CASE REPORT

The significance of florid giant cell component in renal cell carcinoma: a case report and review of the literature

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FARAGALLA H, AL-HADDAD S, STEWART R, YOUSEF GM. The significance of florid giant cell component in renal cell carcinoma: a case report and review of the literature. The Canadian Journal of Urology. 2010;17(3):5219-5222.

Background: *Renal cell carcinoma (RCC) with multinucleated giant cells has been reported in the literature. Different types of multinucleated giant cells have been described, including the osteoclast-like giant cells, rhabdoid cells, syncytial giant cells and tumor multinucleated giant cells.*

Results: *We describe a unique case of a clear cell RCC with extensive giant cell component. Tumor giant cells were arranged in an alveolar pattern and formed more than 50% of the tumor. The rest of the tumor was a classic clear cell renal cell carcinoma. A rhabdoid component was also focally seen. The immunohistochemical profile of the giant cells showed positivity for RCC, vimentin and, very focal positivity for cytokeratins, and negatively for CD68. A traditional spindle cell sarcomatoid component was not seen. The patient had advanced disease at presentation with metastasis to peri-aortic lymph nodes.*

Conclusion: *Giant cells can rarely constitute a major component of renal cell carcinoma and it is not clear if these represent a sarcomatoid component or merely a higher grade of the epithelial component. These cells may have different immunohistochemical profiles in different cases and may therefore be of different derivation. This may necessitate the revision of current classification schemes for renal cell carcinoma. It is also not clear how the presence of the various types of giant cells in renal cell carcinoma and their amount affects the clinical outcome.*

Key Words: renal cell carcinoma, kidney cancer, giant cells, case report, conventional renal cell carcinoma, clear cell, RCC, pathology, syncytial giant cells, giant cell

Introduction

Giant cells, usually multinucleated, have been described in cancers of various organs such as the lung, thyroid, and pancreas. Renal cell carcinoma (RCC) with a multinucleated giant cell (MGC) component is rarely reported in the literature. Different types of giant cells are described in RCC. These include osteoclast-like giant cells, tumor multinucleated giant cells, syncytial multinucleated giant cells and rhabdoid giant cells. The osteoclast-like giant cells are characterized by centrally aggregated small monotonous nuclei with small central nucleoli. They show strong positivity for CD68, and are thought to represent a host response to the tumor.[1] Multinucleated tumor giant cells are also described, usually as a minor component, in RCC with sarcomatoid differentiation or rhabdoid features, and they are associated with a high Fuhrman nuclear

Accepted for publication January 2010

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grade and poor prognosis.[2] They are characterized by pleomorphic bizarre giant cells with high grade nuclear features, and epithelioid differentiation. Interestingly, Chetty and Cvijan reported a unique case of RCC that is composed almost exclusively of bizarre multinucleated giant cells with positivity for both CD68 and epithelial markers.[3] Syncytial multinucleated giant cells (SGC) are also described in RCC.[4-6] They are characterized by an orderly array of regular nuclei with homogeneously large nucleoli. The significance of these syncytial cells and the prognostic implications are not clear, as they have been described with both low and high grade tumors. Finally, rhabdoid giant cells are also documented in RCC.[7]

In most cases, the giant cell component is only minimal with only few multinucleated giant cells dispersed among tumor cells or in the surrounding stroma. In only two reports did the MGC component represent a significant proportion of the lesion.[3,5] Interestingly, the type of giant cells was different in these cases. It is also worth mentioning that in only one report, were the tumor MGCs not associated with a traditional sarcomatoid component.[3]

We describe a case of a high grade clear cell RCC with conventional clear cell component and a second component of bizarre giant cells forming over 50% of the tumor. To our knowledge, this is the first case with extensive giant cell component arranged in an alveolar pattern. The immunohistochemical profile of the giant cells was also unique and had not been reported before.

Case report

A 58-year-old male initially presented with a 2 month history of fever, weight loss, and cachexia. Imaging of the abdomen and pelvis showed a large enhancing heterogeneous mass arising from the right kidney, Figure 1, and a large necrotic lymph node located anterior to the aorta. He underwent right radical nephrectomy. The patient is still alive 12 months after the surgery, until writing this report.

Pathologic findings

The kidney showed a large hemorrhagic solid lesion measuring 13.5 cm x 8.5 cm x 8 cm within the mid and lower part of the kidney, Figure 2. The tumour has large areas of hemorrhage and necrosis and is formed of two components; areas of clear cell RCC of classical morphology, Figure 3a, and a second component of bizarre, multinucleated giant cells (forming more than 50% of the tumor) arranged in an alveolar pattern separated by delicate scanty fibrovascular stroma, Figure 3b, 3c. The giant cells have ample eosinophilic cytoplasm with 2-40 haphazardly arranged, highly pleomorphic nuclei and macronucleoli. A rhabdoid component was also focally noted in addition to vascular space invasion. There was no traditional spindle cell sarcomatoid component. A peri-aortic lymph node (4.5 cm) that was almost entirely replaced by tumor was also present.

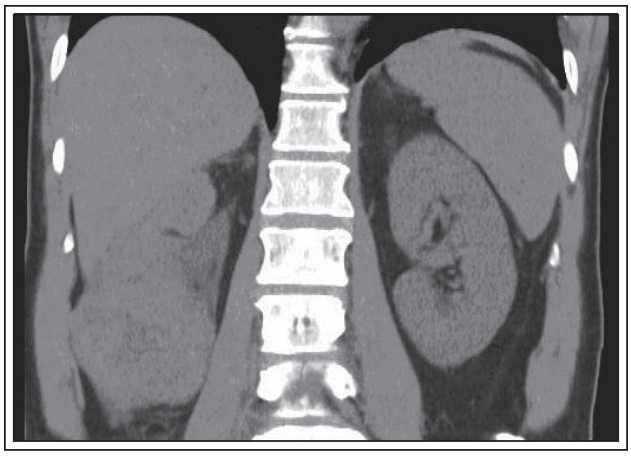

Figure 1. CT scan showing a heterogenous right kidney mass.

Immunohistochemistry

The tumor giant cells were positive for vimentin, CD10, Figure 4a, RCC, Figure 4b, and very focally positive for EMA, pancytokeratin and low molecular weight cytokeratin. Smooth muscle actin, desmin, B-HCG and CD68 were negative.

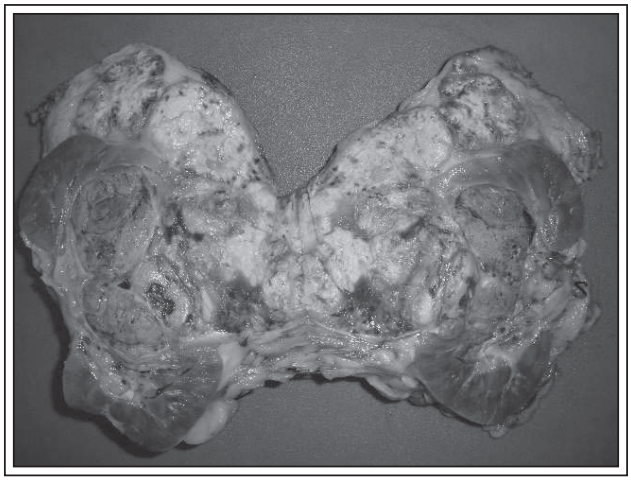

Figure 2. Gross photomicrograph of the right radical nephrectomy showing the tumor mass.

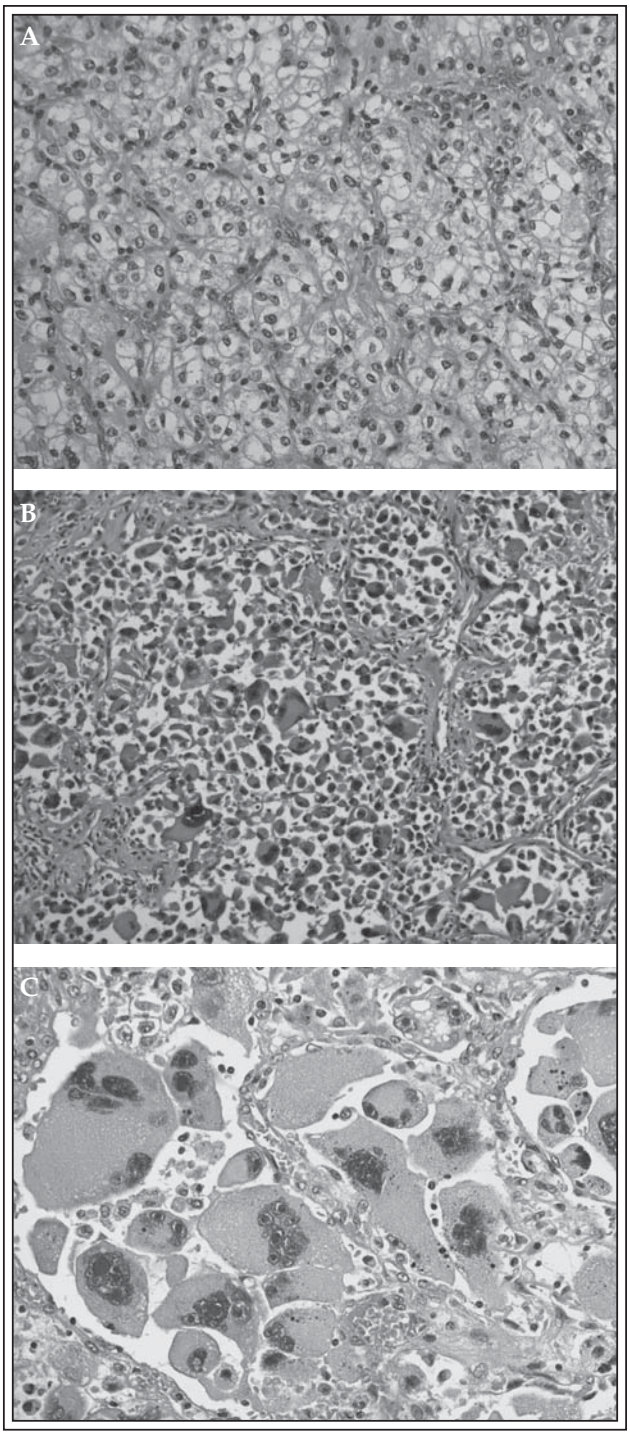

Figure 3. The histomorphology of the tumor. **a)** photomicrograph showing conventional clear cell carcinoma (H&E original magnification x 200). **b)** photomicrograph of areas formed of the multinucleated giant cells in a nested pattern (H&E, original magnification x 100). **c)** higher magnification of the multinucleated giant cells (H&E, original magnification x 400).

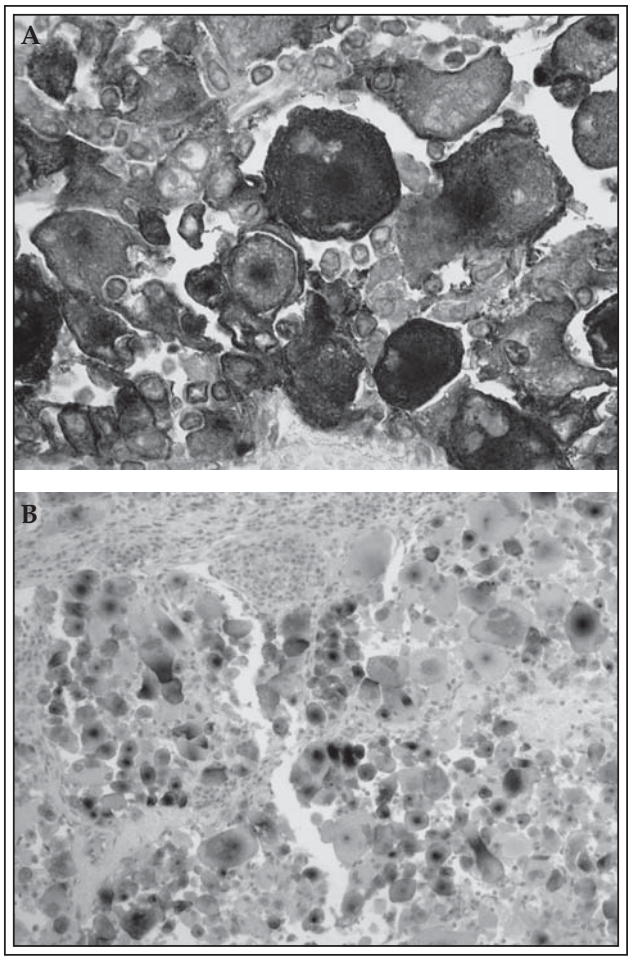

Figure 4. Immunohistochemistry showing the tumour to be positive for CD 10 (H&E, original magnification x 200). **a)** renal cell carcinoma antigen. **b)** (H&E, original magnification x 100).

Discussion

To date, the classification of RCC with giant cells is not clear and neither is their prognostic significance. The current WHO and AFIP classifications of renal cancers does not include an entity for renal cell carcinoma with giant cells. The classification of giant cell subtype of sarcomatoid carcinoma in other organs, e.g. the lung, necessitates that 30%-50% of the tumor to be formed of giant cells.[8] In addition, giant cell carcinomas described in other organs are associated with an aggressive clinical behavior and high tumor grade.

Approximately 5% of clear cell RCCs have a sarcomatoid component. Sarcomatoid carcinoma can occur with any renal cell carcinoma subtype and is not recognized in the current classification as a separate entity. Molecular profiling has shown that

both clear cell and sarcomatoid RCC arise from the same progenitor cell but show different patterns of allelic loss indicating genetic divergence during clonal evolution.[9] In the kidney, a sarcomatoid component is usually diagnosed by the presence of a malignant spindle cell component most commonly resembling fibrosarcoma or malignant fibrous histiocytoma.[2] Unlike most cases, the MGCs in our case were not associated with any sarcomatoid component. Our case might thus represent a distinct subgroup of RCC with a significant giant cell component that needs to be recognized as a separate entity. In order to justify a need for such a new classification, more case reports are needed. Molecular features of these tumors are yet to be elucidated and can be helpful in this regard. In addition, the prognostic significance of this putative entity needs to be assessed on larger series of cases.

The immunohistochemical staining profile of the giant cells is similar to reported examples of tumor giant cells, being positive for CD10, vimentin, RCC and very focally positive for EMA and cytokeratins. This IHC profile is different from reported cases of "syncytial giant cells" that are moderately to strongly positive for epithelial markers and weakly positive for vimentin,[5,6] and another case where the giant cells were positive for epithelial markers and CD68.[3]

The presence of a sarcomatoid component always implies a very poor prognosis. Our case highlights the importance of distinguishing the different subtypes of MGCs in RCC in order to assess the prognostic significance of each. Whereas the osteoclast-like giant cells are indicative of a possible host response, their prognostic significance is not yet clear.[1] Syncytial giant cells have been reported to be associated with either favorable or worse prognosis. Tumor giant cells and rhabdoid cells are associated with high grade tumors and worse prognosis. It is not clear however, if the extent of the MGC component can affect prognosis. Also, our case shows that the rare cases of presence of giant cells without other sarcomatoid components still indicates poor prognosis. This is yet to be confirmed by more reports. In all cases, extensive sampling may be needed and IHC may be helpful.

The mechanism of giant cell formation in RCC is largely unknown. The osteoclast-like giant cells may be the result of chemotactic factors secreted by the tumor that attract macrophages.[1] It is also suggested that tumors with osteoclast-like giant cells may produce a parathormone-like substance that promotes their formation.[10] The formation of multinucleated tumor giant cells and SGCs, on the other hand, is thought to result from either fusion of mononuclear tumor cells or a defect in cell division.[6]

In conclusion, we report a case of clear cell RCC with extensive giant cell component (> 50% of the tumor). The tumor had an aggressive clinical behavior. More cases are needed to establish the clinical significance of this category and whether tumors with this florid giant cell component should be grouped into a separate sub-category or grouped with sarcomatoid RCC. □

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