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CASE REPORT

Hyalinizing clear cell carcinoma of the lung: A rare case with long-term follow-up

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ABSTRACT

Hyalinizing clear cell carcinoma of the lung: A rare case with long-term follow-up

Primary salivary gland-type lung cancers are extremely rare, accounting for less than 1% of all lung tumors. Hyalinizing clear cell carcinoma (HCCC) of the lung, an even rarer subtype, presents diagnostic challenges due to its similarity to other endobronchial lesions, such as carcinoid tumors or mucoepidermoid carcinoma. Here, we aimed to present a case of a 53-year-old male non-smoker who presented with recurrent respiratory symptoms. Initial chest X-ray showed consolidation, and subsequent computed tomography (CT) revealed a left lower lobe endobronchial nodule with post-obstructive pneumonia. Positron emission tomography-CT imaging demonstrated mild F-18 fluorodeoxyglucose uptake, and bronchoscopy with biopsy led to the diagnosis of HCCC. The patient underwent a left lower lobectomy, and histopathological analysis confirmed the diagnosis. The five-year follow-up was unremarkable, with no signs of recurrence. This case underscores the importance of considering HCCC in the differential diagnosis of endobronchial lesions, particularly in non-smokers.

Key words: *Lung cancer; computed tomography; hyalinizing clear cell carcinoma; rare*

ÖZ

Akciğerin hyalinize berrak hücreli karsinomu: Uzun dönem takipli nadir bir vaka

Primer tükürük bezi tipi akciğer kanserleri son derece nadirdir ve tüm akciğer tümörlerinin %1'inden daha azını oluşturur. Akciğerin hyalinizan berrak hücreli karsinomu (HBHK), daha da nadir görülen bir alt tip olarak, diğer endobronşiyal lezyonlar, örneğin karsinoid tümörler veya mukoepidermoid karsinom ile benzerliği nedeniyle tanısal zorluklar oluşturur. Bu yazıda, tekrarlayan solunum semptomları ile başvuran 53 yaşındaki sigara içmeyen bir erkekte tespit edilen HBHK vakasını sunuyoruz. İlk göğüs radyografisinde non-spesifik konsolidasyon saptandı ve ardından yapılan akciğer bilgisayarlı tomografi (BT) taramasında, tıkayıcı (obstrüktif) pnömoniye neden olan sol alt lobda endobronşiyal bir nodül tespit edildi. Endobronşiyal nodül, pozitron emisyon tomografisi-BT görüntülemesinde hafif F-18 florodeoksiglukoz

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tutulumu gösterdi ve bronkoskopi ile alınan biyopsi sonucunda HBHK tanısı düşünüldü. Hastaya sol alt lobektomi yapıldı ve histopatolojik değerlendirme HBHK tanısını doğruladı. Hastanın beş yıllık takibi sorunsuz geçti ve takip görüntülemelerinde nüks belirtisi görülmedi. Bu vaka, özellikle sigara içmeyen hastalarda, endobronşiyal lezyonların ayırıcı tanısında HBHK'nin göz önünde bulundurulmasının önemini vurgulamaktadır.

Anahtar kelimeler: *Akciğer kanseri; bilgisayarlı tomografi; hyalinize edici berrak hücreli karsinom; nadir*

INTRODUCTION

Primary salivary gland-type lung cancers are very unusual, accounting for less than 1% of all lung tumors. These cancers arise from the minor salivary glands located beneath the bronchial mucosa (1,2). The 2021 World Health Organization (WHO) classification of chest tumors identifies several types of salivary gland-type lung epithelial tumors, including pleomorphic adenoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, epithelial-myoepithelial carcinoma, myoepithelioma, myoepithelial carcinoma, and hyalinizing clear cell carcinoma (HCCC) (3). Imaging plays a crucial role in diagnosing and managing primary salivary gland-type lung cancers (4). Advanced imaging techniques, such as computed tomography (CT) and positron emission tomography (PET)-CT, help in accurately identifying the location, size and extent of these rare tumors (5,6). Furthermore, imaging is essential in distinguishing these malignancies from other lung tumors, guiding biopsy procedures, and assessing treatment response. Although only a few case reports describe pathological findings of the disease due to its rarity, radiological characteristics are even less well-documented. Herein, we aimed to emphasize the multimodality imaging and pathological findings of HCCC.

CASE REPORT

A 53-year-old male non-smoker presented to the emergency room with symptoms of cough, fever, and chills. A posteroanterior (PA) and lateral chest X-ray revealed consolidation in the left lower lobe. The patient was started on antibiotics and instructed to follow up with his primary care physician. A few months later, the patient returned to the emergency room with similar symptoms. Given the recurrence, a contrast-enhanced chest CT was performed, revealing a left lower lobe, well-defined hypodense endobronchial nodule with post-obstructive pneumonia (Figure 1). The patient was again started on intravenous antibiotics, and a pulmonary consultation led to bronchoscopy with biopsy. The endobronchial biopsy raised the differential diagnosis of poorly differentiated squamous cell carcinoma versus HCCC of the lung. The patient underwent a PET-CT scan for further evaluation and staging of the tumor. PET-CT images showed mild F-18 fluorodeoxyglucose (FDG) uptake within the nodule and post-obstructive pneumonia without evidence of metastasis (Figure 2). The patient subsequently underwent a left lower lobectomy. The pathological findings revealed a neoplasm composed of nests, glands, and trabeculae embedded within the hyalinized stroma, with tumor cells displaying

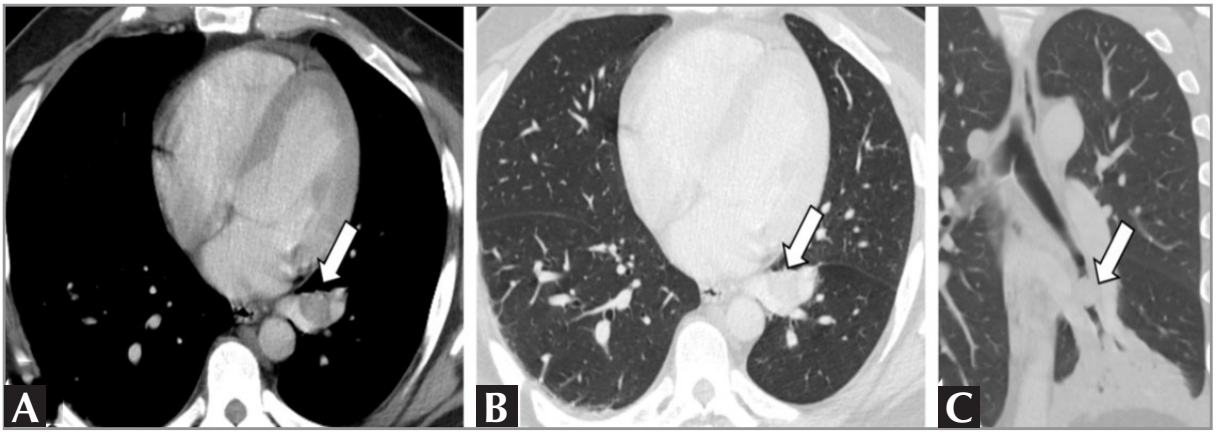

Figure 1. (A,B). Axial contrast-enhanced chest CT images (mediastinal and lung window, respectively) depict a well-defined endobronchial lesion arising from the left lower lobar bronchus. **(C).** Cropped coronal chest CT image shows a smooth, solid endobronchial nodule (arrows).

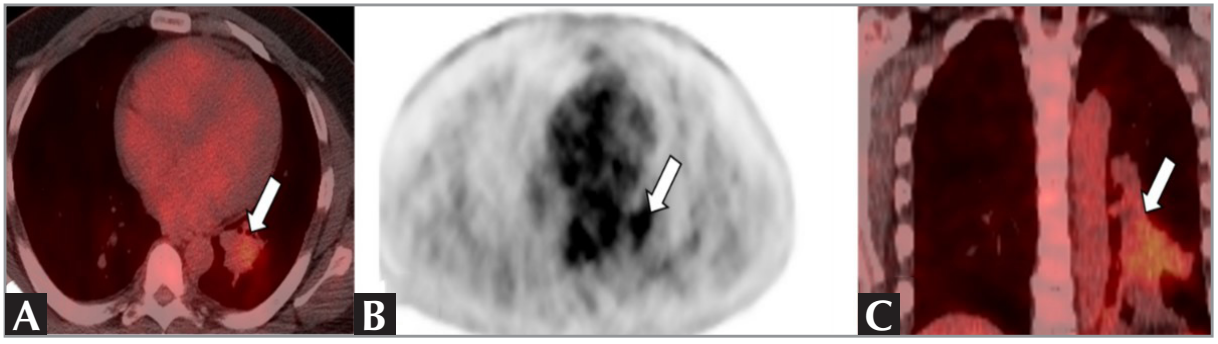

Figure 2. (A-C). Axial PET-CT images show mild FDG uptake within the nodule (arrows) and post-obstructive pneumonia.

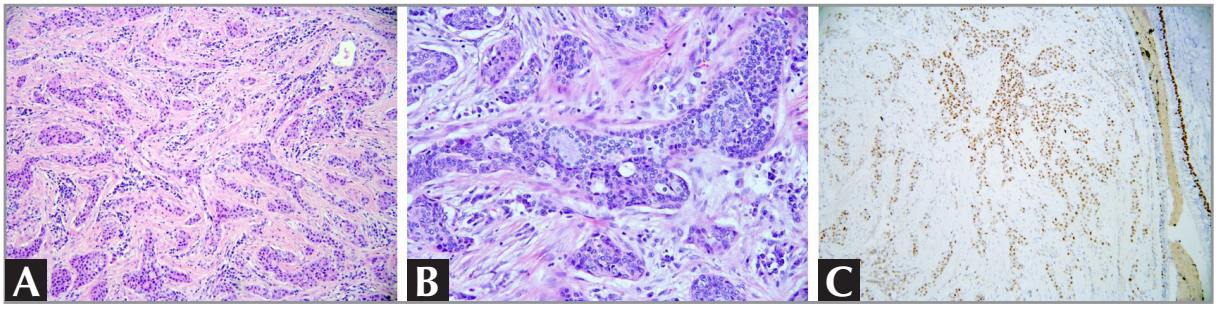

Figure 3. Histopathological features of the neoplasm. **(A).** Low power view showing the neoplasm arranged in nests, glands, and trabeculae within hyalinized stroma. **(B).** High power view showing tumor cells with relatively uniform nuclei, minimal atypia, and variable cytoplasm from eosinophilic to clear. **(C).** Immunohistochemical stain for p40 demonstrates positivity in tumor nuclei. Note internal control on right where the basal layer of bronchial epithelium is staining positive.

relatively uniform nuclei, minimal atypia, and varying cytoplasm from eosinophilic to clear, consistent with HCCC. Immunohistochemistry showed positive nuclear staining for p40 in the tumor cells, with an internal control highlighting the basal layer of bronchial epithelium (Figure 3). The patient's five-year follow-up after surgery was unremarkable, with no signs of recurrence.

DISCUSSION

Primary salivary gland-type lung cancers are extremely rare, accounting for less than 1% of all lung tumors. These cancers arise from the minor salivary glands beneath the bronchial mucosa (1,2). The 2021 WHO classification of chest tumors identifies several types of salivary gland-type lung epithelial tumors, including pleomorphic adenoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, epithelial-myoepithelial carcinoma, myoepithelioma, myoepithelial carcinoma, and HCCC (3,4).

HCCC of the lung is an exceptionally rare subtype of salivary gland-type tumors, with only a few cases reported in the English-language medical literature since its first description by García et al. in 2015 (1). Due to its rarity, diagnosing HCCC poses a significant challenge since its radiologic and clinical presentation often mimics other endobronchial lesions, such as carcinoid tumors or mucoepidermoid carcinoma (4-8).

The histopathological findings in HCCC are critical in differentiating this rare neoplasm from other pulmonary lesions (1-3). In this case, a low-power examination revealed the tumor arranged in nests, glands, and trabeculae embedded within a hyalinized stroma, a hallmark of HCCC. At higher magnification, the tumor cells displayed uniform nuclei with minimal atypia and cytoplasm ranging from eosinophilic to clear. Immunohistochemical analysis confirmed positivity for p40 in the tumor nuclei, consistent with its epithelial origin, while internal controls validated the staining pattern. These features, particularly the clear cytoplasm and hyalinized stroma, are essential for distinguishing HCCC from other differential diagnoses, such as poorly differentiated squamous cell or mucoepidermoid carcinoma (1-3,7,8).

HCCC typically occurs in the 4th to 6th decades of life, predominantly affecting males, and unlike other lung tumors, it has no known association with smoking (5). The present case is consistent with these demographic features, as our patient was a 53-year-old male non-smoker. Importantly, HCCC originates from the mucous and serous glands of the tracheobronchial tree, a site that rarely gives rise to neoplasms that are histologically similar to those found in the salivary glands of the head and neck (1-7). Therefore, distinguishing primary pulmonary HCCC from metastatic disease originating in the head and neck requires a detailed clinical history and PET-CT imaging evaluation.

PET-CT scans play a valuable role in the diagnostic workup and staging of HCCC, as demonstrated in the present case, where mild FDG uptake was observed within the nodule. This finding aligns with the low metabolic activity and well-defined borders often associated with these tumors (8). However, given the typically mild FDG uptake in HCCC, it is essential not to rely solely on PET-CT results for diagnosis. Instead, biopsy remains the gold standard for confirming the nature of the lesion (1-6). These features were critical in differentiating HCCC from other potential diagnoses, such as our patient's poorly differentiated squamous cell carcinoma.

Due to the rarity of HCCC, long-term follow-up data is limited. However, our patient's 5-year follow-up was uneventful, with no signs of recurrence. This favorable outcome is consistent with the limited literature, suggesting that early-stage HCCC, when treated with complete surgical resection, may have a favorable prognosis (9). As the understanding of salivary gland-type tumors continues to expand, it is essential to recognize that they can also arise primarily in the lungs (9,10). A high suspicion index and thorough clinical and histopathological evaluation are crucial to accurately diagnosing and ensuring appropriate management of this rare entity.

CONCLUSION

HCCC of the lung is an exceptionally rare neoplasm, often presenting with non-specific respiratory symptoms and overlapping radiological features with other endobronchial tumors. This case highlights the importance of considering HCCC in the differential diagnosis of endobronchial lesions, especially in non-smokers with central airway involvement. While imaging, including PET-CT, is helpful for evaluation and staging, definitive diagnosis relies on histopathological examination. Surgical resection remains the treatment of choice, and long-term follow-up is essential to monitor for recurrence, as demonstrated by our patient's favorable five-year outcome. Early recognition and appropriate management can result in an excellent prognosis for this rare pulmonary tumor.

PATIENT CONSENT

Patient consent was obtained.

Peer-review: Externally peer-reviewed.

CONFLICT of INTEREST

The authors have no conflict of interest to declare.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: All of authors

Analysis/Interpretation: All of authors

Data Acquisition: All of authors

Writing: All of authors

Clinical Revision: All of authors

Final Approval: All of authors

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