Sarcoid-Like Reaction Associated with Renal Cell Carcinoma - A Case Report.

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Case report

Sarcoid-like reaction associated with renal cell carcinoma – A case report

Asma Iftikhar, Muhammad A.I. Cheema, Preethi Ramachandran, Sonu Sahni

1. Introduction

Renal cell carcinoma (RCC) is a highly vascular tumor, which may spread to the lungs and other organs via the hematogenous or lymphatic route. Patients with RCC can present with local or systemic manifestations which may be due to metastases or paraneoplastic syndromes. The pulmonary manifestations of RCC are many and varied as patients may present with hemoptysis, pleural effusion, pulmonary embolism or arteriovenous fistulas [1]. Though rare, RCC may also spread through the lymphatic system and involve the mediastinal lymph nodes. This may lead to mediastinal and hilar lymphadenopathy. In the absence of any evidence of systemic sarcoidosis they are referred to as sarcoid-like reactions. Non-caseating epithelioid granulomas, also regarded to sarcoid-like granulomas have been described in association with certain malignancies such as carcinomas of the breast, colon, seminoma, and Hodgkin’s lymphoma. However, sarcoid like reaction associated with renal cell carcinoma is uncommon. Herein we present a rare case of a patient with renal cell carcinoma with mediastinal lymphadenopathy initially thought to metastatic disease, though revealed a sarcoid-like reaction with review of literature.

2. Case report

A 45-year-old obese Asian female with only significant past medical history of RCC diagnosed one year prior for which she underwent left partial nephrectomy presented to our outpatient with a chief complaint of progressively worsening dyspnea on exertion, palpitations and wheezing over the previous 3 months. She denied any history of smoking or alcohol use. She also denied history of chest pain, dizziness, weight loss or fever. Her weight was noted to be 88.9 kg with a BMI of 37.69 kg/m². Vital signs were within normal limits with a blood pressure of 130/90 mmHg, pulse of 74 beats/min and O₂ saturation of 96% on room air. On physical examination, she was noted to be obese with no evidence of respiratory distress. Lungs were clear to auscultation bilaterally. Abdominal and neurological examination were unremarkable. Laboratory values are summarized in Table 1. Patient underwent CT scan of the chest with contrast for persistent dyspnea which revealed bilateral enlarged hilar lymph nodes measuring 1.4 × 1.7 cm and 2.1 × 3.1 cm which have been shown in Fig. 1.

A subsequent positron emission tomography (PET) scan revealed that there were several mildly enlarged, mildly hypermetabolic mediastinal and bilateral hilar lymph nodes. A right paratracheal lymph node had a measurement of 1.3 × 1.0 cm. The patient then underwent bronchoscopy with biopsy which showed endobronchial lesion in the anterior segment of their right superior lobe, subcarinal and right hilar lymphadenopathy. The biopsy showed evidence of non-necrotizing granulomatous inflammation. Fungal and AFB stains were negative. Histological slides have been displayed in Fig. 2. The patient has remained well and has been following as an outpatient. Periodic spirometry and flow volumes loops are being conducted without ant observed changes in pulmonary function.

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ABSTRACT

Renal cell carcinoma (RCC) is a highly vascular tumor, which may spread to the lungs and other organs. It often presents with localized or systemic manifestation, including paraneoplastic syndromes. Sarcoidosis is a systemic granulomatous inflammatory disease characterized by non-caseating granulomas that typically affects the respiratory system. In the absence of any evidence of systemic sarcoidosis they are referred to as sarcoid-like reactions. Non-caseating epithelioid granulomas, also regarded to sarcoid-like granulomas have been described in association with certain malignancies such as carcinomas of the breast, colon, seminoma, and Hodgkin’s lymphoma. However, sarcoid like reaction associated with renal cell carcinoma is uncommon. Herein we present a rare case of a patient with renal cell carcinoma with mediastinal lymphadenopathy initially thought to metastatic disease, though revealed a sarcoid-like reaction with review of literature.

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3. Discussion

Granulomatous inflammation is a type of chronic inflammatory process that is characterized by accumulation of epithelioid and multinucleated giant cells [2]. In the absence of systemic sarcoidosis granulomas are traditionally formed in response to perceived foreign substances that the immune system is unable to eliminate or they immune mediated. Foreign body granulomas form around commonly iatrogenic material such as talc, sutures or other fibers that are large enough to preclude phagocytosis by a single macrophage. Immune mediated granulomas may be caused by numerous agents including bacterial and fungal organisms however it is possible that granulomas may be formed idiopathically.

3.1. Sarcoid-like reaction

Sarcoid-like reactions refer to the development of non-caseating epithelioid cell granulomas in patients who do not fulfill the criteria for systemic sarcoidosis. It has been reported that approximately 4–14% of cancer patients exhibit sarcoid-like reactions [3]. The sarcoid-like reaction was first described by Wolbach in 1911 [4] and has been reported in multiple different malignancies such as breast, rectal, cystic duct carcinoma [5] and in renal cell carcinoma [6,7]. Cancer associated sarcoid reactions have been observed in both patients with hematologic malignancies or solid tumors [8]. The etiologies of sarcoid-like reactions are not clear. A proposed theory focuses on soluble antigenic factors, shed by tumor cells or released in tumor necrosis in which these soluble factors are carried by lymphatic vessels to the draining lymph nodes, where they may induce a T cell mediated host response similar to a hypersensitivity reaction leading to the formation of epithelioid cell granulomas [9,10].

3.2. Features of sarcoid-like reactions

Histologically, the granulomas of sarcoid-like reaction are indistinguishable from those of systemic sarcoidosis. They usually consist of central focus of epithelioid cells admixed and surrounded by rim of lymphocytes [11]. Giant cells of both the Langerhans and foreign body type are common. Some investigators have reported epithelioid cell granulomas in lymph nodes accompanied by the sinus histiocytes [12]. Sarcoid like reactions are relatively infrequent directly at the tumor site and frequently occur in organs which can be reached by dendritic cells but without direct tumor involvement [9]. The pathogenesis is poorly understood, but the granulomatous inflammation has been related by an anti-neoplastic immune response [3].

Sarcoid reactions are characterized by the by T-zone in lymph nodes and composed of different inflammatory cells within the epithelioid cell granuloma and contain dendritic cells and T lymphocytes. Distribution and demarcation of the granuloma can be correlated with the ratio of CD4/CD8 cells. Thus, T cell mediated immune response and antigen dependent pathways are common for the formation of granulomas. This pathogenesis is the same same for sarcoidosis and sarcoid-like reactions. In sarcoid-like reactions, CD8 cells are present more frequently when compared to the CD4 cells [13].

Table 1

<table>
<thead>
<tr>
<th>Laboratory Test</th>
<th>Results</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hemoglobin</td>
<td>13.3 g/dl</td>
</tr>
<tr>
<td>Hematocrit</td>
<td>47.7%</td>
</tr>
<tr>
<td>White blood cells</td>
<td>7.7 K/ul</td>
</tr>
<tr>
<td>Platelets</td>
<td>288 K/ul</td>
</tr>
<tr>
<td>Sodium</td>
<td>140 mmol/L</td>
</tr>
<tr>
<td>Potassium</td>
<td>3.7 mmol/L</td>
</tr>
<tr>
<td>Chloride</td>
<td>105 mmol/L</td>
</tr>
<tr>
<td>Blood urea nitrogen</td>
<td>13 mg/dl</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.7 mg/dl</td>
</tr>
<tr>
<td>Glucose</td>
<td>89 mg/dl</td>
</tr>
<tr>
<td>Thyroid stimulating hormone</td>
<td>0.61 μl U/ml</td>
</tr>
</tbody>
</table>

Fig. 1. Computer tomography of the chest with contrast which showed enlarged mediastinal lymph nodes.
3.3. Sarcoid-like reaction in renal cell carcinoma

Incidence of lymph node metastasis of renal cell carcinoma is inconsistent ranging from 5% to 50% [14]. Only 5% to 8.8% of RCC cases have been reported to metastasize after limited hilar or regional lymph node dissection [15,16] and up to 38% with formal extended retroperitoneal lymphadenectomy [17]. The discovery of sarcoid-like reaction in the setting of renal cell carcinoma is rare with very few cases being reported in the literature. A few of such cases have been outlined in Table 2.

Sarcoid-like reaction was noted primarily to the kidney except for one case reported by Bottone et al. in which the sarcoid-like granuloma was present in liver and abdominal lymph nodes [19]. Though the role of lymph node dissection is still controversial in the setting of RCC it is important to understand the drainage of lymph in and around the renal system. As lymphatic drainage of kidney differs

Table 2

Cases of renal cell carcinoma with granulomatous sarcoid-like reaction.

<table>
<thead>
<tr>
<th>Clinical features</th>
<th>Renal tumor histology</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>60 y.o. M - left renal mass, lung nodules of clear cell adenocarcinoma with extensive SLR</td>
<td>Not microscopically examined</td>
<td>Moder et al. (1990) [18]</td>
</tr>
<tr>
<td>55 y.o. F - Renal mass in kidney infiltrated by sarcoidosis, liver solid masses and abdominal lymph nodes consistent with sarcoidosis</td>
<td>Clear cell RCC with sarcoidosis</td>
<td>Bottone et al. (1993) [19]</td>
</tr>
<tr>
<td>56 y.o. M - Renal mass</td>
<td>RCC with SLR</td>
<td>Cambell et al. (1993) [20]</td>
</tr>
<tr>
<td>44 y.o. M - Renal failure with renal mass</td>
<td>Papillary-type RCC with SLR</td>
<td>Marinides et al. (1994) [21]</td>
</tr>
<tr>
<td>39 y.o. M - Renal mass</td>
<td>Clear cell RCC with sarcoidosis</td>
<td>Lucchi et al. (2002) [6]</td>
</tr>
<tr>
<td>72 y.o. M - Renal Mass</td>
<td>Sarcomatoid RCC with SLR</td>
<td>Piscioli et al. (2008) [21]</td>
</tr>
<tr>
<td>44-65 y.o./3M - Renal mass</td>
<td>Clear cell RCC without SLR</td>
<td>Narasimhaiah et al. (2011) [22]</td>
</tr>
<tr>
<td>62 y.o. M - Renal mass</td>
<td>Peritumor sarcoïd-like reaction</td>
<td>Simon et al. (2012) [23]</td>
</tr>
<tr>
<td>41 y.o. M - Renal cell mass</td>
<td>RCC with SLR within tumor</td>
<td>Burhan et al. (2013) [24]</td>
</tr>
<tr>
<td></td>
<td>Bone marrow sarcoïd-like reaction</td>
<td>Timothy et al. (2014) [25]</td>
</tr>
</tbody>
</table>

F – Female; M – Male; RCC – Renal cell carcinoma; SLR – Sarcoid-like reaction.
from right to left, right renal tumors mostly drain in the interaortocaval nodes and left sided tumors drain to post aortic and paraaortic nodes. Formation of a granulomatous reaction is not dependent upon the lymph node drainage but in fact, sarcoid-like reactions may be a marker of an immunologically mediated antitumor response of macrophages activated by T-lymphocytes [9].

Active granulomatous inflammatory conditions such as tuberculosis, sarcoidosis, Cryptococcus may cause accumulation of fluorodeoxyglucose (FDG) on PET scanning and may cause false positives in the setting of malignancy. FDG measurement on PET scanning provides quantitative data in the form of standardized uptake value (SUV). A value 2.5 SUV or greater has been used as cut off value indicative of malignancy though various inflammatory cells such as neutrophils and activated macrophages may also show increased uptake.

Clinicians should also take into consideration the possibility of true sarcoidosis in the setting of malignancy. Review of the literature has identified a moderate association between sarcoidosis and malignancies. In the setting of kidney cancer there appears to be a relative risk of 1.55 for developing sarcoidosis [26]. For a clinician it is important to differentiate between diagnosis of systemic sarcoidosis associated with malignancy and sarcoid like reaction. In the diagnostic workup certain characteristics favor one diagnosis over another. Granulomas isolated to the vicinity of tumor or to the draining lymph node of tumor are seen more commonly in sarcoid like reactions. In addition, presence of B-cells and sinus histiocytes in the granuloma workup certain characteristics favor one diagnosis over another. The discovery of sarcoid-like reaction in the setting of renal cell carcinoma is rare with very few cases has being reported in the literature. In our case sarcoid-like reaction was found in the lung and was found to be secondary to RCC, after other causes of granulomatous disease such as tuberculosis and sarcoidosis were excluded. It is important to know that these reactions may mimic metastatic disease.

Conflicts of interest
None.

Financial disclosure
None.

Appendix A. Supplementary data
Supplementary data to this article can be found online at https://doi.org/10.1016/j.rmcr.2019.100847.

References