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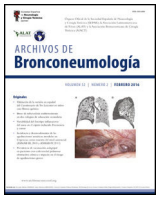

Clinical Letter

Pneumomediastinum as an Early Manifestation in Birt–Hogg–Dubé Syndrome

To the Director,

Birt–Hogg–Dubé syndrome (BHDS) is a rare, multiorgan disorder that results from a pathogenic variant in the folliculin-encoding gene *FLCN*.[1] Some cases may be diagnosed before significant organ involvement.

A 22-year-old male who began evaluation in a familial interstitial lung disease program since he carried the same *FLCN* likely pathogenic canonical splicing gene variant (NM_144997.7:c.1177-1G>A) as his grandmother, mother and uncle. He had no fibrofolliculomas, kidneys were normal, and a chest computerized tomography (CT) was reported as normal. He presented to the Emergency department six months later with a four-day history of swelling of the neck and anterior thorax, with crackling of the skin. A thoracic CT scan (Fig. 1) revealed extensive subcutaneous emphysema and pneumomediastinum; posterior analysis revealed a pericentimetric cyst in the lower left lobe (LLL; Fig. 1). He was conservatively managed and discharged four days later. A CT scan performed eight months later showed resolution of pneumomediastinum, with the cyst in the LLL present, slightly enlarged, as well as other smaller, lenticular, thin-walled cysts. A retrospective analysis of the initial CT scan through a careful reconstruction identified that cyst was already present. The patient is currently asymptomatic and follows regular functional and radiological controls.

BHDS is a rare autosomal dominant monogenic disorder, caused by pathogenic variants in the *FLCN* gene. It is characterized by the development of skin fibrofolliculomas, lung cysts and renal cancer.[1,2] Although the increased risk of pneumothorax is well established, the occurrence of pneumomediastinum is not,[1] with only one previously published case of pneumomediastinum in a patient with BHDS.[1] Initial lung screening did not identify cysts and only a revision with image reconstruction identified a cyst next to an incomplete fissure, which could have caused the pneumomediastinum. This suggests that patients with BHDS may be at risk of cystic rupture, independently of their number or location, as the cysts are likely to progress in number and size. It is interesting to note that, although he is the youngest known carrier in the family, our patient was the first to present an acute event related to BHDS.

A literary review attempted to establish recommendations for management of BHDS, stating that there is no clear indication for routine CT follow-up.[3] While there may not exist clear indications (especially due to the small number of patients), the importance of performing follow-up CT scans should be tailored and may be adequate in selected cases. There is currently no approved therapy for the treatment or prevention of cystic lung disease in BHDS; therefore, all carriers of pathogenic *FLCN* variants should be informed of their increased risk for complications such as pneumothorax and pneumomediastinum. The authors believe that patients should be given behavioral recommendations, regardless of disease severity, such as avoiding diving, high altitudes, smoking and chest trauma.

In conclusion, our case highlights the need for a proactive approach in monitoring and preventive awareness even without clear cystic disease. Regular thoracic imaging could be crucial in detecting early cyst formation and could be used to monitor disease evolution; it remains uncertain whether it could prevent life-threatening events. There is a need to revisit current guidelines and consider personalized management strategies.

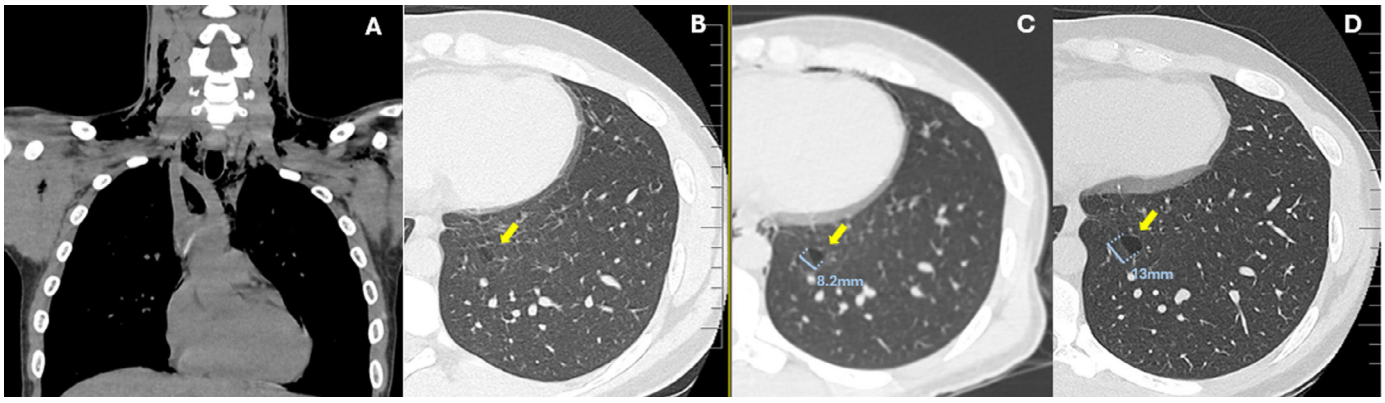

Fig. 1. (A) Thoracic computerized tomography scan (coronal view) showing pneumomediastinum and subcutaneous emphysema; (B–D) Thoracic computerized tomography scans showing a cyst in the lower left lobe (yellow arrows), performed eight months before pneumomediastinum (B), during the pneumomediastinum episode (C) and eight months after (D).

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Conflicts of Interest

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Artificial Intelligence Involvement

None of the material was produced with influence from any artificial intelligence software or tool.

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