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Pulmonary metastases from low grade sarcoma in a patient with pulmonary sarcoidosis. Sarcoidosis or sarcoid-like reaction?

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Abstract. An asymptomatic man with previous histopatological diagnosis of pulmonary sarcoidosis in radiological follow-up (stable for about 4 years) presented massive right pleural effusion. After drainage, CT of the chest showed an increase in number and size of pulmonary nodules compared to the last check (8 months before). Surgical pulmonary biopsies were performed with the diagnosis of metastases from low grade sarcoma. The primary tumor was localized to the right buttock. Given the absence of symptoms, the extent of disease and many comorbidities the patient underwent only treatment with gemcitabine that was not tolerated and discontinued after the first few cycles 1 year ago. At the present the patientis still asymptomatic even if the CT of the chest shows a slow but continuous progression of the disease. The question is: is this an association between sarcoidosis and malignancy? or was this a sarcoid-like reaction during malignancy? *(Sarcoidosis Vasc Diffuse Lung Dis 2016; 33: 171-174)*

Key words: sarcoidosis, sarcoid-like reactions, sarcoma

Sarcoidosis is a multisystem disease of unknown etiology whose diagnosis is based on typical clinical and radiographic findings, exclusion of other diseases, and presence of non-necrotizing epithelioid-cell granulomas in tissue (1). However, non-necrotizing epithelioid-cell granuloma is not equivalent to sarcoidosis because it may be identified in a number of infectious and noninfectious disorders, including neoplastic diseases and hypersensitivity pneumonitis. When non-necrotizing epithelioid-cell granuloma occur without other criteria for systemic sarcoidosis, the term "sarcoid-like reaction" has been used (2,3).

Sarcoid-like reactions have been reported in association with a variety of solid and hematologic malignancies (4,5). On the other hand, patients may develop typical sarcoidosis occurring before, during or after the diagnosis of cancer (6). In this case the differential diagnosis between sarcoidosis and sarcoid-like reactions is critical to avoid unnecessary or, conversely, delayed optimal therapy.

In this paper, we described the occurrence of sarcoma with pulmonary metastases in a man with previous diagnosis of pulmonary sarcoidosis. This is also the evolution of a case described as "pulmonary sarcoidosis mimicking multiple pulmonary metastases" in a previous paper (7).

Briefly: a 67-year-old, asymptomatic, non-smoker man was referred to our attention for a second opinion regarding multiple pulmonary nodules

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found during a colorectal cancer long-term follow-up. The initial suspected metastatic disease was revised in view of 1) pulmonary biopsies showing non-necrotizing epithelioid granulomas with negative stains and cultures for fungi and mycobacteria; 2) absence of symptoms; 3) absence of radiological progression after months; 4) F-18 fluorodeoxyglucose (FDG) positron emission tomography excluding FDG uptake in the lung nodules; and 5) exclusion of other diseases. All these data, along with the medical history of a recent antiviral therapy for chronic hepatitis C virus, led us to make the diagnosis of interferon-induced sarcoidosis. We described this case (7) emphasizing the importance to obtain tissue before the diagnosis of pulmonary metastases is established.

The patient remained asymptomatic and the computed tomography (CT) scan of the chest stayed the same for about 4 years until a massive right pleural effusion occurred (April 2013). After drainage, CT of the chest showed an increase in number and size of pulmonary nodules (Figure 1) compared to the last check (8 months before, Figure 2). Surgical pulmonary biopsies were performed with the diagnosis of metastases of low grade sarcoma (Figure 3). The primary tumor was localized to the right buttock (in absence of pathological findings on physical examination) (Figure 4). Given the absence of symptoms, the extent of disease and the comorbidities (coronary artery and liver diseases) the patient underwent only treatment with gemcitabine that was not tolerated and discontinued after the first few cycles 1 year ago. At the present (August 2015) the patient is still asymptomatic even if the CT of the chest (June 2015) shows a slow but continuous progression of the disease (Figure 5).

The question is: is this an association between sarcoidosis and malignancy? or was this a sarcoid-like reaction during malignancy?

The differential diagnosis between sarcoidosis and sarcoid-like reaction may be very difficult. The histological findings are the same and sarcoidosis is a diagnosis of exclusion.

In our case, the absence of extrapulmonary symptoms and the lack of lymphoadenomegaly, nodes calcification and pulmonary nodules without an obvious perilymphatic distribution at CT, could have led us to doubt the diagnosis of sarcoidosis. On the other hand, F-18 fluorodeoxyglucose (FDG) positron emission tomography (PET) excluded FDG uptake in the pulmonary nodules and the relationship between sarcoidosis and interferon treatment is well understood (8,9).

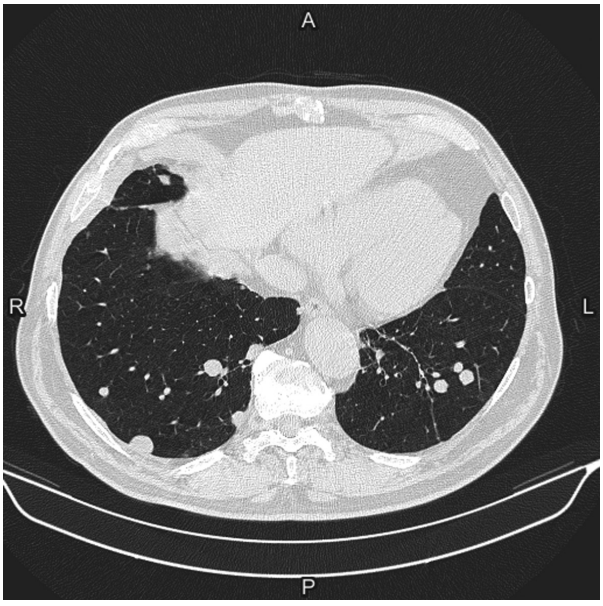

Fig. 1. CT scan of the chest in April 2013 showing increased number of pulmonary nodules in comparison to the last check (8 months before)

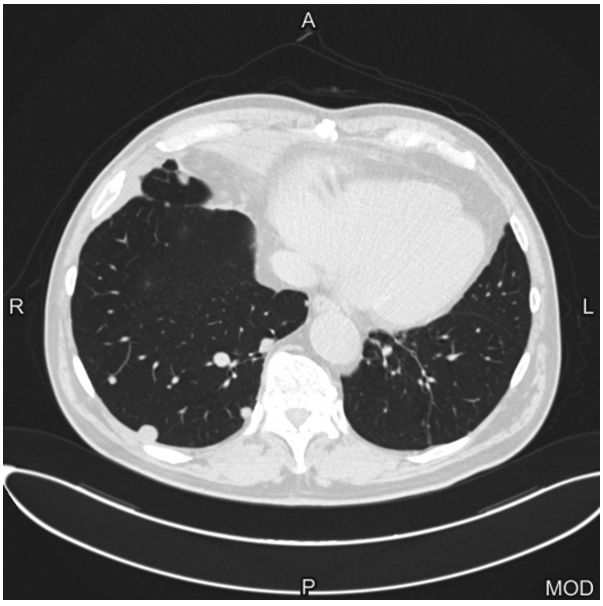

Fig. 2. CT scan of the chest in August 2012 showing multiple pulmonary nodules unchanged for about 4 years

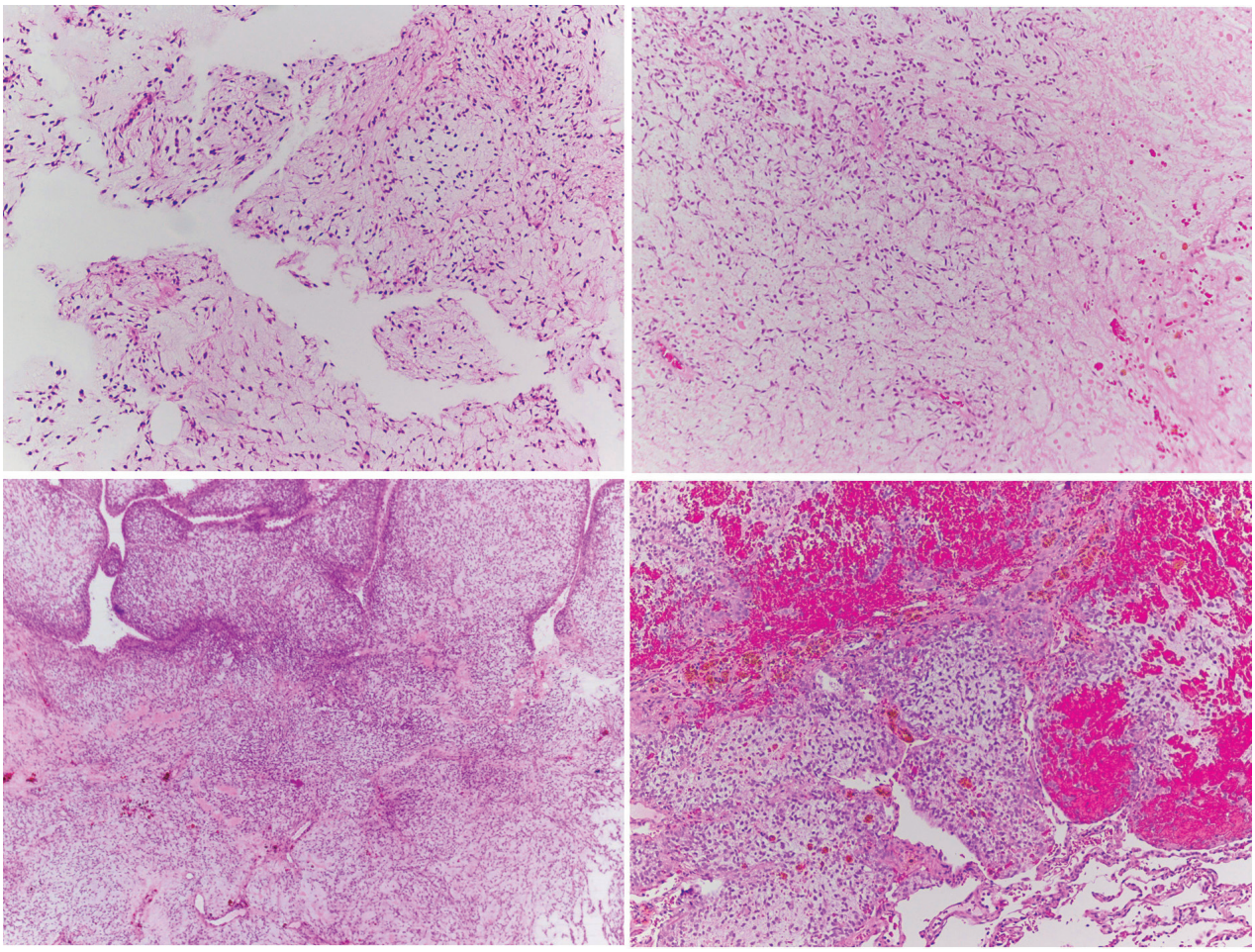

Fig. 3. Hematoxylin and Eosin staining of the lung specimens obtained by surgical biopsy at low magnification (10 x). This figure shows spindle cells with oval slightly atypical nuclei immersed in abundant myxoid stroma frame type (top left and right) with a lobulated pattern of growth (bottom left); there are also hemorrhagic areas with presence of siderofagi (bottom right)

In favour of two distinct diseases there is the absence of neoplastic cells in transbronchial biopsies performed at the time of the first diagnosis of sarcoidosis and the absence of epithelioid granulomas

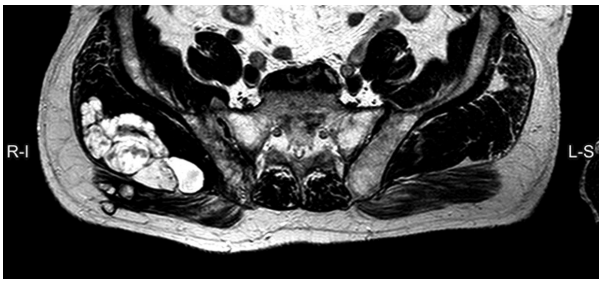

Fig. 4. Magnetic resonance imaging (MRI) of the right buttock showing a bulky (size of 5x11x16 cm) and multiloculated lesion in the context of the gluteus medius muscle

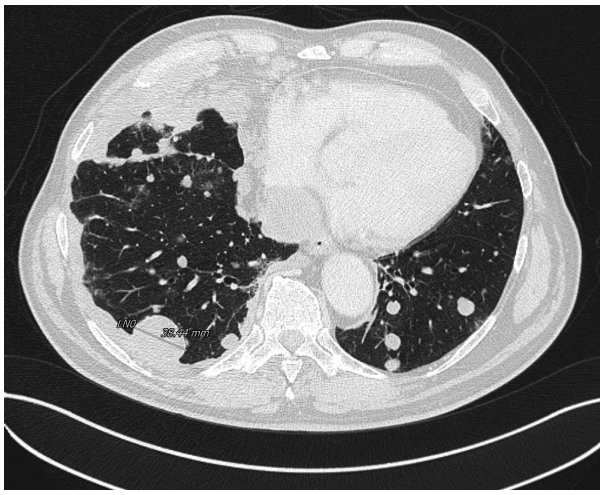

Fig. 5. CT scan of the chest in June 2015 showing a continuous progression of the disease

within the neoplastic tissue removed with surgical biopsies. One could argue that sarcoidosis was diagnosed on transbronchial biopsy and that a larger surgical biopsy could include neoplastic tissue. On the other hand a sarcoid-like reaction during a neoplastic disease may also affect areas not neoplastic so, even with a surgical biopsy, we could achieve the same result (sarcoidosis). In addition, sarcoidosis is a disease that has a histologic pattern predictive of good diagnostic yield with transbronchial biopsy so that a more invasive procedure is not indicated.

Another issue in favor of two distinct diseases is the fact that the first documentation of pulmonary nodules dates back to 2008 and these nodules remained unchanged until 2012; is it possible that metastatic lesions remain unchanged for 4 years? A definite answer does not exist. When encountering an atypical presentation, biopsies from two noncontiguous sites could be useful (10).

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