CASE OF THE MONTH

Characteristic CT appearance of lung cysts prompting the diagnosis of a rare genodermatosis

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Clinical history

A 75-year-old male presented to the emergency department with severe chest pain. The patient had never smoked and had a long-standing skin disorder. Physical examination revealed multiple small skin-coloured papules on his face, chest and back.

A CT angiogram was performed, which excluded aortic dissection and pulmonary embolus.

However, incidental pulmonary findings were found (Figure 1).

Based on these images, what is your differential diagnosis?

What is your best diagnosis given the clinical history and physical exam findings?

Given this diagnosis, what other organ might be abnormal?

Figure 1. (a) Axial CT image at the level of upper lobes showing two small thin-walled cysts (arrows). (b) Multiple cysts of varying sizes are shown, the largest of which are seen in left lower lobe anterior along inferior major fissure. Cysts on either side abut and encase lower lobe pulmonary artery branches (arrows). Intervening lung parenchyma is normal. (c) Coronal image reconstruction shows multiple peripheral cysts with a medial basilar predominance (arrows).

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Findings

A chest CT scan demonstrated multiple round and oval thin-walled pulmonary cysts of varying sizes with a medial-basilar predominance (Figure 1). The cysts measured 0.5–4.5 cm in diameter. Some of the cysts abutted the proximal portions of lower pulmonary arteries and veins, while others were located along the pleura, particularly the fissures. Only a few small cysts measuring 0.5–1.5 cm were present in the upper lobes. The lung parenchyma between the cysts was normal. The visualised portions of the kidneys were normal.

Diagnosis

The chest CT scan findings in an elderly lifelong non-smoker with small skin-coloured papules were highly suggestive of Birt–Hogg–Dubé Syndrome (BHDS). This prompted dermatological re-evaluation of the patient. Skin biopsies revealed a fibrofolliculoma (Figure 2), which confirmed the diagnosis of BHDS.

Discussion

The main differential diagnosis considerations for this case of pulmonary cystic disease includes pulmonary lymphangioleiomyomatosis (LAM), pulmonary Langerhans cell histiocytosis (PLCH), lymphocytic interstitial pneumonitis (LIP), *Pneumocystis jirovecii* (carinii) pneumonia (PCP) and BHDS. In this case, all of these diagnoses except BHDS can be excluded on the basis of imaging and/or clinical grounds.

LAM is a rare disease that occurs almost exclusively in women. It is characterised on chest CT scans by round,

thin-walled cysts of variable size and contour, and is uniformly distributed throughout the lungs. PLCH typically affects younger adults in their third to fourth decade of life, and are typified by irregular-shaped cysts and peribronchiolar upper lung predominant nodules. LIP is a rare benign lymphoproliferative disorder, which is associated with autoimmune diseases, such as Sjogren's disease and human immunodeficiency virus (HIV). LIP typically manifests on CT with areas of ground-glass attenuation and interlobular septal thickening with scattered thin-walled cysts seen in 50% of patients. PCP can present radiologically as diffuse thin-walled cystic lesions [most often in acquired immune deficiency syndrome (AIDS) patients] with associated ground-glass opacities or interlobular septal thickening.

BHDS is a rare genodermatosis affecting multiple organ systems with autosomal dominant inheritance that was originally characterised by the dermatological triad of fibrofolliculomas, trichodiscomas and acrochordons [1], which are now believed to represent different histological sections of the same lesion. These skin lesions are seen clinically as multiple skin-coloured dome-shaped papules involving the head, neck, chest, back and arms. BHDS is diagnosed dermatologically in patients who have at least five facial or truncal papules and at least one histologically confirmed fibrofolliculoma [2]. BHDS patients do not always have skin findings and may have pulmonary and/or renal manifestations.

The CT appearance of lung cysts in BHDS has been well characterised. Recently, Tobino et al [3] demonstrated BHDS patients typically have multiple thin-walled pulmonary cysts of various sizes predominantly in lower medial and subpleural regions of the lung with the universal presence of cysts that either abutted to or encase the proximal portion of lower pulmonary vessels. Cyst shapes were most commonly irregular. Varying sizes of cysts were found in each patient with the largest cysts in the lower medial lung. Cysts that bordered pleural spaces were also noted to commonly be large and irregular.

BHDS patients with pulmonary involvement may present with spontaneous pneumothorax. Toro et al [4] demonstrated that the incidence of spontaneous pneumothorax correlated with the number of lung cysts, total lung cyst volume, largest cyst volume and largest cyst diameter. Smoking was not found to be a risk factor for the development of pneumothorax in this population.

Renal tumours are the least common BHDS manifestation affecting 29–34% of patients [5]. The majority of renal masses associated with BHDS present at an older age than other hereditary renal tumours (median age, 48 years) and are of less aggressive pathology with chromophobe, oncocytoma, clear cell and hybrid oncocytic tumours comprising the majority of neoplasms. Nonetheless, since renal tumours are seven times more likely in BHDS patients than in their unaffected siblings and are most often bilateral and multifocal, screening for renal masses is recommended [5, 6]. One set of guidelines [5] recommends a baseline CT or MRI with contrast at time of diagnosis, which if negative, can be followed by CTs or MRIs every 2–3 years. If the patient has two negative CTs or MRIs and no family history of renal cancer, an ultrasound could be used to screen patients instead.

Figure 2. A papule from the patient's right posterior auricular area was biopsied, and pathology shows a fibrofolliculoma. Note the finger-like projections from a dilated follicle extending into a fibrotic stroma.

Conclusion

While the dermatological manifestations of BHDS can be classic, they are not universal. Thus, it is important for radiologists to be familiar with this syndrome as it can present with either pulmonary findings (lung cysts or spontaneous pneumothorax) or renal masses. The institution of a screening program for BHDS patients is paramount to preventing a life-threatening renal malignancy or renal failure.

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