

Renal Medullary Carcinoma

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Abstract

Renal medullary carcinoma (RMC) is a rare, aggressive renal malignancy affecting young individuals who have sickle cell hemoglobinopathy. Imaging shows an infiltrative central renal mass, often with distant metastases. Diagnosis is supported by renal biopsy. While the disease may be cured with early detection, RMC is often diagnosed at an advanced stage, making the overall prognosis poor.

Keywords: Oncology, Malignant, Renal

Case Summary

An adolescent with a history of juvenile idiopathic arthritis presented with shortness of breath. Chest radiograph (not provided) showed multiple pulmonary nodules.

Imaging Findings

CT of the abdomen and pelvis (Figure 1) showed a poorly defined mass in the upper pole of the right kidney. Multiple pulmonary metastases were present at the lung bases.

Diagnosis

Renal medullary carcinoma (RMC). The differential diagnosis for a solid renal mass in child and adolescent includes renal cell carcinoma.

Discussion

RMC is a rare form of non-clear cell renal cell carcinoma that originates from

the renal medulla.^{1,2} It comprises <0.5% of renal cell carcinomas and disproportionately affects males, adolescents (mean age at diagnosis is 13 years), and individuals with sickle cell hemoglobinopathies.³⁻⁵ Most patients with RMC have sickle cell trait, and the disease is believed to originate as a result of chronic hypoxia in areas where red blood cell sickling is pronounced, such as the renal medulla.³

Patients often present with abdominal or flank pain and hematuria. Other symptoms can include weight loss, cough, hypertension, scrotal pain, fever, urinary tract infection, and enlarging neck mass.⁶ Since the tumor often occupies a central location in the kidney, it is predisposed to infiltrate adjacent tissue, achieve lymphatic spread, and have a delayed presentation, often with initial symptomatic metastases.⁴ The tumor is more common in the right kidney than the left, though currently there is no established explanation for this disparity.^{5,7}

Imaging plays an important role in the diagnosis of RMC, which more often initially reveals advanced-stage metastatic disease compared with cases of isolated

primary renal tumor.² In addition to determining primary tumor size, shape, and exact location, imaging allows for characterization of local infiltration, lymphatic spread, and vascular invasion.⁵ Furthermore, imaging findings guide management decisions regarding the feasibility of surgical resection, the need for systemic therapy, or the use of radiation therapy for local control or palliation of symptoms.^{4,7}

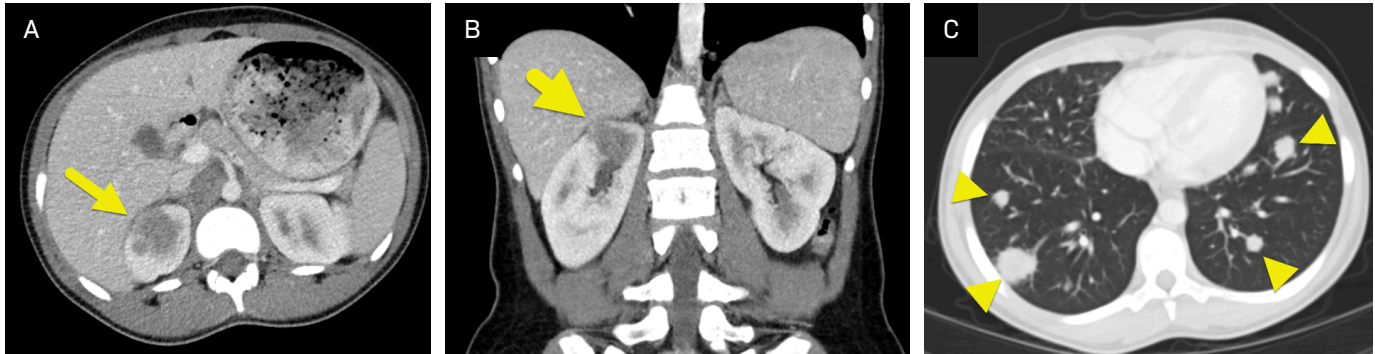
US is often the initial imaging study performed in an adolescent with flank pain and hematuria. It shows a hypoechoic renal lesion.^{5,7} CT and MRI reveal an infiltrative central renal mass with indistinct margins and associated caliectasis.⁷ Other findings that may be present include tumor necrosis, intra-tumoral or subcapsular hemorrhage, and retroperitoneal adenopathy. On CT, RMC appears hypodense compared with the normal renal parenchyma during the cortical, medullary, and delayed phases.² On MRI, the tumor is hypointense on contrast-enhanced T1 sequences and on T2 sequences.⁷ Tumor necrosis, renal caliectasis, and para-aortic lymphadenopathy are common associated findings.⁵ While both CT and MRI are able to detect the tumor, MRI is better able to identify intra-tumoral hemorrhage, hepatic metastasis, and renal vein and inferior vena cava thrombus.^{2,8}

Diagnosis of RMC typically involves a combination of clinical evaluation,

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Figure 1. (A) Axial and (B) coronal contrast-enhanced CT showing a poorly defined mass (arrow) within the upper pole of the right kidney. The mass does not enhance compared with adjacent renal parenchyma. (C) CT of the chest showing multiple pulmonary metastases (arrowhead). The metastases have a spiculated margin, and the largest lesion in the right lower lobe has mild adjacent ground-glass opacity.



imaging studies, and histopathological examination, which shows poorly differentiated tumor cells with high-grade nuclear features, arranged in a reticular pattern.³ Gene sequencing and immunohistochemistry help confirm the diagnosis of RMC. Genetic analysis shows RMC to have inactivating mutations in the *SMARCB1/INI1* tumor suppressor gene.³ Translocation renal cell carcinoma, another tumor in the differential diagnosis, does not demonstrate loss of *SMARCB1*.⁴ Immunohistochemistry is required for the diagnosis of RMC, which demonstrates INI1 loss in all cases.³ RCC unclassified with medullary phenotype also demonstrates INI1 loss but arises in older patients without hemoglobinopathy and can be differentiated demographically from RMC, which presents in younger patients with sickle cell trait.³

The prognosis of RMC is poor, with >90% of patients having stage 3 or 4 disease at diagnosis.⁴ When metastases are present, they are most commonly located in the mediastinal lymph nodes, lungs, liver, and bone.⁶ Lymphatic and vascular invasion are common, and lymphangitic spread, particularly in the lungs, contributes to the severe clinical presentation and complicates treatment strategies.^{3,8} Unfortunately, patients with

stage 4 disease fare poorly with a median survival of 11.1 months.⁹

Treatment of RMC is similar to that of other non-clear cell renal cell carcinomas, with curative intent nephrectomy considered for localized stage 1-3 disease.⁹ Stage 4 or unresectable disease has a poor prognosis and requires systemic therapy, including cytotoxic chemotherapy, molecularly targeted agents, and biologics.⁹ Surgical or radiation therapy may be a supportive option for patients with symptomatic metastases.

Conclusion

RMC is a rare, aggressive renal malignancy affecting young individuals who have sickle cell hemoglobinopathy. Imaging shows an infiltrative central renal mass, often with distant metastases. Diagnosis is supported by renal biopsy. While the disease may be cured with early detection, RMC is often diagnosed at an advanced stage, making the overall prognosis poor.

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