Case Report

Renal cell carcinoma and sarcoid-like epithelioid granuloma: Case report of a rare association

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ABSTRACT

Noncaseating epithelioid granuloma, also designated as sarcoid-like granuloma, has been described in association with malignancies. These granulomas are rare in carcinoma, more so when associated with renal cell carcinoma. Here, we describe an association between clear cell renal cell carcinoma and noncaseating granulomas in a 50-year-old female. We also discuss the differential diagnosis that should be considered before establishing such diagnosis, which might have therapeutic and prognostic implications.

Key words: Granuloma, noncaseating, renal cell carcinoma, sarcoid-like

INTRODUCTION

Granulomas are focal, compact accumulation of epithelioid histiocytes, lymphocytes, and multinucleated giant cells, with or without necrosis. Granulomatous inflammation may have varied etiologies, including infections, immune reactions, and neoplasms.[1] Sarcoid-like granuloma is a noncaseating granuloma, which occurs due to immune reaction. Association of these granulomas with malignancies is rare, more so if the granuloma is found within the stroma of an epithelial malignancy or within the draining lymph node. Few cases of granulomatous reaction associated with breast, colon, and hepatocellular carcinomas have been reported in literature.[2-4] Occurrence of granuloma is rarer in renal cell carcinomas, with few published reports.[5-7] We report a case of a clear cell renal cell carcinoma with the presence of noncaseating sarcoid-like granuloma within the tumor stroma. We also outline the differential diagnosis which should be considered in such cases, which might have profound management and prognostic implications.

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CASE REPORT

A 50-year-old female presented to our institute with a complaint of diffuse, nonradiating left flank pain for the last 1 year. The patient was afebrile. She was a known hypertensive on regular medication. There was no history of gross hematuria or pyuria. On initial work-up, her routine laboratory parameters were unremarkable, except for mild neutrophilic leukocytosis. Chest X-ray, electrocardiography (ECG), and echocardiography were normal. Computerized tomography (CT) scan of the abdomen revealed a well-defined multilobulated soft tissue lesion in the lower pole of the left kidney, suggestive of renal cell carcinoma, stage T2N0M0 [Figure 1]. No lymph node enlargement was noted. The patient was scheduled for radical nephrectomy, and the specimen was sent for histopathological examination (HPE).

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On gross examination, a 12 cm × 8 cm × 6 cm, relatively circumscribed tumor was seen in the lower pole of the kidney, compressing the surrounding renal parenchyma. The tumor was predominantly solid with few cystic areas and had a variegated appearance. No lymph node was identified on gross examination. HPE showed a clear cell renal cell carcinoma, Fuhrman nuclear Grade II, and pathological T2-stage [Figure 2]. No area of sarcomatoid differentiation or necrosis was found. No capsular breach, perinephric fat, or renal vessel involvement was seen. Surgical margins were uninvolved. Multiple compact, sarcoid-like noncaseating granulomas were noticed within the tumor, close to the tumor margin around the pelvicalyceal region. The granuloma consisted of epithelioid cells, Langhans giant cells, and mild mononuclear inflammatory cells. There was no evidence of necrosis or presence of any foreign body [Figures 2 and 3a]. No tumor cells were found within the granulomas. Ziehl–Neelsen (ZN) stain failed to reveal the presence of any acid-fast bacilli [Figure 3b], and fungal stain was negative [Figure 3c]. No asteroid and Schaumann bodies were found. No granuloma was identified in the surrounding renal parenchyma. On immunohistochemistry, the tumor cells were positive for pancytokeratin [Figure 4a] and vimentin [Figure 4b], confirming it to be a clear cell renal cell carcinoma.

The postoperative recovery was uneventful, and the patient is under regular follow-up.

DISCUSSION

The presence of noncaseating sarcoid-like granulomatous reaction is reported to occur with a frequency of 4.4% in carcinomas, 13.8% in Hodgkin's disease, and 7.3% in non-Hodgkin's lymphoma.[8] Association of renal cell carcinoma with granulomatous reaction is rare. However, before establishing this diagnosis, multiple differential

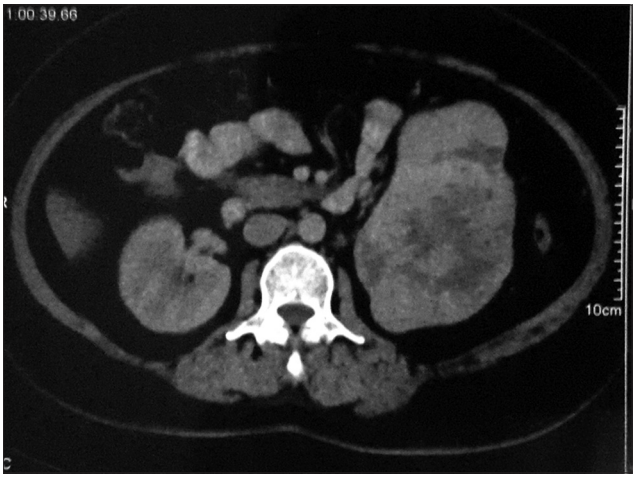

Figure 1: Computerized tomography scan showing a mass in the lower pole of the left kidney

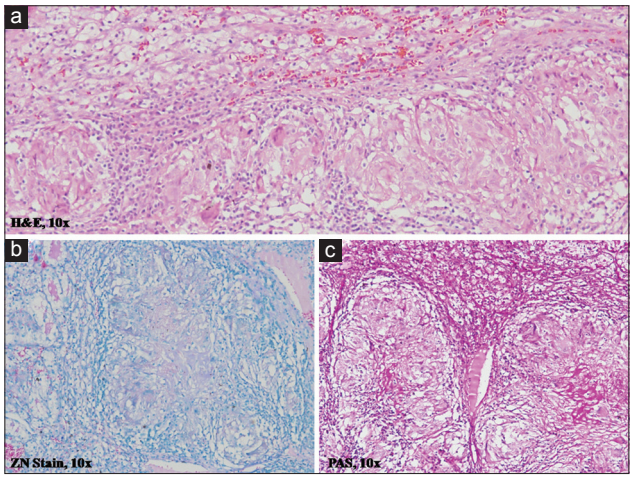

Figure 3: (a) Clear cell renal cell carcinoma with noncaseating epithelioid granuloma showing the presence of giant cells (H and E, ×100); (b) stain for acid-fast bacilli is negative (ZN stain, ×100); (c) no fungus was identified on fungal stain (periodic acid-Schiff, ×100)

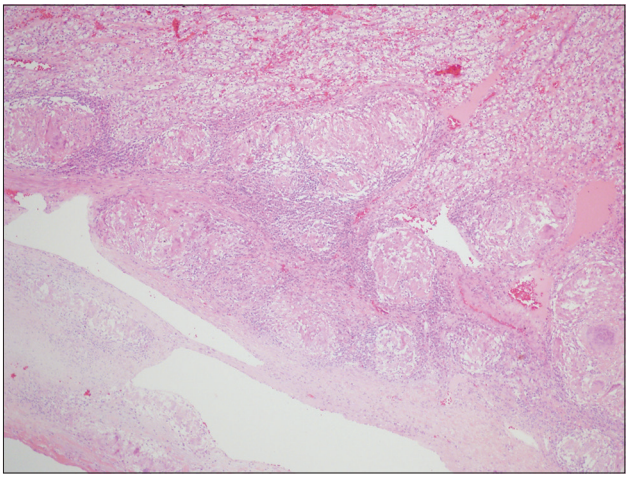

Figure 2: Clear cell renal cell carcinoma (upper right) with multiple noncaseating epithelioid granuloma (lower left) (H and E, ×40)

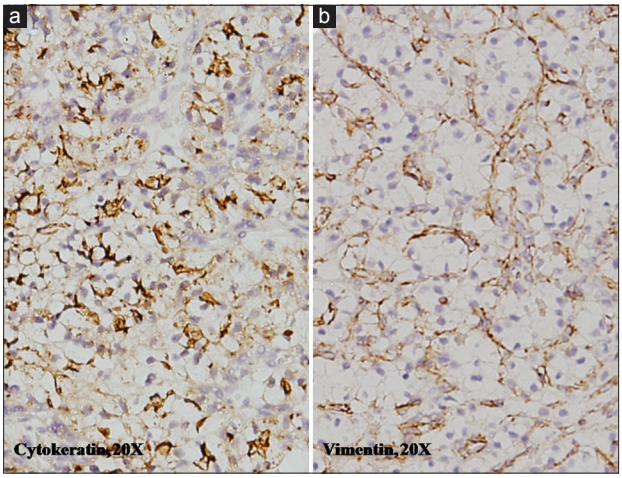

Figure 4: Immunohistochemistry showing (a) cytokeratin positivity (×200) and (b) vimentin positivity (×200) in tumor cells

diagnoses which may lead to granuloma formation should be considered and ruled out.

Tuberculosis (TB) is the most important differential diagnosis which should be considered owing to the exceptionally high incidence of TB in this region.[9] In addition, association of TB has significant management implications and hence should be appropriately ruled out.[10] In our case, TB was excluded through clinical examination and by the absence of the mycobacteria on ZN stain performed on the HPE slide. However, polymerase chain reaction (PCR) for TB could not be performed. Nonetheless, a positive PCR does not rule in an active tubercular infection in a high prevalence region like ours. Similarly, fungal granuloma was ruled out by periodic acid-Schiff stain.

Sarcoidosis is another important consideration, and systemic sarcoidosis should be excluded.[5] In our case, clinical examination did not show any lung, skin, joint, or ocular signs suggestive of sarcoidosis. Relevant radiological investigations including chest X-ray and abdominal CT scan failed to reveal any evidence of systemic sarcoidosis. ECG, liver function test, renal function test, and peripheral blood counts were normal. On HPE, no asteroid or Schaumann bodies were identified, thus ruling out systemic sarcoidosis.

Other consideration is the presence of granulomatous reaction secondary to tumor cell rupture, chemical exposure, or any neoadjuvant therapy.[6] These conditions may produce a granulomagenic substance which might incite the granulomatous reaction.[1] In our case, there was no evidence of the presence of tumor cell within the granuloma, which rules out the possibility of granuloma formation due to tumor cell rupture. Furthermore, there was no history of neoadjuvant therapy or any chemical exposure in the patient, ruling out the above-mentioned possibilities.

Other considerations for granuloma formation such as presence of foreign body[11] were appropriately ruled out on HPE. No foreign body was noticed on serial section HPE examination.

The most probable explanation for granuloma formation in our case is a T-cell mediated immune response mounted against the tumor antigen expressed by the neoplastic cells. Soluble tumor antigen may incite similar reaction in the lymph node located in the vicinity of the tumor.[6] The prognostic implications of such granulomatous response are conflicting; however, as pointed out by Pavic *et al*. in gastric adenocarcinomas and Hodgkin's disease, presence of granuloma might have a role in the prevention of tumor metastasis.[12]

CONCLUSION

Presence of noncaseating granuloma in conventional renal cell carcinoma is unusual and has prognostic implications with its role in the prevention of metastasis. Granulomatous reaction necessitates thorough clinical, radiological, and laboratory examination to rule out the other important differential diagnoses. This effort is necessary as granuloma may be a pointer to systemic disease, and consideration of the differential diagnosis may prevent unnecessary treatment to the patient.

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Conflicts of interest
There are no conflicts of interest.

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