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Adenoid Cystic Carcinoma of the Trachea: A Case Report

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Study Design A
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Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
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Patient: Male, 62
Final Diagnosis: Adenoid cystic carcinoma of trachea
Symptoms: Cough • dyspnea
Medication: —
Clinical Procedure: —
Specialty: Surgery

Objective: Rare disease
Background: Adenoid cystic carcinoma of trachea (ACCT) is an unusual low-grade tumor from the tracheal and bronchial wall glands. The histological structure and biological behavior of ACCT are similar to that of tumors found in the salivary glands. ACCT occurs most commonly in the upper trachea, being found in the articular cartilage in the posterior aspect of the trachea.

Case Report: We describe the case of a 62-year-old male ex-smoker 25 years/pack (abstinence 20 years ago), who began with mild dyspnea 2 years ago, with intense evolution and cough. He was evaluated as an outpatient and was treated for sinusitis and later bronchitis after pulmonary function tests. With the worsening of the aforementioned symptoms, he sought prompt care, with hospitalization and computed tomography (CT) of the chest being indicated, showing an expansive lesion in the anterior wall of the trachea with an extension of approximately 3.1 cm, ending at the level of the carina, measuring 3.4×2.8 cm, with moderate stenosis of the tracheal lumen, with an exophytic component to the mediastinum. Bronchoscopy of the lesion was done, and later immunohistochemistry showed a probable pleomorphic adenoma. However, in a new analysis, after the removal of the surgical specimen, it was observed that it was a ACCT.

Conclusions: ACCT is a rare tumor that should be diagnosed as soon as possible in order to ensure its best prognosis. Moreover, it is evident that the analysis of the surgical specimen is sovereign to immunohistochemistry with regard to histological typing.

MeSH Keywords: Carcinoma, Adenoid Cystic • Immunohistochemistry • Trachea

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Background

Adenoid cystic carcinoma (ACC) is a fairly common cancer that is believed to affect small salivary glands, accounting for 10% to 15% of all tumors in the head and neck. It presents as a submucosal mass of slow and asymptomatic growth, provoking benign symptoms like dyspnea. ACC is characterized by invasion of adjacent tissues in its evolution, and it is usually diagnosed very late in many patients. It is commonly diagnosed in patients between the 5th and 7th decade of life and it is a tumor equally distributed between the sexes [1]. The most frequent localization of ACC is in the oral cavity and pharynx, with a predilection for larger salivary glands. Other areas may also be affected, such as the digestive system (esophagus, pancreas, and anal canal), respiratory system (nasal cavity, larynx, trachea, lungs, and bronchi), female genital system, male genital system (prostate), and tear glands [1,2].

Within the group of tracheal tumors, the incidence of ACC ranges from 18% to 59%, right after epidermoid carcinoma; ACC is not related to the existence of smoking habits. Trachea ACC originates in the seromucous glands located in the submucosal layer of the trachea. It presents with slow growth and has a high potential for local invasion. Distant metastasis is more frequent at the pulmonary level and recurrence can occur even after an extended period of time. Resectable tumors have a good survival rate, with 5-year and 10-year survival rates of 75% to 91% and 76% to 55%, respectively. Surgery is the treatment of choice and the indication for this therapy depends on

the location and extent of the lesion. Trachea tissue is radio-sensitivity, and radiotherapy is indicated as adjuvant therapy, particularly if there is tumor involvement of the surgical margins, as well as in the unresectable lesions, and may be associated with endobronchial therapy [1].

Case Report

Our patient, JGR, was a 62-year-old, male, white, ex-smoker of 25 years/pack (abstinence 20 years ago). His condition began with mild dyspnea 2 years ago, with intensity evolution and cough. He was evaluated as an outpatient and was treated for sinusitis and later bronchitis after pulmonary function tests. With worsening of the aforementioned symptoms, he sought prompt care (PA), with hospitalization and CT of the chest being indicated, showing an expansive lesion in the anterior wall of the trachea with an extension of approximately 3.1 cm, ending at the level of the carina, measuring 3.4×2.8 cm, with moderate stenosis of the tracheal lumen, with an exophytic component to the mediastinum (Figure 1).

He was submitted to a bronchoscopy, which confirmed the finding of vegetative, vascularized and friable lesion to manipulate in a distal portion of the trachea of 1 cm, that of the main carina, causing an important obstruction to airflow. He was submitted to endotracheal biopsy of multiple fragments and histopathology confirmed by pleomorphic adenoma immunohistochemistry, presenting CD117/C-kit (YR145), p63,

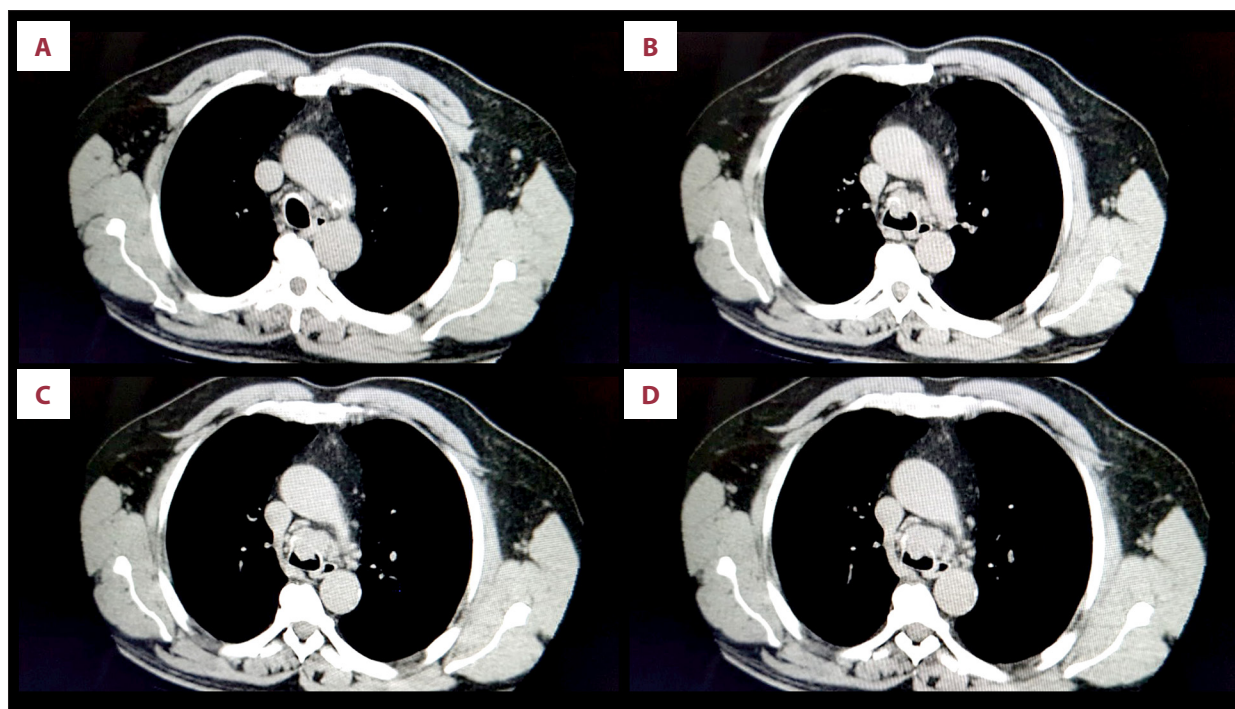


Figure 1. Computed tomography showing the tracheal lesion.



Figure 2. Bronchoscopy evidencing the vegetative lesion.

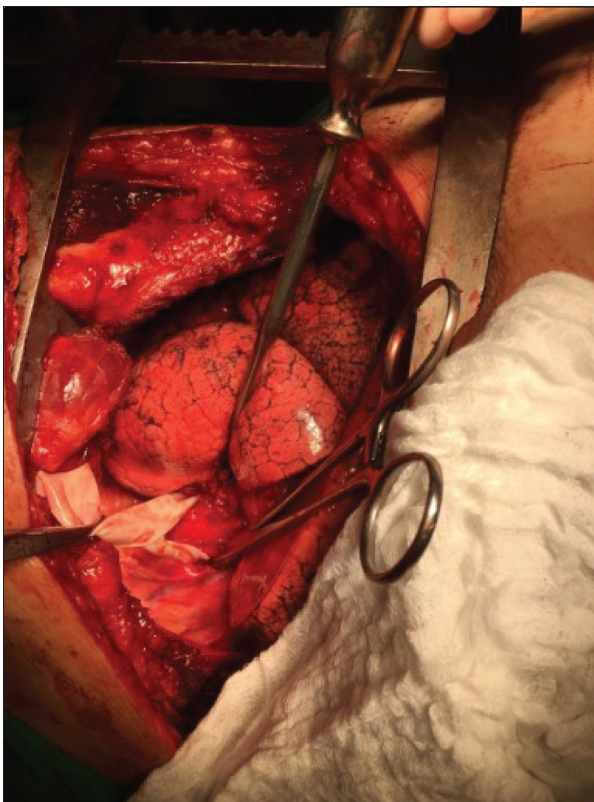


Figure 3. Plane used for tumor excision.

cytokeratin 5, low molecular weight cytokeratin 8/18 (CK 8/18), S100 positive protein in several cells and Ki-67 (MIB-1) with reactivity index was estimated to be 8% to 10% (Figure 2).

Patient submitted to right lateral posterolateral thoracotomy with resection and distal tracheal anastomosis with resection in tumor block remaining postoperative for 2 days in the intensive care unit (ICU). The patient recovered thoracic drainage 4 days later, being discharged on the 5th postoperative day (Figures 3, 4).

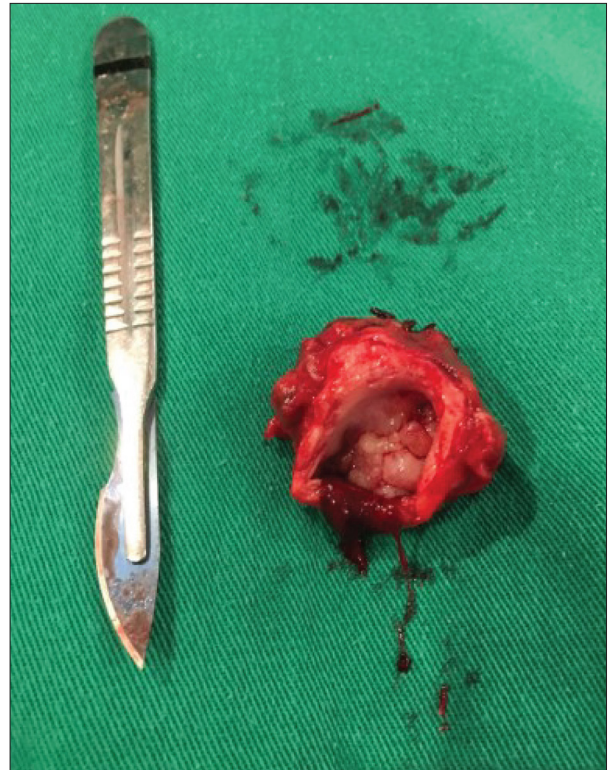


Figure 4. Surgical specimen withdrawn after the procedure.



Figure 5. Post-surgical flexible bronchoscopy video.

The definitive result of histopathology of the surgical specimen was the diagnosis of low-grade cystic adenoid carcinoma confirmed by immunohistochemistry, presenting cytokeratin AE1/AE3, cytokeratin 7, CD117, p63, and ki-67 positive, 2.5 cm in size, with compromised microscopic margins, with

infiltration of cartilage and adjacent soft tissues, as well as perineural and angiolymphatic invasion. The patient was in outpatient follow-up, referring to an absolute improvement of clinical status, being indicated adjuvant radiotherapy. Performed posterior bronchoscopy with good healing (Figure 5).

Discussion

About 90% of all primary trachea tumors are malignant in adults, compared to 10% to 30% in children. The incidence of tracheal neoplasms is approximately 0.1 to 100 000 people per year, equivalent to approximately 0.2% of all tumors of the respiratory tract and 0.02% to 0.04% of all malignancies [3]. Among the primary malignant tracheal tumors, mucoepidermoid carcinoma is the most common, followed by cystic adenoid carcinoma, pleomorphic adenoma, acinar cell carcinoma, and epithelial-myoeipithelial carcinoma [4].

ACC of the trachea (ACCT) is an infrequent low-grade tumor that arises in the glands of the tracheal and bronchial walls. The histological structure and biological behavior of ACCT are similar to that of tumors found in the salivary glands. This pathology occurs most commonly in the upper trachea, being found in the articular cartilage in the posterior aspect of the trachea. The primary ACCT metastasizes more frequently to the lungs and bones. It rarely involves the thyroid, and it can be misdiagnosed as a thyroid neoplasm [5].

In a retrospective study of 108 patients who underwent resection of ACCT, 85% presented with tumors with extramural extension: 15% were intramural; in 20% there was invasion of adjacent structures, 15% involved esophageal muscular layers, 9% involved the thyroid gland, 6% involved recurrent laryngeal nerve, 4% involve infrahyoid muscles, 1% involved large vessels and the pericardium. In several cases, invasion occurred in more than one organ [6]. The aforementioned was an ACCT case with a mediastinal element.

The main tracheal neoplasm symptoms are due to tumor-induced tracheal blockage. Dyspnea is frequently found, with gradual growth over several months, later followed by stridor. Other symptoms include wheezing, coughing, chest pain, and hemoptysis [4]. The interval between the beginning of symptoms of the disease and the setting of a diagnosis is lengthy: 18.3 months in patients with resectable malignancies and 23.7 months in patients with inoperable neoplasms [7]. Patients are commonly treated for asthma for a significant period of time before a correct diagnosis is made. Nonspecific clinical symptoms are often the reason for late diagnosis or misdiagnosis [8]. In the presented case, the male patient had dyspnea 2 years ago and his cough and symptoms indicating upper airway obstruction were being treated initially as sinusitis. This

situation corroborates the findings in the literature, evidencing similar clinical behavior.

The results of pulmonary function tests of patients with primary ACC in a tracheobronchial tree are rarely published in the literature. Such tests can provide important evidence for tracheal tumor diagnosis, and these tests use non-invasive devices that are accessible and easy to operate. However, it is necessary to assess the determinants of the outcome of anatomical lesions on maximum airflow tests, like the location, type (variable or fixed) and extent of the obstruction [1]. In this sense, 3 striking flow volume loop patterns for large airway obstruction can be defined: fixed, intrathoracic variable, and extra-thoracic variable. With the fixed obstruction of the tracheal tumors, a plateau is generated in the inspiratory and expiratory flow loops that evidences the resistance of the airways, regardless of the changes in the transmural pressure. However, such tumors may also cause a single plateau pattern of the expiratory loop with a normal inspiratory loop, characteristic of a variable intrathoracic obstruction [9]. Thereby, even in the lack of an obstructive spirometric standard, endoscopic examination is encouraged when central airway disorder is suspected [1].

Bronchoscopy is the most useful test in tracheal cancer diagnosis. Bronchoscopy provides a precise evaluation of the tumor's nature and extent. The site and length may be associated with anatomical landmarks, such as carina and cricoid cartilage, and tumor sizes may be correlated with the airway caliber. Furthermore, for pathological evaluation, a tumor biopsy may be done. The main pillars for the diagnosis and staging of primary tracheal tumors are CT scans of the chest and neck together with trachea-bronchoscopy. CT scans are useful in assessing the depth of the invasion and the possible involvement of adjacent structures, and in finding lymphogenic and distant metastases or primary synchronous lesions [10].

Histologically, cystic adenoid carcinoma is characterized by cribriform growth pattern, and cells with angulated nuclei and scarce cytoplasm. Perineural invasion is a frequent characteristic. The sampling of peribronchial soft tissue is important because the tumor often infiltrates beyond visible macroscopic margins [10]. Other tumors of tubular and cribriform structures (such as low-grade polymorphous adenocarcinomas, basaloids such as basal cell adenoma and basal cell adenocarcinoma) and with a double population of ductal and myoepithelial cells, such as pleomorphic adenoma, are the main differential diagnoses [11]. In cases of cellular polymorphic adenoma with scarce stroma or in those cases containing hyaline globules, the distinction between ACC and pleomorphic adenoma in needle aspiration biopsy becomes challenging [11,12].

Faced with these diagnostic difficulties, ancillary techniques such as immunohistochemistry and molecular studies are

advantageous and of prognostic importance [12]. Markers of ductal and myoepithelial/basal cells, such as SMA, calponin, CAM 5.2, SOX10, CK7, p63, and S100 are expressed by ACC. Most of these also show strong and diffuse c-KIT expression. In those with high-grade transformation, high rates of Ki-67 and p53 were found in the malignant components. Finally, Myb appears to be an appropriate indicator to differentiate a subset of ACC from other salivary gland tumors. The pleomorphic adenoma, on the other hand, exhibits CK7, CEA, MSA, CEA, SMA, CK14, SMMHC, S100, vimentin, p63, Wilms tumor 1 (WT1), calponin, and GFAP. The PLAG1 protein is a sensitive and specific marker for and may be helpful in differentiating it [13].

The preferred treatment is complete resection of tracheal tumors, which alleviates airway obstruction concomitantly with the treatment of the disease. For inoperable tumors and for treatment of severe symptoms, radiotherapy is indicated as adjuvant after resection [14].

A Surveillance, Epidemiology, and End Results (SEER) health database review included 94 cases of tracheal malignancies from 1973 to 2004 with respect to the prognosis. The statistics showed that the overall 5-year survival rate of patients

with tracheal ACC was 74.3%, while if the condition was diagnosed at a highly developed loco-regional stage, the survival rate was 90%, which shows the better the prognosis the more limited the lesion [15].

Conclusions

In conclusion, we report a case of adenoid cystic carcinoma of trachea (ACCT), in which different conclusions were observed in immunohistochemistry (e.g., pleomorphic adenoma) and in the analysis of the surgical specimen (e.g., ACC), which indicated that the macroscopic analysis was sovereign for histological type detection. Thus, it is clear that ACCT is a rare tumor that must be promptly diagnosed in order to guarantee treatment in its less invasive form, i.e., locoregional form, allowing the best prognosis for the patient.

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