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Tracheobronchial Tumors: Radiologic–Pathologic Correlation of Tumors and Mimics

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Tracheobronchial masses encompass a broad spectrum of entities, ranging from benign and malignant neoplasms to infectious and inflammatory processes. This article reviews the cross-sectional findings of tracheal tumors and tumor-like entities, correlates imaging findings with histologic pathology, and discusses pearls and pitfalls in accurately diagnosing and classifying tracheal tumors and mimics.

Tracheobronchial Lesions

Tracheobronchial tumors can be benign or malignant, and they can be thus classified or be ranked based on being focal or diffuse. Tumors are mainly focal, whereas tumor mimics are mostly diffuse. Classification of these pathologies is summarized in Table 1. Diagnosis of most of these lesions is often delayed because associated nonspecific symptoms such as cough, pneumonia, or lobar atelectasis are often nonspecific; and unless tracheal lesions are found on thoracic cross-sectional imaging such as computed tomography (CT) or magnetic resonance imaging (MRI), often incidentally, they usually present in their late stages.[1,2]

Normal Anatomy of the Trachea

The trachea extends from the lower border of the larynx, at 2 cm below the level of the vocal cords, to the carina. The average length of the trachea spans 10 to 12 cm. The typical angle of tracheal bifurcation at the carina is 70+/−20 degrees. The trachea is composed of four layers: mucosa, submucosa, cartilage, and muscle. The cartilaginous layer consists of 18 to 22 incomplete semicircular rings of cartilage connected by annular ligaments of fibro-connective tissue anteriorly and laterally. The posterior wall consists of the trachealis muscle and fibrous connective tissue with an average wall thickness of 1-3 mm. The normal transverse internal diameter of the trachea is 15 to 25 mm in males and 10 to 21 mm in females. More distally in the tracheobronchial tree, bronchi are differentiated from bronchioles by the presence of cartilage in bronchial walls. Blood to the trachea is supplied through the inferior thyroid, bronchial, and intercostal arteries. The trachea is innervated by the recurrent laryngeal nerve[3-5] (Fig 1).

Imaging Diagnostic Approach

A chest radiograph is the first step in patients with nonspecific respiratory symptoms. However radiography is of low sensitivity in the detection of tracheobronchial pathologies, and many lesions can be missed. Multidetector computed tomography is the modality of choice to investigate suspected airway pathologies. The advantages of CT include excellent spatial resolution and the ability to generate multiplanar reformats and three dimensional (3D) reconstructions, CT allows for rapid and noninvasive evaluation of the tracheobronchial tree. Importantly, with current CT detectors, the spatial resolution is preserved in the axial, coronal, and sagittal planes. Multidetector computed tomography is an excellent diagnostic tool to find, localize, and investigate the extent of airway pathologies with both local and distant disease involvement. Virtual bronchoscopy using 3D reconstruction from CT images is a useful diagnostic tool that offers a noninvasive technique for investigation of the tracheobronchial tree.[6,7]

Tumors

Epidemiology of Malignant Tracheobronchial Tumors

Primary tumors are rare and make up less than 0.4% of all tumors, producing 0.1% of cancer deaths worldwide. Primary malignant tumors typically arise from surface epithelium or salivary glands. Current imaging modalities of choice to evaluate tracheal tumors are CT

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TABLE 1
Tracheal lesions

Tracheal Lesions		
Focal Lesions		Diffuse Lesions
Primary malignant tumors	Bronchogenic adenocarcinoma	Relapsing polychondritis
	Squamous cell carcinoma	Wegner's granulomatosis
	Small cell carcinoma	Infection
	Carcinoid	Metastasis
	Mucoepidermoid carcinoma	Amyloidosis
	Adenoid cystic carcinoma	Osteochondroplastic tracheobronchopathia
Endobronchial metastases		Papillomatosis
Benign Lesions		
	Tracheal leiomyoma	
	Lipoma	
	Pleomorphic adenoma	
	Granular cell tumors	

with 3D reconstructions and PET/CT.[8-12] Malignant involvement of the trachea can result from direct invasion by tumors arising from adjacent organs such as the thyroid, lung, esophagus, and larynx, or by hematogenous metastasis from distant organs such as kidney, breast, colon, and melanoma.[13]

Squamous Cell Carcinoma

Squamous cell carcinoma (SCC) is the most common primary tracheal tumor, with higher male prevalence, and is highly associated with smoking. Tumors can produce symptoms when enlarged to obstruct more than half of the tracheal cross-sectional area, leading to cough, hemoptysis, and dyspnea. Imaging characteristics of SCC include a polypoid or sessile lesion, causing eccentric narrowing of the airway lumen or circumferential wall thickening in the lower third of trachea. Irregular margins are seen as the tumor arises from the surface epithelium, often with mediastinal invasion by direct extension or lymphatic spread. Lymph node metastasis and distant metastases at presentation are sometimes observed[14,15] (Fig 2). SCC tends to exhibit high uptake on FDG PET/CT.[16]

Adenoid Cystic Carcinoma

Adenoid cystic carcinoma (ACC) is the second most common tracheal tumor, with similar incidence among males and females, and with younger age predilection than SCC. ACC is often a submucosal

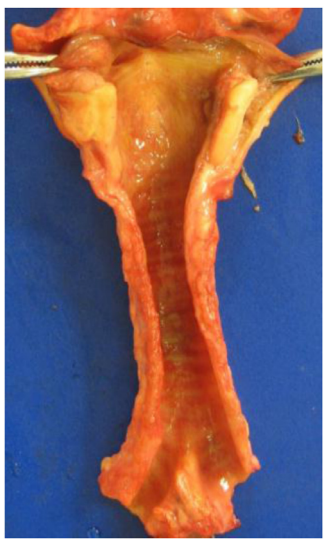

FIG. 1. Normal larynx, trachea, and proximal bronchi opened from the posterior aspect.

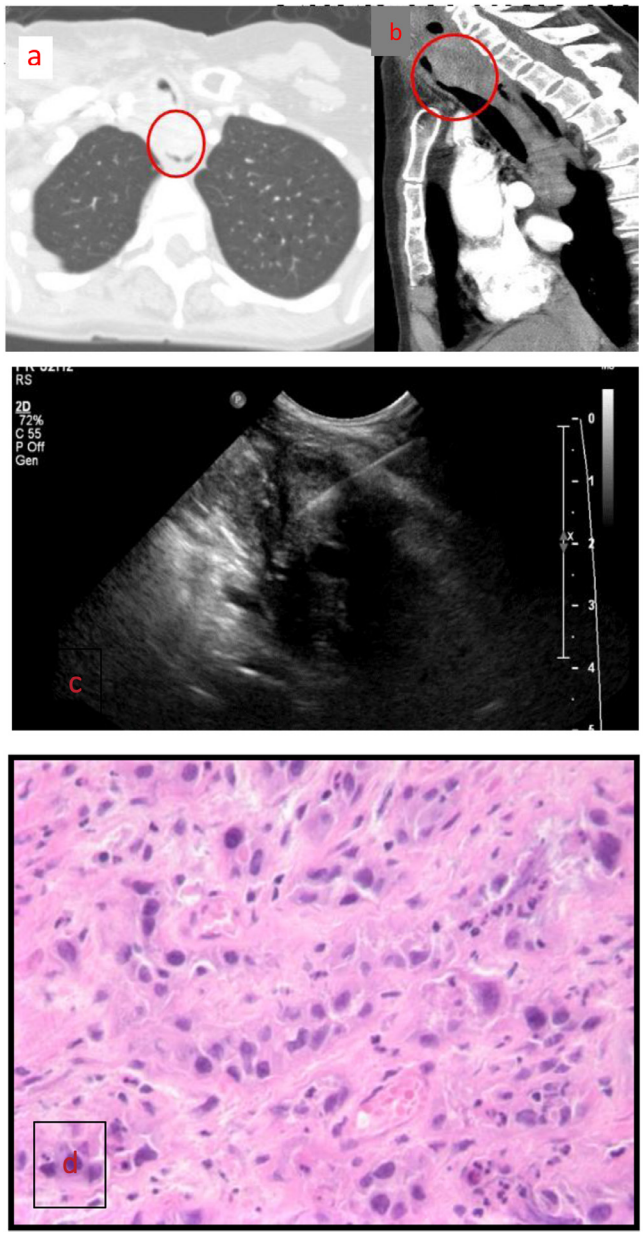

FIG. 2. (a, b) Axial and sagittal CT images demonstrating squamous cell carcinoma centered in the superior trachea with posterior extension into the esophagus. (c) Ultrasound-guided biopsy of an enlarged right supraclavicular lymph node was performed. (d) Infiltration by large atypical neoplastic cells with ample amount of eosinophilic cytoplasm and prominent nucleoli. Numerous mitoses are identified.

tumor with intact overlying mucosa and smooth contour. Presenting symptoms also include cough, hoarseness, dyspnea, and wheezing. CT imaging often demonstrates a smooth focal mass in the trachea or main bronchi with a longer extent of longitudinal involvement than cross-sectional involvement. 3D reconstruction is helpful in the evaluation of the extent of disease. Lymphadenopathy and distant metastasis are uncommon in ACC.[17-19] Surgical resection is a treatment option in localized disease (Fig 3).

Mucoepidermoid Carcinoma

Mucoepidermoid carcinoma is a tumor of the salivary-gland type that originates from the submucosal glands of the tracheobronchial tree. Presenting symptoms include cough, hemoptysis, wheezing, and postobstructive pneumonia, but may also be asymptomatic. It classifies as low-grade or high-grade based on histologic findings. On CT

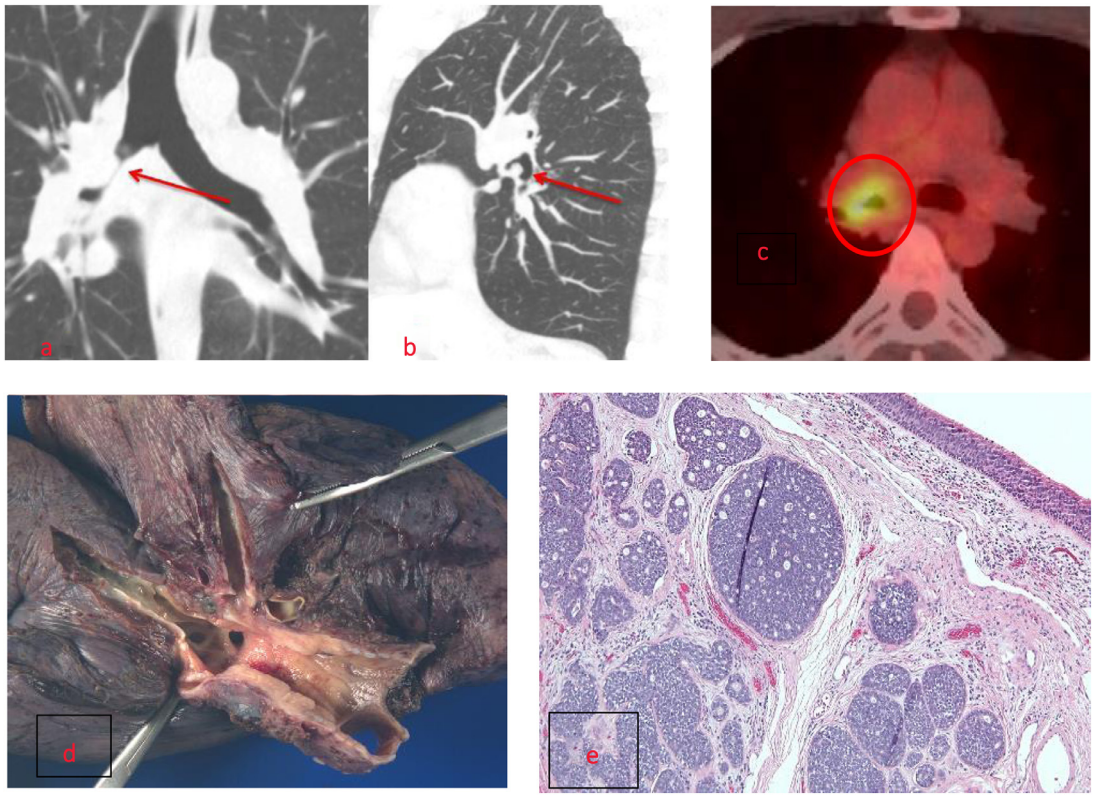

FIG. 3. (a, b) Adenoid cystic carcinoma presenting as intraluminal mass within the proximal right main stem bronchus. Note the smooth contours and extent of longitudinal involvement that is longer than axial involvement as seen on coronal and sagittal CT imaging. (c) FDG PET-CT is demonstrating avid radiotracer uptake. (d, e) Gross pathology demonstrates ill-defined firm white-tan mass is enveloping the trachea measuring t 3.6 × 5 × 0.8 cm and extending into the right superior lobar bronchus. 10 X image with H&E staining demonstrates respiratory mucosa at the top with nests of ACC tumor cells below.

the presentation is a nodule or mass in the lower trachea or lobar bronchi. Surgical resection is the treatment of choice with a good prognosis[20-22] (Fig 4).

Carcinoid

Carcinoids compose of 1%-2% of all pulmonary neoplasms and 25% of all carcinoid tumors. These tumors are more common in adolescent and younger adults than other primary tracheal tumors and are more often located centrally. Symptoms include cough, hemoptysis, postobstructive pneumonia, and wheezing. In less than 5% of the time, carcinoid can present with symptoms of carcinoid syndrome, including flushing, diarrhea, and wheezing. On CT, endobronchial carcinoids present as well-defined spherical or oval lesions with lobulated borders and intense contrast enhancement. Twenty-five percent of carcinoid tumors contain calcification. On MR, these tumors are T2 hyperintense and T1 hypointense with evidence of avid enhancement on postcontrast sequence. FDG-PET is of limited utility as that carcinoid are often associated with minimal uptake. The somatostatin avid PET radiotracer 68-Ga DOTATATE PET/CT received US FDA approval in June 2016 and demonstrated a higher level of uptake in carcinoid. The higher resolution of PET-CT can also be advantageous as compared to 111-In pentetreotide SPECT-CT. Carcinoid metastases to the liver are associated with right heart valvular disease due to paraneoplastic effects from tumor release of vasoactive substances, including serotonin and prostaglandin[23] (Fig 5).

Endotracheobronchial Lymphoma

Endobronchial lymphoma is a rare manifestation of Hodgkin's and Non-Hodgkin's lymphoma, arising de novo from the bronchus-associated lymphoid tissue. The onset of presenting symptoms are insidious with airway obstruction, coughing, and wheezing with a reported median age of 44 years (4-81 years).[24,25]

Bronchus-associated lymphoid tissue lymphoma is a rare low-grade subtype of marginal zone lymphoma which mostly occurs in distal bronchi. Conditions such as follicular bronchiolitis, smoking, and chronic infections may lead to its development. Some of the entities associated with bronchus-associated lymphoid tissue lymphoma include AIDS, Sjogren's syndrome, amyloid deposition, and dysgammaglobulinemia.[26-28] There is no specific radiologic finding to suggest lymphoma and diagnosis is based on biopsy. However CT is useful to detect associated mediastinal/hilar lymphadenopathy. Treatment is with chemotherapy. Surgery is only suggested when there is airway compromise/obstruction (Fig 6).

Tracheal Chondrosarcoma

A rare cartilaginous tumor mostly has been reported in elderly male patients. They can grow in any part of the trachea; however lower third followed by upper, and Mille thirds are the order of prevalence. Bronchoscopy is the gold standard for diagnosis and CT is the imaging modality of choice to determine the size, presence of calcification, location, the degree of luminal obstruction and presence of extratracheal extension. In the early stages, the mass spares the posterior wall of the trachea because of lack of cartilage, but in later stages, there will be invasion to the posterior wall. They tend to be low grade with a low risk of metastasis. The treatment of choice is surgical resection[29-31] (Fig 7).

Metastases

Metastasis is a rare entity, which can result from local invasion or hematogenous spread, with direct invasion being far more common.

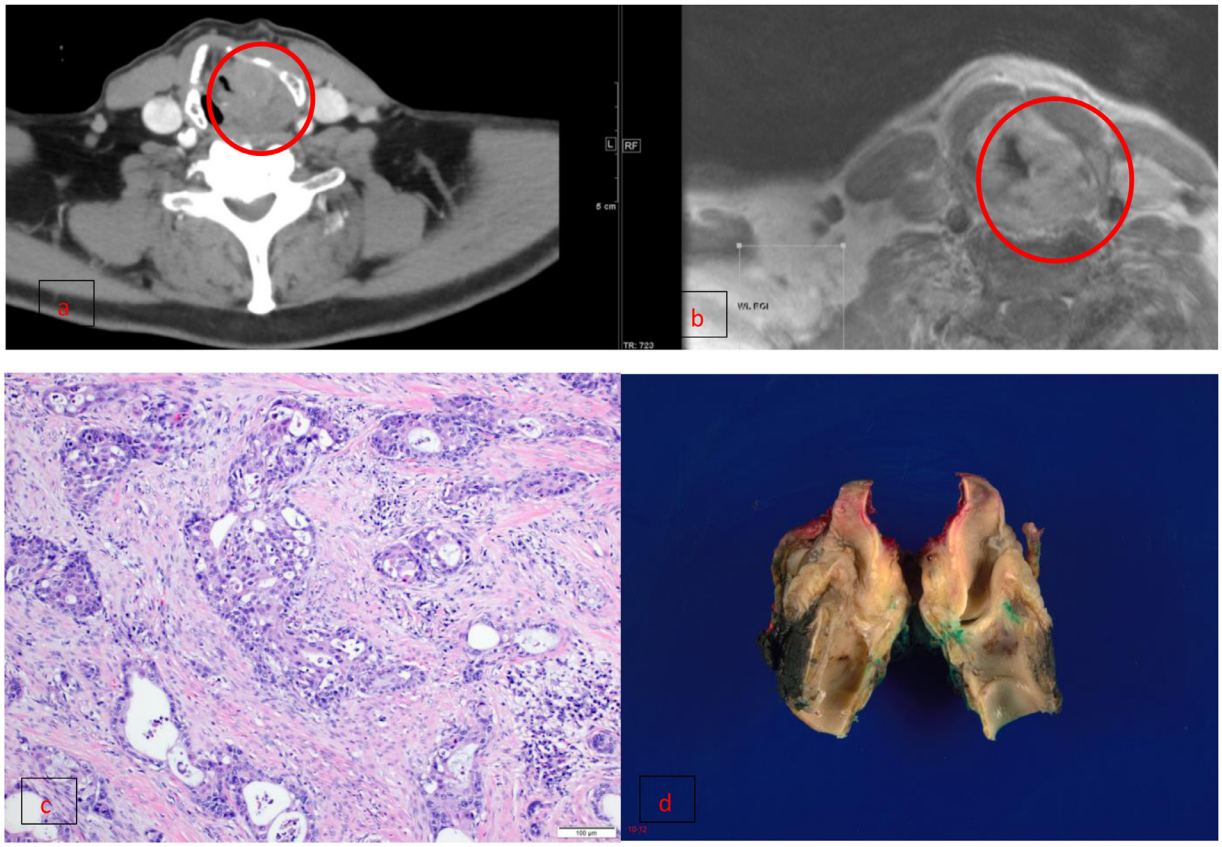

FIG. 4. (a, b) Left glottic enhancing mass involving the left paraglottic fat and aryepiglottic fold. The mass infiltrates the true vocal cord and left cricothyroid space and abuts the left thyroid, arytenoid, and cricoid cartilages. Left: Contrast-enhanced neck CT, Right: Axial IDEAL T1 w/ contrast. (c, d) Sections demonstrate sheets and nests of infiltrating tumor cells characterized by enlarged, pleomorphic nuclei with ample amounts of eosinophilic cytoplasm with extensive microcystic and cribiforming architectures. Overall the features are diagnostic of intermediate-grade mucoepidermoid carcinoma.

Given their proximity, tumors originating from lung, esophagus, and thyroid are the most common sources of local invasion. Tumors producing tracheal metastases include renal cell carcinoma, breast, colon, hepatocellular carcinoma, and melanoma. Metastases can present as solitary or multiple airway nodules[13,14] (Fig 8).

Tumor-Like Lesions and Mimics

Infections

Viral

Diffuse swelling associated with signs of upper airway obstruction is seen in the setting of childhood infections, such as with parainfluenza types 1–3, influenza A and B viruses; adenoviruses; coronavirus NL63; and respiratory syncytial virus. In adults, upper airways obstructive symptoms are unlikely due to the larger diameter of the adult trachea as compared to children. Infectious processes in adults are associated with risk factors such as immunocompromised states or focal damage to the tracheal mucosa from etiologies such as intubation or tracheostomy.[32-35] Overall, most of the cases of viral tracheitis stem from parainfluenza or respiratory syncytial virus infection, which can lead to subglottic or laryngeal narrowing.

Tuberculosis

Around 10%-40% of patients with tuberculosis exhibit features of endobronchial involvement with the thickened and irregular wall with active disease. Tuberculosis tracheitis is considered one of the most communicable patterns of tuberculosis. The extension of the disease to the trachea is more commonly from neighboring mediastinal lymph nodes or peribronchial lymphatics. Smooth residual airways stenosis can be seen after completion of treatment.[36]

Rhinoscleroma

Rhinoscleroma presents as a chronic granulomatous condition of the nose and upper airway structures. The known causative microorganism is *Klebsiella rhinoscleromatis*. It is more common in female patients, and between ages 10 yearsand 30 years. Rhinoscleroma infection often has a chronic course with a 25% chance of relapse. The treatment includes antibiotics, and surgery if complicated by focal airways, obstructs narrowing[37] (Fig 9).

Noninfectious Pathologies

Granulomatosis With Polyangiitis (GPA, Formerly Wegner Granulomatosis)

Granulomatosis with polyangiitis is a systemic necrotizing granulomatous vasculitis mainly affecting the respiratory system, in which 90% of patients present with pulmonary involvement. Granulomatosis with polyangiitis is associated with positive Antineutrophil cytoplasmic antibodies (ANCA), and there is often concurrent glomerulonephritis as a part of the pulmonary-renal syndrome. CT scanning often shows tracheal wall thickening with ulceration, posterior wall involvement, and predilection for the subglottic trachea which can produce subglottic stenosis. Pulmonary parenchymal findings include cavitary nodules, consolidations, and ground glass opacities[38] (Fig 10).

Amyloidosis

Amyloidosis is a rare disorder of deposition of abnormal proteinaceous material in the trachea. CT shows diffuse nodular thickening or may present as short segment stenosis. The subglottic larynx and adjacent cervical trachea are most commonly involved. Amyloid nodules

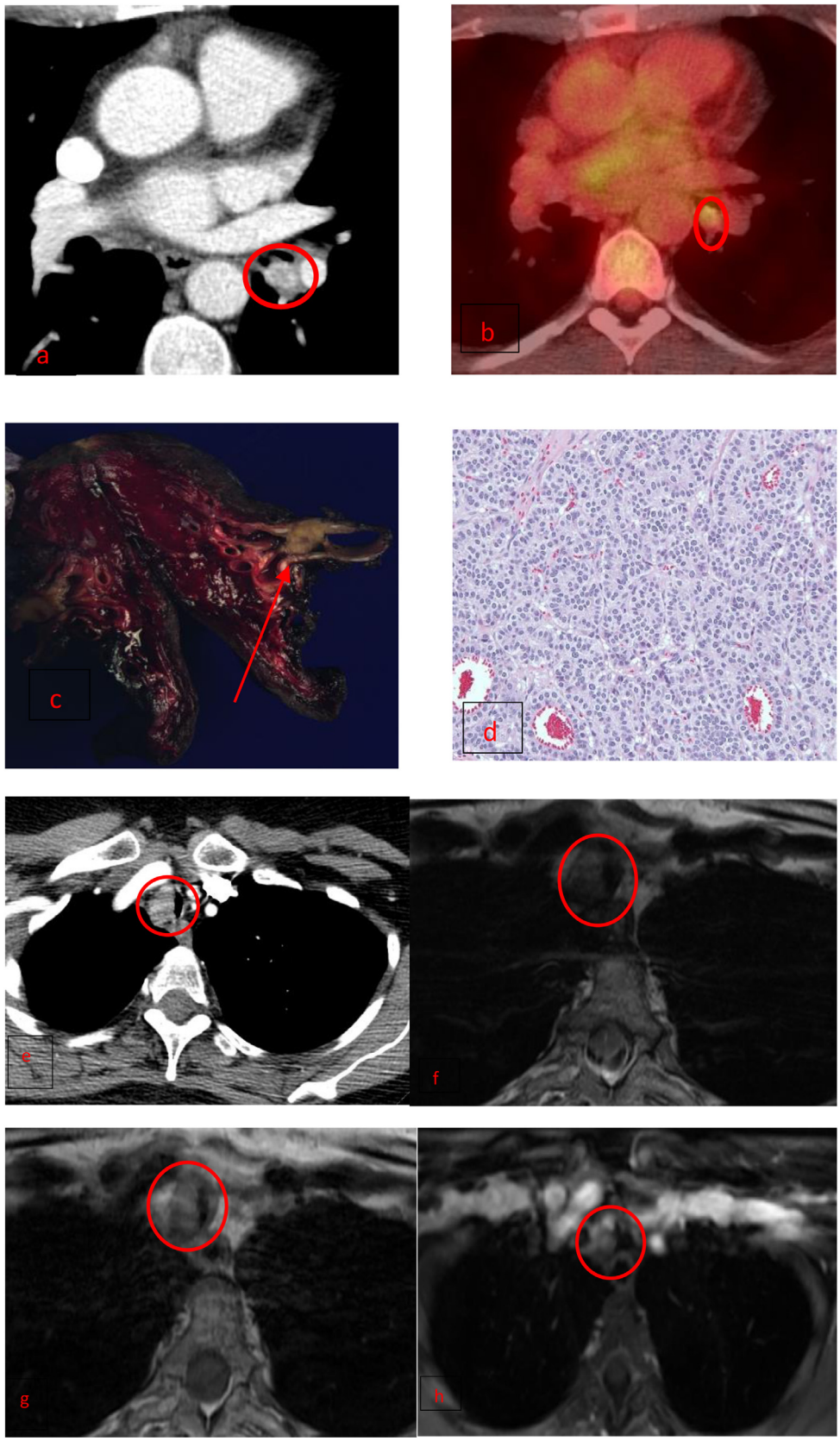

FIG. 5. (a) Endobronchial carcinoid visualized as an enhancing, well-defined ovoid nodule arising from the left lower lobar bronchus. (b) Carcinoid is demonstrating low FDG avidity on PET/CT. (c) Gross pathology is demonstrating a 1.6 × 1.0 × 1.0 cm well circumscribed, endobronchial, tan-white nodule arising from the left lower lobe bronchus, within 0.5 cm of the inked specimen edge, and 0.5 cm to the inked bronchial specimen edge. (d) 20 X H&E stain showing small nests of uniform cells representing a typical carcinoid. (e-h) Partial obstruction of the mid trachea by an enhancing mass which is mild hyperintense on T2 (f) and isointense on T1(g). The lesion is avidly enhancing with contrast. This mass was found to be a cardinoid.

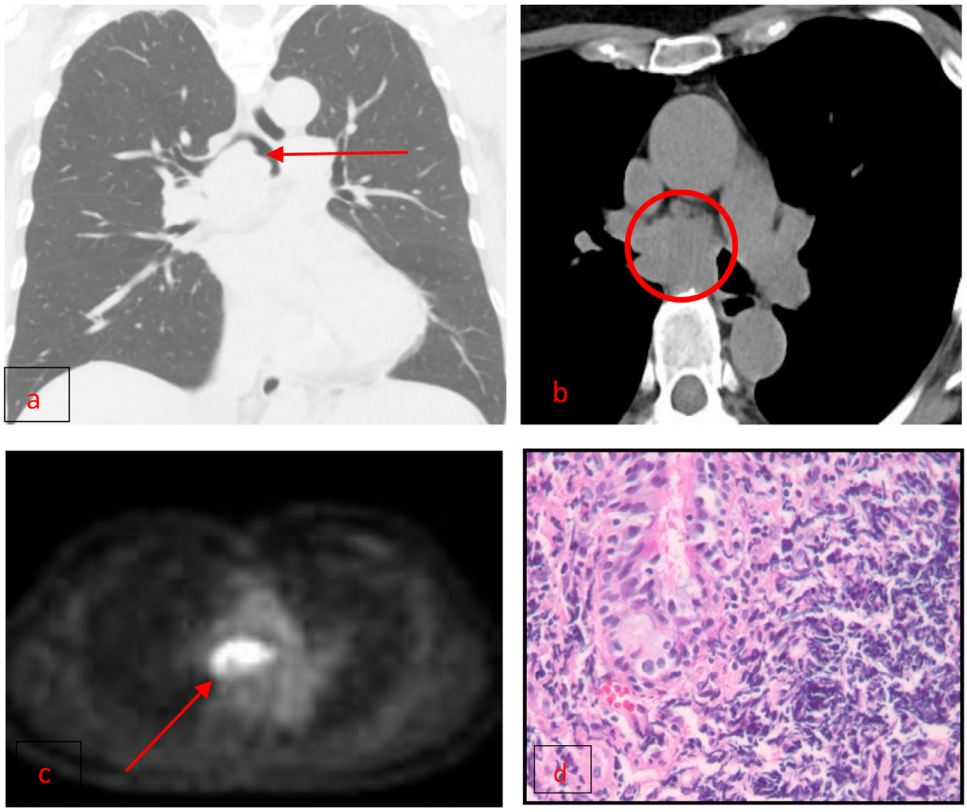

FIG. 6. (a, b) Endobronchial lymphoma is manifesting as a large intraluminal mass expanding the right main bronchus and extending into the bronchus intermedius. (c) FDG PET is showing intense uptake corresponding to the intraluminal soft tissue mass and subcarinal lymphadenopathy. (d) H&E stained sections show bronchial mucosa with a lymphoid infiltrate expanding the submucosa, composed of predominantly small sized cells with condensed chromatin and irregular nuclei. The findings are consistent with bronchial involvement by non-Hodgkin's lymphoma.

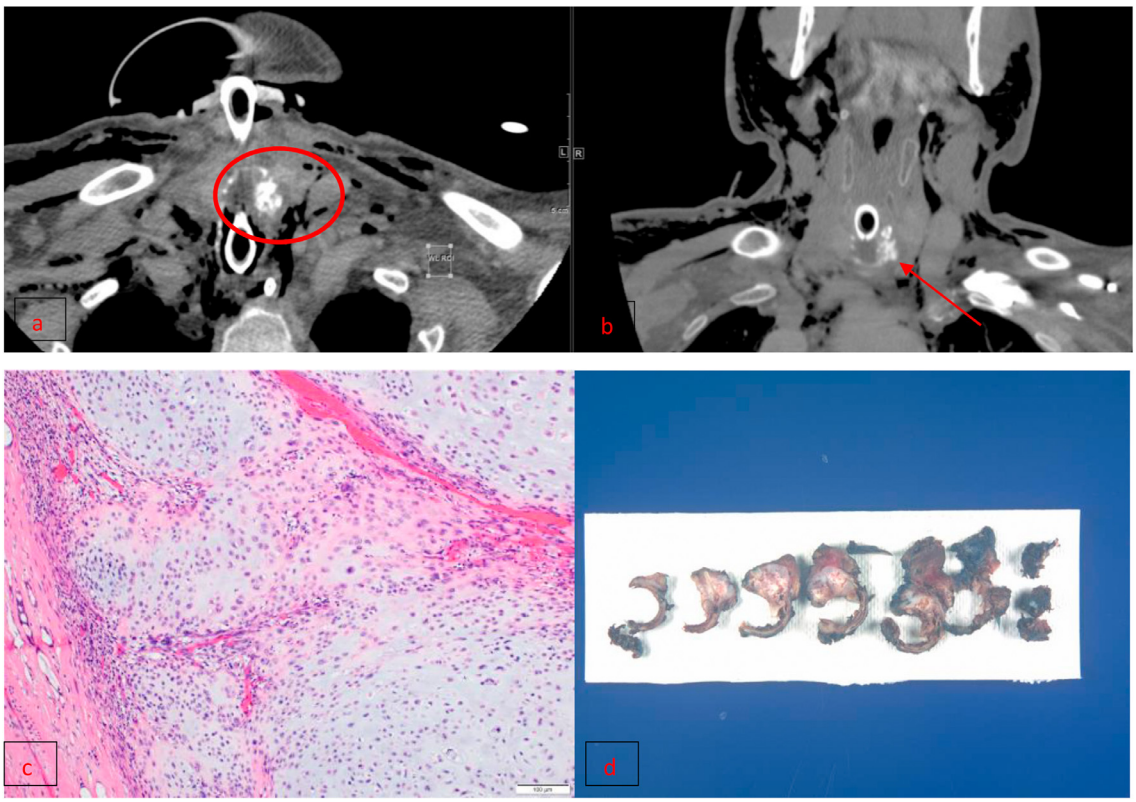

FIG. 7. (a, b) CT in the axial (left) and coronal planes (right) demonstrates a laryngopharyngeal mass with abnormal soft tissue and internal irregular calcifications consistent with chondroid matrix eroding the left aspect of the upper trachea. This mass extends into the postcricoid larynx and glottic larynx. Tracheostomy cannula and post-tracheostomy pneuma-mediastinum and subcutaneous emphysema are also demonstrated. (c, d) Portions of the current resection specimen show chondrosarcoma with foci of low-grade cellularity (grade 1).

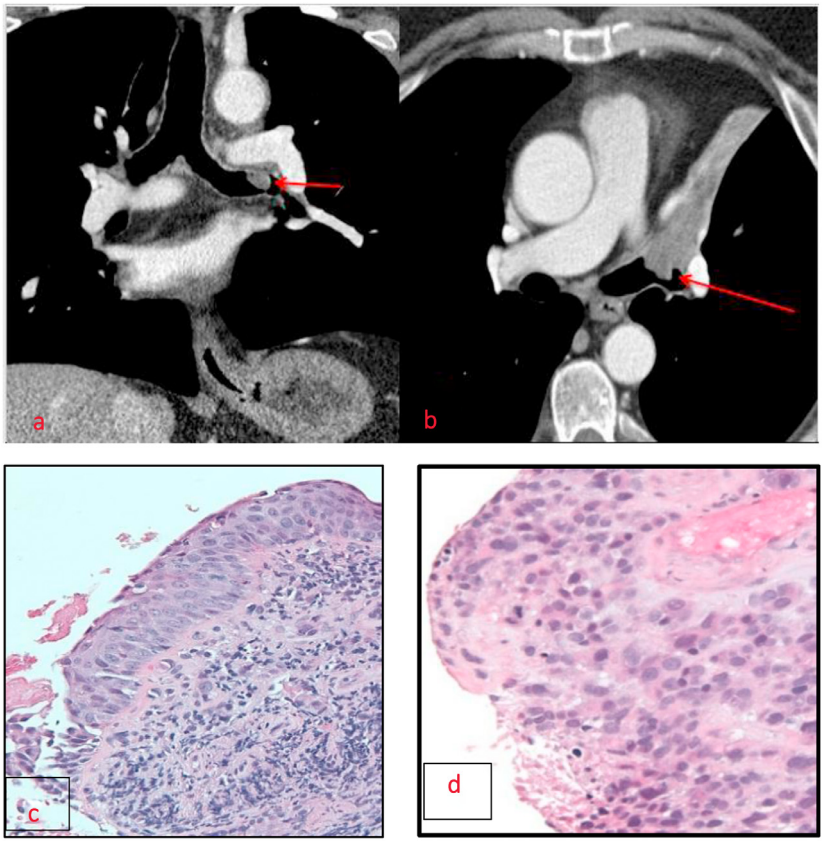

FIG. 8. (a, b) Enhancing nodule in the left main bronchus producing the partial collapse of the left upper lobe in a patient with a known history of melanoma. (c) Fragment of respiratory mucosa. (d) Fragment of metastatic melanoma.

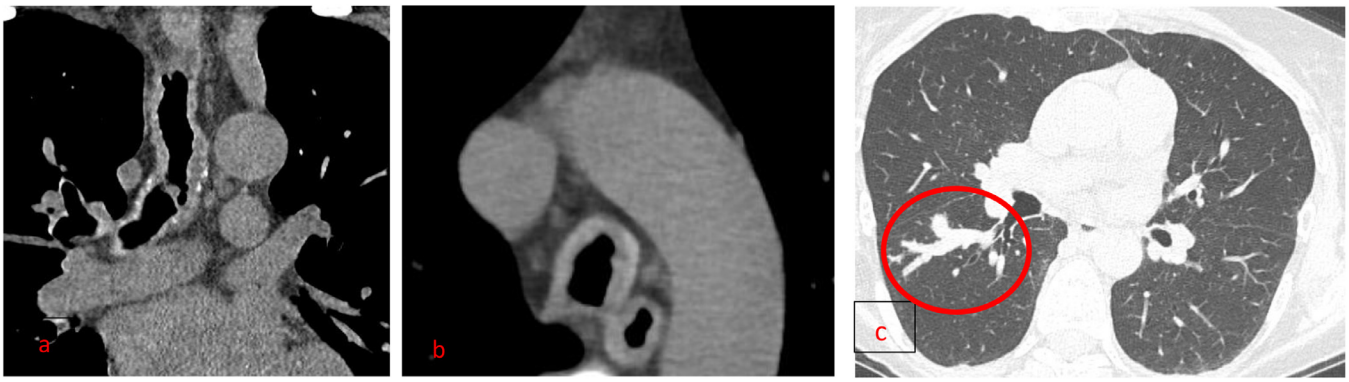

FIG. 9. (a, b) Diffuse tracheal wall thickening with mild nodularity without calcification is compatible with Rhinoscleroma. (c) Mucoid impaction within the lobar bronchus (finger in glove sign), which can be seen in airways infection and ABPA. Such as Aspergillosis.

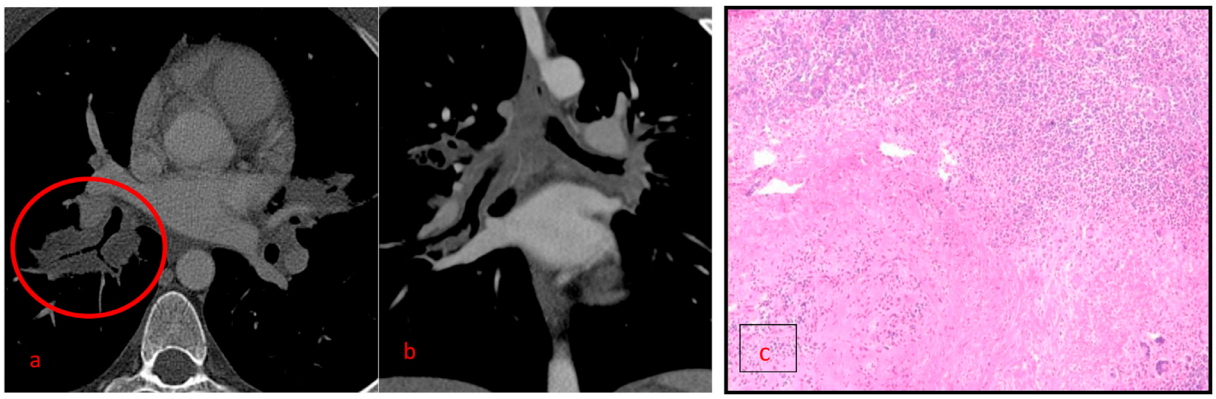

FIG. 10. (a, b) Diffuse tracheal wall thickening producing bronchial stenosis. (c) Acute and chronic inflammation, follicular bronchiolitis, dense interstitial lymphoplasmacytic infiltrate, and blood vessels with granulomatous inflammation and fibrosis.

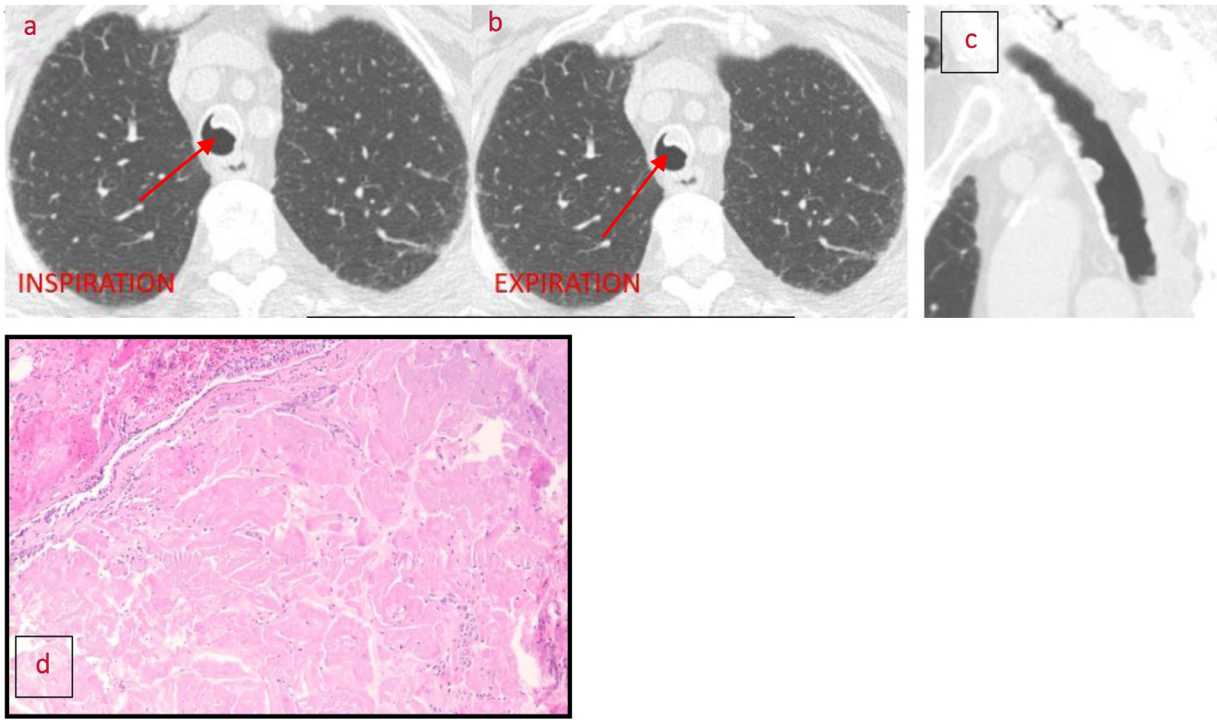

FIG. 11. (a) Multiple partially calcified soft tissue nodules in the trachea, with the involvement of the posterior membrane as seen on sagittal view. (b) Low magnification image demonstrates eosinophilic amorphous material compatible with amyloid deposition.

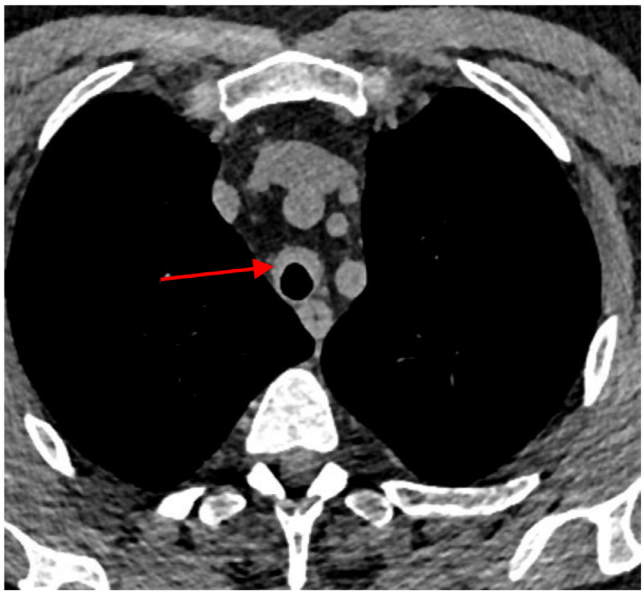

FIG. 12. Diffuse smooth tracheal wall thickening is sparing the posterior wall in a patient with relapsing polychondritis.

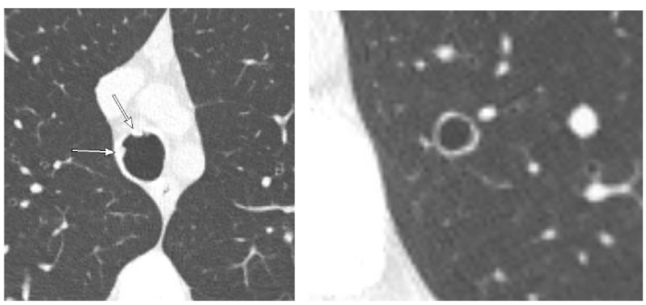

FIG. 13. Endoluminal nodules in the trachea with thin-walled cysts and nodules in the lung parenchyma reflecting respiratory papillomatosis.

may calcify and resemble tracheopathia osteochondroplastica (TPO). Amyloidosis involves the posterior wall and presents with dyspnea, wheeze, cough, hemoptysis, and recurrent pneumonia[39] (Fig 11).

Relapsing Polychondritis

Relapsing polychondritis is a recurrent inflammation involving cartilage, including in the trachea and bronchi. The incidence is 1 in 28,5000. It involves trachea in half of the cases, and mortality from this disease is often due to pneumonia. Relapsing polychondritis presents with diffuse smooth tracheal and bronchial wall thickening sparing the posterior wall. Other presentations include subglottic stenosis, air trapping, and tracheal cartilage calcification. Treatment options include medications such as corticosteroid and azathioprine administration vs surgical with limited indications, such as focal symptomatic stenosis or to maintain airway patency[40,41] (Fig 12).

Respiratory Papillomatosis

Infection leading to respiratory papillomatosis is associated with inhalation of HPV at the time of birth and genital-oral sexual transmission. It presents with voice change and stridor, cough, recurrent pneumonia, and dyspnea. CT of the lung parenchyma shows multiple bilateral thin-walled cysts and nodules, and the trachea exhibits endoluminal nodules. Treatment is with cryotherapy. Neoplastic nodules of respiratory papillomatosis have the potential to transform into SCC malignantly[42,43] (Fig 13).

Tracheobronchopathia Osteochondroplastica

TPO is a benign idiopathic entity. It presents with submucosal osteocartilaginous nodules. TPO is more common in men and is mostly seen in patients over 50-year-old. It more commonly involves lower 2/3 of the trachea and main bronchi with sparing of the posterior wall. Majority of the cases are incidentally found. No malignant transformation potential has been reported[44,45] (Fig 14).

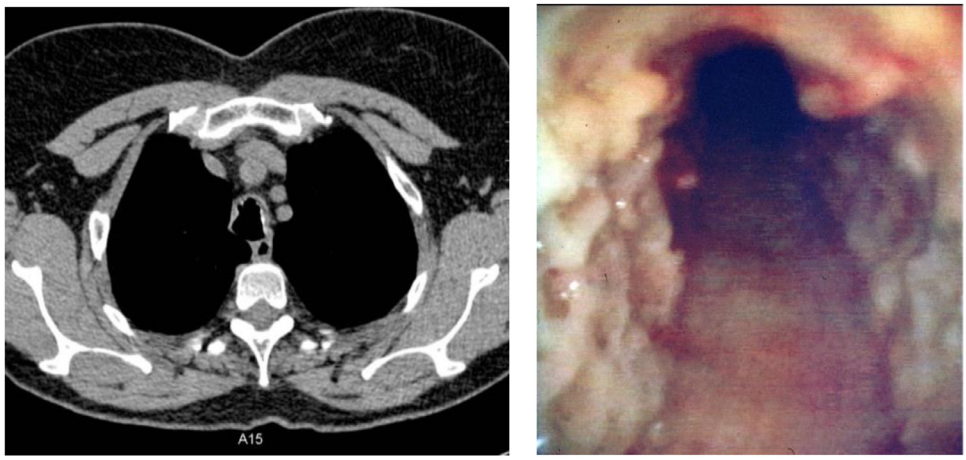

FIG. 14. Osteocartilaginous nodules are sparing the posterior trachea reflecting Tracheobronchopathia Osteochondroplastica (TPO) with a bronchoscopic view of the trachea (Image courtesy of Justus Roos, MD).

Foreign Body/Mucus Plug

It can be seen in both children and adults but is more common in children. The presence of an obstructing foreign body is accentuated by ipsilateral air trapping in expiratory phase imaging. Endoluminal obstruction can present with postobstructive collapse/atelectasis. CT with virtual bronchoscopy is the best noninvasive modality for localization[46-48] (Fig 15).

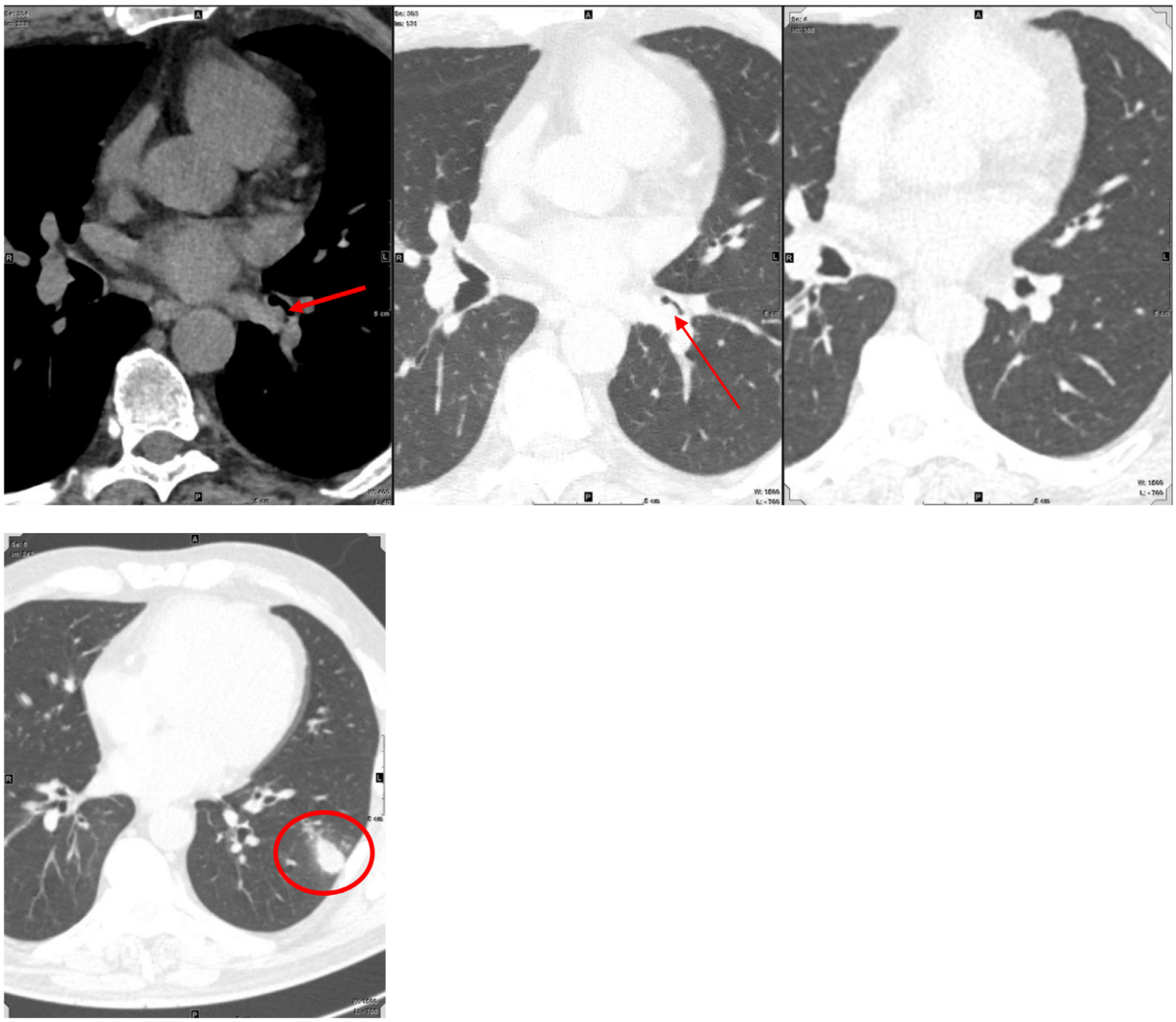

FIG. 15. (From left to right) 65-year-old man with cough lasting several weeks. An endoluminal lesion at the origin of the left lower lobe basilar segmental bronchi was noted on CT at presentation (red arrows, A, mediastinal window; panel B, lung window). Bronchoscopy confirmed the presence of an aspirated peanut, which was removed and patency of the airway was restored (panel C). The patient developed a subsegmental area of aspiration pneumonia (image 2), which subsequently resolved on follow-up imaging (Image courtesy of Alex Bratt, MD). (Color version of figure is available online).

Conclusion

Tumors and tumor-like conditions of the airways are rare. Majority of airway tumors are malignant. CT is the modality of choice for anatomical localization. FDG-PET/CT provides an assessment of tumor metabolic activity. Combining clinical, imaging, and pathology data can facilitate appropriate management strategy

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