



Case report

Recurrent spontaneous pneumothorax in a patient with Birt–Hogg–Dubé syndrome[☆]

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Received 8 April 2010; received in revised form 1 June 2010; accepted 9 June 2010

Abstract

Recurrent spontaneous pneumothorax is a disorder often managed by thoracic surgeons. Most etiologies are benign in nature; however, there are several syndromes that are associated with potentially fatal pulmonary or systemic manifestations. One such example is Birt–Hogg–Dubé syndrome, a rare inheritable syndrome characterized by papular skin lesions involving the scalp, head, face and neck; pulmonary cysts; and a propensity to develop renal carcinoma. In our report, we describe a patient, who was diagnosed with Birt–Hogg–Dubé syndrome after presenting with a history of recurrent spontaneous pneumothorax, and a family history of spontaneous pneumothorax and renal cell carcinoma. This case is of particular interest to the cardiothoracic surgery community as the patient described as well as several of his family members were managed by multiple thoracic surgeons, who did not appreciate the diagnosis.

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Keywords: Birt–Hogg–Dubé syndrome; Spontaneous pneumothorax; Pulmonary cysts; Renal carcinoma; Skin lesion

1. Introduction

Birt–Hogg–Dubé syndrome was initially described as a dermatologic disorder characterized by multiple, dome-shaped, whitish papules located on the scalp, forehead, face, and neck [1]. Systemic manifestations are now recognized as components of this syndrome. Pulmonary cysts are the most common comorbidity and are present in up to 90% of those diagnosed with the syndrome [2]. Commonly subpleural in distribution, these cysts frequently result in spontaneous pneumothoraces [2], and the majority of these patients will suffer from multiple episodes [3]. Almost 25% of those diagnosed with the syndrome will also develop renal carcinomas [4]. Both pulmonary and cutaneous manifestations are more common and may precede the development of renal cancers, which provides the opportunity for clinicians to make the diagnosis and appropriately screen patients and family members for renal carcinoma.

2. Case report

A 41-year-old male nonsmoker presented to the emergency room with a history of progressive dyspnea for 2 days. Past medical history was significant for a right-sided spontaneous pneumothorax 9 years prior to presentation that was managed by video assisted thoracic surgery (VATS) blebectomy. Upon further questioning, a family history of renal cancer and spontaneous pneumothorax was discovered (Fig. 1). His initial vital signs were stable and his physical examination was unremarkable other than for several pale, dome-shaped, papules inferior to the brow, bilaterally (Fig. 2(A)).

A chest X-ray revealed bilateral pulmonary parenchymal cysts and a loculated right basilar pneumothorax. Concurrent chest computed tomography (CT) confirmed the presence of a moderate loculated right basilar pneumothorax and multiple, thin-walled, subpleural and intraparenchymal cysts ranging from <1 cm to 4 cm in diameter (Fig. 2(B)). A chest tube was inserted and the pneumothorax promptly resolved. The Department of Thoracic Surgery was consulted regarding pleurodesis, given the patient's previous history of spontaneous pneumothorax. At the time of thoracoscopic pleurodesis, multiple subpleural, thin-walled cysts were appreciated. The remaining lung parenchyma was normal in appearance.

Following the procedure, folliculin (*FLCN*) genetic testing was obtained, which confirmed the diagnosis of Birt–Hogg–

[☆] Support: Doris Duke Clinical Research Foundation research grant to Jarrold D. Predina and the Lavin Family Supporting Foundation.

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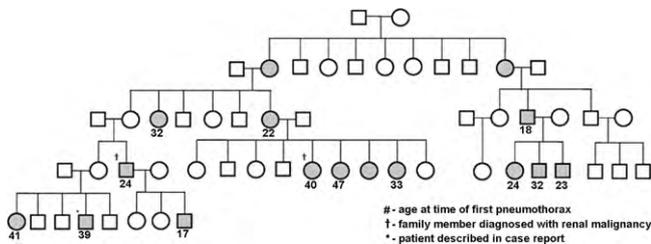


Fig. 1. Pedigree of patient's family with history of spontaneous pneumothorax. Inheritance pattern is autosomal dominant with evidence of incomplete penetrance, consistent with Birt–Hogg–Dubé syndrome.

Dubé syndrome. Additional CT of the abdomen and pelvis was performed and revealed no evidence of malignancy.

3. Discussion

Birt–Hogg–Dubé syndrome was initially described in 1977 as an autosomal dominant disorder characterized by multiple, dome-shaped, whitish papules located on the scalp, forehead, face, and neck [1]. Histology of the cutaneous lesions is consistent with fibrofolliculomas (skin tags), trichodiscomas, or acrochordons [5]. Dermatologic lesions are benign but, when prominent, may be cosmetically distressing. Effective permanent treatments do not exist.

It is now accepted that, other than the skin, the lung is the most commonly involved organ. More than 85% of patients will have findings of cystic lung disease, and these changes may precede dermatologic involvement [4]. Detection of pulmonary involvement can be made by CT scan of the chest [1]. Characteristic findings include the presence of bilateral cysts that are typically few in number, irregular in shape, variable in size, and often subpleural in distribution. In addition to Birt–Hogg–Dubé, syndrome the differential

diagnosis for these findings includes lymphangioleiomyomatosis (seen exclusively in women), Langerhans cell histiocytosis (seen almost exclusively in current and ex-smokers), and lymphocytic interstitial pneumonia (typically seen in association with Sjogrens or systemic lupus erythematosus). Almost 25% of Birt–Hogg–Dubé syndrome patients with lung pathology ultimately develop pneumothorax, often recurrent [4]. Treatment of the first episode should be conservative, involving observation or chest tube insertion. However, in the case of an initial pneumothorax requiring surgical intervention or recurrent pneumothoraces, we advocate the use of pleurodesis, as additional pneumothoraces are likely [4]. Although cyst biopsy may play a role in confirming other diagnoses for cystic lung disease, cyst biopsy should not be used solely to establish the diagnosis of Birt–Hogg–Dubé syndrome as lung pathology associated with the syndrome is nonspecific.

The most life-threatening complication of the syndrome is the development of renal cancer. The two most common variants include chromophobe renal carcinoma and renal oncocytoma [1]. Renal neoplasms are diagnosed in approximately 25% of those with the syndrome and maybe unilateral or bilateral. Because these malignancies develop after the third decade, annual surveillance with abdominal magnetic resonance imaging (MRI) or renal ultrasound should begin near the age of 20 years [1]. Patients with Birt–Hogg–Dubé syndrome have been diagnosed with multiple other tumors, but direct causality has not been proven [1].

The genomic abnormality resulting in Birt–Hogg–Dubé syndrome has recently been traced to the folliculin (*FLCN*) gene located on chromosome 17p11.2 [6,7]. The *FLCN* protein is a tumor-suppressor protein expressed in many tissues including the skin, lungs, and kidneys [7], and spontaneous mutations resulting in protein truncation have been described in families with the syndrome [8]. For patients with suggestive histories, *FLCN* mutation analysis confirms the diagnosis in the majority of cases [1]. An additional diagnostic criterion is the presence of five or more papules with at least one confirmed to be fibrofolliculoma or trichodiscoma [9].

Birt–Hogg–Dubé syndrome is a rare, autosomal dominant condition that should be considered in patients presenting with spontaneous pneumothorax and radiographic evidence of multiple pulmonary cysts. The presence of multiple papular skin lesions involving the head or neck, a past history of renal cancer, or a family history of pneumothorax, or renal malignancy, provides important diagnostic clues. When suspicious of the diagnosis, confirmation can be obtained using appropriate genetic testing or histological analysis of the skin lesions. Patients with Birt–Hogg–Dubé syndrome should subsequently undergo renal ultrasound or abdominal MRI, high-resolution CT of the chest, and genetic counseling.

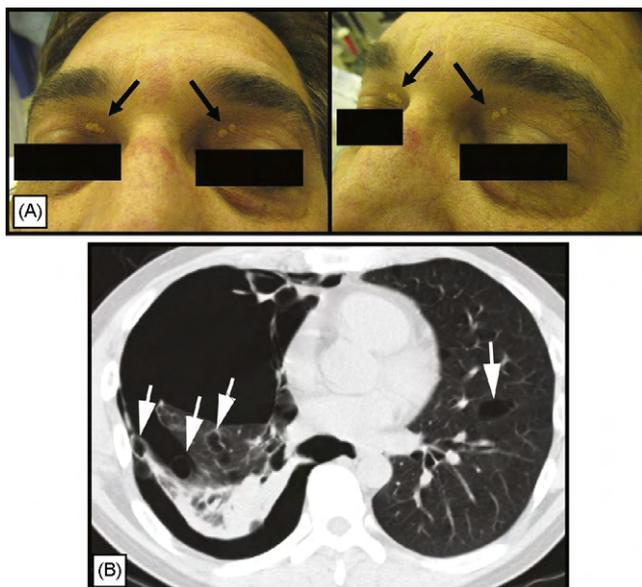


Fig. 2. (A) Multiple fibrofolliculomas located inferior to the brow (B) Computed tomography of the chest revealing a right pneumothorax, right lower lobe atelectasis and multiple bilateral thin-wall cysts. Findings are characteristic of Birt–Hogg–Dubé syndrome.

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