (OR: 3.45) (Table 4). Computerised tomography revealed endoluminal tumour mass in 7 (46.7%) patients with benign tumours, and 12 (24%) patients with malignant tumours. Endoluminal tumour was revealed in 9 patients with atelectasis, in 3 patients with normal chest x-ray and in patients with consolidation and hyperinflation (2 each). In 3 of 26 patients with radiographically detected tumour mass, CT also revealed endoluminal tumour. Virtual bronchoscopy was performed in only 2 of our patients (Figs. 5A and 5B).

Bronchoscopic Findings

On bronchoscopy, tumours were visible in 11 (73%) benign cases and 35 (70%) malignant cases. Signs of inflammation were detected in 3 malignant cases. Extraluminal compression was observed in 1 patient with benign tumour. Fifty-eight patients underwent surgery (44 lobectomies, 5 bronchotomies, 6 tumour extirpations, 2 tracheal resections) and in 4 cases, the tumours were removed bronchoscopically. In 3 patients, the tumour were unresectable. Diagnosis was made on tissue samples obtained through bronchoscopy in 50 patients, through surgically resected material in 12, through thoracoscopy in 2, and through percutaneous transthoracic biopsy in 1.

Table 4. Probability of Some Radiological Findings in Benign and Malignant Tumours

Chest X-ray findings	Malignant	Benign	χ^2 *P* value	Odds Ratio (CI ± 95%) Malignant vs Benign
Normal	2 (4.0%)	1 (6.7%)	$P = 0.681$	OR: 0.596 (95% CI, 0.05 to 7.07) RR: 95% CI: 0.0596 < RR<6.2913
Atelectasis	9 (18.4%)	5 (33.3%)	$P = 0.219$	OR: 0.450 (95% CI, 0.12 to 1.64) RR: 95% CI: 0.2179 < RR<1.3934
Tumour Mass	23 (46%)	3 (20.0%)	$P = 0.063$	OR: 3.450 (95% CI, 0.73 to 16.35) RR: 95% CI: 0.8172 < RR < 6.7404
Nodule	7 (14.3%)	2 (13.3%)	$P = 0.926$	OR: 1.083 (95% CI, 0.19 to 5.87) RR: 95% CI: 0.2485 < RR < 4.619
Consolidation	5 (9.3%)	3 (20.0%)	$P = 0.315$	OR: 0.454 (95% CI, 0.08 to 1.95) RR: 95% CI: 0.1378 < RR < 1.8896
Pleural effusion	3 (6%)	0	no testing	no testing
Hyperlucency	1 (2%)	1 (6.7%)	$P = 0.367$	OR: 0.292 (95% CI, 0.02 to 4.96) RR: 95% CI: 0.0204 < RR < 4.6047

McNemar's Test = 44.3077, df = 1, P <0.0001
Odds ratio: 3.4500 (95% CI, 0.7280 to 16.3500)

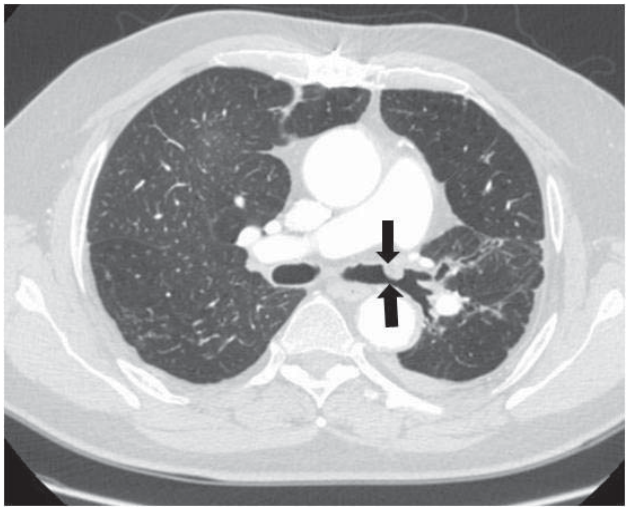

Fig. 5A. Chest CT in patient with carcinoid tumour. CT scan shows tumour mass in left main bronchus (arrows).

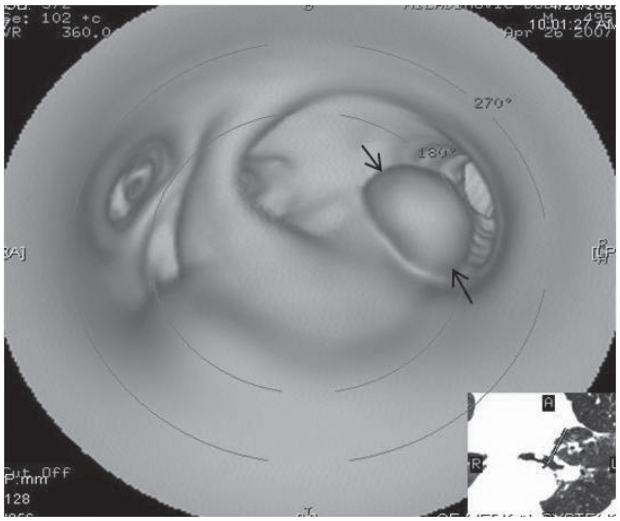

Fig. 5B. Virtual bronchoscopy of the same patient shows a tan spherical, smooth-surfaced tumour in left main bronchus (arrows).

Discussion

We presented a series of 65 primary tracheobronchial tumours, which are rare neoplasms found in the trachea, carinal and endobronchial regions. It was possible to obtain such a series owing to a large number of patients referred to our teaching hospital. Although tracheobronchial tumours represented only 0.6% of all the pulmonary tumours, they are clinically very important. They often mimic asthma, chronic obstructive pulmonary disease or other malignant neoplasms, and could potentially lead to complete bronchus destruction and/or parenchymal damage due to post-obstructive pneumonia.[4,6]

Most tumours of the tracheobronchial tree are malignant[2] and our study confirmed this. Our results showed that the patients with malignant tumours were significantly younger than those with benign ones (P <0.004). However, due to the small number of benign cases, the result needs to be further examined with a larger sample size. Among malignant tumours in our series, tumours with low-grade malignancy were dominant (92%) with carcinoid tumour being the most common.

We found 30 central and 12 peripheral carcinoids. Central bronchial carcinoids most frequently manifested as a hilar or perihilar mass. The mass is usually a well-defined, round or ovoid lesion and may be slightly lobulated at radiography and CT. Because of the central location of carcinoids, initial radiographs may demonstrate findings related to bronchial obstruction while the other radiographical findings are less common and non-specific. Bronchoscopy enables location like this, as in the majority of these tumours, reachable. They have a characteristic bronchoscopic appearance.[7,8]

Peripheral carcinoids manifested mostly as nodules (6 of our cases) followed by non-segmental infiltrates and pleural effusion (3 each). These findings are concordant to those previously reported.[7,9-13] Other malignant endobronchial tumours with low-grade malignancy were less frequent and included mucoepidermoid carcinoma and tracheal adenoid cystic carcinoma. Patients with mucoepidermoid carcinoma had non-specific symptoms and radiological features.[14,15] Patients with tracheal tumours experienced wheezing and dyspnoea. Though the chest x-ray appears normal, CT however, revealed the presence of endotracheal tumour. Tracheal tumours are rare. Reported frequencies ranged from 0.075% in autopsy series to 0.19% of all the patients with malignancy of the respiratory tract.[16-18]

Adenoid cystic carcinoma is the second most common primary tracheal tumour next to squamous cell carcinoma. It should be considered as differential diagnosis, particularly in younger adults.[19-21] High-grade endobronchial tumours were diagnosed in only 8% of our patients and corresponded to primary lung carcinoma. Their clinical and radiographical features were indistinguishable from other endobronchial malignant tumours. Secondary malignant tumours occur as a result of either haematogenous metastasis or direct invasion by a malignancy from an adjacent structure. Haematogenous metastases usually originate from renal cell carcinoma, breast cancer, colon cancer, hepatocellular carcinoma, or melanoma. Their CT manifestations are similar to those of primary malignant tumours.[22]

Benign tracheobronchial tumours in our study are even more rare compared to malignant ones, accounting for just 0.13% (15/10,995) of all the primary pulmonary tumours in our series—similar frequency as reported in the literature.[2] These tumours are quite different and not concentrated in

several groups as the malignant ones. Unlike malignant tumours, many benign neoplasms are slow growing and present with symptoms of bronchial obstruction.[1,2,23,24]

Most commonly, our patients sought treatment because of cough, chest pain and haemoptysis.[25] The duration of their symptoms were very similar to those reported in literature.[26] The clinical and radiographical features of these tumours may resemble malignant tumours. The radiographical findings are usually non-specific and may include atelectasis, pneumonia, bronchiectasis, and mediastinal shifts.[1,2,4]

In our study, 10 patients with benign tumours have had recurrent pneumonia in the same lung lobe before definitive diagnosis and 2 were misdiagnosed as having asthma. Possible presence of tracheobronchial tumour should be kept in mind when 'asthmatic' patient experienced repeated pulmonary infection at the same location with or without atelectasis. Early recognition and diagnosis of benign endobronchial lesions may allow conservative treatment and favourable disease outcome.[1-3,27] Therefore, a cross-sectional CT imaging is an important and complementary tool with bronchoscopy although it underestimates the extent of submucosal invasion.

In 7 benign and 12 malignant cases, CT showed endoluminal mass that explained the cause of radiological findings. CT features are helpful in definitive diagnosis of fatty tumour within the bronchial lumen because CT is highly specific and sensitive in fat detection.[27-31] Four of our patients had benign endoluminal tumour of fatty density. Virtual bronchoscopy (VB) performed in only 2 of our patients, is a 3-dimensional reconstruction that shows a real-like anatomical view of the tracheobronchial tree. This imaging method is accurate, non-invasive for evaluating obstructions, endoluminal masses and poststenotic areas within the airway. VB has some disadvantages: it lacks the detail of real bronchoscopy and does not show mucosal or submucosal extensions.

However, this imaging modality provides information regarding bronchial and peribronchial anatomy that may be beneficial in the management of patients with tracheobronchial tumours.[32-35] Because of the predominant location of these tumours in the large bronchus, bronchoscopic examination and biopsy were necessary in the confirmation of diagnosis.[36-38] In 76.9% of our patients, diagnosis was made on tissue samples obtained through bronchoscopy. Various histological types of primary lung tumours with endoluminal growth pattern were diagnosed. Benign and malignant lung tumours of both epithelial and mesenchymal origin were histologically diagnosed. A fluorine 18 fluorodeoxyglucose (FDG) positron emission tomography (PET) is increasingly used in the diagnostic work-up of various tumours that are suspected of being malignant. At FDG PET, most squamous cell carcinomas show high uptake, whereas adenoid cystic carcinoma and mucoepidermoid carcinoma show variable uptake depending on the grade of differentiation. Carcinoid tumours usually have a lower uptake at FDG PET than what would be expected of a malignant tumour.[39]

We hope that our paper increases clinicians' awareness on tracheobronchial tumours which can mimic bronchial asthma or recurrent pulmonary infections. Careful clinical evaluation and imaging together with endoscopic examination are necessary for the confirmation of endoluminal tracheobronchial lesions. Knowledge of the CT characteristics and PET manifestations of tumours in the tracheobronchial tree can aid in the diagnosis and differentiation of malignant tumours from benign ones. Henceforth, proper treatment can be administered.

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