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Mediastinopulmonary sarcoidosis mimicking metastatic renal cell carcinoma: About a case report

Ramzi Mejri [a,*], Kays Chaker [b], Bibi Mokhtar [b], Sami Ben Rhouma [b], Yassine Nouira [b]

[a] Departement of Urology, Hospital Mongi Slim La Marsa, Tunisia
[b] Departement of Urology, La Rabta Hospital, Tunisia

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ABSTRACT

There is a well-established association between sarcoidosis and many solid and hematologic malignancies, but it is less commonly described in patients with renal cell carcinoma. The majority of the cases described presented local sarcoid-like reactions in the immediate vicinity of the tumor with comparatively few reports of the disease further away. In view of the relatively small number of cases, there remains great uncertainty about the clinical behavior of sarcoidosis in renal cell carcinoma. In this observation, we illustrate a case of mediastinopulmonary sarcoidosis, which behaved like a true paraneoplastic syndrome of a renal tumor.

1. Introduction

Sarcoidosis is a multisystem inflammatory disease characterized histologically by non-caseous granulomas in multiple organs throughout the body, most commonly the lungs, intra-thoracic lymph nodes, skin or eyes. The etiology remains unknown. It can present with a multitude of all non-specific symptoms and its diagnosis remains difficult to perform. Sarcoidosis affects people of all racial and ethnic groups and occurs at all ages, although it usually develops before the age of 50 years, with the incidence peaking at 20–39 years.[1] Most cases of sarcoidosis are considered idiopathic only a portion has been associated with malignancies, antineoplastic therapies, or immune check point inhibitors. While sarcoidosis and sarcoid-like reactions are well-described phenomena in a variety of solid and hematologic malignancies,[2] they are more rarely reported in patients with renal cell carcinoma. In addition, in patients with renal cell carcinoma, non-necrotizing granulomas have mainly been found to occur within or adjacent to the primary tumor. The involvement of distant organs such as the pulmonary parenchyma, the thoracic lymph nodes and the bone marrow is little known and presents a great clinical challenge because it can mimic advanced metastatic pathology and lead to unnecessary exploration and aggressive treatment. In this observation, we report an original case of mediastinopulmonary sarcoidosis, which behaved like a true paraneoplastic syndrome of a renal tumor.

2. Case report

A 46-year-old female presented to an urgent care clinic with a five-day history of deaf left flank pain with hematuria, a dry cough, anorexia, asthenia and weight loss. Her past medical history was significant for diabetes mellitus, hypertension, chronic back pain. She denied any family history of malignancy. Clinical examination shows a large mass which fills the left lumbar fossa, firm, sensitive and which is palpable by bimanual palpation of the kidney. Laboratory test showed a normal level of inflammatory markers and a normal renal function.

An ultrasound of the urinary tract showed a solid mass at the expense of the kidney. The chest x-ray showed an enlargement of the mediastinum related to lymphadenopathy associated with diffuse interstitial lung syndrome (Fig. 1).

A thoraco-abdominal CT scan was performed showing an inferior polar tumor of the left kidney of 13 cm, heterogeneous, strongly taking the contrast product (Fig. 2A). The thorax was the site of symmetrical mediastinal ganglion lesions with centrimetric nodules diffuse throughout the pulmonary parenchyma (Fig. 2B). Mediastinoscopy with biopsy of the ganglions revealed mediastinopulmonary sarcoidosis (Fig. 3A and B).

A left radical nephrectomy was performed. No incident was observed in the postoperative follow-up. Our patient recovered quickly from her surgery, she resumed her professional activity in good physical and mental health. Histological examination showed clear cell renal cell carcinoma (Fuhrman grade 3) and absence of epithelioid granulomas

* Corresponding author.
E-mail address: ramzimejrimed@yahoo.fr (R. Mejri).

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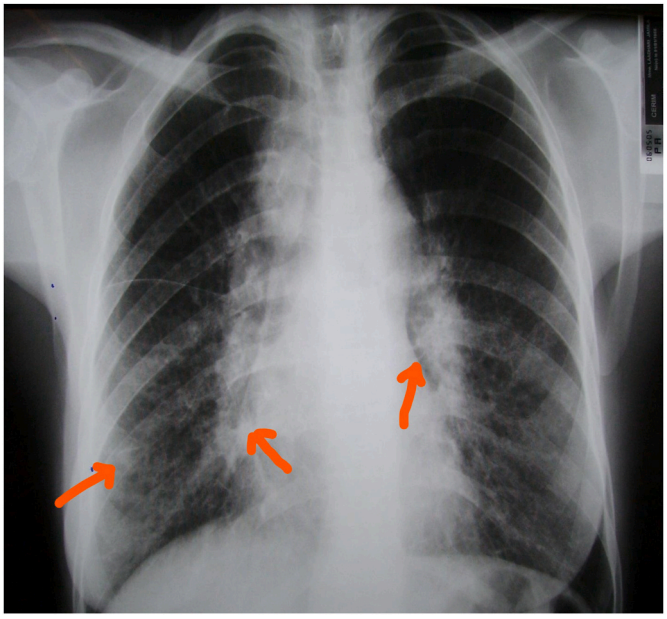

Fig. 1. Preoperative thorax x-ray: Mediastinal lymphadenopathy with diffuse interstitial syndrome.

throughout the tumor, classified as pT2 N0 (Fig. 3C and D). The lymph nodes removed were free from metastases and the histopathological study showed a significant inflammatory reaction. With a follow-up of 10 months, clinically the respiratory symptoms have completely regressed. A repeat chest x-ray showed a marked decrease in lung lesions and lymphadenopathy.

3. Discussion

Sarcoidosis is a systemic disease characterized by inflammatory granulomatous histologic lesions without necrosis. The etiopathology of this disease is unknown, but the production of cytokines by T lymphocytes and macrophages appears to play a primary role in the pathogenesis of this granulomatosis.

Tumor cells produce antigens which induce cell-mediated immune reactions in the stroma, in particular T lymphocytes. This activation of T lymphocytes produces interleukins (IL1, IL2) which induce the formation of inflammatory granulomas.[3] Although a multitude of paraneoplastic syndromes have been described in the renal cell carcinoma, it has a rarely well established association with sarcoidosis and sarcoid-like reactions, with less than fifteen cases reported in the literature to date. It has been well established that sarcoidosis associated with malignancy and the idiopathic form are histologically identical. The degree of the behavior of sarcoidosis associated with malignancy in terms of clinical progression and target organ damage is less clear. The pathogenesis of sarcoidosis seems to involve the interplay of antigen, HLA class II molecules, and T-cell receptors[4] A variety of chemokines and cytokines have been associated with the granulomatous response in sarcoidosis, including tumor necrosis factor α (TNF-α).[5] One mechanism that has been suggested for sarcoidosis associated with neoplasia is that, either through release or excretion during necrosis, malignant cells release soluble tumor antigenic factors that can induce a complex immune response cascade.

The clinical manifestations of sarcoidosis are multiple. Asymptomatic in 30–60% of cases, this disease is often discovered incidentally on a chest x-ray. Persistent respiratory symptoms such as dyspnea, dry cough or chest pain may be present. The onset symptoms are accompanied by systemic manifestations in one third of patients.

To our knowledge, this is the third case of pulmonary parenchymal involvement of sarcoidosis in a patient with lesions suggestive of clear cell renal carcinoma. Our patient presented clinical and radiological signs of sarcoidosis at the initial stage of the disease, he did not receive any immunological treatment before the diagnosis. All of this scientific evidence suggests that the development of sarcoidosis in this patient was probably related to his underlying malignancy.

Sarcoidosis is therefore a systemic disease that can coexist with certain neoplasms, without them being specific. The lesions regress spontaneously after removal of the tumor, responding to the characteristics of a true para-neoplastic syndrome. Its existence should lead to the search for an underlying neoplasia in cases where its etiology remains unexplained. Sarcoidosis should always be considered in the differential diagnosis of patients with a history of neoplastic pathologies who develop lymphadenopathy. It is crucial to obtain a histological diagnosis before initiating treatment for a suspected cancer recurrence.

4. Conclusion

The association of renal neoplasia and mediastino-pulmonary sarcoidosis is probably due to certain immunological interactions between the two conditions. Treatment for granulomatous lesions consists of removing the kidney tumor. On the other hand, the discovery of epithelial-giganto-cellular granulomas should prompt a search for an

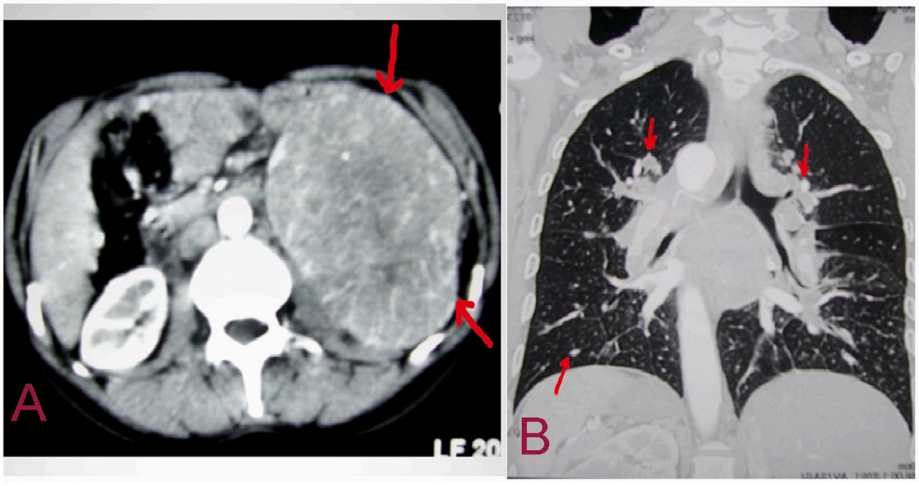

Fig. 2. a. Abdominal CT: Left renal tumor.
b. Thoracic CT: Mediastinal lymphadenopathy associated with parenchymal nodules.

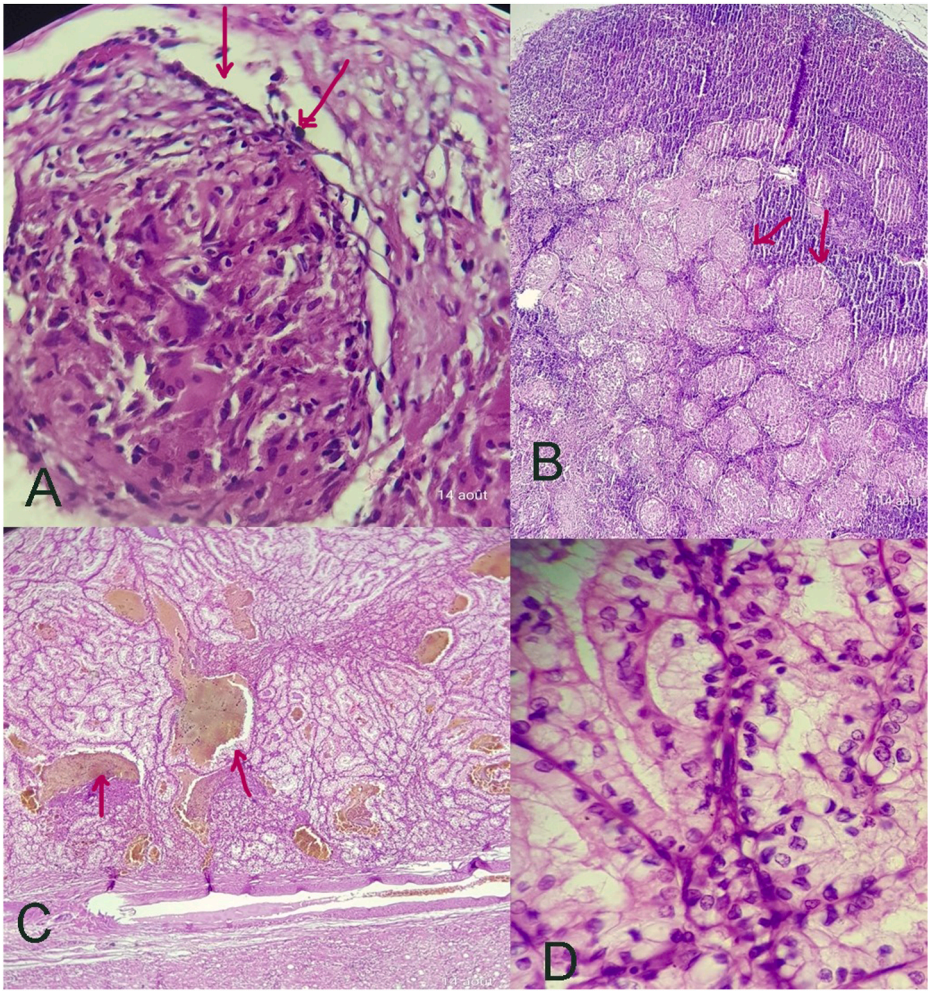

Fig. 3. a. Pulmonary sarcoidosis Non-necrotizing granulomas are distributed along the bronchovascular bundles. Granulomas contain very compact epithelioid cells and giant Langhans cells, surrounded by lymphocytes without evidence of malignancy.
b. Lymph node sarcoidosis, several non-confluent granulomas.
c. Clear cell renal cell carcinoma (Fuhrman grade 3).
d. Optically-clear cells high magnification.

underlying neoplasia.

Authors contributions

R. Mejri: participated in the writing of the manuscript.
K.Chaker: participated in the writing of the manuscript.
M.Bibi: participated in the writing of the manuscript.
S. Ben Rhouma: participated in the writing of the manuscript and its correction.
Y. Nouira: participated in the writing of the manuscript and its correction.

Declaration of competing interest

The authors declare that there are no conflicts of interest regarding the publication of this article.

References

1. Rybicki BA, Major M, Popovich Jr J, Maliarik MJ, Iannuzzi MC. Racial differences in sarcoidosis incidence: a 5-year study in a health maintenance organization. *Am J Epidemiol*. 1997;145:234–241.
2. Chee A, Tremblay A. EBUS, granulomas, and cancer: what does this represent? *J Bronchology Interv Pulmonol*. 2013;19(3):171–173.
3. Kovacs J, Varga A, Bessenyei M, Gomba S. Renal cell cancer associated with sarcoid-like reaction. *Pathol Oncol Res*. 2004;10(3):169–171.
4. Moller DR, Chen ES. Genetic basis of remitting sarcoidosis: triumph of the trimolecular complex? *Am J Respir Cell Mol Biol*. 2002;27:391–395.
5. Ziegenhagen MW, Rothe E, Zissel G, Muller-Quernheim J. Exagerated TNFalpha release of alveolar macrophages in corticosteroid resistant sarcoidosis. *Sarcoidosis Vasc Diffuse Lung Dis*. 2002;19:185–190.