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An Unusual Combination of Diffuse Pulmonary Cysts and a Nodule



Una combinació infreqüent de quistes pulmonars difusos i un nòdul

Dear Editor:

A 59-year-old asymptomatic woman was referred to our outpatient clinic to investigate a diffuse cystic lung disease (DCLD) incidentally found on abdominal computed tomography (CT). Her past medical history revealed obstructive sleep apnea and Paget disease, for which she used zoledronic acid. She denied smoking and had no relevant exposure. Physical examination was normal and her peripheral oxygen saturation was 98% on room air. Chest high-resolution CT (HRCT) revealed multiple thin-walled pulmonary cysts diffusely distributed in both lungs and a 10 mm ground-glass nodule in the right upper lobe (Fig. 1). Pulmonary function tests (PFTs) showed normal spirometry, air trapping (RV, 166% of predicted; RV/TLC ratio, 0.51) and a mild reduction in DLCO (60% of predicted). Serum markers of inflammatory activity, protein electrophoresis, alpha 1 antitrypsin serum dosage were normal, and antinuclear antibodies, rheumatoid factor, anti-Ro/SSA and anti-La/SSB were negative. The serum level of vascular endothelial growth factor-D was 407 pg/mL and abdominal ultrasound and scintigraphy of salivary glands were normal. She refused to

undergo a surgical lung biopsy for diagnostic elucidation. The nodule remained stable during the follow-up.

After 5 years of follow-up, PFTs were stable and there was an increase in the nodule size (13 mm), with a solid composition (Fig. 1). There was a mild increase of glycolytic metabolism (SUV 2.6) on the combined positron emission tomography/CT. There was no evidence of lymph node enlargement or extrapulmonary disease. A right upper lobectomy with lymphadenectomy was performed after an adenocarcinoma has been confirmed in the intraoperative frozen section. Histopathological analysis revealed a predominantly acinar invasive adenocarcinoma, with lepidic and micropapillary components, which was classified as Stage IA (T1aN0M0). The lung parenchyma around the tumor revealed a heterogeneous small airway disease characterized by variable narrowing of the small airways, abnormal bronchioles with subepithelial fibrosis and scattered chronic inflammatory cells, associated with peribronchiolar alveolar overdistension, which was consistent with constrictive bronchiolitis (Fig. 1).

The differential diagnosis of DCLD is broad and establishing a definite diagnosis may be challenging. Although chest HRCT has substantially contributed to the approach of DCLD, lung biopsy may be necessary to confirm the etiology.^{1,2} Constrictive bronchiolitis is rarely included in the differential diagnosis of DCLD, but it is a potential etiology.^{1,2} The proposed physiopathology involved is a bronchiolar check-valve mechanism, with air trapping and distension of distal airspace resulting in cysts formation.³ Our case

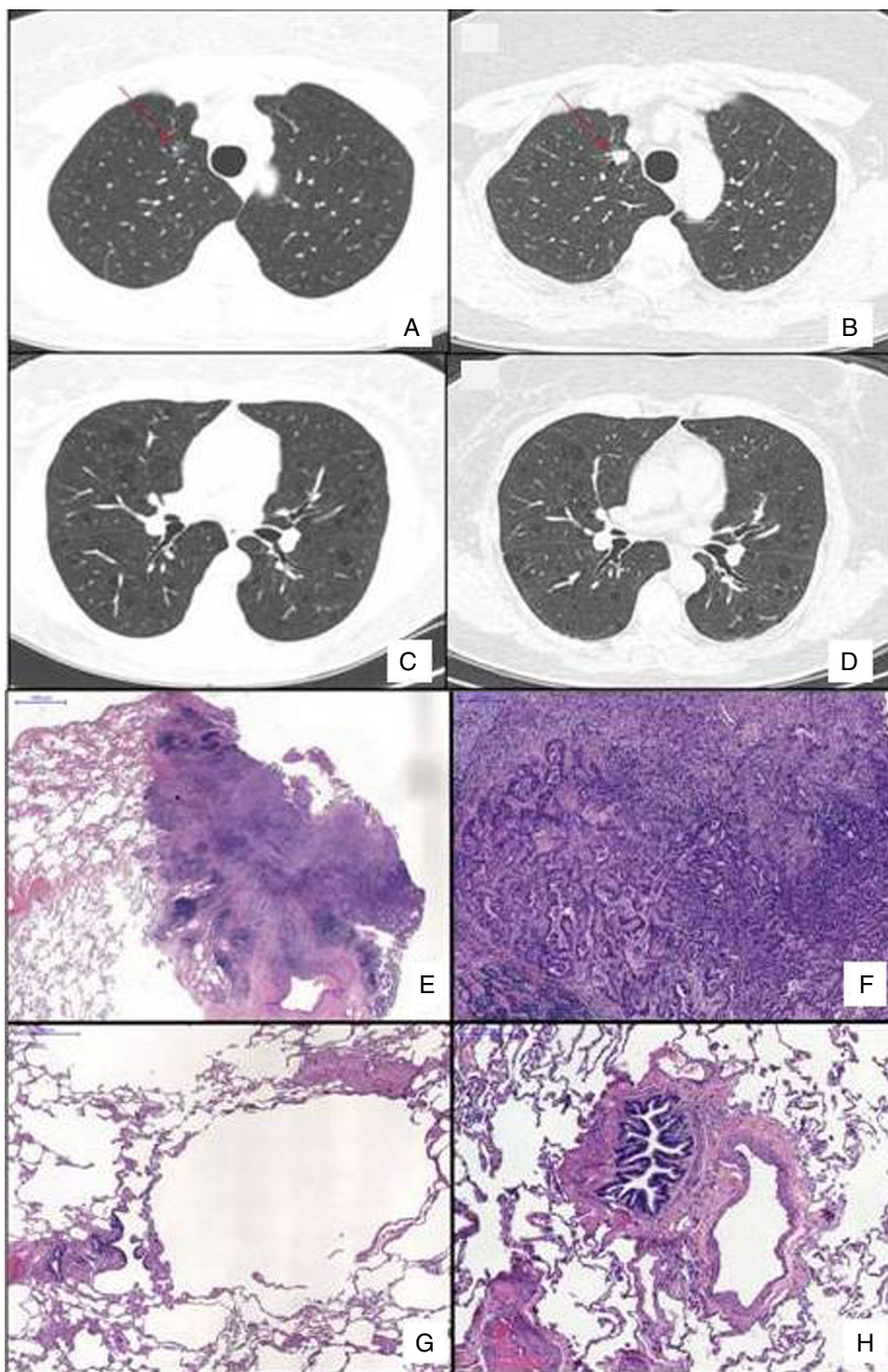


Fig. 1. Chest HRCT scans showing diffuse cystic lung disease and a solitary pulmonary nodule (red arrow) in the beginning of follow-up (A and C) and five years later (B and D). (A) Regular and thin-walled pulmonary cysts and a 10 mm pure ground-glass nodule in the right upper lobe. (B) CT image at the same level as Fig. 1A after five years of follow-up showing a significant increase in the size of the nodule (13 mm) and change in its composition (a solid nodule). (C) Random and multiple thin-walled cysts. (D) Stability of diffuse pulmonary cysts five years later. (E) A low-power view of the tumor with a dense area of scarring. (F) Invasion area with desmoplastic tissue, irregular glands and micropapillae. (G) Constricted airway and peribronchiolar alveolar overdilation. (H) Bronchiole with submucosal fibrosis and focal inflammatory cell infiltrate. (H&E stains, original magnification (A) $\times 10$, (B) $\times 50$, (C) $\times 40$ and (D) $\times 100$).

corroborates such hypothesis, supported by the finding of downstream hyperdistension of distal airways and alveolar spaces.

One may also speculate about the relationship between the small airway disease and the incidental lung cancer. The initially detected ground glass opacity was compatible with a spectrum of early neoplastic or pre-malignant lesions comprising atypical

adenomatous hyperplasia, adenocarcinoma in situ and minimally invasive adenocarcinoma, which progressed to a solid nodule, proven to be an invasive adenocarcinoma. Early genetic or epigenetic changes leading to altered function or aberrant cellular pathways, thought to develop through lung tissue injury, are recognized as precursors of premalignant changes, such as cell

metaplasia/dysplasia or clonal patches.⁴ We speculate that the molecular changes in the airway epithelium of an affected bronchiole in the context of constrictive bronchiolitis might account for the increased risk of developing non-small-cell lung carcinoma in our patient, although this association requires further confirmation. In conclusion, constrictive bronchiolitis should be included as a differential diagnosis of DCLD and it is speculated that it may determine an increased risk of lung cancer.

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Calcified Pulmonary Nodules in an Oncological Patient



Nódulos pulmonares calcificados en un paciente oncológico

Dear Director:

A 50-year-old female patient underwent thoracic and abdominal computed tomography examinations for oncological follow-up.

The images showed multiple lung nodules, some of which were calcified (Fig. 1A and B), a calcified hepatic mass, and an expansile osteolytic lesion with internal foci of calcification on the ischiopubic ramus of the right hip (Fig. 1C). The patient had undergone colonoscopy 3 years previously due to rectal bleeding, which showed an exophytic and stenosing rectal lesion. The biopsy findings were compatible with well-differentiated tubular adenocarcinoma. Surgical resection confirmed the anatomopathological

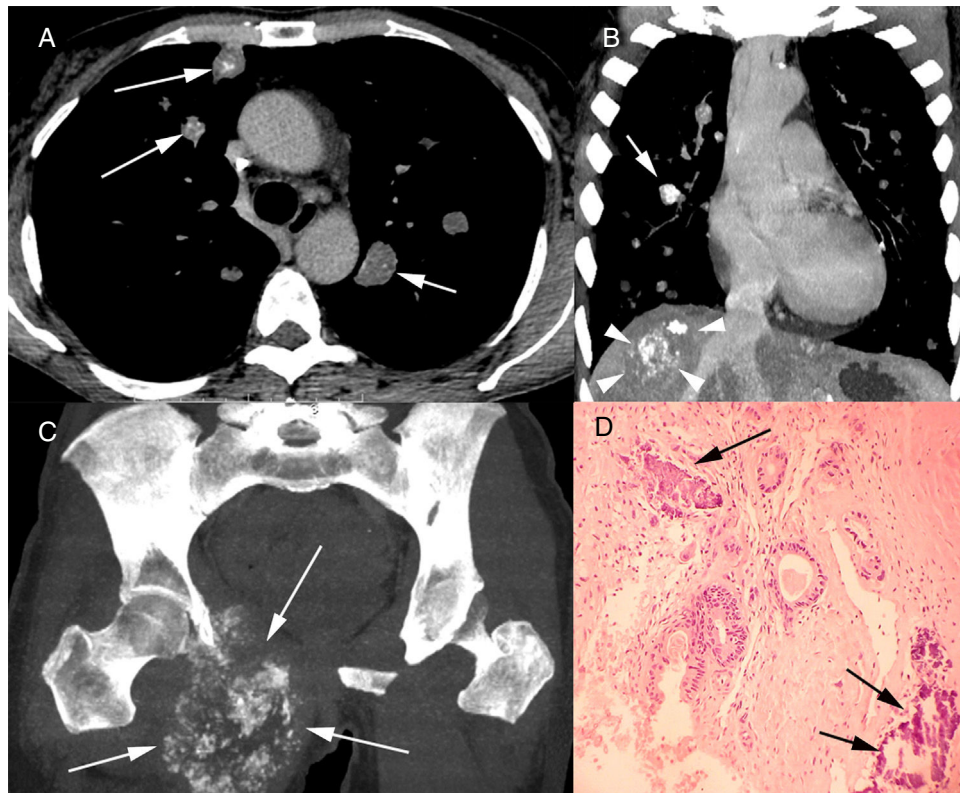


Fig. 1. Chest computed tomography with axial (A) and coronal (B) reconstruction showing multiple pulmonary nodules, some with calcification (arrows). Note also in B a calcified mass in the right lobe of the liver (arrowheads). In C, computed tomography of the pelvis with coronal acquisition MIP reconstruction, showing an osteolytic lesion with internal foci of calcification (arrows) and invasion of surrounding soft tissue. In D, histological section of the pulmonary nodule demonstrating atypical neoplastic glands infiltrating the connective tissue amid desmoplastic stroma. Note also the amorphous basophilic material, compatible with extracellular deposition of calcium adjacent to the neoplastic process (arrows; hematoxylin and eosin stain, ×100).