Radiological Diagnosis of Pulmonary Tumor Thrombotic Microangiopathy: A Non-bronchial Cause of «Tree-in-Bud» Pattern on Computed Tomography

Diagnóstico radiológico de microangiopatía trombótica tumoral pulmonar: una causa no bronquial de patrón de «árbol en brote» en tomografía computarizada

Dear Editor,

Pulmonary tumor thrombotic microangiopathy (PTTM) is a rare and generally fatal form of pulmonary tumor embolism that generally presents with rapidly progressing dyspnea in patients with disseminated malignant disease. Clinical diagnosis is difficult, and unfortunately PTTM is generally only confirmed post mortem.1,2

We report the case of a 58-year-old man, former smoker (20 pack-years), who presented with a 2-week history of progressive dyspnea and dry cough. Significant clinical history included prostate adenocarcinoma (Gleason score 6), treated with radiation therapy with curative intent 6 years previously, with no biochemical evidence of tumor relapse. Clinical examination revealed tachypnea and fine crackles on auscultation. Basal oxygen saturation was 88% and laboratory test findings did not suggest infection, although D-dimer levels were elevated. A chest radiograph showed bilateral diffuse interstitial involvement and prominent lung hila. Chest CT angiogram ruled out embolism on the main pulmonary, lobar or segmentary arteries, although multiple mediastinal and hilar lymphadenopathies were detected, along with severe interstitial involvement consistent with thickening of the subpleural pulmonary interstitium (Fig. 1A) and the presence of numerous centrilobular nodules and “tree-in-bud” images (Fig. 1B and C).

Multiple focal bone lesions, predominantly sclerotic, were also observed in the vertebrae and sternum, consistent with metastasis (Fig. 1D). Given these radiological findings, PTTM secondary to prostate adenocarcinoma was suggested as an initial diagnosis, although other possibilities such as sarcoidosis or infection with an unusual pathogen were not ruled out. Four days after admission, the patient developed rapidly progressing respiratory failure that required urgent intubation. A few hours later, he suffered an episode of cardiorespiratory arrest with asystole and died despite prolonged attempts at cardiopulmonary resuscitation. The diagnosis of PTTM was confirmed on autopsy, which revealed an unsuspected undifferentiated occult gastric “signet ring” adenocarcinoma, with extensive metastases and multiple tumor embolisms in the small-caliber peripheral pulmonary arteries.

PTTM is a rare form of pulmonary arterial tumor embolism, in which small tumor cell embolisms cause fibrocellular proliferation in the intima of small-caliber pulmonary arteries. These changes lead to stenosis/occlusion of the pulmonary arteries and a subsequent rise in pulmonary vascular resistance, which in turn leads to rapidly progressing precapillary pulmonary hypertension.3 Clinically, patients tend to develop acute/subacute cor pulmonale and respiratory failure. Most patients who develop PTTM have

Fig. 1. (A) Axial image of chest CT (pulmonary parenchymal window) showing linear thickening of the subpleural lung interstitium (arrows). (B) Maximum intensity projection (MIP) axial reconstruction (pulmonary parenchymal window) of left lung, showing a peripheral “tree-in-bud” pattern consisting of linear opacities forming predominantly subpleural branches (circled). See also the presence of small centrilobular nodules (arrow). (C) MIP coronal reconstruction (pulmonary parenchymal window) of the left lung, also showing the “tree-in-bud” pattern (circled). (D) Chest CT sagittal image (bone window) revealing multiple focal bone lesions (arrows) in the sternum and several vertebrae, consistent with bone metastases.

documented metastatic cancer, the most common tumor being gastric adenocarcinoma followed by lung cancer, but on occasions (as in our case) it can occur in patients with no diagnosis of metastatic disease. In a recent review, none of the 30 cases scrutinized was due to disseminated prostate cancer. Unfortunately, most PTTMs are diagnosed post mortem on autopsy, and only some isolated cases have been described in surgical biopsies ante mortem. Only a high clinical suspicion and consistent radiological findings will prompt the physician to make a clinical diagnosis of PTTM and to plan the appropriate treatment, which is generally based on a combination of chemotherapy, anti-coagulants and corticosteroids. Significant radiological signs of PTTM described on CT include the “tree-in-bud” pattern. This is practically the only vascular cause of this radiological pattern, and should be distinguished from the bronchial presentation that is generally observed in patients with infectious bronchiolitis.

PTTM should be suspected in oncological patients with worsening respiratory function and/or who develop acute/subacute cor pulmonale, particularly in the absence of pulmonary artery embolisms on chest CT angiogram. Detection of a “tree-in-bud” pattern without clinical signs of respiratory infection should also alert to this diagnosis.

Efficacy of Double Bronchodilation (LABA+LAMA) in Patients with Chronic Obstructive Pulmonary Disease (COPD) and Lung Cancer

Dear Editor,

The prevalence of chronic obstructive pulmonary disease (COPD) among patients with a new diagnosis of lung cancer (LC) is 40%–70%. Both underdiagnosis of COPD and absence of treatment are common in these patients, and in curable cases these factors influence the choice of surgery or radiation therapy to treat LC, and affect tolerance to chemotherapy and radiation therapy. International LC guidelines recommend smoking cessation and respiratory rehabilitation, but do not make any explicit statements on intensive, short-term COPD treatment other than those given in the specific COPD guidelines.

Our aim was to study functional improvement of COPD in patients with LC after treatment with double bronchodilation (DBD) with a long-acting beta-adrenergic agent (LABA) and a long-acting muscarinic antagonist (LAMA). We conducted this prospective study in a population of outpatients seen in a lung cancer rapid diagnosis unit with spirometry performed on their first day in this unit showing forced expiratory volume in 1 second/forced vital capacity (FEV1/FVC) ratio <70% and a post-bronchodilator predicted FEV1 <80%. Patients who were already receiving DBD treatment and those with an alternative diagnosis of bronchial asthma were excluded. The effect of DBD on lung function was evaluated at 4 weeks. The choice of the LAMA and the LABA were selected according to medical criteria and the ability and capacity of the patient to follow the treatment. Participants receiving inhaled corticosteroids before inclusion continued to receive this therapy. During this period, all other laboratory, endoscopic and imaging tests required for diagnosis, staging, and multidisciplinary therapeutic decision-making were also performed. At 4 weeks, before LC treatment in all cases, spirometry was repeated to evaluate the impact of DBD on FEV1 and FVC.

Results

Thirty-seven patients with LC and COPD were included; patient characteristics are shown in Table 1. Six had a previous diagnosis of COPD and were receiving bronchodilator treatment, none of which was DBD-based; 4 of these were fluticasone combined with salmeterol. The most commonly used LABA was indacaterol (83.8%), followed by salmeterol, vilanterol, and olodaterol. The most commonly used LAMA was glycopyrronium (51.4%), followed by aclidinium and tiotropium. After 4 weeks of DBD treatment, FEV1 increased by 200 ml (interquartile range [IQR] 40–320) and 8% (IQR 9–11) and FVC by 290 ml (IQR 75–665) and 6.5% (IQR 1.5–14) on average with respect to baseline values. In 40% of patients, FEV1 and/or FVC increased by 400 ml or more, although no response predictors or differences in LC staging were detected on a multivariate analysis. In 5 of the 10 potentially resectable patients who initially presented poor lung function, improvements in FEV1 and FVC after DBD permitted surgical resection for LC to be performed without the need for an oxygen consumption test.

In this pilot study, we observed a notable improvement in lung function among patients with a diagnosis of COPD and LC who received DBD, allowing curative surgical interventions in a high percentage of patients.

In a study with a similar objective to ours that also explored postoperative pulmonary complications in 2 intervention groups who received DBD (formoterol+tiotropium) alone vs DBD+budesonide found comparable improvements to those described in our series in both groups, while the group that received budesonide had significantly better outcomes, including fewer postoperative complications. A lower incidence of postoperative

References


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Análisis de la eficacia de la doble broncodilatación (LABA+LAMA) en pacientes con enfermedad pulmonar obstructiva crónica (EPOC) y cáncer de pulmón

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