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Case Report

Radiology Section

More than Just a Pneumothorax: Unmasking Birt-Hogg-Dubé Syndrome through the Lungs

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ABSTRACT

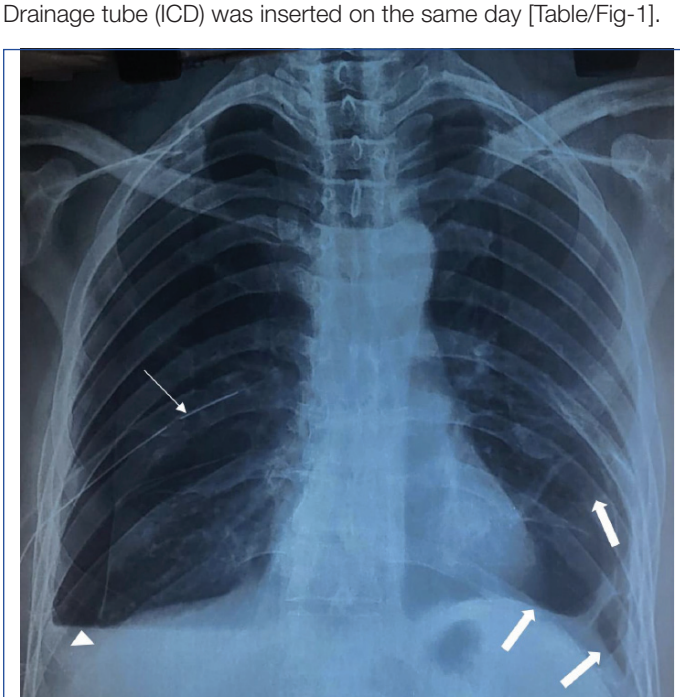
Birt-Hogg-Dubé (BHD) syndrome is a rare autosomal dominant disorder caused by pathogenic mutations in the FLCN gene located on chromosome 17p12q11.2. It is characterised by cutaneous fibrofolliculomas, pulmonary cysts often associated with spontaneous pneumothorax, and an increased risk of renal neoplasms. The pulmonary features, particularly the pattern and morphology of cysts on CT, are key diagnostic clues in differentiating BHD from other cystic lung diseases. We report a case of a 34-year-old male presenting with dyspnoea and right-sided pneumothorax. Imaging revealed bilateral variable-sized cysts predominantly in the lower lobes, paramediastinal and perifissural locations, with intervening normal lung parenchyma. Dermatological examination showed multiple fibrofolliculomas, while genetic testing identified a heterozygous pathogenic FLCN variant, confirming BHD. The presence of basal lung cysts or pneumothorax with skin lesions should prompt genetic testing at the earliest, as early diagnosis not only helps in timely surveillance of renal lesions but also enables screening and management for at-risk family members.

Keywords: Cystic lung disease, Fibrofolliculomas, HRCT thorax, Radiology

CASE REPORT

A 34-year-old male presented to the emergency department with dyspnoea on exertion grade I-II for 25 days. There was no history of trauma, cough, haemoptysis, fever, or palpitations. No history of previous similar episodes or known comorbidities was noted. There was no history of smoking, family history of pneumothorax, renal cancer or fibrofolliculomas. Patient denied all other addictions. Patient was conscious, oriented and vitally stable at the time of presentation. Complete blood count results were unremarkable.

A chest X-ray PA view was performed, which revealed right sided pneumothorax. The patient was admitted, and an Intercostal Drainage tube (ICD) was inserted on the same day [Table/Fig-1].



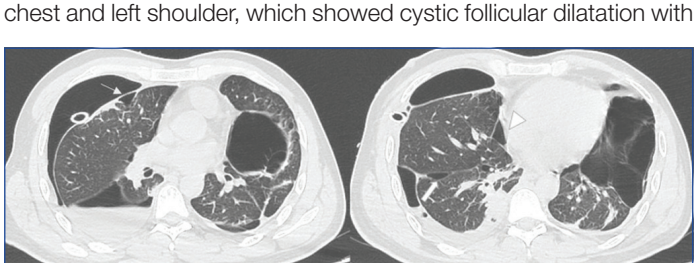
[Table/Fig-1]: Chest X-ray PA view showing right-sided hydropneumothorax (arrowhead) with ICD noted in situ (thin white arrow). Few varying sized well defined cystic lesions are noted in left lower zone (thick white arrows).

Clinical examination revealed numerous small dome-shaped skin-coloured papules on the neck, as well as multiple non-tender lesions scattered over the chest, abdomen, and extremities, not increasing in size [Table/Fig-2]. A few small skin tags were also seen.

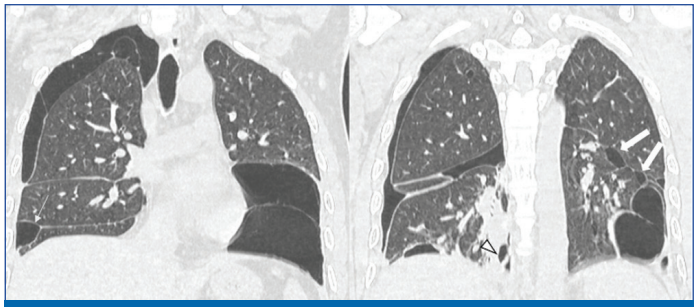
[Table/Fig-2]: Numerous small dome-shaped skin coloured papules on the neck and chest (thick white arrows).

The CT imaging revealed moderate right-sided hydropneumothorax with a few septae of variable thickness within, and ICD was seen in situ. Multiple varying-sized thin-walled cysts, few of them showing thin septae within were seen in intraparenchymal and subpleural (including paramediastinal and perifissural) location in bilateral lower lobes [Table/Fig-3-5]. However, visualised kidney sections revealed no evidence of any focal lesion.

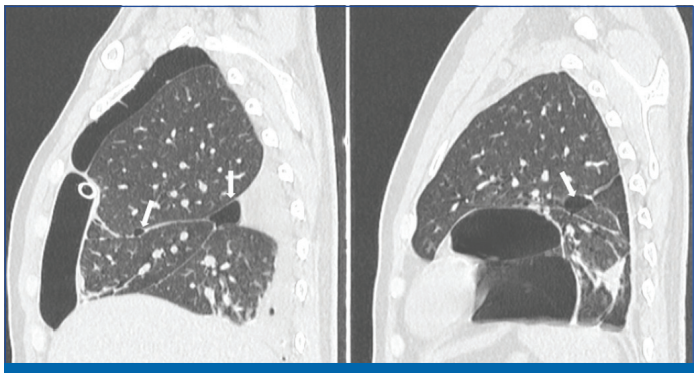
Further skin biopsy from a skin-coloured papule was taken from the chest and left shoulder, which showed cystic follicular dilatation with



[Table/Fig-3]: High Resolution CT (HRCT) axial sections in lung window showing moderate right sided hydropneumothorax with ICD in situ and multiple varying sized thin-walled cysts in subpleural (thin arrow), paramediastinal (arrowhead) and perifissural (thick arrow) location in bilateral lower lobes.

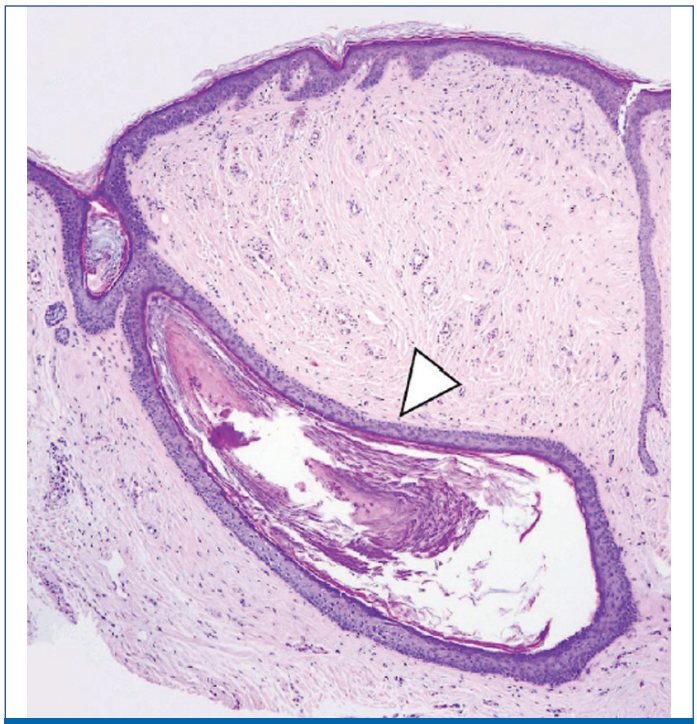


[Table/Fig-4]: High Resolution CT (HRCT) coronal sections in lung window showing multiple varying sized thin-walled subpleural (thin arrow), paramediastinal (arrowhead) and perifissural (thick arrow) cysts in bilateral lower lobes with normal intervening lung parenchyma.



[Table/Fig-5]: High Resolution CT (HRCT) sagittal sections in lung window showing multiple varying sized thin-walled perifissural (arrows) cysts in bilateral lower lobes with normal intervening lung parenchyma.

keratinous material, elongated thin strands of basaloid epithelial cells surrounding the cyst, along with fibrous stromal proliferation peripheral to it suggestive of fibrofolliculoma [Table/Fig-6].



[Table/Fig-6]: Histopathological image of fibrofolliculoma showing cystic dilatation of follicle (arrowhead).

Patient underwent ICD insertion for pneumothorax, and once the pneumothorax resolved, ICD was removed, and the patient was kept on follow-up ultrasound abdomen every six months. Furthermore, he was counselled regarding screening of family and avoiding activities like air travel and scuba diving, which would increase the risk of pneumothorax. He subsequently underwent genetic testing. Analysis revealed a pathogenic variant in the FLCN gene, FLCN c.285T>A (p.Tyr95Ter) heterozygous, confirming the diagnosis of BHD syndrome.

DISCUSSION

The BHD syndrome is a rare, often underdiagnosed, genetic disorder having an autosomal dominant inheritance with a deletion mutation in the Folliculin (FLCN) gene located on the short arm of chromosome 17 (17p12q11.2) [1].

It primarily presents with skin lesions known as fibrofolliculomas, pulmonary cysts, and a significantly increased risk of spontaneous pneumothorax-occurring in up to 38% of cases with a recurrence rate that warrants pleurodesis after the first episode [2]. Another major concern is the elevated risk of renal tumours, often malignant, with chromophobe and oncocytic types being most common. These renal manifestations may be multifocal or bilateral, and their detection should prompt evaluation for BHDS.

Agarwal PP et al., characterised the thoracic manifestations of BHD syndrome, noting that lung cysts in this population are typically thin-walled, lower-lung predominant, and bilateral. Their analysis of 17 patients revealed that BHD cysts often vary in shape, ranging from lentiform to multiseptated, with the larger cysts consistently found at the lung bases [3]. Sane IA et al., reported a case of BHD syndrome where spontaneous pneumothorax served as the primary clinical indicator, and CT identified characteristic thin-walled pulmonary cysts with a clear preference for the subpleural, basilar, and mediastinal lung zones [4].

Importantly, the surrounding lung parenchyma was normal in both studies [3,4] and there was no evidence of cyst progression over time. The distinct imaging characteristics are of diagnostic significance, especially in differentiating BHD from other cystic lung diseases such as Lymphangioleiomyomatosis (LAM), Langerhans Cell Histiocytosis (LCH), and emphysema [5,6]. The findings support the utility of chest CT as a non-invasive screening tool for BHD, particularly in patients with spontaneous pneumothorax or atypical cystic lung disease.

According to Stamatakis L et al., management of BHD remains largely preventive, with a focus on early detection of renal tumours-the most life-threatening aspect of the syndrome [7]. Renal cancer associated with BHD is often multifocal or bilateral and includes characteristic oncocytoma or chromophobe renal cell carcinoma. Surveillance using annual MRI is recommended starting from the age of 20 years, with nephron-sparing surgeries favored to preserve renal function [1,7]; however, this is not always possible in limited-resource settings. Once renal tumours are identified, they should be followed with interval imaging studies until the largest tumour reaches 3 cm in maximal diameter, at which point nephron-sparing surgery should be ideally pursued [7].

CONCLUSION(S)

Recognising BHD syndrome early is important for referring physicians, as the management is mostly preventative. Patients often present with common symptoms like chest pain or dyspnoea on exertion, which can be due to an undiagnosed pneumothorax. However, these symptoms may overshadow other subtle signs like skin lesions or renal malignancies. General practitioners and physicians play a key role by staying alert to these subtle clues, referring patients for dermatological evaluation and appropriate radiological investigations.

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