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Case Reports

Renal Cell Carcinoma Metastasis to the Left Atrium

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Only 13 cases of renal cell carcinoma metastasis to the left atrium of the heart have been described. We report the case of a man in his 50s who had undergone radical nephrectomy for renal cell carcinoma in 2006 and presented with amnesia at our neurology department in 2020. Magnetic resonance images of the brain showed metastatic lesions; subsequent computed tomograms of the chest, abdomen, and pelvis revealed a mass in the left atrium and multiple metastases in the lung, pleura, and pancreas. Our cardiologists advised against surgical removal of the left atrial mass because of a poor prognosis, so radiation therapy and immunotherapy were initiated instead. ***(Tex Heart Inst J 2022;49(3):e207452)***

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Cardiac neoplasms are rare and are almost always metastatic in origin. In an autopsy study of 266 cases involving cardiac neoplasms, only 2 tumors (0.8%) were primary.[1] In another study of 12,485 autopsies, the incidences of primary and secondary heart tumors were 0.06% and 1.23%, respectively.[2] The pericardium is the most frequent site of metastasis.[1,2]

Renal cell carcinoma (RCC) accounts for 2% to 3% of all cancers.[3] It is highly aggressive, typically metastasizing to the lungs, liver, bones, and brain. In contrast, RCC metastasis to the heart is unusual, and metastasis to the left atrium (LA) is even rarer.[3] We report a case of RCC with metastasis to the LA.

Case Report

A man in his late 50s presented at our neurology department in 2020 with self-reported amnesia and loss of coordination during the past week. He had a history of stage 2 clear cell RCC for which he had undergone left-sided nephrectomy in 2006. In 2011, he had undergone wedge resection of 2 pulmonary nodules.

Brain magnetic resonance images with contrast medium revealed 2 large lesions in the frontal and parietal lobes. A contrast computed tomogram (CT) of the chest, abdomen, and pelvis revealed a large tumor extending from the inferior pulmonary vein (PV) into the LA (Fig. 1). The CT also showed an increase in the number and size of pulmonary, pleural, and perihilar masses when compared with the patient's 2011 CT data, along with multiple new masses in the pancreatic tail. Echocardiograms showed a 3 × 2.5-cm oval mass in the LA (Fig. 2). Our cardiologists advised against surgical resection because of a poor prognosis, so we prescribed the patient a 10-session regimen of 3-dimensional conformal radiation therapy, 5 mg of axitinib twice daily, and 200 mg of intravenous pembrolizumab 3 times weekly.

At the patient's 4-month follow-up examination, his memory recall had improved substantially. He still had no symptoms to suggest an atrial mass, such as syncope, dyspnea, chest pain, cough, or peripheral edema.[4] The radiotherapy had brought 70% to 75% subjective improvement. An echocardiogram revealed a 3 × 2.5-cm oval, pedunculated, mobile mass attached to the LA posterior wall. Valvular structures and excursions were normal, and no pericardial pathologic condition was observed. We observed mild (grade 1) diastolic impairment, preserved left and right ventricular systolic function, and no notable valvular abnormalities. Blood test results were within normal limits. The patient's therapeutic regimen was reduced to 400 mg/d of oral pazopanib.

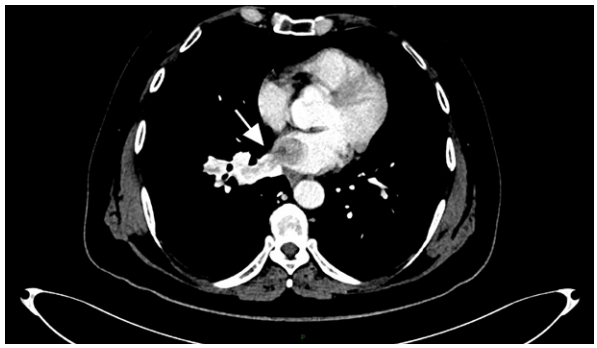

Fig. 1 *Computed tomogram (axial view at the level of the cardiac chambers) shows a hypodense mass (arrow) extending from the pulmonary vein into the left atrium.*

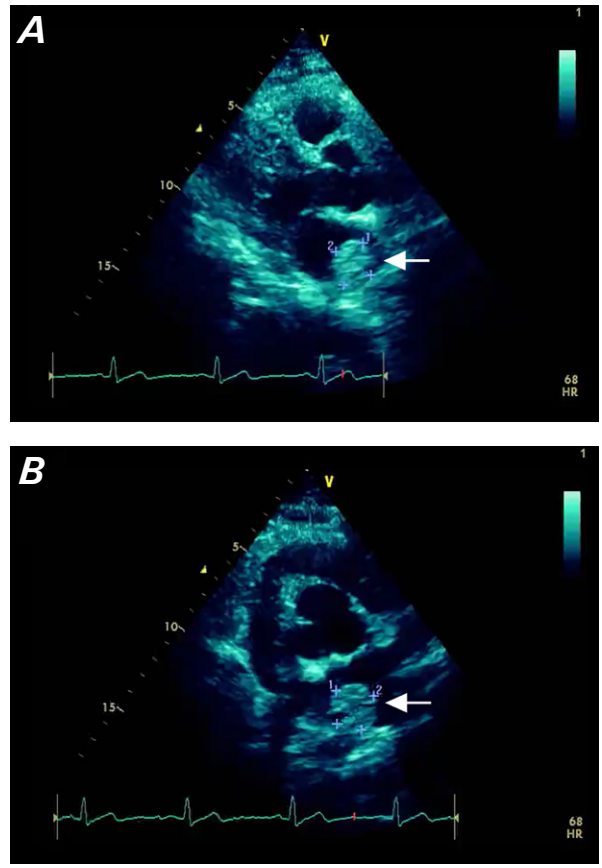

Fig. 2 *Transthoracic echocardiograms in **A**) parasternal long-axis view and **B**) parasternal short-axis view at the aortic valve level show a left atrial mass (arrows).*

Discussion

Our patient presented with LA metastasis 14 years after a nephrectomy for RCC, slightly longer than the longest interval (13 yr) reported previously for any similar case.[3] He had purely neurologic symptoms and none indicating cardiac involvement.

Renal cell carcinoma is the 12th most prevalent cancer worldwide; the highest incidence is in North America, Europe, and Australia.[5] Chief among RCC's multiple histologic subtypes is clear cell RCC, which accounts for 75% of all primary kidney tumors. The characteristic triad of hematuria, flank pain, and palpable abdominal mass is present in only 10% of patients who have RCC. Most cases are diagnosed incidentally during imaging studies, such as abdominal ultrasonography or CT.[5]

Because RCC rarely metastasizes to the heart, its diagnosis is difficult. In addition, affected patients are mostly asymptomatic and can present variably. Hypertension occurs in 20% to 38% of patients; other cardiac presentations include syncope, dyspnea, chest pain, cough, and peripheral edema.[4] Cardiac tumors can also compress or occlude one or more coronary arteries, leading to myocardial infarction or heart failure.[6] Pericardial involvement with effusion and cardiac tamponade is the typical cause of hemodynamic compromise.[7]

Although CT is usually used to evaluate metastases in the chest, it is not ideal for investigating cardiac metastases. Viteri Malone and colleagues[8] suspected that the incidence of cardiac involvement in patients with metastatic RCC is underestimated because refined cardiac imaging techniques, such as cardiac magnetic resonance (CMR), ultrafast CT, echocardiography, and multigated acquisition, are not routinely used in cancer detection. Czarnecka and associates[9] recommended CMR in these patients.

Lymburner[10] identified 4 pathways through which carcinoma spreads to the heart: direct invasion, the bloodstream, lymphatic structures, and combined hematogenous/lymphatic metastasis. Lymphatic spread is often associated with metastasis to the left side of the heart. The carinal lymph nodes and parasternal lymph vessels collect drainage from the posterior wall of the heart. It is thought that the metastasis reaches the carinal lymph nodes through the lymphatic pulmonary drainage; it then reaches the pericardium and left-sided myocardium through reverse lymphatic flow caused by the node metastasis. Another pathway, hematogenous spread, is through the renal vein to the heart. This route is more often associated with metastasis to the right side of the heart.[3,11] Unlike left-sided heart metastasis from RCC, which is frequently associated with metastasis to other sites, right-sided metastasis does not appear to spread to other sites.[12]

Almost all reported cases of RCC-to-LA metastasis involve the PV, suggesting that RCC metastasizes to the LA through the PVs. Our case reinforces this hypothesis. We know of only one case of RCC metastasis to the LA in which no PV tumor thrombus developed; however, coronary sinus invasion in that case suggested another pathway through which LA metastasis might occur.[3]

It is possible, although unlikely, that a mass found incidentally in a patient with RCC and metastasis is

instead an atrial myxoma. Our patient's mass had some features of an atrial myxoma (clear definition and pedunculation with a stalk); however, we were unable to confirm this histologically because surgical excision was not performed.

Treatments for metastatic RCC are evolving. In a network meta-analysis,[13] first-line treatment for metastatic RCC was determined in accordance with clinical risk group, toxicity, and efficacy endpoints. The results of that meta-analysis suggested that, for intermediate-risk and poor-risk groups, pembrolizumab plus axitinib, avelumab plus axitinib, and cabozantinib produced superior progression-free survival, and pembrolizumab plus axitinib produced superior overall survival.[13] In contrast, no such treatment regimen is available for RCC metastasis to the heart.

Given the risk of sudden cardiac death, most cardiac masses are removed surgically as soon as possible. For inoperable metastases, molecular targeted therapy is used.[3] Temsirolimus, a mammalian target of rapamycin inhibitor, produced excellent clinical and radiographic responses with acceptable tolerability in one patient.[14] Nivolumab, a programmed death-1 receptor inhibitor, reduced the size of an intracardiac RCC metastasis by 70% in another patient.[15] Sunitinib, a tyrosine kinase inhibitor, completely eradicated myocardial metastasis during the second cycle of drug administration in one patient.[16]

Conclusion

Atrial masses can be detected in patients years after nephrectomy and may not produce obvious symptoms, so patients with RCC should undergo regular cardiovascular evaluation and investigation of any cardiac mass. If surgery is inadvisable, the patient should be started on immunotherapy, and the cardiac mass should be monitored regularly for structural changes.

Given that there is no established algorithm for managing cardiac metastases from RCC, a surgical approach seems most feasible. For inoperable metastases, molecular therapy is an alternative, although further studies are needed to determine efficacy and safety profiles.

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