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SINE QUA NON CLINICOPATHOLOGIC CORRELATION

An Autopsy Report of an Adenoid Cystic Carcinoma Arising in the Trachea

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Abstract

While adenoid cystic carcinoma is a common malignancy to arise within the salivary glands (21.9%) (Kokemueller et al. in Int J Oral Maxillofac Surg 33:25–31, 2004), it is seldom encountered as a tracheal mass and represents < 1% of all lung cancers. Tracheal tumors are an uncommon cause of dyspnoea due to their relatively rare occurrence (Baydur and Gottlieb in JAMA 234:829–831, 1975). They pose considerable diagnostic challenge clinically as their symptoms mimics more commoner ailments like asthma and chronic bronchitis. As they carry good prognosis, a timely diagnosis is highly warranted for appropriate therapeutic intervention. We describe a rare autopsy case of an adenoid cystic carcinoma in a middle-aged gentleman who presented with severe breathlessness and dyspnoea and succumbed to his illness after a brief hospital stay. Because the symptoms were non-specific, he was treated on lines of asthma and bronchitis.

Keywords Adenoid cystic carcinoma · Trachea · Autopsy · Salivary gland tumor of trachea

History

A 36-year-old man presented with complaints of shortness of breath for past 3 days (which progressed from NYHA class II–IV), associated with orthopnea, palpitations and anxiety. There was no history of chest pain or syncope. There was history of fever lasting for 2 days, 10 days ago. He received a course of antibiotics from a local practitioner. There was no history of jaundice, pain abdomen, decreased urine output, seizures, loss of consciousness, blood in vomitus or black tarry stools. There was past history of pulmonary tuberculosis 7 years ago, for which he received anti-tubercular treatment for 12 months, however he had poor compliance for the treatment. He also gave history of myocardial infarction 3 years ago, but no coronary angiography was done and currently he was not on any medication. There was history of dyspnea on exertion since 2.5 years. His addictions included smoking, tobacco and alcohol intae. On examination, no pallor, icterus, pedal edema, clubbing or cyanosis was noticed. His jugular venous pulse was normal. He had tachycardia with respiratory rate of 40/min and blood pressure of 110/70 mm of Hg. He was severely dyspneic with respiratory rate of 40/min along with bilateral diffuse crepitations and harsh vesicular breath sounds. S1 and S2 sounds were heard on cardiovascular examination. Liver and spleen were not palpable. No focal neurological deficits or meningeal signs were noted on central nervous system examination. Investigations revealed leucocytosis (TLC = 25,800 cells/mm^3) with normal haemoglobin and platelets. Arterial blood gas parameters were deranged with signs of hypoxia, showing decreased pO_2 levels of 53.2 and O_2 saturation of 85%. Coagulogram was maintained with INR of 1.16. Renal and liver function tests were normal. Troponin I was negative, however CK-MB levels were marginally raised to a level of 33 IU/L. Chest X-ray revealed left lower zone consolidation and prominent descending right pulmonary artery (Fig. 1). No opacities or effusion was noted (Fig. 1). ECG showed evidence of ventricular premature complexes and ST depression in leads II, V4–V6. He was managed symptomatically however he suffered a sudden cardiac arrest and succumbed to his illness after a brief hospital stay of 1 day.

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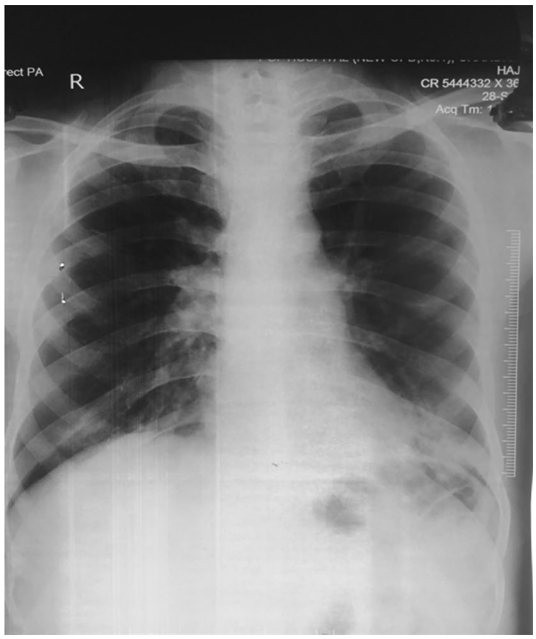

Fig. 1 Chest radiograph showing left lower zone consolidation and prominent descending right pulmonary artery

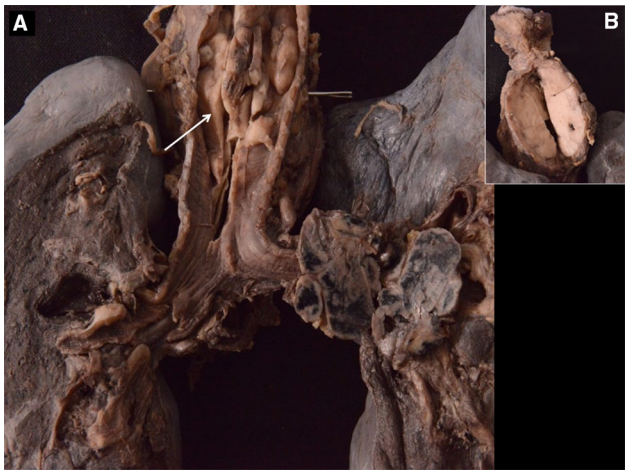

Fig. 2 **a** and **b** Gross photograph of tracheobronchial tree showing greyish-white growth filling up the tracheal lumen in the middle one-third and extending to upper one-third (arrow); **b** Cut surface reveals tumor with solid, homogenous appearance

Pathology Findings

A partial autopsy performed after an informed consent revealed normal serous cavities. Both lungs weighed 1120 g. The middle 1/3rd of trachea revealed a mass (8 × 5 × 4 cm) arising from the posterior wall, encasing the trachea and protruding into its lumen. On cut surface it was fleshy, firm, greyish white, and homogenous without any haemorrhage or necrosis (Fig. 2a, b). Hilar lymph nodes were enlarged but no metastatic deposits were identified on gross examination. The pleural aspect of both lungs was dull but no fibrinous exudates or tags were seen. Lower lobes of both lungs revealed diffuse hemorrhagic consolidation. Inspissated secretions were seen in the bronchioles. Microscopy revealed a nodular tumor arising from the sub-mucosal glands and defined by characteristic cribriform and tubular patterns (Fig. 3a, b). No solid areas were seen. The tumor cells exhibited mild pleomorphism with distinctive round to angulated nuclei and scant cytoplasm (Fig. 3c). No areas of necrosis or increased mitosis were seen. Multiple pseudocysts with thin basophilic secretions in the lumen were also noted. Basement membrane-like material deposition was also noted within the stroma around some of the tumor islands. The tumor was seen infiltrating the surrounding skeletal muscle (Fig. 3d). No significant atypia or areas indicative of high-grade transformation were noted. The tumor cells showed strong and diffuse immunoreactivity for Pan-CK and epithelial membrane antigen (EMA) was focally positive in the epithelial cells (Fig. 4a, b). p63, myoepithelial cell marker was diffusely positive in the luminal cells while c-kit revealed focal positivity in the abluminal cells (Fig. 4c, d). The lymph nodes did not reveal any metastatic deposits microscopically.

Other regions from the lower lobes showed alveolar haemorrhage along with ulceration of the bronchiolar lining epithelium and features of confluent bronchopneumonia (Fig. 3c, d). Some of the pre-acinar arteries showed early fibrin thrombi, however, these were not seen in any of the major vessels. CD34 immunostain highlighted capillary angiomatosis within the alveolar interstitium causing interstitial widening, probably secondary to long standing hypoxia. Heart weighed 320 g, all chambers and valves were essentially normal. The coronaries revealed a fibro-intimal atheromatous thickening 3 cm from the origin in the left anterior descending artery. Rest of the organs including liver, pancreas, spleen, kidneys, gastrointestinal tract, adrenals and bone marrow was within normal limits.

Diagnosis

The morphology and immunohistochemical features are characteristic of adenoid cystic carcinoma of trachea, Grade 1.

Discussion

Adenoid cystic carcinoma is a common tumor arising in the salivary gland with an incidence of 21.9% [1]. Primary salivary gland tumors of tracheobronchial tree are exceedingly

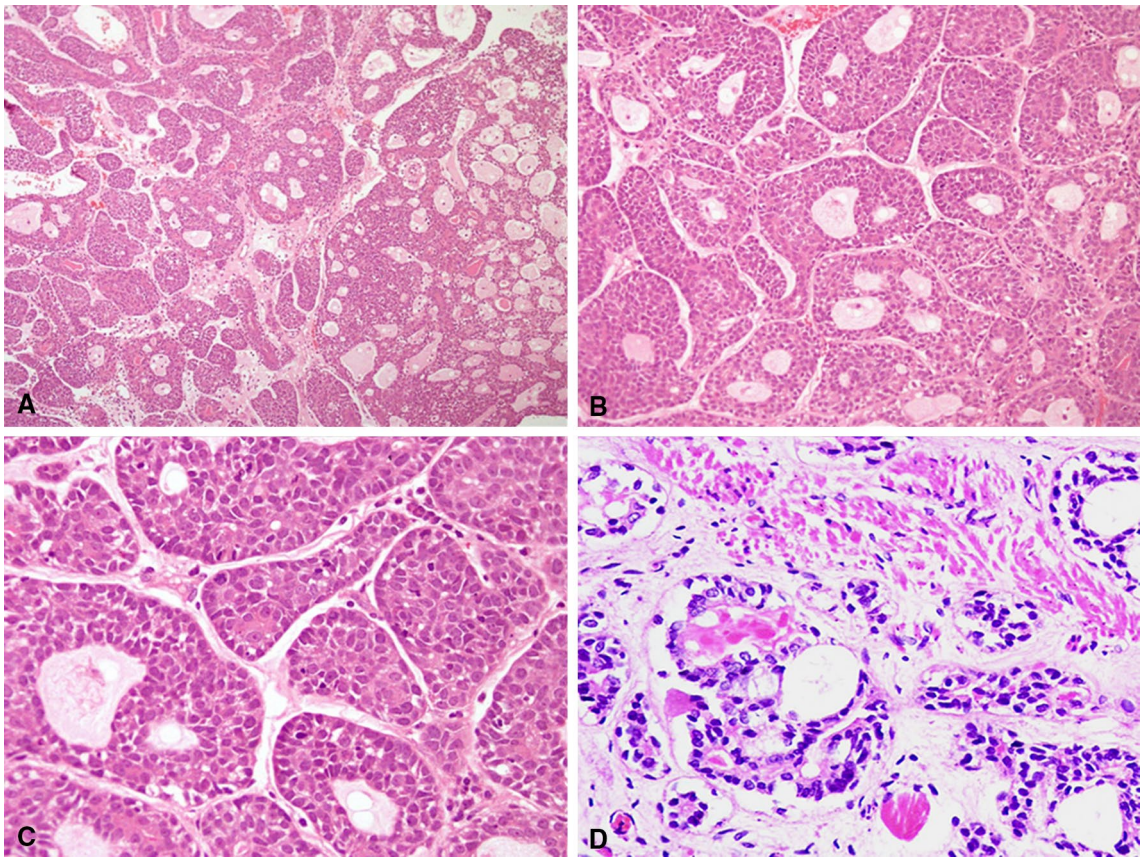

Fig. 3 **a** Low magnification depicts a tumor arranged in islands and nests and characteristic cribriform pattern (H&E ×100); **b** tubular pattern noted at places with formation of pseudocysts (H&E ×200); **c** high magnification shows basaloid cells with mild pleomorphism, distinct round to angulated nuclei and scant cytoplasm (H&E ×400); **d** tumor cells seen infiltrating the surrounding skeletal muscle (H&E ×200)

rare and represent 0.1% of respiratory malignancies [2, 3]. Mucoepidermoid carcinoma is the commonest among them followed by adenoid cystic carcinoma, pleomorphic adenoma, acinic cell carcinoma and epithelial-myoepithelial carcinoma [3]. Within the trachea, they commonly arise at the distal one-third of the trachea and involvement of the proximal trachea and larynx is extremely rare [4]. Non-specific clinical symptoms are often the reason for delayed diagnosis or misdiagnosis. Rarely, it may invade the upper aero-digestive tract and cause dysphagia [5]. Whereas the index case described here was a smoker, adenoid cystic carcinoma are not classically associated with smoking unlike squamous cell carcinoma [6]. These have an indolent growth and are generally diagnosed at a late stage until the airways are significantly obstructed. The tracheal lumen has a large functional reserve and thus the tumor may not cause any symptoms until they occlude 50–75% of the luminal diameter. Patients present with non-specific symptoms of cough, wheezing and exertional dyspnoea and thus are often misdiagnosed as chronic obstructive pulmonary disease (COPD), asthma or upper respiratory tract infections. Chest radiographs are rarely diagnostic although they are the first-line of investigations. Endoscopic evaluation, biopsy and imaging with computed tomography (CT) scan are standard imaging modality recommended for assessment of endobronchial growth [7]. Magnetic resonance imaging helps in delineating the extent of spread. Early demise in the index case did not give an opportunity to investigate the patient in detail. Histologically, adenoid cystic carcinoma is characterized by cribriform growth pattern, cells with angulated nuclei and scant cytoplasm. Perineural invasion is a frequent feature. Sampling of peribronchial soft tissue is important as tumor frequently infiltrates beyond the visible macroscopic margins. Other diagnostic possibilities of a tracheal mass include carcinoid tumor, basaloid squamous cell carcinoma and small cell carcinoma. All these are distinguished by morphology supplemented by immunohistochemistry. Moreover, basaloid squamous cell has a high proliferative index unlike adenoid cystic carcinoma.

Recent studies have indicated involvement of *MYB* gene alterations with *MYB-NFIB* fusions resulting in upregulation of MYB transcriptional regulatory activity in the tumor cells

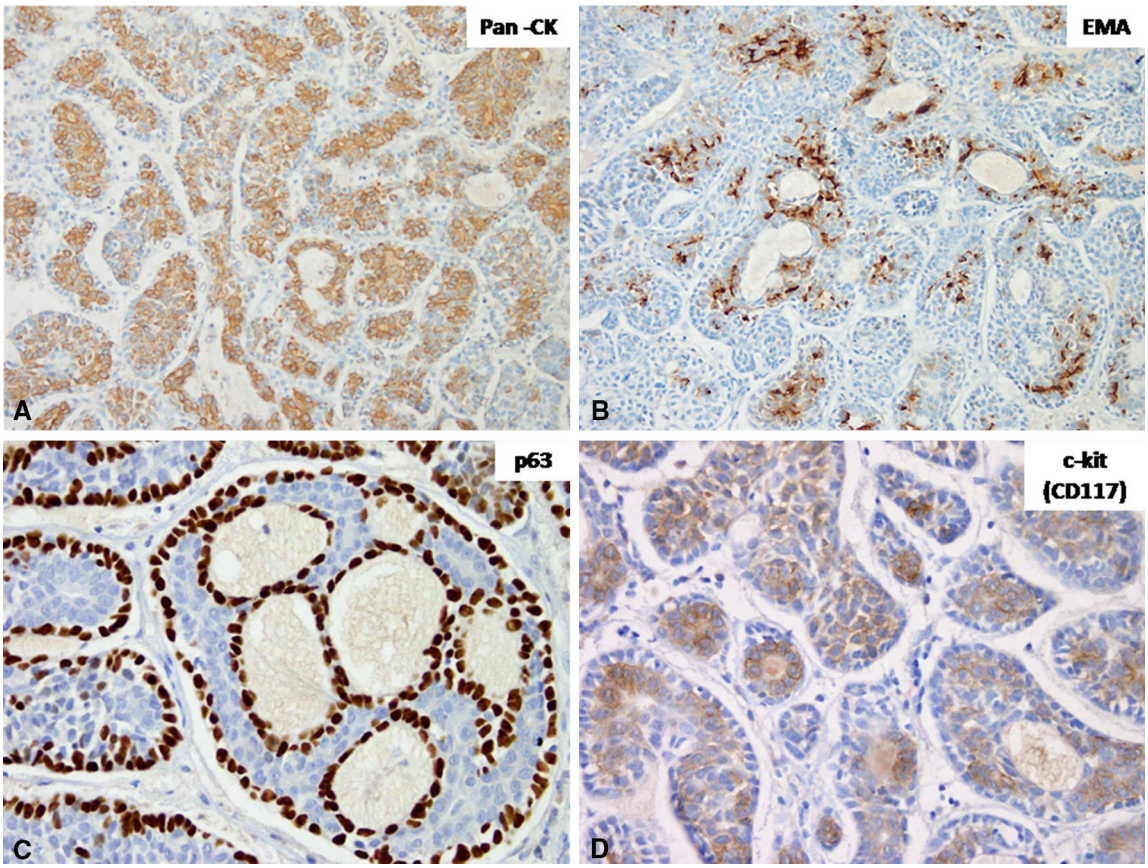

Fig. 4 **a** Tumor cells exhibiting strong and diffuse immunoreactivity with Pan-cytokeratin (immunoperoxidase ×200); **b** focal positivity with epithelial membrane antigen (immunoperoxidase ×200); **c** p63 highlights the myoepithelial cell along the luminal aspect (immunoperoxidase ×400); while c-kit reveals focal positivity in the abluminal cells (**d**) (immunoperoxidase ×400)

[8]. However, the prognostic relevance of this fusion is yet to be established. Since the clinical behaviour of these tumors is different from the conventional lung tumors, it is important to accurately diagnose them. Resection is the main stay of treatment. Unresectable cases are given radiotherapy [9]. As the clinical presentation often mimics COPD or asthma, it is often misdiagnosed. In conclusion, awareness about its clinical symptoms and histology is essential for a timely diagnosis.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflicts of interests.

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