

Renal Medullary Carcinoma; A Rare Entity

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Abstract

Renal medullary carcinoma (RMC) is an uncommon aggressive neoplasm of the kidney. RMC is biologically aggressive with a very poor prognosis, and metastasis is seen in up to 95% of the patients at diagnosis or shortly thereafter. The common sites of metastasis are respectively lymph nodes, lungs, livers, and adrenal glands in order of frequency. The presence of poorly differentiated eosinophilic cells in a characteristic fibro-inflammatory stroma is seen in histological examination. The origin and pathogenesis of RMC are unclear. The radiographical and pathological findings suggest that RMC probably originates in the calyceal epithelium in or near the renal papillae, which could be the result of chronic ischemic damage in the renal papillae epithelium by sickled erythrocytes. Positivity of VEGF and HIF-1 α supports the chronic hypoxia that may be caused in the pathogenesis of RMC. Other factors such as genetic or environmental factors are important. Although hemoglobinopathy is very common, RMC is very rare. An understanding of the molecular and genetic factors of this rare disease is important for its prevention and treatment. We herein describe an adult Turkish patient, who presented with hematuria. The diagnosis was RMC after pathological examination.

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Keywords • Medullary carcinoma • Kidney neoplasms • Case reports

Introduction

Renal medullary carcinoma (RMC) is a very rare malignancy that accounts for less than 1% of all renal neoplasms.¹ RMC exhibits a highly aggressive behavior and is usually seen among young men aged between 10 and 40 years. Most patients are young African-American men.² RMC occurs in the right kidney of more than 75% of the patients. The reported patients were associated with sickle cell hemoglobinopathy, mainly with sickle cell trait and less frequently without sickle cell disease.³

The prognosis is very poor because the tumor is very aggressive and resistant to conventional chemotherapy.³ The average length of survival after diagnosis is approximately 4 months. We report a case of RMC that occurred in an adult Turkish male patient and was treated with surgery and radiotherapy.

Case Presentation

A 36-year-old man presented with gross hematuria of 1 month's duration. Physical examination was normal. Laboratory results were within normal ranges. Blood urea nitrogen and

What's Known

- Medullary renal tumors are rare kidney neoplasms. These tumors usually occur in patients with hemoglobinopathy and African origin.

What's New

- Our patient had no hemoglobinopathy and had Turkish nationality.

creatinine levels were 15 mg/dL (<23 mg/dL) and 1.28 mg/dL (0.8–1.3 mg/dL), respectively, and hemoglobin and hematocrit levels were 13.1 g/dL (12–15 g/dL) and 39.2% (40%–52%), correspondingly. Ultrasonography revealed mild hydronephrosis in the right kidney. Computed tomography showed a 5×4 cm mass localized in the central area of the right kidney, with grade II hydronephrosis (figure 1). The patient underwent open radical nephrectomy and regional lymphadenectomy. Pathological examination confirmed the diagnosis of RMC with positive lymph nodes. The tumoral mass was 6×5×4 cm in size and was located in the corticomedullary area (figure 2). The renal vein was infiltrated by the tumor cells, and the surgical margin was positive. There was tumoral infiltration in the renal cortex in microscopical examination. The tumor cells had infiltrated into the renal pelvis and shown an inflammatory reaction (figure 3). Positive lymph nodes were detected in 4 of 5 and 4 of 7 in the perihilar and interaortocaval areas. Immunohistochemical study revealed total loss of INI-1 expression (figure 4); positive staining

of vimentin (figure 5), panCK (figure 6), CK19 (figure 7), and PAX8; and negative staining of CK7, CK20, p63, uroplakin, CD 10, and 34βE12 (figure 8). After the diagnosis, electrophoresis was done for the diagnosis of sickle cell hemoglobinopathy. The result was negative for sickle cell hemoglobinopathy, and HbA1 and HbA2 bands were 85% and 15%, respectively. The patient received 50 Gy/25 fr radiotherapy. He is alive with pulmonary metastasis at 15 months' follow-up after the initial diagnosis.

Discussion

Davis et al.⁴ first described RMC on the basis of their observation of 34 patients with sickle cell trait. RMC is a very rare subtype of renal cell carcinoma which usually occurs in children and young adults with sickle cell trait and disease.⁵ There are fewer than 100 cases in the literature, with the patients' age ranging between 8 and 69 years.³ Most of the patients are of African descent and are usually associated with sickle cell trait and or disease.

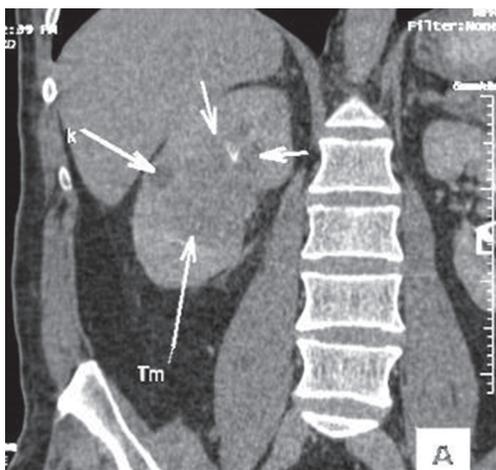


Figure 1: Computed tomography shows the mass in the central area of the kidney.

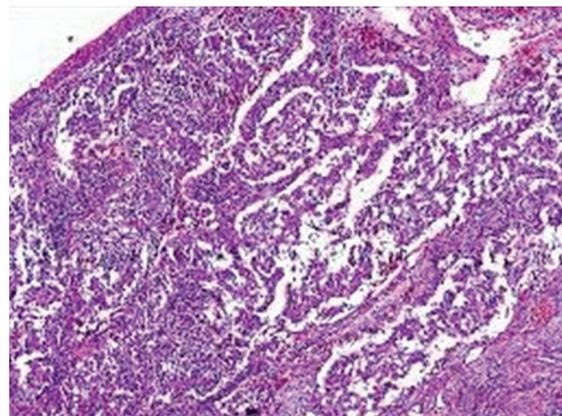


Figure 3: Tumor cells have infiltrated into the renal pelvis (HE&400).



Figure 2: It shows Gross-section of the excised kidney.

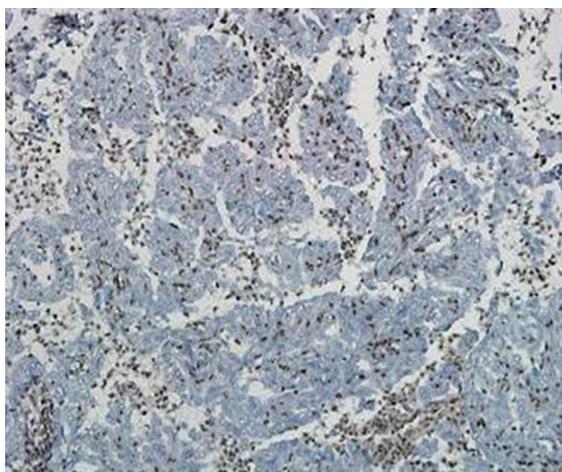


Figure 4: Tumor cells have a loss of INI-1 expression (×200).

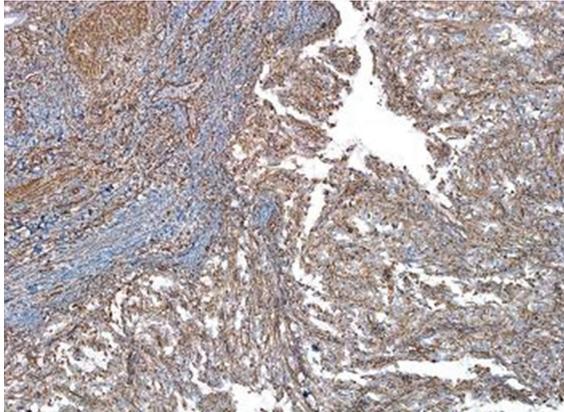


Figure 5: Cytoplasmic area is depicted with positive staining of vimentin ($\times 200$).

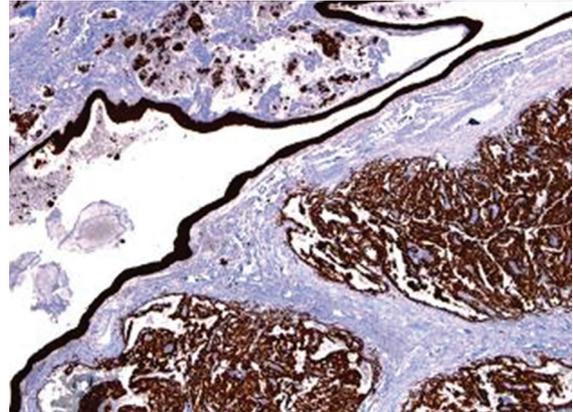


Figure 7: Positive staining of the tumor cells with CK19 is depicted ($\times 100$).

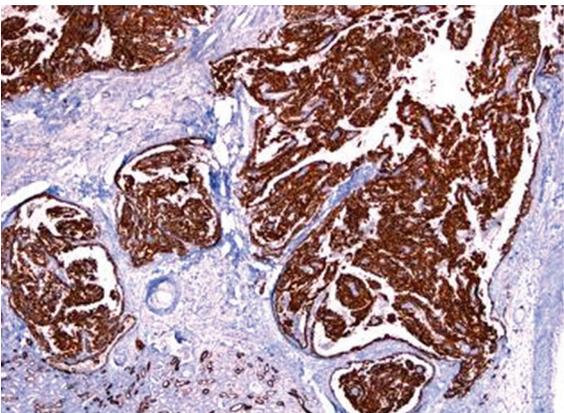


Figure 6: Positive staining of the tumor cells with panCK is illustrated ($\times 200$).

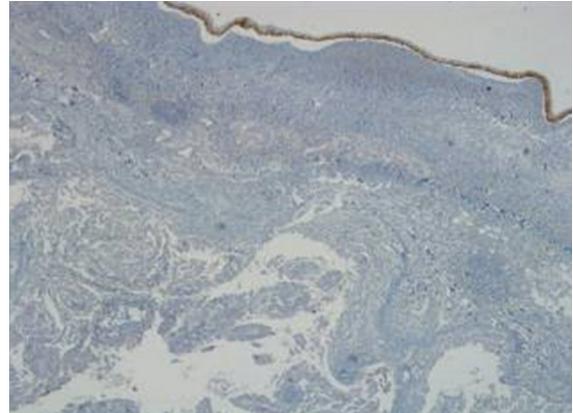


Figure 8: Cells are negative for the expression of uroplakin, P63, CK7, CK20, and 334 β E12 ($\times 100$).

Our patient was white and Turkish and had no hemoglobinopathy.

The clinical presentation of RMC includes gross hematuria, flank pain, weight loss, palpable flank mass, and enlarged lymph nodes.⁵ Most of the patients usually present with at least 1 component of classic renal triad, and some patients may present with symptoms of metastatic disease.³ The common sites of metastasis are regional lymph nodes, adrenal glands, lungs, livers, inferior vena cavae, and peritoneum. The clinical presentation of the present case was hematuria, and positive lymph nodes were detected in pathological examination.

Radiological imaging findings of RMC are nonspecific and usually manifest as an infiltrative renal mass with necrosis, caliectasis, lymphadenopathy, and heterogeneous contrast enhancement due to hemorrhage and necrosis.⁵ The treatment modalities are surgery, chemotherapy, radiotherapy, and biological agents.¹ Unfortunately, there are no effective treatment options in advanced RMC.⁵ Early diagnosis and treatment may change the survival time, with reported survival of up to

8 years in nonmetastatic tumor patient. The 2 most commonly used standard chemotherapy regimens are MVAC (methotrexate, vinblastine, doxorubicin, and cisplatin) and PCG (paclitaxel, carboplatin, and gemcitabine).³

RMC has reactive stromal elements and fair amounts of inflammatory infiltrates, unlike the other subtypes of renal cell carcinoma.³ Transitional cell carcinoma, renal lymphoma, and collecting duct carcinoma may present with a central location and an infiltrative pattern. These malignancies must be differentiated from RMC with clinical findings (ethnicity and hemoglobinopathy) and immunohistochemical studies. A panel comprising PAX8, p63, and INI1 is most optimal for distinguishing RMC from transitional cell carcinoma and collecting duct carcinoma, as all these tumors show a similar staining pattern with CK7 and vimentin.² PAX8+, p63-, and INI1- support the diagnosis of RMC. In our patient, P63, CK7, CK20, 34 β E12, and INI 1 were negative in immunohistochemical studies and PAX8 and CK19 were positive.

Although treatment options include surgery, chemotherapy, and palliative radiotherapy, there is no consensus on this topic.³ Chemotherapy

regimens are high-dose intensity MVAC (methotrexate, vinblastine, doxorubicin, and cisplatin) and PCG (paclitaxel, carboplatin, and gemcitabine).³ Unfortunately, neither chemotherapy nor radiation therapy has been found to be effective for the patients.⁶ RMC has a poor response to immunotherapy and chemotherapy.⁷ Tannir et al.⁸ reported that targeted therapy had a low efficacy when used as monotherapy. In contrast, Kondagunta et al.⁹ reported complete remission without evidence of disease in a metastatic RMC treated with bortezomib for 7 months in a follow-up >27 months. Interestingly, an 8-year-old African-Brazilian patient with RMC having been alive and free of recurrence 8 years after diagnosis was reported.¹⁰ Pulmonary metastasis occurred in our patient during the follow-up period. There is no consensus on the treatment options for RMC in the postoperative period because of the small population of the disease in the literature.

Conclusion

RMC is a very rare aggressive malignancy that affects all age groups. RMC has a poor survival because metastatic disease is almost universal at the time of diagnosis, with a median survival of about 4 months. It typically presents in young African patients with sickle cell trait or disease, with the involvement of the right kidney characteristically in over 75% of the cases. Advanced stage at the time of presentation and relative resistance to chemotherapy decrease the median survival time of the patients. Radiotherapy can be combined with surgery for the treatment. Early diagnosis is important for patients in high-risk groups (young patients with sickle cell trait or disease and presentation with hematuria).

We treated our patient with surgery and radiotherapy. Pulmonary metastasis occurred at the end of the first year after the diagnosis. Physicians should consider that RMC is a very aggressive neoplasm and has metastasis potential at the time of diagnosis or thereafter. Radiotherapy can be combined with surgery for survival.

Conflict of Interest: None declared.

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