Co-existing Sarcoidosis and Clear Cell Renal Carcinoma: A Case Report

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Abstract Systemic sarcoidosis has been described in association with many primary tumors. Although it is more seen in carcinomas than in hematologic malignancies, it is very rarely reported in renal carcinoma. Here, we describe a rare association of systemic sarcoidosis and clear cell renal carcinoma in a 62-year-old-female. At 36 months follow-up, she had no recurrence.

Keywords Systemic sarcoidosis; Clear cell renal carcinoma

1 Introduction
Sarcoidosis is a multisystem disease due to non-caseating epithelioid granulomatous inflammation in affected organs. Diagnosis requires a consistent clinical picture and a biopsy with typical non-caseating granulomas, excluding diseases that can cause similar granulomatous reactions (Statement on sarcoidosis, 1999). Few reported cases of systemic sarcoidosis were associated to the occurrence of cancers such as lung cancer (Yamasawa et al., 2000), cutaneous cancer (Alexandrescu et al., 2011) or testicular cancer (Rayson et al., 1998). We report hereby the case of a 62-year-old patient with a diagnosis of a concomitant sarcoidosis and renal clear cell carcinoma.

2 Observation
A 62-year-old-female patient without medical history was referred to our department for chronic dry cough and shortness of breath. She denied any family history of malignancy. Physical examination revealed bilateral crackles on lung auscultation, lymph nodes enlargement on the cervical area, and spleen enlargement on abdominal palpation. Laboratory tests revealed lymphopenia of 1 000 cells/mm$^3$ at blood count. Serum electrophoresis, calcium and phosphate levels in blood and urine, proteinuria of 24 hours were within normal range. Immunologic findings including antinuclear antibodies were negative. HCV and HBV serology and tuberculin skin test were negative. Chest X-ray showed bilateral interstitial syndrome. Thoracoabdominal computed tomography revealed mediastinal lymphadenopathy, bilateral ground glasses at bases (Figure 1), spleen enlargement and a 3-centimeter hypervascularized lower pole renal mass (Figure 2). Bronchial endoscopy was performed and biopsies revealed non-caseating epithelioid granulomas. Salivary gland biopsy showed granulomatous sialadenitis. Bronchoalveolar lavage concluded to a lymphocytic alveolitis with a CD4/CD8 ratio of 2.8. An open left heminephrectomy was performed through a flank incision. Pathological examination concluded to a stage T1a, clear cell renal cell carcinoma (Figure 3, 4). The diagnosis of systemic sarcoidosis associated to renal carcinoma was retained and the patient underwent a course of corticosteroids treatment (1 mg/kg/day for 4 weeks with progressive tapering of the doses). The evolution was marked by an improvement of the dry cough and normalization of the biological hepatic parameters. The CT scan control showed an improvement of the interstitial lesions and a size normalization of spleen and lymph nodes. There was no tumor recurrence. The decline is 36 months.

3 Discussion
Sarcoidosis is a multisystem granulomatous disease of unknown origin with pulmonary and extrapulmonary manifestations. Cancer can eventually occur in patients who have an established diagnosis of sarcoidosis and sarcoidosis can also develop subsequently in an oncologic patient. The sarcoidosis-related cancer includes not only lymphomas but also other hematologic malignancies and solid tumors (Reich, 2006). In our
Figure 1 Thoracic computed tomography: bilateral ground glasses at bases

Figure 2 Abdominal computed tomography: spleen enlargement and a 3-centimeter hypervascularized lower pole renal mass

Figure 3 Carcinoma composed of sheets and alveolar structures, separated by an abundance of thin-walled blood vessels (HEx10) *(show with arrow)*

Figure 4 Tumor cells with distinct cell membranes and clear cytoplasm. Nuclei are round and uniform; nucleoli are absent (HEx40) *(show with arrow)*

cases, the diagnosis of systemic sarcoidosis was made concurrently with the discovery of the neoplasm. We report hereby the case of a 62-year old patient admitted for an investigation of chronic dry cough. She did not complain of any history of lumbar pain and did not report any urological symptoms. Our investigations concluded to a sarcoidosis, confirmed histologically on mediastinal lymph node biopsy and salivary gland biopsy. CT scan revealed a suspicious inferior polar mass of the left kidney leading to a tumorectomy, which confirms the diagnosis of renal clear cell carcinoma. This means that in our case, sarcoidosis could be considered as a paraneoplastic syndrome. Paraneoplastic sarcoidosis is defined as the onset of sarcoidosis that is coincidental within 1 year with the discovery of an unsuspected cancer, and is more commonly reported in hematologic malignancy (Karakantza et al., 1996). Paraneoplastic sarcoidosis occurs less frequently in oncologic patients with solid tumors. To our knowledge, sarcoidosis was diagnosed concurrently with the detection of malignancy in patients with kidney cancer as renal cell carcinoma in two cases (Logan and Bensadoun, 2005; Willis et al., 2011). These two reported cases consisted of an undiagnosed condition of sarcoidosis complicating the staging of renal cell carcinoma. In the two cases, the patients did not report any symptoms and had no physical signs related to sarcoidosis, in contrast to our case, where the patient complained of dry cough and shortness of breath. This was probably due to a relatively advanced stage of the sarcoidosis contrasting with an early stage of the carcinoma. There is a postulated association between sarcoidosis and malignancy secondary to an induced T-cell-mediated host response to soluble antigenic tumor factors (Brincker, 1986). The antigenic factors may be either shed by the tumor cells or released during tumor necrosis. Subsequently, lymphatic vessels transport the factors to draining lymph nodes where the host’s immune response, similar to a hypersensitivity reaction, results in the formation of the non caseating epithelioid granulomas (Bassler and Birke, 1988). In our case, pathology of the renal mass demonstrated a stage T1a clear cell carcinoma. Pathologic margins were negative. This is to say that although the diagnosis of malignancy was hazardous, it is considered at early stage. In fact, the presence of sarcoïd reaction has been shown to have positive prognostic significance.
in patients presenting malignant tumors such as Hodgkin disease (Kurata et al., 2005) or gastric cancer (Sacks et al., 1978). No published data concerning sarcoidosis and renal carcinoma were found. However, we conclude from this case that this association leads to the positive global outcome of the carcinoma.

4 Conclusion
This case illustrates a rare association of a sarcoidosis to clear cell carcinoma in a 62-year-old patient without any urological symptoms. This case reveals an unusual picture of sarcoidosis as a paraneoplastic syndrome and, again, the occurrence of cancer in patients with sarcoidosis, which remains not clear.

The authors have no competing interests.

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