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Case report

Secondary pneumothorax associated with Birt-Hogg-Dubé syndrome: a case report^{☆,☆☆}

Raphael T. Pagger^{a,*}, Kaveh Akbari^a, Franz A. Fellner^{a,b}, Alexander Firmötz^a

^aCentral Radiology Institute, Kepler University Hospital, Medical Faculty of the Johannes Kepler University, Krankenhausstraße 9, 4021 Linz, Austria

^bFriedrich-Alexander-University Erlangen-Nürnberg, Erlangen, Germany

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ABSTRACT

Birt-Hogg-Dubé syndrome (BHDS) is a rare autosomal-dominant inherited disease. Typical clinical features include skin lesions, pulmonary cysts, and renal tumors. However, the syndrome remains to be underdiagnosed as a result of its heterogeneous clinical manifestation. In this report, we present the case of a 75-year-old male patient who was referred to the emergency department with pneumothorax, leading to the diagnosis of BHDS. Based on characteristic morphologic features, radiologists have the opportunity to propose BHDS as a differential diagnosis. Establishing the diagnosis in a timely manner is crucial, as these patients require lifelong screening examinations for renal cancer.

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Introduction

Birt-Hogg-Dubé syndrome (BHDS), described by Birt, Hogg, and Dubé in 1977 [1], is an autosomal dominant inherited disease [2]. To date, only 663 affected families have been reported in literature [3]. It consists of the typical triad skin lesions, pulmonary cysts, and renal tumors. As these clinical features are typically treated by different medical specialties, the syndrome remains to be underdiagnosed [4] and there is a long delay in establishing the correct diagnosis from the first onset of the symptoms [5].

The patient in our case report was referred to the emergency department with spontaneous pneumothorax, a common complication of BHDS and often its first clinical manifestation [5]. While primary spontaneous pneumothorax occurs in patients without an underlying lung disease, secondary spontaneous pneumothorax is classified as air in the pleural space in patients with lung disorders; therefore, a computed tomography (CT) examination can be necessary to establish the underlying cause of pneumothorax [6].

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* Corresponding author.

E-mail address: raphael.pagger@kepleruniklinikum.at (R.T. Pagger).

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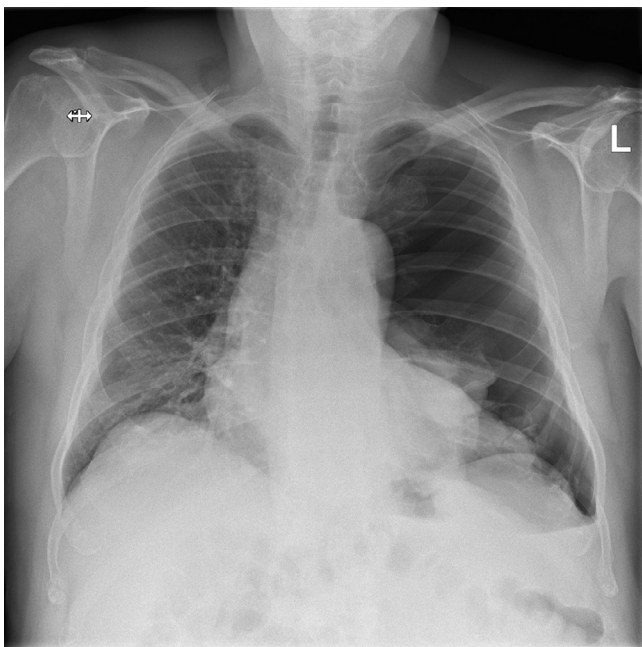


Fig. 1 – Posterior-anterior chest X-ray demonstrating tension pneumothorax with lung collapse on the left side.

Case report

A 75-year-old male patient was referred to our emergency department from a resident pulmonologist with radiologically evident tension pneumothorax with lung collapse on the left side (Fig. 1). For about 10 days, he had been complaining about shortness of breath and irritable cough symptoms. There was no evidence of previous pulmonary illnesses in his medical record. After chest tube insertion, the patient presented himself symptom free. A blood test showed increased creatinine levels, corresponding to chronic kidney disease 3a. An abdominal ultrasound examination was performed to evaluate the morphology and the perfusion of the kidneys, which revealed multiple bilateral renal cysts. In order to differentiate the un-

derlying pathology of the pneumothorax and to evaluate the renal cysts, a subsequent thoracic and abdominal CT scan was undertaken, showing multiple predominantly basally located pulmonary cysts of various size (Fig. 2) as well as one Bosniak II and several Bosniak I cysts (Fig. 3). Considering the typical clinical features and a positive family history for pneumothorax, BHDS was established as a differential diagnosis. Genetic testing identified a mutation in the FLCN gene, securing the diagnosis of BHDS.

Discussion

Although first described by Hornstein and Knickenberg in 1975, the genetic disorder is named after Birt, Hogg, and Dubé, who published a case report 2 years later, delineating the same syndrome [7]. The cause of this genetic disease is a mutation in the FLCN gene located on chromosome 17p11.2, coding a folliculin (FLCN) protein. The FLCN is thought to be a tumor suppressor, playing a role in the mTOR pathway [8]. With up to 90%-95% of patients developing clinical features, the penetrance is estimated to be very high [2]. The prevalence is considered to be 1-9/1,000,000 [9]; to date, only 663 affected families have been published [3]. However, due to a lack of awareness, the BHDS remains to be underdiagnosed. The typical clinical triad of BHDS consists of skin lesions, renal tumors, and lung cysts [4].

The skin lesions, including fibrofolliculomas, trichodiscomas, and acrochordons, usually become evident after the age of 20 years. They are predominantly located on the nose, cheeks, and the neck. However, up to 25% of affected patients do not show any skin manifestation [10]. The therapeutic approach of fibrofolliculoma and trichodiscoma consists of laser ablation with variable results [11].

Another manifestation of BHDS consists of renal tumors, which usually affect middle-aged and elderly patients [8]. The risk for developing renal cancer varies largely among previous studies, ranging from 6.5%-34% [12]. The predominant histological subtype is a hybrid tumor (chromophobe/oncocytoma), clear-cell carcinoma is less common. Nephron-sparing surgery is the method of choice

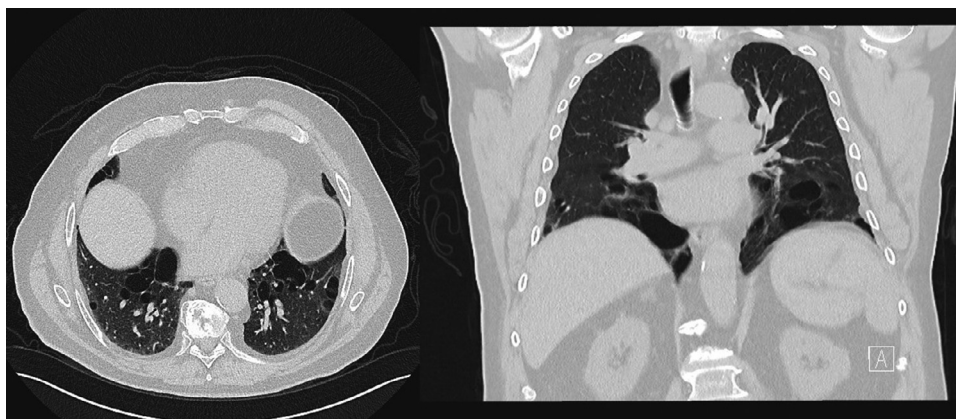


Fig. 2 – Contrast enhanced CT of the thorax showing multiple basally located pulmonary cysts.

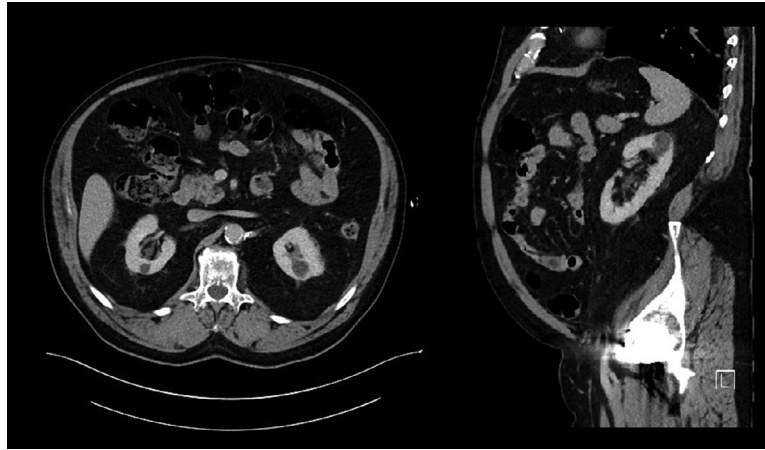


Fig. 3 – Contrast enhanced CT of the abdomen revealing several bilateral renal cysts.

for the treatment of solid nephric tumors with a diameter of more than 3 cm. Smaller lesions are usually monitored [13].

A very common feature of BHDS are lung cysts, with more than 80% of patients affected. Contrary to the typical apical location of cysts in emphysema or primary spontaneous pneumothorax [14], these cysts are frequently found in the basal regions of the lung. The number of cysts varies largely within the patients. The cysts are usually small, irregular-shaped and are often located adjacent to the pleural surfaces [15]. Pulmonary langerhans cell histiocytosis, amyloidosis, lymphoid interstitial pneumonia, and lymphangioliomyomatosis are differential diagnosis for lung cysts. The most common manifestation of pulmonary cysts is spontaneous pneumothorax. The mean age of occurrence of pneumothorax is in the third decade of life, with affected individuals having a 50-fold increase in the probability of developing a pneumothorax compared to the general population [14]. To reduce the recurrence rate, pleurodesis is usually performed after the second episode of ipsilateral pneumothorax [5]. Pneumothorax is usually diagnosed with a chest X-ray examination [6]. A subsequent thoracic CT examination is often needed to differentiate the underlying pathology of pneumothorax, as the detection of pulmonary cysts is extremely limited in chest X-ray examinations [16].

The skin lesions as well as the lung cysts do not necessitate periodical examinations [2]. However, due to the increased risk of renal malignancies, annual magnetic resonance examination of the kidneys is recommended as a screening examination. Ultrasonography of the kidneys has a too low sensitivity to detect small lesions, while periodical CT scans would result in an unacceptably high lifetime radiation dose [10].

The patient in our case report presented himself with pneumothorax, a typical clinical feature [5]. In the subsequent thoracic and abdominal CT scans, the pathognomonic features of predominantly basally located thoracic and kidney cysts could be revealed. Skin manifestation was not present, which occurs in up to 25% of affected patients [10]. Due to the rarity of the BHDS, the correct diagnosis of this syndrome is often delayed [14]. However, based on the typical morphological features, radiologists have the opportunity of establishing

BHDS as a differential diagnosis in a timely manner, enabling genetic testing and screening examinations [17].

Conclusions

BHDS is a rare genetical disease caused by a mutation in the FLCN gene. It consists of the typical triad skin lesions, pulmonary cysts and renal tumors. Pneumothorax is a common clinical manifestation. Therefore, including BHDS in the differential diagnosis of pneumothorax, pulmonary cysts and skin lesions is crucial, as these patients require life-long surveillance for renal tumors [4]. The diagnosis can be confirmed with genetic testing [2].

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