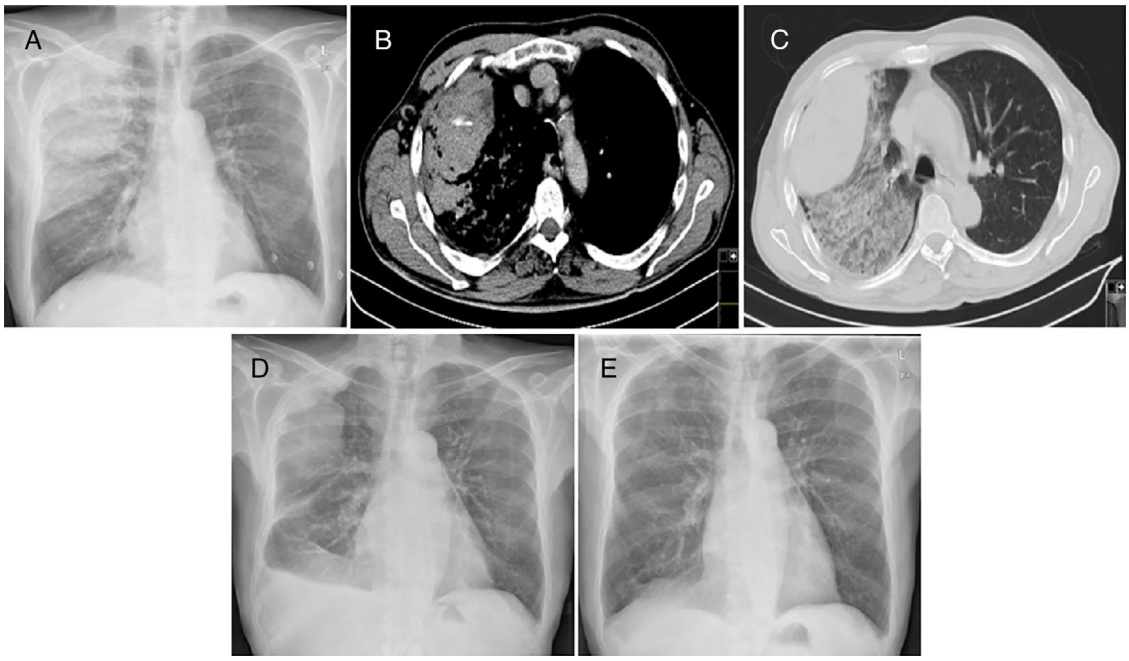

Fig. 1. (A) Postero-anterior chest X-ray showing a heterogeneous opacity in the right superior lung lobe. (B) Chest CT showing a subpleural hematoma on the right lung with active bleeding. (C) Chest CT showing subpleural hematoma and scaterred infiltrate on the right upper lobe. (D) Postero-anterior chest X-ray performed at hospital discharge, showing reduction of the hematoma in the right superior lung lobe and right small volume pleural effusion. (E) Postero-anterior chest X-ray performed after 7 months, showing complete disappearance of hematoma.

patients can be a real challenge and the disclosure of theses rare cases may help to improve knowledge about the best therapeutic strategy.

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1579-2129/

Pleuroparenchymal Fibroelastosis and Silicosis: An Unexpected Association

Fibroelastosis pleuropulmonar y silicosis: una asociación inesperada

Dear Editor:

Idiopathic upper lobe fibrosis was described in 1992[1] and characterized by elastotic fibrosis in pleura and subpleural lung parenchyma, with a predilection for the upper lobes. In 2004 Frankel et al.[2] applied the term pleuroparenchymal fibroelastosis (PPFE) for the first time, highlighting the pathologic findings of the disease. The latest update of international multidisciplinary classification of idiopathic interstitial pneumonia[3] (IIP) includes PPFE in the section of rare IIP. Despite the initial thought that it represented a specific entity, current literature suggests that PPFE may likely represent a much more common form of chronic lung injury,[4] associated with a variety of clinicopathologic conditions, such as infections, drugs, transplantation, autoimmune and interstitial lung diseases. We report a case of silicosis and PPFE, a possible association not yet established.

A 47-year-old man, ex-smoker (22 pack-year), working as a plumber in a construction company without any relevant previous medical history before a clinical presentation with dry cough, low-grade fever and weight loss for a month. After an initial primary health care observation, a chest X-ray, which showed fine nodular opacities, was prescribed. The patient was treated with antibiotics with resolution of the symptoms, but the radiological findings did not improve. The high resolution computed tomography

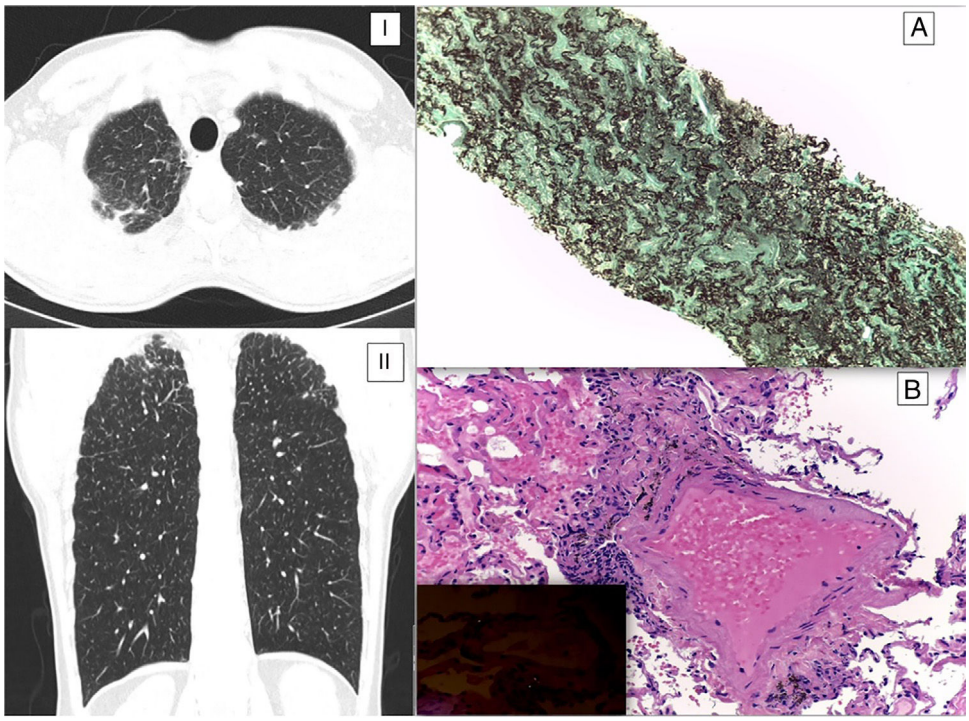

Fig. 1. (I) Axial and coronal (II) HRCT image show pleural and sub pleural thickening with mild fibrotic changes in the marginal parenchyma with apical-caudal distribution. (A) Preservation of the alveolar architecture; marked elastosis in the alveolar septa and obliteration of airspaces by fibrosis (EVG, 100×) – suggestive of pleuropulmonary fibroelastosis. (B) Small aggregates of histiocytes and anthracose pigment around bronchioles (H&E; 200×); birefringent silicate crystals are identified using polarized light (inset) – suggestive of early silico-anthracosis.

(HRCT) of the thorax revealed diffuse micronodular pattern with random distribution, mainly in the upper lobes, apical pleural thickening with extension to the pulmonary parenchyma (Fig. 1 – I and II) and mediastinal and hilar lymphadenopathies. Since radiological features were interpreted as possible mycobacterial lung infection, he was submitted to videobronchofibroscopy with bronchoalveolar lavage for microbiological scrutiny that was negative. Afterwards, a transthoracic core biopsy guided by CT to the apical subpleural lesions was performed and pulmonary parenchyma with fibrosclerosis and extensive septal elastosis (more than 80% of fibroelastic changes in this sample), associated with a discrete lymphoplasmocytic inflammatory infiltrate were reported on histological examination, according with PPFE; no silicate type refractive particles or granulomas were identified (Fig. 1A). The clinical case was then discussed in the diffuse lung diseases multidisciplinary team meeting and although the apical radiological features were consistent with PPFE, the micronodular pattern was not clarified suggesting silicosis/sarcoidosis. Therefore, the patient was submitted to transbronchial lung cryobiopsy that revealed macrophages in peribronchovascular location with anthracotic pigment and the presence of acicular refractive particles in polarized light compatible with silicosis (Fig. 1B).

The etiology of PPFE is not well established and is considered idiopathic when none of the known associated conditions are identified.[5] There are reports of patients with PPFE and dust exposure, but only one has histological confirmation of that exposure (aluminum, silicon and oxygen).[6] The present case is the first association with silicosis described, highlighting the eventual relevance of this entity in silica exposure scenario. Occupational exposure to respirable crystalline silica dust particles occurs in many industries. Diagnosis of silicosis needs carefully documented records of occupational exposure and radiological features, with exclusion of other competing diagnoses.[7]

Concluding, PPFE needs to be considered also in the context of occupational exposure and data are needed regarding the implication of this association in the disease clinical course and prognosis.

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Extrapulmonary Tumors and Sarcoidosis: An Incidental or Real Association?☆

Tumores extrapulmonares y sarcoidosis. ¿Relación casual o real?

To the Editor:

Sarcoidosis is a systemic granulomatous disease of unknown etiology that usually affects young patients, with an estimated incidence in Spain of 1.36/100 000 inhabitants.[1] The pathogenesis of sarcoidosis is thought to be related with exposure to certain environmental factors in genetically predisposed individuals.[2,3] Whether or not patients with sarcoidosis have a greater risk of developing cancer is debatable,[4,5] but reports in the literature of the tumor appearing before the diagnosis of sarcoidosis are rare and limited to case series. We report a series of 14 patients who were diagnosed with sarcoidosis during oncological follow-up of extrathoracic cancers.

We performed a retrospective, descriptive, observational follow-up (January 2012–June 2017) of patients with extrathoracic tumors referred to the bronchoscopy unit for the exploration of new mediastinal lymphadenopathies on a chest computed tomography (CT).

A total of 2420 patients were evaluated, of which 437 candidates met the study criteria; 404 were finally included. Reasons for exclusion were contraindication for endobronchial ultrasound for various reasons (12 cases), mediastinal lymphadenopathies already present at the time of cancer diagnosis (15 cases), or patient's refusal to perform more diagnostic tests (6 cases). All patients underwent linear endobronchial ultrasound for lymphadenopathy aspiration (Olympus BF-UC180F; Olympus ViziShot needle NA-201SX-4022, 21G) under sedation with midazolam. Fourteen patients (7 men and 7 women; mean age at diagnosis of the tumor 54.2 ± 13.9 years) were diagnosed with sarcoidosis on the basis of clinical and radiological criteria with histological confirmation[6] (mean age at sarcoidosis diagnosis: 56.6 ± 13.7 years). Mean time between both diagnoses was 2.4 ± 2.3 years. The most common tumors were gastrointestinal (three cases), breast, gynecological, and oropharyngeal (two each) (Table 1). Two patients had two tumors (cervical-ovarian and epiglottal-tonsillar; interval between diagnoses 36 and 4 months, respectively). Most tumors were diagnosed in early stages [stages I–II; 12/16 (75%); stage III: 3/16 (18.8%); stage IV: 1/16 (6.2%)]. The stations most often aspirated were the subcarinal (7; 100%) and lower right paratracheal [4R; 9/14 (64.3%)]. Eight patients (57.1%) had sarcoidosis at radiological stage II and six patients presented stage I (42.9%). Eight of the 14 patients (57.1%) were asymptomatic, 4 (28.6%) had arthralgia, 2 (14.3%) had asthenia, 1 (7.1%) had polyneuropathy, and another (7.1%) had skin involvement. In all cases, cultures to identify *Mycobacterium tuberculosis* in lymphadenopathy samples were negative. In addition to bilateral enlargement of the mediastinal lymph node chains, seven patients (50%) had diffuse bilateral millimetric pulmonary nodules. Increased mediastinal uptake on positron emission tomography was observed in 7 of the 14 patients (SUVmax 16.2 ± 12.9; range 4.2–24.9). Only 10 of the 14 patients received chemotherapy (four cisplatin and two docetaxel) (Table 1). Two patients were treated with corticosteroids (those with polyneuropathy and skin involvement) for 3 and 24 months (maximum doses of 50 and 30 mg prednisone, respectively). Response was favorable in both cases. Mean patient follow-up was 57.8 ± 24.1 months after diagnosis of the tumor (with only one tumor relapse and no deaths), and 28.1 ± 15.8 months after the sarcoidosis diagnosis.

This study shows that the development of new mediastinal lymphadenopathies in a cancer patient does not necessarily mean tumor extension, even if hyperenhancement is observed, and the possibility of sarcoidosis (or other diseases) must be considered.[7] Histological confirmation is always needed.[8] Another important finding is that the diagnosis of sarcoidosis was always subsequent to the tumor diagnosis. The inverse order has been described more often, and very few published series report a diagnostic chronology of tumor followed by sarcoidosis.[9,10]

It is sometimes difficult to differentiate between sarcoidosis, tuberculosis or a sarcoid-like reaction. The diagnosis of tuberculosis, a real possibility in our region which has an incidence of 21.3 cases/100 000 inhabitants/year,[11] was ruled out in all cases by a negative culture for *M. tuberculosis* in a sample of mediastinal lymphadenopathy obtained by endobronchial ultrasound. A sarcoid-like reaction (development of non-caseifying epithelioid cell granulomas in patients who do not fully meet the criteria for sarcoidosis) can occur in cancer patients in the first regional lymph node chain to which a particular tumor might metastasize, taking into account the strategic position occupied by each nodal group.[12,13] This phenomenon is more common in testicular cancers and lymphomas. As mediastinal lymphadenopathies would be the first chains to which lung and pleural cancers would metastasize, these tumors were excluded from the study. Moreover, the fact that our patients were in remission, yet presented systemic symptoms or mediastinal lymphadenopathies with uptake on PET[7] (six and seven of our patients, respectively), was suggestive of a diagnosis of sarcoidosis. However, even with these differentiating factors, it may be difficult to distinguish between these two entities.

Although the association between cancer and sarcoidosis was formerly believed to be incidental, the current thinking is that certain etiopathogenic mechanisms may be involved in genetically predisposed individuals, such as immune hyperresponsiveness of the host to the cancer itself (or antigens produced by the tumor),[9] or the treatment of the tumor itself,[12] as in the case of nivolumab in metastatic melanoma.[13]

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