Cystic Lung Disease in Birt-Hogg-Dubé Syndrome: A Case Series of Three Patients

Birt-Hogg-Dubé Sendromunda Görülen Kistik Akciğer Hastalığı: Üç Hastalık Olgu Serisi

Abidin Kilincer¹, Orhan Macit Ariyurek¹, Nevzat Karabulut²

¹Department of Radiology, Hacettepe University Faculty of Medicine, Ankara, Turkey
²Department of Radiology, Pamukkale University Hospital, Denizli, Turkey

Abstract

Birt-Hogg-Dubé syndrome is characterized by clinical manifestations such as hamartomas of the skin, renal tumors and lung cysts with spontaneous pneumothoraces. Patients with Birt-Hogg-Dubé syndrome may present with only multiple lung cysts. We report the chest computerized tomography (CT) features of three patients with Birt-Hogg-Dubé syndrome. Each patient had multiple lung cysts of various sizes according to chest CT evaluation, most of which were located in lower lobes and related to pleura. The identification of unique characteristics in the chest CT of patients with Birt-Hogg-Dubé syndrome may provide an efficient mechanism for diagnosis.

Key Words: Birt-Hogg-Dubé syndrome, chest CT, lung cyst

Introduction

Birt-Hogg-Dubé (BHD) syndrome is a rare autosomal dominant, inherited genodermatosis that was first described in 1977 and is characterized clinically by skin fibrofolliculomas, lung cysts, spontaneous pneumothoraces, and renal cancer [1, 2]. Renal cancer often presents with mixed chromophobes and oncocytic histology in patients with BHD syndrome. Additionally, benign renal tumors, such as renal oncocytoma, may be observed in BHD patients [2]. BHD is caused by germline mutations in the FLCN gene, which encodes a protein of unknown function called folliculin [2, 3]. Multiple lung cysts may be the only manifestation in patients with BHD syndrome without any other features [2, 4]. Therefore, incidental detection of lung cysts on chest CT should alert the radiologist to include BHD syndrome in differential diagnosis. We report the chest CT features of three patients with BHD syndrome.

Case Reports

Case 1

A 39-year-old male smoker was admitted to our institution with a spontaneous pneumothorax. Multislice CT of the chest showed numerous bilateral lung cysts and a limited pneumothorax on the right side (Figure 1). The majority of the lung cysts (93 of 154 cysts) were related to pleura. The largest cyst was in left lower lobe, measuring 45x24x22 mm in diameter. Physical examination revealed papular skin lesions on the nose and neck. Family history revealed that two of the patient’s cousins had episodes of spontaneous pneumothorax and that his father had documented lung cysts. Renal ultrasonography showed two simple renal cysts in the left kidney without any solid lesions.

Case 2

A 53-year-old man was admitted to our institution with right upper quadrant pain. Abdominal CT showed a contrast-
enhancing mass in the right kidney measuring three centimeters in diameter. A subsequent chest CT scan, performed for staging, showed numerous bilateral lung cysts (Figure 2). Most of the lung cysts (72 of 120 cysts) were associated with pleura. The largest cyst was in the right middle lobe, measuring 93x114x128 mm in diameter. Physical examination revealed papular skin lesions.

The patient underwent right partial nephrectomy. Pathologic examination of the kidney revealed clear cell renal cell carcinoma.

Case 3
A 38-year-old woman with a family history of recurrent pneumothorax was admitted to our institution. Chest CT showed multiple bilateral lung cysts. The largest cyst was in the right lower lobe, measuring 22x23x16 mm in diameter. Physical examination revealed papular skin lesions on the neck. The patient’s father had similar skin lesions. Dermatological examination confirmed the skin lesions to be fibrofolliculoma. Renal ultrasonographic evaluation was normal.

Discussion

Chest CT is a practical method for the initial diagnostic examination of patients with suspected BHD syndrome. None of the presented patients had a diagnosis of BHD syndrome at the time of the initial evaluation. All the patients had multiple lung cysts of various sizes (ranging from 2 mm to 12 cm), predominantly distributed in the lower regions of the lung. Furthermore, most of the lung cysts were related to pleura. In all patients, BHD syndrome was diagnosed after the CT scan of the chest. Table 1 summarizes the demographic and imaging characteristics of the presented cases in addition to those published in previous studies.

In the largest study to date, Toro et al. [5] reported that lung cysts were observed in the chest CT images of 89% of patients with BDH syndrome. They also reported that 24% of patients screened for lung cysts had a history of spontaneous pneumothoraces. In that study, they showed that the number of lung cysts were significantly associated with spontaneous pneumothoraces. Tobino et al. [6] reported that most lung cysts were small (<1 cm) and most commonly affected the lower medial zone. They described that approximately 40±12% of lung cysts bordered pleura. In a recent study, Agarwal et al. [7] reported that lung cysts were predominantly distributed in the lower lung (87% of patients) and that the largest cysts were also primarily found in the lower lung (93% of patients). In that study, 15 of 17 patients had lung cysts, which were bilateral in 13 patients (87%). Likewise, in the present report, lung cysts were typically bilateral, the largest of which were

Figure 1. Coronal reformatted CT scan of Patient 1 demonstrates a limited pneumothorax in the right lung; also note multiple bilateral lung cysts. CT: computed tomography

Figure 2. a, b. Coronal and axial CT images of Patient 2 show multiple bilateral lung cysts (a). The largest cyst in the right lung is related to pleura and in the middle lobe (b). CT: computed tomography
located in the lower lung in all patients. Interestingly, Kluger et al. [8] reported that two patients with a history of spontaneous pneumothoraces did not have cystic lesions on the CT scan. Lung cyst characteristics for the reported cases and the two published studies are shown in Table 2.

Cystic lung disease in BHD syndrome needs to be distinguished from other lung diseases that are characterized by multifocal or diffuse cystic changes, including lymphangioleiomyomatosis, pulmonary Langerhans cell histiocytosis, lymphocytic interstitial pneumonitis and emphysema [9-11].
Lymphangioleiomyomatosis is characterized by diffuse thin-walled, typically round cysts (measuring 2-20 mm in diameter). Cysts in lymphangioleiomyomatosis show an equal distribution in upper and lower lung zones. Cystic cavities in emphysema are usually seen in upper lobes and have no definable walls. In contrast, cysts in BHD syndrome are usually distributed in lower lung zones. In pulmonary Langerhans cell histiocytosis, thin-walled cysts may be seen in the final stage, although other parenchymal abnormalities, such as nodules, may also be observed [12]. Likewise, in lymphocytic interstitial pneumonitis, ground-glass opacities or centrilobular nodules may be seen separately from cysts [13].

In conclusion, we considered the diagnosis of BHD syndrome in our patients because of the features of lung cysts in chest CT evaluation. As chest CT findings may be an important mechanism for the fortuitous diagnosis of this syndrome, radiologists should be aware of the imaging features and clinical characteristics of this syndrome and should include BHD in the differential diagnosis when they encounter multiple thin walled cysts in the lung.

Informed Consent: Written informed consent was obtained from patients who participated in this case.

Peer-review: Externally peer-reviewed.


Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this case has received no financial support.

References