CLINICAL IMAGE

Familial pneumothoraces: Birt–Hogg–Dubé syndrome

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Cystic lung diseases constitute a significant proportion of rare disorders including tuberous sclerosis, lymphangioleiomyomatosis, alpha-1 antitrypsin deficiency, Ehlers–Danlos syndrome, Marfan syndrome, neurofibromatosis, amyloidosis, lymphoid interstitial pneumonia, Langerhans cell histiocytosis, and Birt–Hogg–Dubé syndrome (BHDS).

We present a case of a 54-year-old woman, a former smoker (1.5 pack/year), who was admitted to our department for evaluation of recurrent bilateral pneumothoraces. First, she experienced left-sided pneumothorax at the age of 34 years, which was treated with pleural drenage. The pneumothorax reoccurred 3 times during the same year. Four years later, she developed a right-sided pneumothorax, and pleurectomy was performed. In addition, she was surgically treated because of breast follicular fibroadenoma, uterine leiomyoma, and skin angiomyolipoma. Her sister, mother, and grandmother had recurrent pneumothoraces. On admission to the hospital, she was in good general condition. She had dyspnea on exertion and pain in the base of both lungs. The results of standard laboratory blood and urinary tests as well as alpha-1 antitrypsin levels were normal. A computed tomography scan showed multiple small, thin-walled cystic lesions, located mainly in the lower parts of both lungs (**FIGURE 1A** and **1B**). The results of pulmonary function tests were normal. The magnetic resonance imaging of the brain did not show any significant lesions, but a few liver and renal cysts were revealed in the abdomen. A genetic analysis revealed heterozygotic mutation c.469_471delTTC(p.Phe157del) in the folliculin (*FLCN*) gene. The clinical, radiological, and genetic examinations allowed a diagnosis of BHDS.

BHDS is an autosomal dominant inherited disease caused by mutations in the *FLCN* gene located on chromosome 17 p12-q11.2. *FCLN* functions as a tumor suppressor. BHDS is a very rare disease with about 600 reported families worldwide. It is characterized by skin lesions (fibrofolliculomas, trichodiscomas, perifollicular fibromas, and acrochordons), pulmonary cysts, pneumothoraces, and renal tumors.[1-5]

BHDS mainly affects adults, with first symptoms appearing between the age of 20 and 40 years. The most common first manifestations are skin lesions and pneumothoraces. The clinical presentation of BHDS varies widely, but 90% of patients were reported to develop skin or pulmonary lesions (or both); 25%, pneumothorax; and 30%, renal tumors. Familial pneumothoraces have been reported in 35% of patients.[3-5]

The age is inversely correlated with the development of a pneumothorax, and the median age at the first episode was reported to be 38 years (range, 22–71 years), without differences between sexes. The majority of patients (75%) had recurrent pneumothoraces. Pulmonary cysts have different sizes, from small to large, with irregular distribution, and are often located in the middle and lower parts of both lungs.[5] Such localization is characteristic of BDHS and discriminates it from a very common disease such as emphysema, in which cysts mainly occur in the upper lung lobes. Diagnosis is based on identification of the pathogenic mutations in the *FCLN* gene.

According to our best knowledge, this is the first case of BHDS reported in Poland, as the disorder is extremely rare and is rarely suspected by practitioners. A genetic assessment to confirm BHDS has only recently become available in Polish laboratories. The diagnosis of BHDS has additional consequences, as patients have 7 times higher risk for renal cancer and require regular ultrasound examinations of the abdomen.

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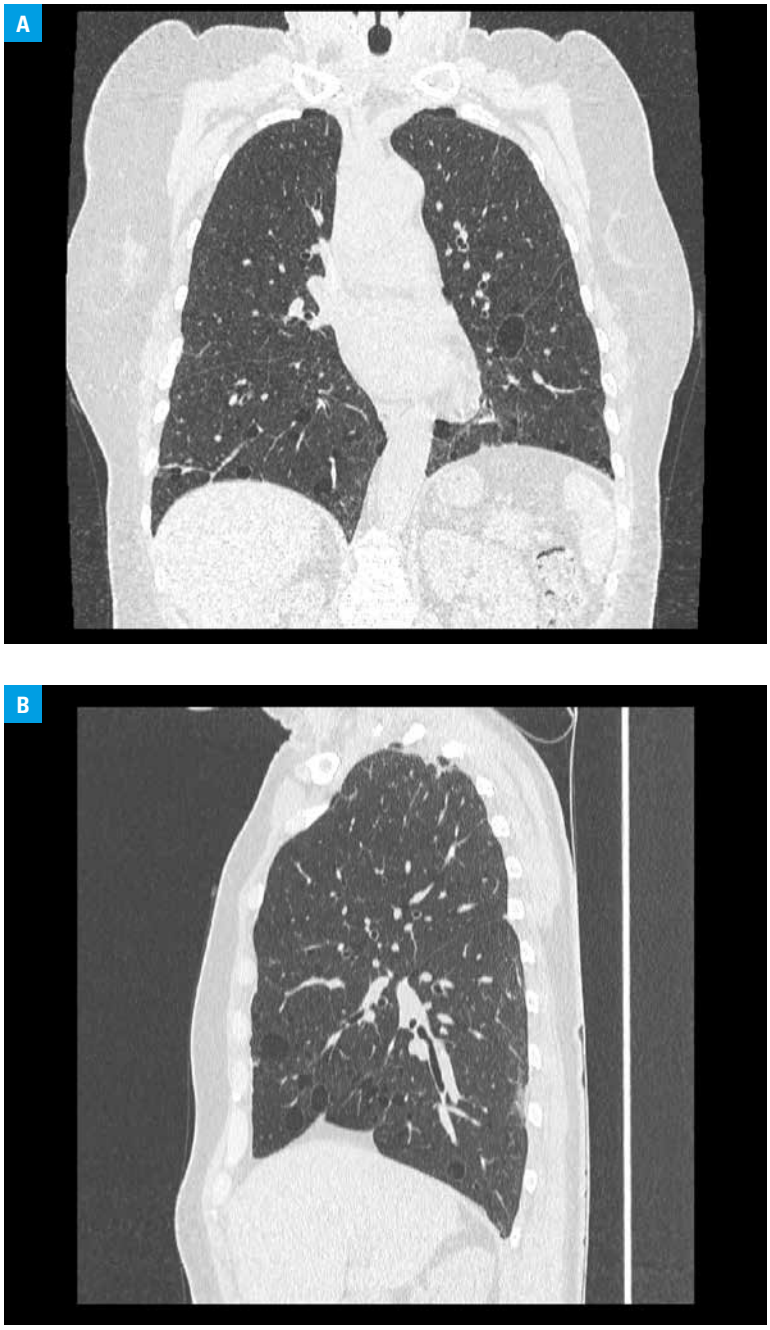

FIGURE 1 Computed tomography scans showing multiple small, thin-walled cystic lesions, located mainly in the lower parts of both lungs

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