Birt-Hogg-Dubé syndrome: A little known cause of pulmonary cysts

Keywords: Lung; Cysts; CT scan; Pneumothorax; Genodermatosis

Dermatologists are more familiar with Birt-Hogg-Dubé syndrome than radiologists are, since the cutaneous symptoms are the dominant feature of this rare syndrome. It is an autosomal dominant genodermatosis classically composed of multiple cutaneous hamartomas, renal tumours, and pulmonary cysts, which are often forerunners of spontaneous pneumothorax. It is rarely considered in the differential diagnosis of pulmonary cysts.

Case report

A 58-year old woman was referred for a thoracic scan to determine the cause of two episodes of spontaneous pneumothorax. Her previous medical history was relatively scant other than undiagnosed cutaneous anomalies that had appeared in adulthood, composed of colourless or yellowish papules disseminated over the face, neck (Fig. 1), torso, and limbs. She had been a moderate smoker, but had given up over 20 years previously.

The CT scan revealed cysts, which were primarily basal, in contact with the peripheral and mediastinal pleura, and along the bronchovascular axes (Fig. 2). These cysts were somewhat irregular, oval, or slightly polylobular, sometimes septate, and rarely round. There was no other parenchymal anomaly. The remainder of the thoracic examination was normal.

The family history revealed identical cutaneous lesions in the mother and daughter.

A thoracic scan performed in both her children aged 25 and 32 years old, also revealed cysts, these were less numerous but of identical morphology and topography (Fig. 3). None of the three family members had a renal tumour. Genetic blood tests performed in the mother confirmed the diagnosis of Birt-Hogg-Dubé syndrome.

Discussion

Birt-Hogg-Dubé syndrome was initially described in 1977 [1] as the association of three characteristic cutaneous lesions (fibrofolliculomas, trichodiscomas, and acrochordons). The first pneumothorax associated with these lesions was described in 1986 [2], and in 1993, renal cancer was reported in a patient with multiple fibrofolliculomas [3]. Many other pathological manifestations have been described in association with this syndrome: intestinal polyposis, parathyroid adenoma, parotid oncocytooma, meningioma, lipoma, etc. [4–6].

It is currently acknowledged that the classic presentation of this syndrome comprises a combination of cutaneous fibrofolliculomas, pulmonary cysts, and occasionally multiple benign or malignant renal tumours.

The gene associated with this disease, known as the FLCN gene, was first identified in 2001 [7]. It is located on chromosome 17p11.2 and codes the synthesis of a protein known as folliculin, which is expressed in the skin, nephrons, and epithelium of pulmonary alveoli.

This rare syndrome has no gender or racial predisposition. The cutaneous lesions appear during the 3rd or 4th decade of life. Fibrofolliculomas are small, asymptomatic, flesh-coloured or yellowish papules of 2 to 4 mm in diameter. The risk of developing a renal tumour is seven times greater than in the general population. The types of
tumour are variable, and include, in decreasing order of prevalence, hybrid tumours associating chromophobe and oncocytic components, chromophobe renal cell carcinoma, clear cell renal cell carcinoma, oncocytomas, and papillary carcinomas [8].

Nearly 80% of patients have pulmonary cysts [9], with no reduction in pulmonary function. These cysts usually precede the onset of cutaneous and renal lesions, which may enable early diagnosis of the disease, as with the patient’s son in this case. The mechanism for the development of these cysts is unclear. They are bilateral, diffuse, but predominantly basal. Their shape is variable, often oval or polylobular. The largest cysts usually develop in the pulmonary bases and may be multiseptate. These cysts often

Figure 2. Axial sections (a and b) and Minip coronal reconstruction (c) showing the primarily basal, sub-pleural, and peribronchiovascular distribution of the cysts and their variable size.

Figure 3. CT sections of the patient’s son (a and b) and daughter (c and d) showing irregular, predominantly basal cysts, less numerous than in the mother.
trigger pneumothorax (24 to 38% of cases) with a mean age at onset of 38 years.

The main differential diagnosis for isolated pulmonary cysts is lymphangioleiomyomatosis, where the cysts are usually round with a more homogenous and diffuse distribution, and with no caudocranial predominance [10]. Other cystic pulmonary diseases that should be considered include cystic metastases, Langerhans cell histiocytosis, lymphocytic interstitial pneumopathy, Sjögren’s syndrome, amyloidosis, and light-chain deposition disease.

To date, there is no treatment for this disease, but the advantage of an early diagnosis is in the instigation of screening for renal tumours. If this syndrome is suspected, a full family and genetic history should be taken owing to the autosomal dominant nature of its transmission and the fact that cutaneous symptoms are often absent, subtle, or late onset. This case illustrates the presence of pulmonary lesions in other members of the family, probably at an early stage of the disease.

Other circumstances that are evocative of this diagnosis include the association of pulmonary cysts and renal tumours and a family history of pneumothorax or pulmonary cystic disease.

Disclosure of interest

The authors declare that they have no conflicts of interest concerning this article.

References


P. Ardilouze a,b, J. Jacquin c, T. Ait Ali c, S. Schneider c

a Pôle imagerie, centre hospitalier de la Côte-Basque, 13, avenue de l’Intégration Jacques-Loëb, 64100 Bayonne, France
b Pôle imagerie, CHU de Bordeaux, place Amélie-Raba-Léon, 33000 Bordeaux, France
c Service de pneumologie, centre hospitalier de la Côte-Basque, 13, avenue de l’Intégration Jacques-Loëb, 64100 Bayonne, France

* Corresponding author.

E-mail address: p.ardilouze@gmail.com

(P. Ardilouze)