

Sarcoidosis or sarcoid-like reaction associated to malignant tumors?

Sarcoidoză sau reacție sarcoid-like asociată cu tumorile maligne?

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Abstract

Malignancy can be associated with sarcoidosis, which can be discovered before, during neoplasia or in the follow-up period of malignant tumors. Any diagnosis of sarcoidosis in patients with a history of malignancy can be a sarcoid-like reaction secondary to cancer, but it can also be a different disease. It is essential to know whether there is an association of two concomitant different diseases or it is a sarcoid-like reaction in patients with neoplasia. It is important to differentiate these two situations, because it can change the therapeutic approach.

Keywords: sarcoidosis, sarcoid-like reaction, malignancy

Rezumat

Neoplaziile pot fi asociate cu sarcoidoza, care poate apărea înainte, concomitent sau în perioada de urmărire a acestora. Orice sarcoidoză diagnosticată la un pacient cu antecedente personale patologice de cancer poate reprezenta o reacție de tip sarcoid-like secundară neoplaziei. În ceea ce privește atitudinea terapeutică, este important de știut dacă e vorba despre două afecțiuni concomitente sau despre o reacție sarcoid-like la un pacient cu cancer.

Cuvinte-cheie: sarcoidoză, reacție sarcoid-like, neoplazie

Background

Sarcoidosis is a multisystemic disease histologically characterized by the presence of noncaseating epithelioid cell granuloma. The etiology of sarcoidosis is unknown. Positive diagnosis is established by clinical symptoms, radiological images and histological results^(1,2). Malignancy can be associated with sarcoidosis and solid tumors can precede or follow sarcoidosis. In the first situation, sarcoidosis can be discovered during neoplasia or in the follow-up period of malignant tumors and the lymph nodes are most commonly affected^(1,2).

We present a clinical case of a patient with lung cancer associated with sarcoidosis. The most important question is whether the sarcoidosis is a primary disease or it represents a sarcoid-like reaction associated with a malignant tumor.

Case report

A 30-year-old male, non-smoker, without occupational exposure, presented with high fever (39.4 C°) and productive cough with yellow sputum. Clinical examination revealed at pulmonary auscultation crackles in the inferior part of the left lung, without other changes. Oxygen saturation was 93% on room air and during rest. Blood tests revealed high level of leukocytes and inflammatory syndrome. The chest X-ray showed left lower lobe consolidation with a central hypertransparency. At that moment, the patient was prescribed antibiotic treatment with amoxicillinum + acidum clavulanicum 1g three times per day (at 8 hours interval), for 7 days, with partial relief of symptoms.

There was no change in chest X-ray image at one-month and two-month evaluations and the patient continued to have dry cough. Further, the pneumologist decided to perform a CT scan that showed a macro nodular opacity, irregular margins in the left lower lobe and mediastinal lymph nodes at the superior limit of normal dimension, without metastatic lesions (Figure 1).

The next step for diagnosis was a fiberbronchoscopy that showed in the posterior segment of the left lower lobar bronchus an irregular tumor, well vascularized, 4 millimeters in diameter, which completely obstructs the bronchus. The histopathological biopsy result was suggestive for a neuroendocrine tumor, but because the tumor was bleeding, not enough material for the immunohistological tests was obtained.

In order to obtain histological confirmation, a thoracic surgery intervention was considered necessary. Consequently, a left lower lobectomy with mediastinal lymph nodes resection was performed. The histopathological result was compatible with a low malignancy mucoepidermoid carcinoma without mediastinal lymph nodes involvement.

After surgery, the patient was referred to the oncologic service and started chemotherapy with etoposide and carboplatin, 4 cures. CT scan reevaluation one week after the oncological treatment revealed no metastasis (Figure 2).

At 6-month reevaluation after chemotherapy, the thoracic CT scan showed an increased diameter of mediastinal lymph nodes, with no other opacities suggesting secondary tumor determinations or tumor relapse (Figure 3). At this point, the suspicion was of neoplastic adenopathies.

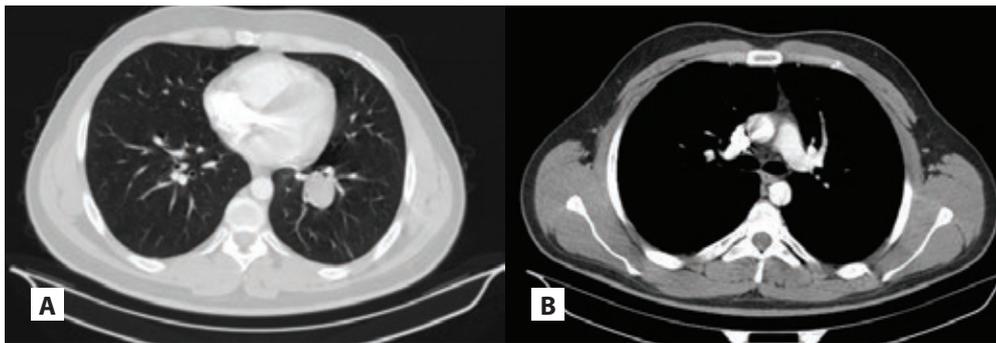


Figure 1. A. Thoracic CT scan - lung parenchyma window showing left lower lobe ovalar opacity. B. Thoracic CT scan - mediastinal window: normal diameter of lymph nodes

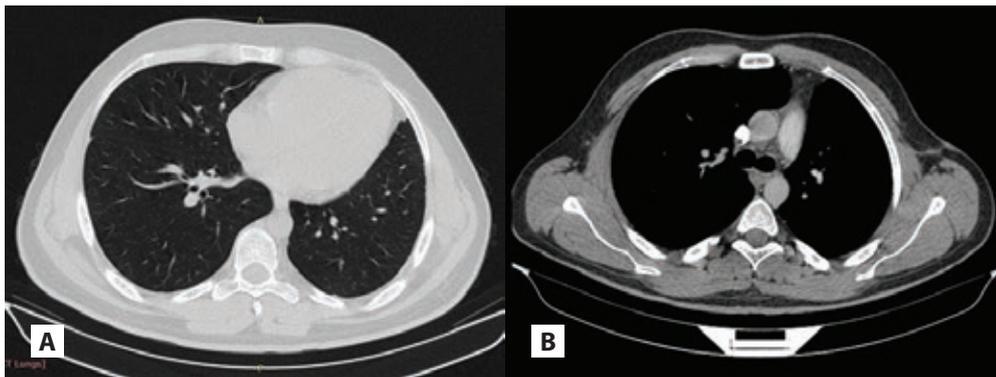


Figure 2. A. Thoracic CT scan - lung parenchyma window showing normal images (after surgery). B. Thoracic CT scan - mediastinal window: normal diameter of lymph nodes

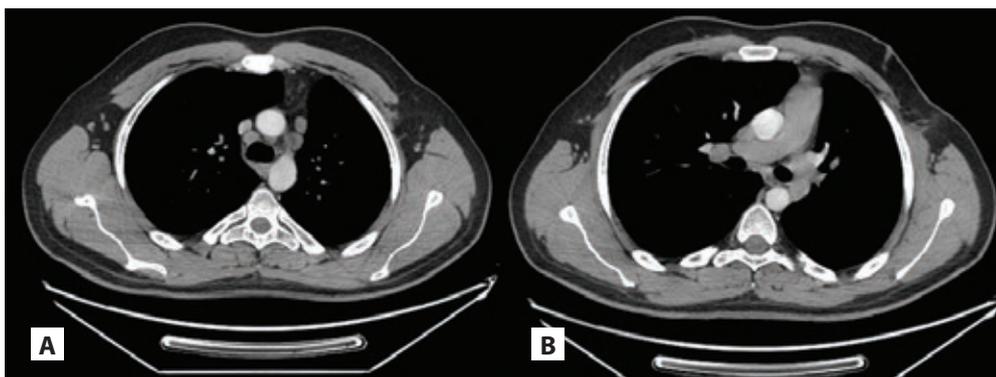


Figure 3. A, B. Thoracic CT scan - mediastinal window: increased diameter of lymph nodes

In order to have a correct diagnosis, a mediastinoscopy with lymph nodes biopsy was proposed. The histopathological result indicated sarcoidosis with the presence of noncaseating epithelioid cell granuloma (Figure 4). The patient was asymptomatic and no other therapy was proposed.

After another 6 months, the patient repeated the thoracic CT scan, which showed dimensional and numerical progression of mediastinal lymph nodes with conglomerate adenopathy and bilateral pulmonary micronodules (Figure 5).

The patient also had increased values of angiotensin converting enzyme (35.8 U/ml; reference range: 15-28 U/ml), but with normal values at pulmonary function tests and without clinical manifestations.

Given the new occurrence of pulmonary nodules (small size), the differential diagnosis was between sarcoidosis with lymph nodes and pulmonary involvement or secondary neoplastic determinations. Surgery was proposed with the resection of the right pulmonary nodule, but the patient refused. The patient is asymptomatic and continues to be monitored regularly (every 3 months) by thoracic CT scan in the service of pneumology and oncology.

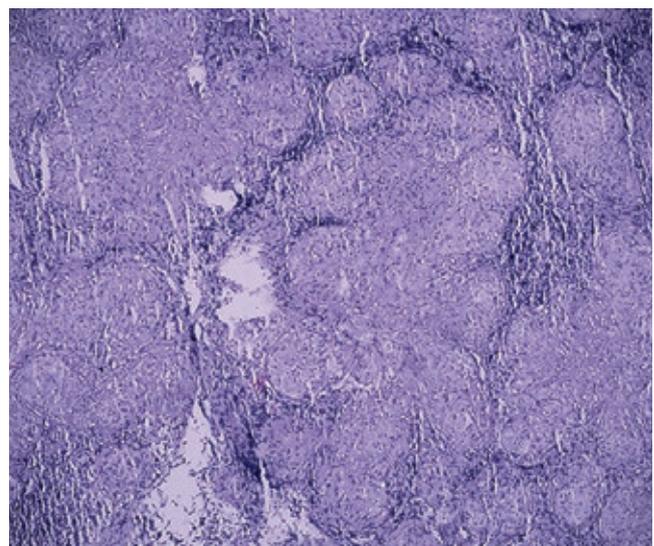


Figure 4. Histopathological aspect of mediastinal lymph node: noncaseating epithelioid cell granulomas, focal areas of giant epithelioid granulomas, isolated, rarely confluent and minimum perinodular sclerohyalinization

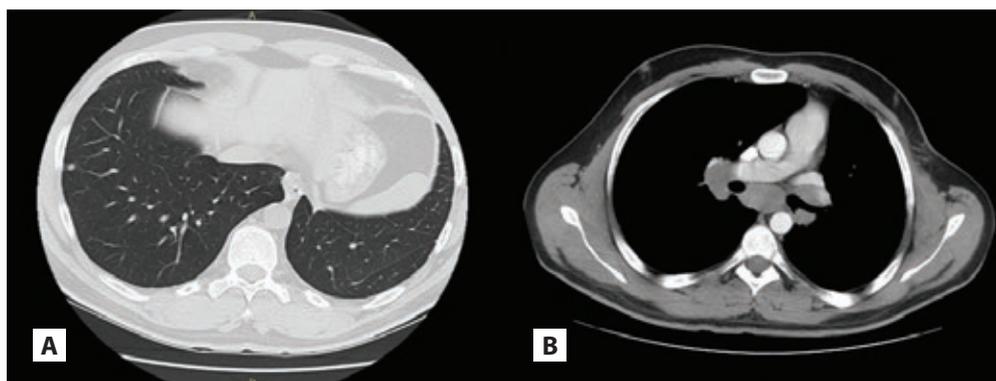


Figure 5. A. Thoracic CT scan - lung parenchyma window showing micronodular opacity in right lower lobe. **B.** Thoracic CT scan - mediastinal window: increased diameter of lymph nodes

Discussions

We presented the case of a young patient with history of lung cancer, diagnosed with mediastinal sarcoidosis one year later (by lymph node biopsy), without clinical manifestations of sarcoidosis, but with lymph node progression and the apparition of micronodules on CT scan.

Although our team decided that it was more likely to obtain the etiology of the lung micronodules by histopathological analysis from nodule resection using thoracic surgery, the patient refused the procedure. Given the situation, we considered that the patient had a mediastinal sarcoidosis, confirmed histopathologically, following a solid lung cancer (as the CT scan images are showing a progression) and pulmonary nodules of uncertain etiology. The sarcoidosis needs no specific treatment because the patient has no clinical symptoms and has normal values at pulmonary function tests, therefore a periodic evaluation was proposed (at every 3 months).

One of the major issues with our patient was the differential diagnosis of lymph node sarcoidosis with lung involvement and metastasis of the previous solid lung cancer. If we are dealing with a neoplasm recurrence, the patient needs to start another oncological treatment, but for that a histological analysis of one of the lung nodules is mandatory⁽³⁾.

Another diagnosis dilemma was whether the biopsy result of the mediastinal lymph nodes was in the context of sarcoidosis or it was a sarcoid-like reaction during neoplasia.

For the diagnosis of sarcoidosis advocates the histological aspect of noncaseating epithelioid cell granuloma from the mediastinal lymph nodes, increased values of

angiotensin converting enzyme and the age of diagnosis (30 years old), similar to data from literature (20-39 years)⁽²⁾.

The differential diagnosis between the two diseases cannot be done using the histopathological analysis of the lymph nodes, because epithelioid granulomas can be seen in both situations: sarcoidosis and sarcoid-like reaction in lung cancer (modified immune response caused by the neoplasia)^(4,5). Also, our patient can also present a sarcoid-like reaction after chemotherapy, described in a small number of case reports^(1,11,12).

The relationship between malignancy and sarcoidosis has been studied over time, and data from literature showed that cancer after sarcoidosis is more common than the reverse situation^(6,7). The most frequent types of cancer developed after sarcoidosis are represented by testicular and breast cancers^(6,7).

The other situation – sarcoidosis after malignancy – was reported in a small number of cases, and cancers were located in lung, head and neck and colorectal^(7,8,9,10). Other studies revealed that the cause of sarcoidosis (lymph nodes and pulmonary involvement) after neoplasia was chemotherapy, and the disease disappeared over time, with or without specific treatment for sarcoidosis^(1,11,12).

Conclusion

When facing a patient with a history of malignancy who develops enlargement of mediastinal lymph nodes, we have to consider sarcoidosis/sarcoid-like reaction for the differential diagnosis. The result of histopathological analysis by mediastinal lymph nodes biopsy does not differentiate these two situations. ■

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