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Case Report

Pulmonary Adenoid Cystic Carcinoma Mimicking Asthma-Like Symptoms: A Case Report and Literature Review

Fan Zhou[a, b] Rong Jiang[a, b] Shenhong Li[a] Xiaojie He[b] Yongxia Li[b]

[a]Kunming Medical University, Kunming, China; [b]Department of Respiratory and Critical Care Medicine, Second Affiliated Hospital of Kunming Medical University, Kunming, China

Keywords

Case report · Pulmonary adenoid cystic carcinoma · Salivary gland-type tumor · Bronchial tumor · Tracheal tumor

Abstract

Introduction: Pulmonary adenoid cystic carcinoma (PACC) is a rare, low-grade malignant salivary gland-type tumor characterized by a dormant onset and slow progression, often leading to misdiagnosis. Due to its rarity, limited cases have been reported in the literature. This report aimed to enhance clinicians' understanding of this infrequent disease. ***Case Presentation:*** We present the case of a 41-year-old female patient diagnosed with PACC. Our report provides a comprehensive analysis of the patient's imaging, pathology, and treatment, with a particular focus on immunohistochemical results. Importantly, we emphasize the significance of considering foreign bodies and tumors in the bronchus when encountering asthma-like symptoms unresponsive to conventional treatments. Due to the uncertain etiology and pathophysiology of PACC, there are currently no established guidelines for chemotherapy and radiotherapy. ***Conclusion:*** PACC predominantly manifests as bronchial lesions without significant clinical heterogeneity. Therefore, it is crucial to consider foreign bodies and tumors in the bronchus when dealing with asthma-like symptoms, especially in patients without chronic lung disease who do not respond to anti-infective, antispasmodic, and antiasthmatic treatments. Additionally, meticulous examination of lesions is essential for timely diagnosis and intervention, ultimately improving patient survival rates.

Correspondence to:
Yongxia Li, yongxiali999@163.com

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Introduction

Pulmonary adenoid cystic carcinoma (PACC) originates from the submucosal serous or mucus glands of the bronchus. PACC constitutes roughly 0.04–0.2% of primary pulmonary neoplasm and accounts for 10% of all bronchial carcinomas, making it the second most common pathological type of primary tracheal neoplasm after squamous cell carcinoma [1, 2]. PACC is frequently observed in middle-aged and young adults without significant gender bias in incidence. The clinical presentation of the disease is nonspecific, often resulting in frequent misdiagnosis or missed diagnosis as a sputum embolus or another form of pulmonary neoplasm.

The majority of PACC lesions occur in the trachea or lobar bronchus. The demarcation of the tumor margin from the surrounding tissues is indistinct to the naked eye, with microscopically cancer cells arranged in solid striated, glandular, or sieve-like structures. These cells infiltrate and grow into and out of the bronchus, or infiltrate along the submucosa of the bronchus to distance. Certain subtypes of solid structure are believed to have strong local aggressiveness according to some pathologists [3, 4].

PACC can span decades from the appearance of an intratracheal mass to the development of obstructive symptoms or distant metastases. Although lymph node metastasis is rare, the disease can metastasize to the hilar lymph nodes or mediastinal lymph nodes, as well as to the liver, bone, brain, and other organs through hematogenous metastasis. The CARE Checklist has been completed by the authors for this case report, attached as supplementary material (for all online suppl. material, see https://doi.org/10.1159/000535505).

Case Report

In October 2022, a 41-year-old female patient presented to our hospital with a history of cough, dyspnea, and chest tightness for over 1 year. These symptoms were exacerbated in the lying position and improved in the sitting position. The patient denied any history of exposure to environmental toxins such as dust, benzene, or cyanide, as well as any family hereditary diseases, smoking, or alcohol consumption.

The patient's vital signs were normal. Cardiac and abdominal examinations were conducted, with no significant abnormalities noted. The respiratory system was examined with inspection, palpation, and percussion, revealing no observable anomalies, but the patient had weakened breath sounds in both lungs, and wheezing rale can be heard on deep inspiration.

Ancillary examination results revealed that a chest computed tomography (CT) conducted on October 28, 2022, showed a small, lamellar, slightly dense shadow and protrusion in the left bronchus, which was diagnosed as a sputum embolism, and tiny solid nodules were found in the posterior segment of the upper lobe apices of the left lung. Following 3 days of intravenous antibiotics, expectorants, and bronchodilator treatment, chest CT contrast enhancement on October 31, 2022, suggested that there was no significant change compared with the previous image. Thickness and adhesion were also detected in the left pleura (shown in Fig. 1). In pursuit of a precise diagnosis, bronchoscopy was employed. Electronic bronchoscopy unveiled a tumor, positioned about 0.5 cm from the upper carina of the left main bronchus. This results in notable lumen narrowing, a smooth mucosal surface, and a pronounced inflammatory response with mucosal congestion and vascular hyperplasia. The tumor, measuring approximately 2–2.5 cm and located at the 6 o'clock direction, exhibits a surface adorned with a thickened, disordered vascular network, enhancing brittleness and susceptibility to bleeding upon contact. Importantly, the lower end of the left main bronchus

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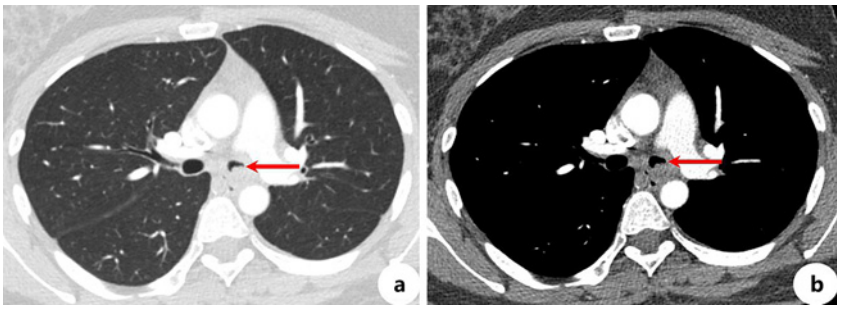

Fig. 1. Chest CT imaging showing a slightly high-density shadow with a narrow lumen in the left bronchus, as indicated by the red arrow in both CT pulmonary window image (**a**) and mediastinal window image (**b**).

and the bronchial openings in each lobe of the left lung remain unobstructed (shown Fig. 2). Additionally, pulmonary function tests showed mixed ventilatory dysfunction, small airway obstruction, mild reduction in pulmonary reserve function, and a positive bronchial dilation test (BDT).

Upon tracheoscopic biopsy, the pathology report indicated the patient was diagnosed with PACC (shown in Fig. 3). The patient's microsatellite stability was determined by the presence of PMS-2 (+), MSH6 (+), and MSH2 (+) markers. As the patient was ineligible for immunotherapy, the physician recommended surgical removal. Using SSTR2, CD56, CgA, and Syn markers, neuroendocrine tumor can be specifically identified if at least one of the last three markers is strongly positive or two or more are positive. Pathological examination of the patient's tissues revealed glandular cavity-like changes with irregular invasive growth, but immunohistochemistry showed the presence of P63 (+), P40 (+), and CK5/6 (+) markers in squamous epithelial cells, indicating the presence of PACC. Ki-67 is a commonly used marker to differentiate between benign and malignant tumor based on proliferative activity. For this patient, a Ki-67 level of 20% was observed, indicating the presence of low-grade malignant tumor proliferation characteristics. Other auxiliary examinations were normal.

Following a multidisciplinary approach involving pathology, imaging, oncology, thoracic surgery, and respiratory medicine, experts unanimously recommended the patient to undergo carina reconstruction operation in the thoracic surgery department to remove the bronchial carcinoma. However, the patient and her family declined surgical treatment and requested discharge. On the 18th day, the patient, experiencing aggravated symptoms, sought care at another hospital, receiving a reaffirmation of PACC. Following a comprehensive evaluation, corrective surgery ensued on the 24th day, encompassing left main bronchial mass resection, bronchial sleeve resection, and carinoplasty. The lesion was entirely excised, and accompanying lymph nodes were meticulously explored and cleared, devoid of observable residual tumor tissue. Intraoperative frozen pathological biopsy confirmed malignancy with a negative stump. Lymph nodes in groups 4, 5, 7, and 10 exhibited no metastasis. The procedure, characterized by a smooth course and approximately 100 mL intraoperative blood loss, ensured unobstructed bronchial openings, as verified by postoperative bronchoscopy. Eight months post-surgery, the evolution is generally favorable, with no recurrence of the tumor or distant metastasis. However, the left main bronchus is completely blocked by granulation tissue and sputum (shown in Fig. 4). Notably, the patient, devoid of postoperative radiotherapy, chemotherapy, or immunotherapy, presently experiences markedly reduced dyspnea symptoms, with occasional coughing and expectoration. Figure 5 presents the event timeline.

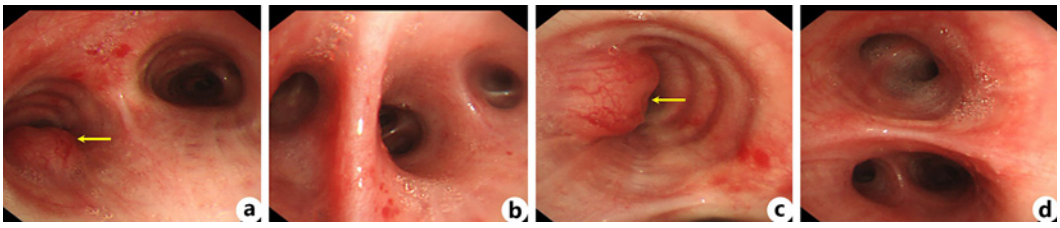

Fig. 2. a–d Observation of new organisms obstructing part of the lumen in the left main bronchus, 0.5 cm from the carina (indicated by yellow arrow). No apparent abnormalities were found in the right main bronchus or any other bronchial segments, except for bronchitis changes.

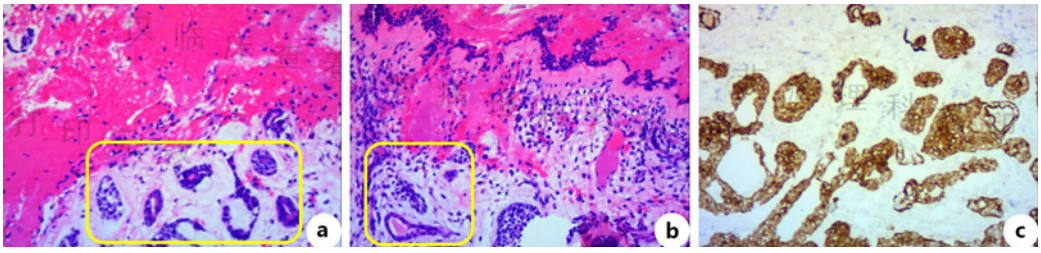

Fig. 3. Pathological biopsy of tissue specimen. Special staining results: silver staining (+). Immunohistochemical results: PMS-2 (+), MSH6 (+), MSH2 (+), MLH1 (+), CK5/6 (+), Her-2 (2+), PD-L1 (TPS: 0%), Ki-67 (20%), SSTR2 (focal+), CD56 (focal+), CgA (−), -Syn (−), P63 (+), P40 (+), Villin (−), CK20 (−), CK7 (+), CKL (focal+). **a**, **b** Tumor morphology with glandular cavity-like changes, irregular and infiltrative growth. **c** CK5/6.

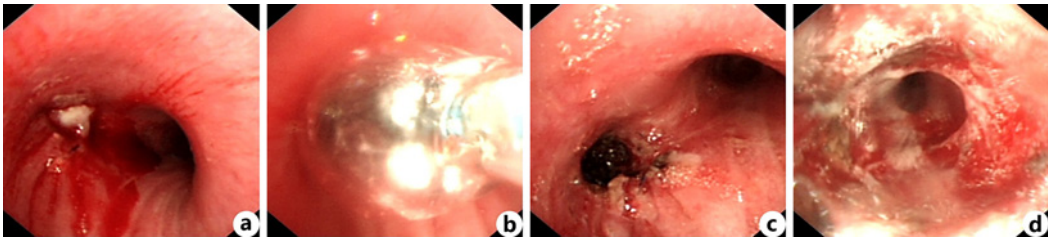

Fig. 4. Follow-up bronchoscopy at 8 months after surgery. **a** The left main bronchus is completely blocked by granulation tissue and sputum. **b** Interventional therapy such as balloon dilation for airway stenosis. **c**, **d** Left main bronchus recanalization after interventional treatment.

Discussion

In this section, we initially provide a comprehensive analysis of the clinical presentation, diagnosis, treatment, and prognosis of the present case. Subsequently, we selectively reviewed relevant case reports of first-time diagnosed PACC in the past 5 years [5–21]. A comparative analysis is presented in Table 1 through a literature review. We then compared these findings with our case, offering our insights to highlight the diagnostic challenges and the importance of reporting this case.

PACC typically exhibits slow growth, predominantly in the upper trachea's upper third segment. Clinical symptoms are nonspecific, challenging chest X-ray detection. Diagnostic emphasis lies on chest CT and bronchoscopy, relying on pathological biopsy confirmation. For

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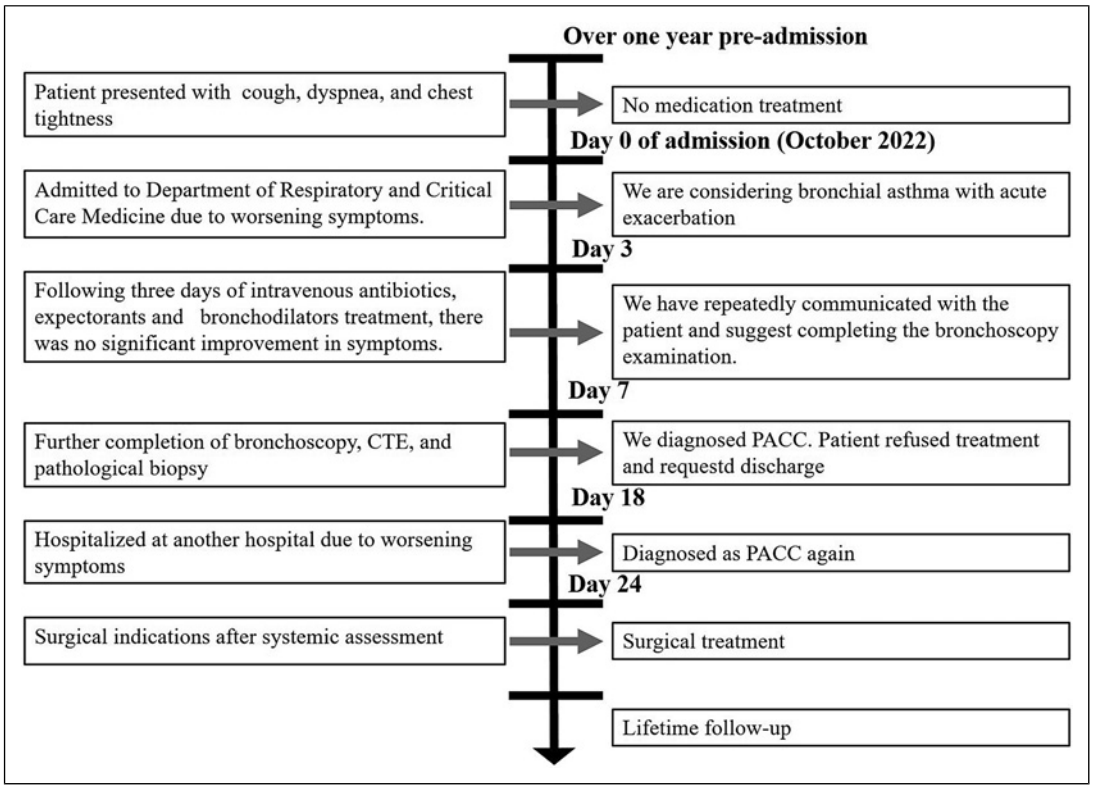

Fig. 5. Timeline of the diagnostic process.

patients with respiratory symptoms, prioritizing chest CT over X-ray aids timely airway lesion detection. In initial stages, small tumors may yield normal lung function, while increasing tumor size leads to positive bronchodilation tests, potentially misdiagnosed as asthma or chronic obstructive pulmonary disease. Early stages often lack overt symptoms, with pronounced difficulties emerging when cavity obstruction exceeds 50–75%, causing breathlessness, cough, and phlegm. Syncope may occur, indicating advanced stages with limited surgical options and a poor prognosis [22–27]. PACC is highly infiltrative and can extend into the lung parenchyma and mediastinum. Complete surgical resection may be challenging when the tumor invades the peripheral nerve, and local recurrence is common; nevertheless, distant organ metastasis is infrequent.

The cytology of PACC is characterized by round, oval tumor cells with sparse cytoplasm, high nucleoplasmic ratio, smooth contours, and no obvious nucleoli, with dense chromatin that contains transparent spheres form dense, bifurcated tubular clusters of cells, which is a pathological feature of the disease [28]. Studies have shown that PACC can differentiate into glandular epithelial, myoepithelial, or intermediate-type cells. Immunohistochemistry primarily expresses the ductal cells marking EMA, CK7, CD117, CEA, and myoepithelial cells marking P63, S-100, Calponin, SMA, CK5/6. Co-expression of CD117 and P63 suggests a more aggressive tumor and a poor prognosis. The higher the expression of CD117, the worse the prognosis [29, 30]. Several studies have suggested that CD117 expression levels are negatively correlated with the prognosis of primary PACC [31].

It is critical to differentiate primary PACC from metastatic PACC originating from other sites during diagnosis. In the current case, there is no evidence of lesions at other sites or adjacent and distant metastases. The pathology report suggests that neoplastic lesions are present, but further analysis is necessary to identify whether they are adenoid cystic

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Table 1. Literature review of the reported cases of PACC

Ref	Age/sex	Clinical manifestation	Dur.	Size	Metastasis of lymph node/ other organs
[5]	43/F	–	–	4 cm	–/–
[6]	37/F	Fever	–	–	N/N
[7]	50/M	Cough, dyspnea	4 mo	Large cystic mass	Y/Y
[8]	58/M	Expectoration, hemoptysis	–	–	N/N
[8]	52/F	Cough, wheezing, dyspnea	4 y	–	N/N
[9]	27/F	Chest discomfort, cough, hemoptysis	1 mo	2.4 × 1.2 × 2 cm	N/N
[10]	28/M	Dyspnea	–	Entire trachea	N/N
[11]	82/M	Dyspnea, dry cough, anorexia, weight loss	–	8.2 cm	–/–
[12]	82/M	Tracheitis, dysphonia	3 mo	4.6 cm	N/N
[13]	62/M	Dyspnea, cough	1 y	3.4 × 2.8 cm	N/N
[14]	30/F	Dyspnea, wheezing, cough	1 y	–	N/N
[15]	43/M	Dyspnea, wheezing	–	–	N/N
[16]	51/M	Dyspnea, cough, lightheadedness, weight loss	8 mo	6.1 × 5.3 cm	Y/Y
[17]	16/F	Dyspnea	5 d	Subglottic region	N/N
[18]	53/F	Dyspnea, hemoptysis	2 y	–	Y/Y
[18]	25/F	Cough, hemoptysis	1 y	–	N/N
[19]	26/F	Dyspnea, dry cough	2 mo	1.1 × 1.3 cm	N/N
[20]	51/M	Discomfort in the pharynx	–	4 cm	N/N
[21]	45/F	Progressive shortness of breath	–	–	Y/Y

Ref	Treatment	Follow-up
[5]	Radiotherapy	Unknown (loss of follow-up)
[6]	Surgical resection (bronchial stump negative)	Distant metastasis occurred 6 years later
[7]	Palliative chemotherapy	In poor general condition
[8]	Surgical resection (bronchial stump negative)	After 7 months of follow-up, no tumor recurrence
[8]	Surgical resection (bronchial stump positive), radiotherapy	Follow-up of 6 months with a clear improvement in dyspnea

(Continued on following page)

Table 1 (continued)

Ref	Treatment	Follow-up
[9]	Surgical resection (bronchial stump positive), radiotherapy	Unknown (three-monthly clinical reviews)
[10]	Radiotherapy, chemotherapy, durvalumab maintenance	No tumor progression after 15 months
[11]	Refusal to treatment	–
[12]	Surgical resection, radiotherapy	Complete response to the radiotherapy after 6 and 12 months of follow-up
[13]	Surgical resection, radiotherapy	Absolute improvement of clinical status in follow-up
[14]	Radiotherapy, cryoablation	Normal healing trachea after 6-month post-radiotherapy
[15]	Surgical resection (bronchial stump positive), radiotherapy	No tumor recurrence
[16]	Removing/lasering 3.5 cm of tumor, radiotherapy, chemotherapy	Progressive metastatic disease and worsening symptoms
[17]	Proton radiotherapy	No recurrence or metastasis till date
[18]	Palliative right sleeve pneumonectomy with resection of the carina	Deceased due to severe pneumonia
[18]	Surgical resection	No tumor recurrence
[19]	Surgical resection	Recent 6-month follow-up shows no tumor recurrence
[20]	Surgical resection (bronchial stump positive), radiotherapy	Tracheal stenosis after 6 months, no metastasis after 1.5 years
[21]	Radiotherapy	Recurrence a year later

F, female; M, male; Y, yes; N, no; y, year(s); mo, month(s); d, day(s); –, unknown.

carcinoma or pleomorphic adenoma. The focal sieve-like structure of pleomorphic adenoma may resemble PACC, but distinguishing between the two can be done based on cell morphology, structural pattern, interstitial composition, and immunohistochemistry. Pleomorphic adenomas share a common histogenesis at the intercalated duct level and often exhibit a combination of neoplastic basaloid cells [32]. Diagnosis of pleomorphic adenomas was unlikely as this benign tumor typically has a Ki-67 value of less than 5%. Optimal PACC treatment involves radical surgery, emphasizing complete resection with adequate margins. Adjuvant radiotherapy is recommended for cases with positive surgical margins, potentially extending overall survival [33]. Nonsurgical patients benefit from palliative measures like tracheal therapy, radiotherapy, or combination therapy to enhance clinical symptoms. Typically, a tumor invading over 50% of tracheal length (>6 cm) or exceeding one-third of the total length in children poses challenges for tracheal reconstruction, constituting a surgical contraindication [34].

Shafiee et al. [9] documented a case involving a 27-year-old pregnant woman initially diagnosed with bronchial asthma 3 years prior. Although initially presumed as an

exacerbation of asthma, treatment with bronchodilators, steroids, and intravenous antibiotics failed to alleviate symptoms. Subsequent diagnostic video-bronchoscopy led to the identification of PACC. In addition to respiratory symptoms, PACC also has neurological symptoms such as dizziness and digestive system symptoms such as anorexia. Thouil et al. [11] reported a PACC case presenting with dyspnea, dry cough, anorexia, and weight loss as primary symptoms in an elderly patient with a sizable tumor. Unfortunately, the patient declined treatment and subsequently lost contact. Additionally, Nagi et al. [16] reported a patient diagnosed with PACC, presenting primarily with dizziness. The patient's treatment has progressed to an advanced stage, accompanied by distant metastasis and a sizable tumor. Despite the removal/laser treatment of a 3.5-cm tumor, airway obstruction persists. As highlighted earlier, PACC patients may present not only with respiratory symptoms but also with dizziness and poor appetite, despite no notable abnormalities in the central nervous and digestive systems. We hypothesize that severe airway obstruction from the tumor induces hypoxia and discomfort, while gradual tracheal enlargement compresses the digestive tract, causing appetite decline. This speculation underscores the importance of chest examinations alongside routine central nervous system assessments for patients primarily manifesting dizziness to prevent potential misdiagnoses. In cases of PACC with distant metastasis [7, 16, 18], palliative treatment is the sole option, contributing to a grim prognosis. One patient [18], subsequently developing severe pneumonia, succumbed to respiratory failure. As per reports [24, 34, 35], patients undergoing solely surgical resection exhibit a 5-year survival rate of 88–100% and a 10-year survival rate of 51–80%. Despite the potential for local recurrence and systemic metastasis post-surgery, lifelong follow-up is essential. Lymph node metastasis and presence of solid structure in the tumor lack a significant correlation with patient survival, whereas peripheral nerve infiltration notably impacts long-term survival rates. Prognostic factors in PACC encompass tumor stage, location, positive surgical margin, and treatment modality [33]. Although these treatments have a better local effect, the risk of long-term effects is higher. At present, there are no established criteria for radiotherapy and chemotherapy, and the use of targeted therapy and immunotherapy for PACC remains controversial and under research. Immunotherapy, a novel cancer treatment, boosts the patient's immune function against cancer cells. Studies [36] indicate a positive correlation between immunotherapy and the complete response rate in cancer treatment. However, challenges persist, such as immune checkpoint inhibitors causing specific treatment-related toxicity, termed immune-related adverse events, stemming from the immune system mistakenly targeting its own antigens [37, 38]. Furthermore, doubts have arisen about the effectiveness of PD-1/PD-L1 expression as a predictive indicator for first-line immunotherapy in advanced NSCLC [39–41]. Recent studies [6] showed promising results for targeted therapy in patients with PACC, such as the use of pyrotinib for patients with ERBB2 amplification, which resulted in a significant reduction in the growth of liver metastases and stable condition. Other targeted therapies, such as icotinib for patients with EGFR exon 19p.E746-A750 del [42] and erlotinib for patients with EGFR exon 21 c.2593G>A [43], also demonstrated beneficial outcomes. So, due to the low incidence of PACC and limited clinical studies, case reports are valuable in providing insights into the disease.

The increasing incidence of bronchial asthma, particularly in patients diagnosed with cough variant asthma, prompts clinicians to consider bronchial tumors when regular medication fails to control symptoms effectively. Some PACC-diagnosed patients, previously identified with bronchial asthma, experienced unsatisfactory treatment outcomes, with confirmation of PACC taking several years. Despite numerous clinical case reports of PACC, we observe a relative scarcity of patients misdiagnosed as acute bronchial asthma attacks, particularly those with a positive BDT, which is more prone to misleading clinicians into considering asthma. Furthermore, we hypothesize that tumors in the trachea induce mucosal

congestion, airway inflammation, and increased airway sensitivity. It is worth considering whether PACC patients present with concomitant bronchial asthma. The scarcity of PACC clinical research underscores the importance of case reports to contribute medical data for future investigations.

Conclusion

This report presents the diagnosis and treatment of a 41-year-old female patient with PACC, highlighting the significance of recognizing foreign bodies and tumors in patients exhibiting asthma-like symptoms. Following PACC resection and carina reconstruction operation, the possibility of metastasis exists even after several years, thus necessitating lifelong follow-up.

Statement of Ethics

Ethical approval is not required for this study in accordance with local or national guidelines. Written informed consent was obtained from the patient for publication of this case report and any accompanying images.

Conflict of Interest Statement

None of the authors have any conflicts of interest to declare.

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Author Contributions

Y.L. conceived and designed the study; F.Z. and R.J. acquired the data; S.L. and X.H. analyzed and interpreted the data; and F.Z. drafted the manuscript. All authors critically revised the manuscript for important intellectual content, gave approval of the version to be submitted, and agreed to be accountable for all aspects of the work.

Data Availability Statement

All data generated or analyzed during this study are included in this article. Further inquiries can be directed to the corresponding author.

References

1 Madariaga MLL, Gaissert HA. Overview of malignant tracheal tumors. Ann Cardiothorac Surg. 2018;7(2):244–54.

2 Wang Y, Cai S, Gao S, Xue Q, Mu J, Gao Y, et al. Tracheobronchial adenoid cystic carcinoma: 50-year experience at the National Cancer Center, China. Ann Thorac Surg. 2019;108(3):873–82.
3 Molina JR, Aubry MC, Lewis JE, Wampfler JA, Williams BA, Midthun DE, et al. Primary salivary gland-type lung cancer: spectrum of clinical presentation, histopathologic and prognostic factors. Cancer. 2007;110(10):2253–9.
4 Moran CA, Suster S, Koss MN. Primary adenoid cystic carcinoma of the lung. A clinicopathologic and immunohistochemical study of 16 cases. Cancer. 1994;73(5):1390–7.
5 Pino RM, Riley LE. Critical tracheal stenosis from adenoid cystic carcinoma during pregnancy: case report. J Clin Anesth. 2022;77:110620.
6 Tang Z, Lin F, Xiao J, Du X, Zhang J, Li S, et al. Case report: efficacy of pyrotinib in ERBB2 amplification pulmonary adenoid cystic carcinoma. Front Oncol. 2021;11:605658.
7 Laklaai Z, Chanoune K, Benjelloune H, Zaghba N, Yassine N. A huge primary adenoid cystic carcinoma of the lung: case report and review of the literature. Ann Med Surg. 2023;85(3):603–5.
8 Saad AB, Kadoussi R, Njima M, Mhamed SC, Fahem N, Abdeljelil NB, et al. Primary adenoid cystic carcinoma of the tracheobronchial tree: report of 2 cases. Pan Afr Med J. 2019;34:137.
9 Shafiee S, Adno A, French B, Johansson C, Frankel A, Williamson JP. Central airway obstruction caused by adenoid cystic carcinoma in pregnancy: a case report and review of the literature. Respirol Case Rep. 2018;6(5):e00317.
10 Mikami E, Nakamichi S, Nagano A, Misawa K, Hayashi A, Tozuka T, et al. Successful treatment with definitive concurrent chemoradiotherapy followed by durvalumab maintenance therapy in a patient with tracheal adenoid cystic carcinoma. Intern Med. 2023;62(18):2731–5.
11 Thouil A, Rhazari M, Baddi FZ, Kouismi H. Cystic adenoid carcinoma: a rare bronchial tumor. Cureus. 2023;15(7):e42476.
12 Spinelli GP, Miele E, Prete AA, Lo Russo G, Di Marzo A, Di Cristofano C, et al. Combined surgery and radiotherapy as curative treatment for tracheal adenoid cystic carcinoma: a case report. J Med Case Rep. 2019;13(1):52.
13 Nicolini EM, Montessi J, Vieira JP, Rodrigues Gd A, Costa Vd O, Teixeira FM, et al. Adenoid cystic carcinoma of the trachea: a case report. Am J Case Rep. 2019;20:1373–7.
14 Davari HR, Vahedi M, Jahanbin B, Mireskandari SM, Mirzaiemoghaddam M, Hajipour A. Proximal airway obstruction caused by adenoid cystic carcinoma in a pregnant woman: a case report. Afr J Thorac Crit Care Med. 2021;27(4):174–6.
15 Djaković Ž, Janevski Z, Cesarec V, Slobodnjak Z, Stančić-Rokotov D. Adenoid cystic carcinoma of distal trachea: a case report. Acta Clin Croat. 2019;58(4):777–9.
16 Nagi T, Dabiri R, Gheit Y, Zaki A, Gan W, Torres A, et al. Rare case of primary adenoid cystic carcinoma of the lung with bilateral kidney and liver metastasis. J Med Cases. 2022;13(11):551–6.
17 Dumitru CȘ, Balica NC. Subglottotracheal adenoid cystic carcinoma in a 16-year-old female-a case report. Medicina. 2023;59(6):1140.
18 Fernández L, Salazar N, Sua LF, Velásquez M. Sleeve pneumonectomy and carinal resection for management of primary adenoid cystic tumor of the lung with carinal extension: report of 2 cases. Respir Med Case Rep. 2019;26:82–6.
19 Lu D, Feng S, Liu X, Dong X, Li M, Wu H, et al. 3D-printing aided resection of intratracheal adenoid cystic carcinoma and mediastinal mature cystic teratoma in a 26-year-old female: a case report. J Thorac Dis. 2018;10(2):e134–7.
20 Amemiya R, Takada I, Matsubara T, Ono S, Morishita Y, Ikeda N, et al. Temporary stenting for anastomotic stenosis after tracheal resection of adenoid cystic carcinoma: a case report. Ann Thorac Cardiovasc Surg. 2023;29(5):256–60.
21 Tun AJ, Hoppe BS, Zhao Y, Makey I, Fernandez-Bussy S, Liang X. Radiation therapy for primary adenoid cystic carcinoma of the trachea: photons, protons, or carbon. Int J Part Ther. 2023;9(4):302–5.
22 Bhattacharyya N. Contemporary staging and prognosis for primary tracheal malignancies: a population-based analysis. Otolaryngol Head Neck Surg. 2004;131(5):639–42.
23 Honings J, van Dijck JA, Verhagen AF, van der Heijden HF, Marres HA. Incidence and treatment of tracheal cancer: a nationwide study in The Netherlands. Ann Surg Oncol. 2007;14(2):968–76.
24 Maziak DE. Biology of adenoid cystic carcinoma of the tracheobronchial tree and principles of management. Thorac Surg Clin. 2018;28(2):145–8.
25 Benn BS, Zhu V. Multimodal bronchoscopic treatment of unresectable tracheal adenoid cystic carcinoma. J Bronchology Interv Pulmonol. 2020;27(2):e17–9.
26 Macchiarini P. Primary tracheal tumours. Lancet Oncol. 2006;7(1):83–91.
27 Bots EMT, van Wyk AC, Janson JT, Wagenaar R, Paris G, Koegelenberg CFN. Syncope due to tracheal adenoid cystic carcinoma. Respirol Case Rep. 2019;7(7):e00452.
28 Zhang Y, Liu X, Gu Y, Zhang S. Clinical, laboratory, pathological, and radiological characteristics and prognosis of patients with pulmonary salivary gland-type tumors. J Cancer Res Clin Oncol. 2023;149(7):4025–39.
29 Zhou Q, Chang H, Zhang H, Han Y, Liu H. Increased numbers of P63-positive/CD117-positive cells in advanced adenoid cystic carcinoma give a poorer prognosis. Diagn Pathol. 2012;7:119.

30 Huang Z, Pan J, Chen J, Wu S, Wu T, Ye H, et al. Multicentre clinicopathological study of adenoid cystic carcinoma: a report of 296 cases. Cancer Med. 2021;10(3):1120–7.
31 Mino M, Pilch BZ, Faquin WC. Expression of KIT (CD117) in neoplasms of the head and neck: an ancillary marker for adenoid cystic carcinoma. Mod Pathol. 2003;16(12):1224–31.
32 Chon SH, Park YW, Oh YH, Shinn SH. Primary peripheral pulmonary adenoid cystic carcinoma: report of a case diagnosed by fine needle aspiration cytology. Diagn Cytopathol. 2011;39(4):283–7.
33 Zhao Y, He G, Zhai Y, Zhou Z, Bi N, Mao Y, et al. Adenoid cystic carcinoma of lobar bronchial origin: 20-year experience at a single institution. Ann Surg Oncol. 2022;29(7):4408–16.
34 Park JH, Jung JW, Kang HW, Joo YH, Lee JS, Cho DW. Development of a 3D bellows tracheal graft: mechanical behavior analysis, fabrication and an in vivo feasibility study. Biofabrication. 2012;4(3):035004.
35 Högerle BA, Lasitschka F, Muley T, Bougatf N, Herfarth K, Adeberg S, et al. Primary adenoid cystic carcinoma of the trachea: clinical outcome of 38 patients after interdisciplinary treatment in a single institution. Radiat Oncol. 2019;14(1):117.
36 Santoni M, Rizzo A, Kucharz J, Mollica V, Rosellini M, Marchetti A, et al. Complete remissions following immunotherapy or immuno-oncology combinations in cancer patients: the MOUSEION-03 meta-analysis. Cancer Immunol Immunother. 2023;72(6):1365–79.
37 Santoni M, Rizzo A, Mollica V, Matrana MR, Rosellini M, Faloppi L, et al. The impact of gender on the efficacy of immune checkpoint inhibitors in cancer patients: the MOUSEION-01 study. Crit Rev Oncol Hematol. 2022;170:103596.
38 Rizzo A, Mollica V, Marchetti A, Nuvola G, Rosellini M, Tassinari E, et al. Adjuvant PD-1 and PD-L1 inhibitors and relapse-free survival in cancer patients: the MOUSEION-04 study. Cancers. 2022;14(17):4142.
39 Hu D, Zhang W, Tang J, Zhou Z, Liu X, Shen Y. Improving safety of cancer immunotherapy via delivery technology. Biomaterials. 2021;265:120407.
40 Rizzo A, Cusmai A, Giovannelli F, Acquafredda S, Rinaldi L, Misino A, et al. Impact of proton pump inhibitors and histamine-2-receptor antagonists on non-small cell lung cancer immunotherapy: a systematic review and meta-analysis. Cancers. 2022;14(6):1404.
41 Rizzo A. Identifying optimal first-line treatment for advanced non-small cell lung carcinoma with high PD-L1 expression: a matter of debate. Br J Cancer. 2022;127(8):1381–2.
42 Song Z, Wu W, Zhang Y. Effective treatment with icotinib in primary adenoid cystic carcinoma of the lung with liver metastasis. J Thorac Oncol. 2014;9(9):e67–9.
43 Mendes MA, Barroso A, Campainha S. EGFR-variant adenoid cystic carcinoma of the lung. J Thorac Oncol. 2018;13(9):e178–81.