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# Birt-Hogg-Dube Syndrome Presenting with a New Pleural-Based Pulmonary Nodule in a Patient with Progressive Cystic Lung Disease and Emphysema: A Case Report

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## Abstract

We describe a 78-year-old man with a 28-pack-year smoking history, moderately severe emphysema, and progressive bilateral cystic lung disease who presented with pleuritic chest pain and a newly identified pleural-based left upper lobe pulmonary mass. Retrospective review of serial computed tomography (CT) imaging from 2019 onward revealed longstanding, predominantly basilar thin-walled pulmonary cysts that had progressively increased in size and number over several years. The distribution and morphology of the cysts were more consistent with a diffuse cystic lung disease than with emphysema alone. Clinical examination revealed multiple cutaneous lesions consistent with fibrofolliculomas, which raised strong suspicion for Birt-Hogg-Dubé (BHD) syndrome.FDG-PET/CT scanning demonstrated an intensely FDG-avid posterolateral left apical mass measuring up to 37 × 65 mm with a maximum standardized uptake value (SUVmax) of 22.8. The mass showed direct invasion into the adjacent posterolateral chest wall musculature and permeative erosive changes involving the left third to fifth ribs. There was no evidence of distant visceral or skeletal metastases. Background findings included scattered bilateral pulmonary cysts consistent with BHD syndrome. CT-guided core biopsy confirmed primary lung adenocarcinoma (TTF-1 positive). The patient was referred to medical oncology and radiation oncology for further management. This case highlights the diagnostic challenges of coexisting smoking-related emphysema and inherited cystic lung disease, the importance of recognizing characteristic cutaneous and radiological features of BHD syndrome, and the need for a multidisciplinary approach that integrates malignancy evaluation, genetic testing, renal surveillance, and family screening.

**Keywords:** Birt-Hogg-Dube syndrome; pulmonary cysts; Fibrofolliculomas; Lung adenocarcinoma; FLCN gene; Cystic lung disease; Emphysema; Spontaneous pneumothorax

## Introduction

Birt-Hogg-Dub (BHD) syndrome is a rare autosomal dominant genodermatosis caused by germline pathogenic variants in the FLCN (folliculin) tumor suppressor gene on chromosome 17p11.2. The folliculin protein plays a critical role in regulating the mTOR signaling pathway, cellular energy sensing, and autophagy. Loss-of-function mutations lead to dysregulated cell growth and the development of hamartomas and tumors. The syndrome classically presents with a triad of manifestations. Cutaneous lesions include multiple fibrofolliculomas and trichodiscomas, which are benign hair follicle hamartomas that typically appear in the third or fourth decade of life as small (2–5 mm), dome-shaped, whitish-to-flesh-colored papules on the face, neck, scalp, and upper trunk. Acrochordons (skin tags) may also be present but are less specific. Pulmonary involvement occurs in more than 80–90% of patients and is characterized by multiple thin-walled, irregular cysts that are often basilar and subpleural in

distribution. These cysts are associated with a significantly increased lifetime risk of spontaneous pneumothorax, which may reach 25–50% and can be recurrent, often occurring at younger ages than in the general population. Renal neoplasms constitute the third major feature, with a lifetime risk of 15–35%. The most common tumors are chromophobe renal cell carcinomas, hybrid oncocytic/chromophobe tumors, and oncocytomas. These tumors are frequently multifocal and bilateral but often follow an indolent clinical course when detected through surveillance. Pulmonary cysts in BHD syndrome are frequently under-recognized and may be misattributed to emphysema or other cystic lung diseases, especially in older patients or those with a smoking history. While BHD syndrome is strongly associated with renal tumors, its association with primary lung cancer is rare and not considered a core feature of the syndrome. Only a limited number of cases have described coexisting lung cancer in patients with BHD, predominantly adenocarcinomas. In these cases, smoking history likely plays the dominant role in oncogenesis, although FLCN haploinsufficiency and mTOR pathway dysregulation may create a permissive cellular environment for tumorigenesis. This rare association underscores the importance of smoking cessation and prompt evaluation of any new solid or pleural-based nodules in patients with known or suspected BHD syndrome.Early recognition of BHD syndrome is critical because of its implications for lifelong renal cancer surveillance, family cascade genetic testing, pneumothorax prevention strategies, and assessment of procedural risks in patients with fragile cystic lung parenchyma [1-6].

## Case Presentation

A 78-year-old man was referred to the respiratory clinic for assessment of a new pulmonary lesion associated with pleuritic chest pain. His medical history included coronary artery disease with percutaneous coronary intervention in 2018 and coronary artery bypass grafting in 2022, atrial fibrillation managed with a permanent pacemaker and apixaban anticoagulation, obstructive sleep apnea treated with continuous positive airway pressure, and a clinical diagnosis of chronic obstructive pulmonary disease with emphysema. He had a 28-pack-year smoking history, which he had ceased several years earlier, and significant occupational exposures from mining and manual labor. Prior respiratory reviews had noted cystic lung changes, but longitudinal coordination and syndromic evaluation had been lacking. He reported a 3- to 4-week history of moderate-to-severe left scapular and shoulder pain with pleuritic features radiating anteriorly. The symptoms had developed after an influenza-like illness with cough that largely resolved, leaving persistent pleuritic discomfort. There was no hemoptysis, significant sputum production, weight loss, night sweats, or signs of acute infection. On clinical examination, he demonstrated features of chronic airflow limitation with hyperinflation. Dermatological inspection identified multiple small dome-shaped papules on the face, neck, and upper trunk that were clinically consistent with fibrofolliculomas. These skin findings, in the context of progressive cystic lung disease, prompted strong suspicion for Birt-Hogg-Dube syndrome. No acute cardiorespiratory decompensation was evident. Pulmonary function tests demonstrated moderate-to-severe airflow obstruction, air trapping, hyperinflation, and reduced diffusing capacity for carbon monoxide, consistent with combined emphysematous destruction and cystic parenchymal loss.

Retrospective review of CT imaging from 2019 onward revealed multiple bilateral thin-walled pulmonary cysts with progressive increase in size and number. The cysts showed a predominantly basilar and subpleural distribution with irregular shapes, features more consistent with a diffuse cystic lung disease than with centrilobular emphysema alone. The February 2026 CT chest confirmed extensive bilateral cystic lung disease and centrilobular emphysema, along with a new left upper lobe subpleural lesion measuring approximately 30 × 22 mm with associated pleural thickening and a small ipsilateral pleural effusion. This lesion was highly suspicious for primary lung malignancy given the smoking history, interval development, morphology, and symptoms. Subsequent FDG-PET/CT scanning demonstrated an intensely FDG-avid posterolateral left apical mass measuring up to 37 × 65 mm with an SUVmax of 22.8. The mass showed direct invasion into the posterolateral chest wall musculature and permeative erosion of the left third to fifth ribs. A small adjacent mildly FDG-avid focus (SUVmax 6.1) with a tiny pleural effusion was also noted. Scattered background pulmonary cysts were consistent with underlying BHD syndrome. Mildly FDG-avid non-enlarged ipsilateral hilar and paratracheal nodes were present, but there was no FDG-avid distant visceral or skeletal metastatic disease. A 19 mm exophytic lesion in the left renal lower pole showed no concerning FDG uptake and was favored to represent a benign hemorrhagic cyst, stable compared with prior imaging. The primary differential diagnosis for the mass was primary lung malignancy, most likely non-small cell lung carcinoma, with local invasion. Less likely considerations included organizing infection or rounded atelectasis, but the overall features strongly favored malignancy. Coexisting smoking-related emphysema and cystic disease complicated recognition of the underlying genetic disorder, but the progressive cystic pattern, cutaneous lesions, and relative symptom preservation supported suspected BHD syndrome. Formal confirmation would require FLCN genetic testing (Figures 1-8).

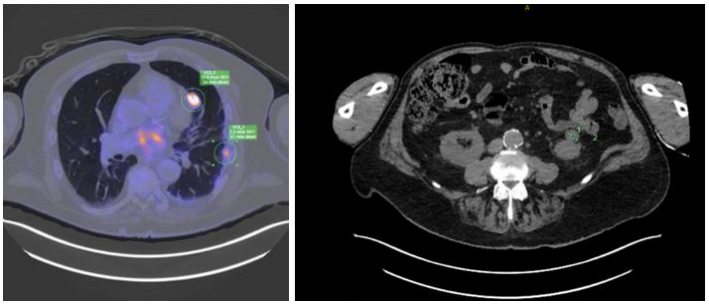
## Management and Clinical Course

A detailed discussion with the patient addressed the uncertain nature of the lesion, the high likelihood of malignancy, the staged

diagnostic pathway, and the elevated procedural risks due to cystic lung disease, emphysema, reduced diffusing capacity, and anticoagulation. The patient demonstrated understanding of the potential for curative or effective treatment despite locally advanced disease.

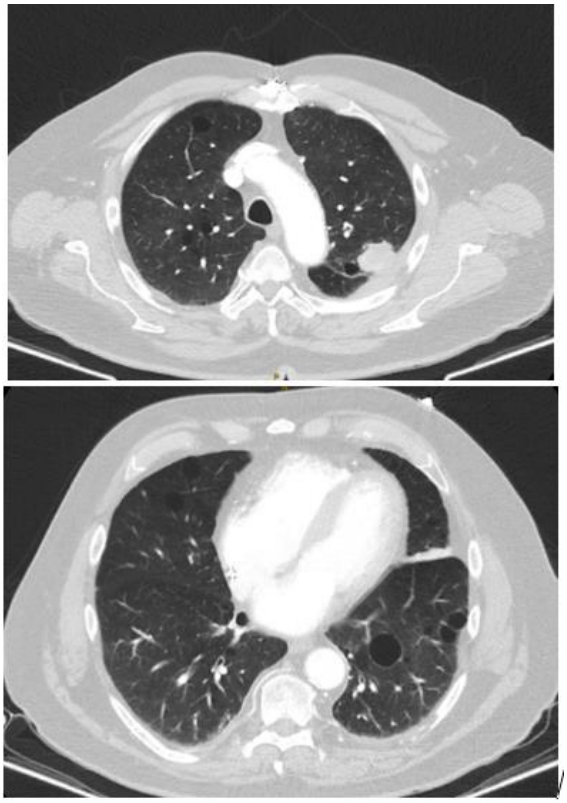


***Figures 1-4:*** *Fibrofolliculomas.*



***Figures 5,6****: PET scan images.*

Following review at the Lung Cancer Multidisciplinary Team meeting, CT-guided transthoracic core biopsy of the FDG-avid mass was performed. Histopathology confirmed non-small cell lung carcinoma with morphological features favoring lung adenocarcinoma. The tumor was TTF-1 positive, confirming primary lung adenocarcinoma. Further management included referral to medical oncology and radiation oncology for comprehensive staging review and discussion of treatment options, which may include systemic therapy, stereotactic ablative radiotherapy, or multimodal treatment depending on performance status, molecular profile, and final staging. In parallel, urgent referral to clinical genetics for FLCN germline testing and counseling was arranged. Dermatology review was planned to confirm fibrofolliculomas, potentially with skin biopsy if required. Renal surveillance with abdominal magnetic resonance imaging will follow ERN GENTURIS guidelines. First-degree relatives will be offered cascade genetic testing once a pathogenic variant is identified. Smoking cessation was reinforced, and education regarding pneumothorax risk reduction (avoidance of scuba diving and caution with air travel) was provided. The patient continues to be managed with close collaboration between respiratory, oncology, genetics, and radiology teams.



***Figures 7, 8:*** *CT cystic changes.*

## Discussion

This case underscores several key points in the management of cystic lung diseases. Inherited disorders such as BHD syndrome remain under-recognized in routine respiratory practice, particularly in older smokers where cystic changes may be ascribed solely to emphysema. Characteristic features, including basally located thin-walled cysts with interval progression, fibrofolliculomas on examination, and a compatible family history, aid differentiation. Smoking may exacerbate cystic changes, accelerate lung function decline, and increase malignancy risk in patients with BHD syndrome. The incidental discovery of suspected BHD syndrome during malignancy evaluation is not uncommon. The coexistence of emphysema and extensive cystic disease creates significant procedural challenges

for interventions such as transthoracic biopsy, necessitating careful risk-benefit assessment and multidisciplinary planning. A staged diagnostic approach beginning with PET/CT followed by biopsy optimizes outcomes while minimizing harm. Comprehensive management of BHD syndrome extends far beyond the lungs. Updated clinical practice guidelines recommend regular renal MRI surveillance, typically starting in the third decade, to detect renal tumors at an early, treatable stage. Genetic confirmation facilitates precise family cascade screening and reproductive counseling. Patient education on pneumothorax prevention is essential. This case illustrates the intricate relationship between acquired smoking-related lung disease and inherited BHD syndrome. It reinforces that dermatological examination should form part of the routine assessment in patients with unexplained or progressive cystic lung disease. Multidisciplinary collaboration involving respiratory medicine, thoracic radiology, medical oncology, radiation oncology, genetics, dermatology, and urology is indispensable for optimal patient outcomes.

## Conclusion

We report suspected Birt-Hogg-Dubé syndrome in a 78-year-old man with progressive cystic lung disease and emphysema, identified during investigation of a suspicious pleural-based pulmonary mass that proved to be locally advanced primary lung adenocarcinoma on FDG-PET/CT and CT-guided biopsy. The case emphasizes the importance of recognizing characteristic cystic patterns and associated cutaneous lesions, the diagnostic pitfalls of coexisting smoking-related disease, and the value of a staged multidisciplinary approach incorporating biopsy, molecular testing, referral to oncology and radiation oncology, genetic testing, renal surveillance, and family screening. Prompt diagnosis facilitates appropriate oncologic care, risk mitigation, and potentially life-saving familial benefits.

## References

1. Schmidt LS, Linehan WM. FLCN: The causative gene for Birt-Hogg-Dube syndrome. Gene. 2018; 640: 28-42.
2. Gupta N, Seyama K, McCormack FX. Pulmonary manifestations of Birt-Hogg-Dubé syndrome. Fam Cancer. 2013; 12:387-396.
3. Dal Sasso AA, Belem LC, Zanetti G, Souza CA, Escuissato DL, Irion KL, et al. Birt-Hogg-Dube syndrome. State-of-the-art review with emphasis on pulmonary involvement. Respir Med. 2015; 109: 289-296.
4. Daccord C, Good JM, Morren MA, Olivier B, Hohl D, Lazor R, et al. Birt–Hogg–Dube syndrome. Eur Respir Rev. 2020; 29: 200042.
5. Menko FH, Van Steensel MAM, Giraud S, Friss-Hansen L, Richard S, Ungari S, et al. Birt-Hogg-Dube syndrome: diagnosis and management. Lancet Oncol. 2009; 10: 1199-1206.
6. Geilswijk M, Genuarid M, Woodward ER, Nightingale K, Huber J, Madsen MG, et al. ERN GENTURIS clinical practice guidelines for the diagnosis and management of Birt-Hogg-Dube syndrome. Eur J Hum Genet. 2024.