

Renal cell carcinoma with rhabdoid and sarcomatoid features presented as a metastatic thigh mass with an unusual immunohistochemical profile

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Abstract

Renal cell carcinoma (RCC) may metastasize anywhere in the body and sometimes the primary tumor is missing and necessitates extensive investigations to detect. In this report, we describe a case of RCC metastasizing to the thigh in a 70 year old male with a highly pleomorphic morphology suggesting a high grade sarcoma that showed unequivocal positivity for desmin directing the diagnosis for pleomorphic rhabdomyosarcoma. After completion of 33 cycles of radiotherapy, the patient developed large intraabdominal mass that showed conventional areas of RCC with immunoreactivity for CD10, CK, EMA, carbonic anhydrase IX and vimentin. The tumor cells in other areas resembled that of thigh mass which raised suspicions whether the two masses represented the same tumor or not. Surprisingly, the tumor cells of thigh mass showed diffuse positivity for CD10 and focal expression for CK, EMA and carbonic anhydrase IX. Extensive investigations failed to detect any primary renal lesions. The present case demonstrated that RCC can metastasize to virtually any body site and can have significant morphologic overlap with other non-renal neoplasms. Absence of primary origin of RCC according to radiological and operative data should not hinder the diagnosis of metastatic RCC. RCC with sarcomatoid and rhabdoid features carries aggressive behavior manifested by great metastatic potential and short survival time.

Introduction

RCC similar to other malignant tumors may undergo dedifferentiation to more aggressive histologic types. It may acquire spindle cell morphology, which is designated as sarcoma-

toid differentiation and it may acquire rhabdoid features, which is designated as rhabdoid differentiation.¹ Rhabdoid features was described in other malignancies including carcinomas,² melanoma,³ and sarcomas.^{4,5} Cohesive epithelioid cells with eccentric vesicular nuclei, prominent nucleoli and intracytoplasmic hyaline eosinophilic globules are the main features of rhabdoid cells.⁶ These cells resembled rhabdomyoblasts in morphology but they differed immunohistochemically and ultrastructurally.¹ The proportion of rhabdoid components in RCC ranges from 1 to 90% of the total tumor volume,^{6,8} however occasional cases were composed entirely of rhabdoid cells without detection of conventional RCC.^{9,10}

Sarcomatoid RCC is a rare renal malignancy with a reported incidence ranging between 0.7 and 13.2% of all renal parenchymal carcinomas.¹¹ Five percent of patients with RCC had sarcomatoid component especially with chromophobe (8.7%) and conventional types of RCC (5%).¹² Regions of rhabdoid differentiation are reported in 15% of sarcomatoid RCC,¹³ whereas in 39%, the two components are intimately admixed.¹⁴ The present study demonstrates some of the unusual features of RCC such as its presentation as a metastatic thigh mass with absence of primary tumor, combined aggressive histologic features such as sarcomatoid and rhabdoid dedifferentiation, expression of desmin as a type of mesenchymal metamorphosis.

Acquiring sarcomatoid morphology, unusual immunophenotyping and presentation as thigh mass have directed the diagnosis towards sarcoma more than carcinoma.

Case Report

Male patient 70 years old presented with a thigh mass measured 35×24×9 cm with grayish white lobulated cut section. Histopathological examination revealed epithelioid sheets of cells exhibiting great pleomorphism and frequent mitoses (Figure 1A-C). Most of these malignant cells showed abundant eosinophilic cytoplasm with occasional eccentric nuclei (Figure 1A, B). Some areas showed clear cell changes (Figure 1C). Malignant multinucleated giant cells and areas of necrosis were also seen. The possibility for sarcoma was highly thought.

Immunohistochemical panel of soft tissue sarcoma was performed including SMA, desmin, vimentin, S100 and pan cytokeratin. The neoplastic cells showed positivity for desmin (Figure 1D) and vimentin and the mass was designated at that time as pleomorphic rhabdomyosarcoma. At this moment, the patient has not submitted to further investigations. The patient received 33 cycles of radio-

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therapy, during which, he suffered from bad wound healing of the thigh wound.

Unfortunately, the patient suffered seven months later from abdominal pain. Abdominal CT revealed huge intra-abdominal mass that was located pararenal and extended to psoas muscle replacing and destroying it and both kidneys were free.

The patient underwent abdominal exploration where the intra-abdominal mass was resected. The mass measured 30×24×10 cm with whitish lobulated cut section (Figure 2A, B).

Microscopic evaluation of the abdominal mass revealed malignant epithelial cells characterized by clear cytoplasm with variable degrees of pleomorphism, where there were areas of moderate pleomorphism to anaplastic areas (Figure 3). The first impression of this mass is RCC *versus* adrenocortical carcinoma.

Stepping sections revealed areas simulating the morphology of thigh mass. Three iliac lymph nodes were dissected and revealed infiltration by the same neoplasm (Figure 4A). The tumor cells were diffusely positive for CD10 (Figure 4B) and vimentin and focally positive for pan cytokeratin (Figure 4C) and EMA (Figure 4D).

The tumor cells were completely negative for inhibin and other sarcoma markers such as SMA, desmin, myogenin and S100. Therefore, the morphological and immunohistochemical pictures indicated the diagnosis of RCC. But investigations failed to prove the presence of any renal masses. Paraffin blocks of thigh

mass were retrieved and were submitted to immunostaining for CD10, EMA, vimentin, pancytokeratin, desmin, myogenin and carbonic anhydrase IX.

For our surprise, the tumor cells of thigh mass were diffusely positive for CD10 (Figure 5A), and vimentin and focally positive for pan cytokeratin (Figure 5B), EMA (Figure 5C) and carbonic anhydrase (Figure 5D) and still showed immunoreactivity for desmin. However, the tumor cells of thigh mass were negative for myogenin.

Therefore, we are now dealing with the same tumor which is RCC metastasizing to the thigh. Patient died within two months after the resection of intra-abdominal mass and receiving one cycle of Doxorubicin.

Discussion

The present case demonstrated several issues, such as the presence of metastatic RCC with absence of primary tumor. Some studies explained this finding by spontaneous regression of the primary cancer, delayed development of the primary tumor or the presence of ectopic tissue giving rise to the neoplasm.¹⁵ According to Johnson *et al.*,¹⁵ RCC was found to be metastasizing to adrenal gland with absence of primary and according to Wayne *et al.*,¹⁶ RCC was metastasizing to three sites (the subcutaneous tissue of the arm, the pancreas and the parotid gland) without detection of primary renal origin.¹⁷

The second issue presented in this case is metastasis to unusual sites such as thigh. Some authors reported the atypical presentation of RCC and its metastatic potential to rare sites including thigh.¹⁸ Skeletal muscle represented a rare site for carcinoma metastasis that reached less than 1% of all carcinomas metastases.¹⁹ Metastases from the lung and gastrointestinal tract are the most common sources of skeletal muscle metastases.^{20,21} Renal cell carcinoma most commonly metastasizes to the lungs, lymph nodes, bone, and liver.²² Grossly, RCC at metastatic site was reported to be grayish white and multinodular.¹⁸

Skeletal muscle is not a preferred site for metastasis in spite of its rich blood supply and huge body mass because of several reported factors, such as resistance to angiogenesis by the produced lactic acid. Also, frequent contractions of the muscle may prevent cancer seeding and metastatic growth through wide variation in blood flow. In addition, high concentrations of free radicals and local temperature fluctuations may also hinder development of metastases in skeletal muscle.²³ Sarcomatoid RCC can metastasize to unusual sites including breast,²⁴ colon and oropharynx.^{25,26}

The third issue in the context of the present

case, is why the tumor cells of the thigh mass expressed desmin? This misled to the diagnosis of rhabdomyosarcoma, which was not confirmed later by using more specific markers

such as myogenin. According to Koga *et al.*,²⁷ sometimes sarcomatoid renal cell carcinoma not only takes the morphology of sarcoma but it may express sarcoma marker and in their

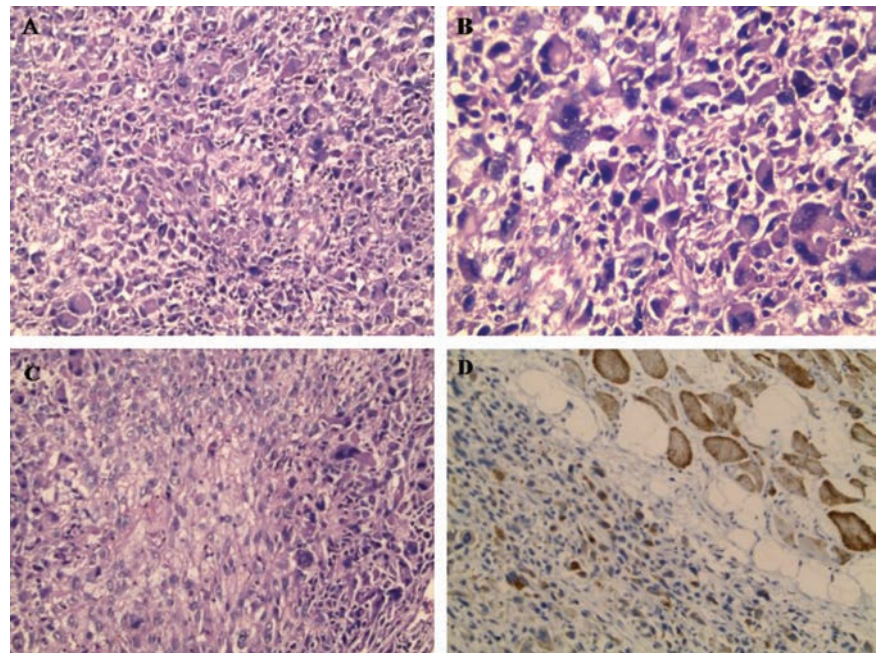


Figure 1. Histomorphology of thigh mass showing sheets of epithelioid cells with pleomorphic eccentric nuclei (A, B and C) that showed immunoreactivity for desmin (D). Skeletal muscle bundles served as internal positive control for desmin (Haematoxylin and Eosin staining $\times 200$ for A and C and $\times 400$ for B, Immunohistochemical staining $\times 200$ for D).

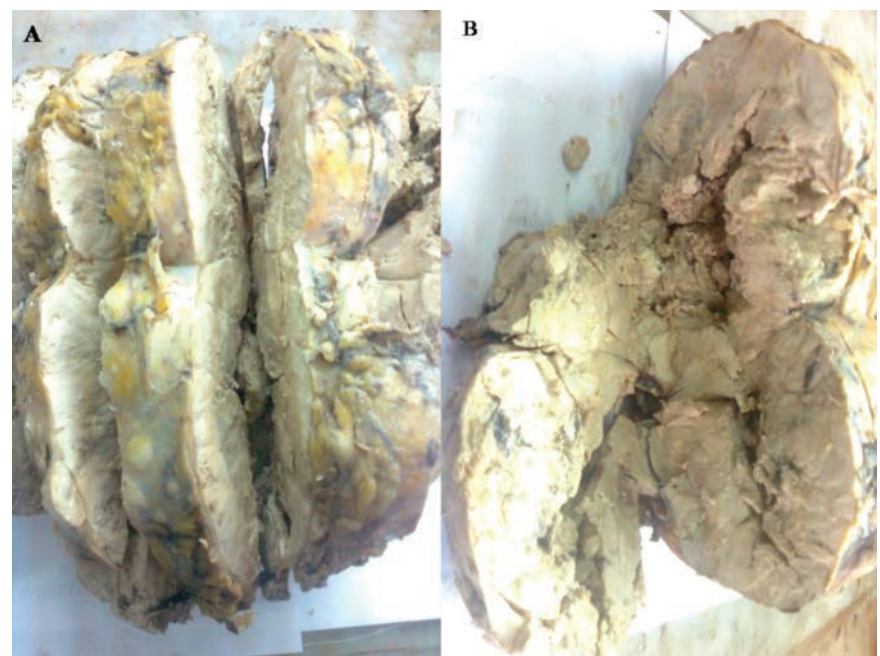


Figure 2. Gross picture of abdominal mass showed grayish white discoloration with friability and necrosis.

described case, it expressed myoglobin as one of skeletal muscle markers and they concluded that their tumor was in process of metamorphosis to rhabdomyosarcoma.

RCC may gain true molecular features of mesenchymal neoplasms with preservation of their epithelial features.^{28,29} Spindle cell carcinoma from different body areas such as larynx, skin and esophagus was reported to express mesenchymal markers such as smooth muscle actin, desmin and vimentin.³⁰ Epithelial-mesenchymal transition has been reported to be an etiological factor in metaplastic carcinoma.³¹ The expression of desmin in the current case especially with absence of myogenin expression suggested the possibility of leiomyosarcoma. However, at histological level, leiomyosarcoma is very rarely to show great pleomorphism and anaplastic areas. Leiomyosarcoma may express epithelial markers focally but still could not show CD10 or carbonic anhydrase expression. Renal leiomyosarcoma is a rare entity that sometimes causes a diagnostic challenge with sarcomatoid RCC,³² necessitating extensive sampling of the tumor and applying the immunohistochemical panel for differentiation.

The present case at the level of morphology showed definite sarcomatoid areas, but still we have seen areas with rhabdoid features manifested by abundant eosinophilic cytoplasm and eccentric nuclei. Rhabdoid variant of RCC or what is called adult RCC with rhabdoid morphology has been described as an entity representing dedifferentiation of RCC similar to the sarcomatoid variant.¹ Both rhabdoid and sarcomatoid areas may represent clonal evolution of definite carcinomatous areas toward biologically aggressive tumors. Unfortunately, our patient died within short period after the intra-abdominal operation. Median survival durations of sarcomatoid RCC without treatment (from the time of diagnosis) are 3.8 to 6.8 months.³³

According to Chivelle *et al.*¹² cancer specific survival rates at 2 and 5 years after nephrectomy were 33.3% and 14.5%, respectively. Therefore, small amounts of sarcomatoid differentiation in RCC may be clinically relevant and should be included in the pathology report. Some authors considered 5-10% of sarcomatoid areas are associated with progressive course.¹⁴

Regarding response to treatment, metastatic sarcomatoid RCC showed partial response to immunotherapy in 33% of patients.³⁴ Similar results with combination chemotherapy regimens such as doxorubicin plus gemcitabine were reported to give complete or partial responses in 40% of cases.³⁵ Unfortunately, the current case under discussion received one cycle of doxorubicin and then the patient died.

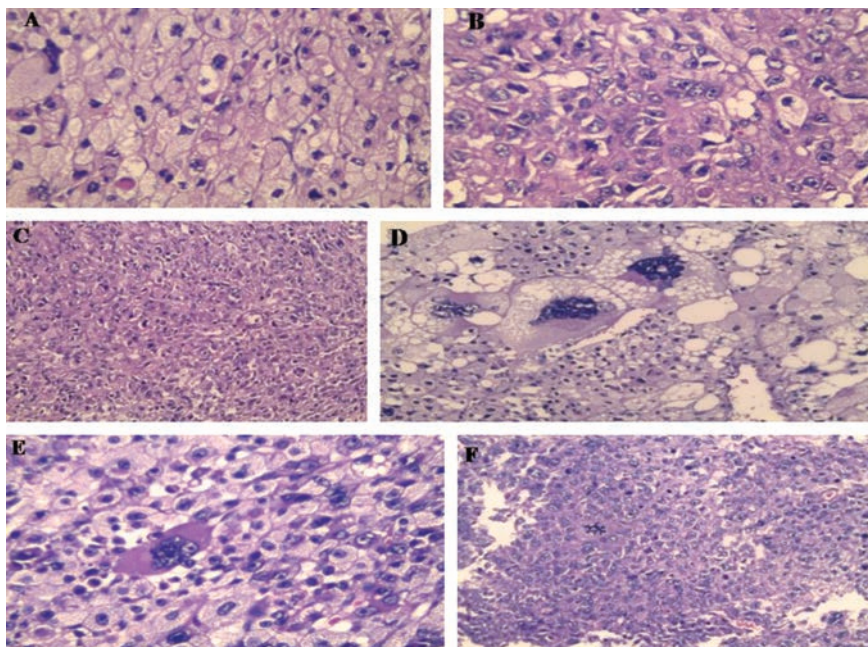


Figure 3. Histopathological picture of abdominal mass showing malignant neoplasm with conventional clear areas (A), granular eosinophilic cytoplasm (B and C), anaplastic areas with monster cells (D and E) and abnormal mitosis (F) (Haematoxylin and Eosin staining $\times 400$ for B, D and E, $\times 200$ for C and F).

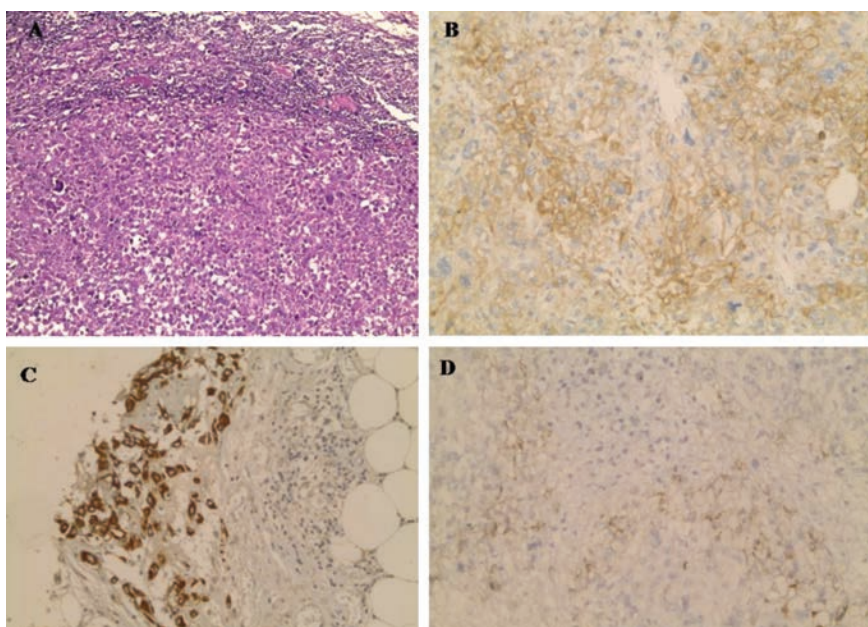


Figure 4. One of metastatic lymph node (A) (Haematoxylin and Eosin staining $\times 200$). The malignant cells of thigh mass showed diffuse positivity for CD10 (B) and focal positivity for CK (C) and EMA (D) (Immunohistochemical staining $\times 200$).

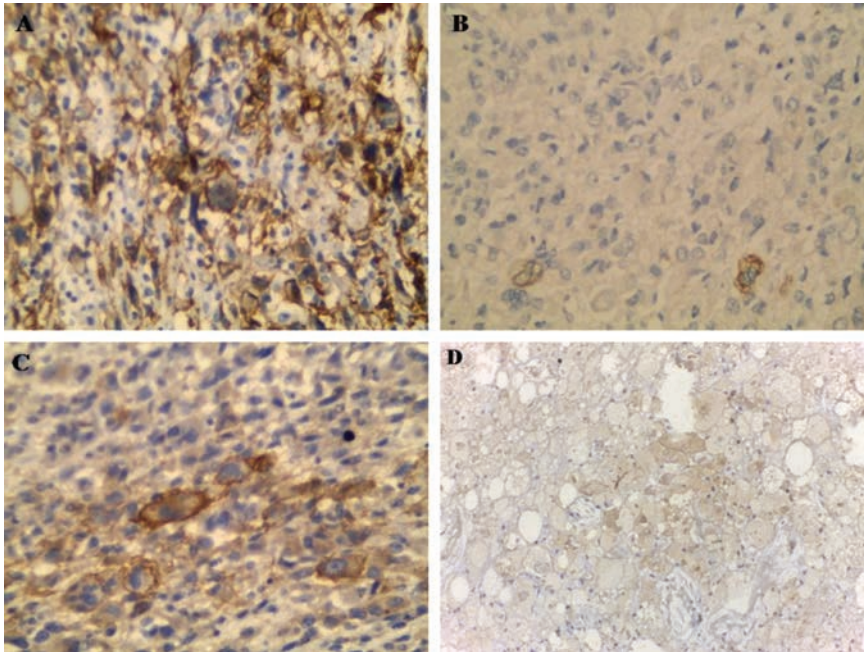


Figure 5. CD10, CK, EMA and carbonic anhydrase IX expression in malignant cells of thigh mass, respectively (Immunohistochemical staining $\times 400$).

Conclusions

Finally, our case represents conventional renal cell carcinoma with sarcomatoid and rhabdoid features metastasizing to abdomen and thigh without evidence of primary tumor. RCC can metastasize to virtually any body site and can have significant morphologic overlap with other non-renal neoplasms. Absence of primary origin of RCC according to radiological and operative data should not hinder the diagnosis of metastatic RCC. RCC with sarcomatoid and rhabdoid features carries aggressive behavior manifested by great metastatic potential and short survival time.

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