

Acute Ischemic Stroke as a Result of Paradoxical Embolus in a Patient with Renal Cell Carcinoma, Intravenous Tumor Thrombus Extension, and Patent Foramen Ovale

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Introduction: Patent foramen ovale is a common congenital cardiac abnormality. An association with acute ischemic stroke is well described. Extension of renal cell carcinoma (RCC) into the adjacent veins is common. Surgical resection is felt to be an effective approach to treatment, even in the setting of extensive venous involvement.

Case Report: A 55-year-old woman with recently diagnosed right renal mass and cavoatrial tumor thrombus was transferred to our facility for surgical resection. She subsequently underwent open radical right nephrectomy, regional lymph node dissection, inferior vena cava and right atrial tumor thrombectomy, and resection of the infrahepatic vena cava. An intraoperative transesophageal echocardiogram confirmed the absence of tumor thrombus from the inferior vena cava and right atrium and also identified a patent foramen ovale (PFO). Upon weaning sedation, she was noted to be agitated and have left hemiplegia. Her National Institutes of Health Stroke Scale (NIHSS) was 30 and Glasgow Coma Scale (GCS) 6. The computerized tomography scan of head revealed extensive hypoattenuation right in the middle and left posterior cerebral artery territories. There was associated cerebral edema and 5-mm midline shift. In the setting of devastating neurological injury, her family elected to transition to comfort care and the patient died on the postoperative day 7.

Conclusions: This is the first reported case of intraoperative paradoxical embolism in the setting of RCC with cavoatrial extension and PFO. The presence of PFO may be a risk factor for severe cerebrovascular complications in the surgical management of RCC with venous involvement.

Key Words: renal cell carcinoma, patent foramen ovale, paradoxical embolism, stroke

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BACKGROUND

Surgical resection is the mainstay of therapy for renal cell carcinoma (RCC).¹ The favorable long-term outcome has been reported in the absence of regional or distant metastatic disease.^{2,3} In addition, resection may be attempted in more advanced tumors to alleviate symptoms, palliate, or as a cytoreductive approach to prepare the patient for immunotherapy.^{4,5} Venous extension in RCC is common and poses unique surgical challenges. In a large retrospective case series from Mayo Clinic in Rochester, Minnesota, invasion of the renal veins was reported in 19% of cases, invasion of the inferior vena cava (IVC) in 7% of cases, and

supradiaphragmatic extension in 1% of cases. The rate of early complications (<30 d) increased significantly with the extent of the tumor thrombus (14%, 18%, and 30% for level II, III, and IV thrombus, respectively).⁶

Patent foramen ovale (PFO) is a common congenital cardiac abnormality that often persists into adulthood and has been associated with cryptogenic stroke. On the basis of autopsy and echocardiographic studies, the prevalence of PFO is estimated at 20% to 30% in the general population.^{7,8} Right-left shunting of blood during early systole and with Valsalva maneuver can allow fragments of the venous thrombus to travel into the arterial circulation and cause ischemic thromboembolic strokes, a process termed a paradoxical embolism.⁹ Recent evidence has demonstrated a role for PFO closure in selected patients with cryptogenic stroke.^{10–12}

We present a case of a catastrophic acute ischemic stroke in a patient with RCC and extensive cavoatrial tumor thrombus because of intraoperative paradoxical embolism in the setting of a PFO.



FIGURE 1. Axial thoracic computerized tomography scan image showing tumor thrombus within the right atrium and right ventricle with visible contrast extravasation across the interatrial septum (red arrow) into the left atrium.

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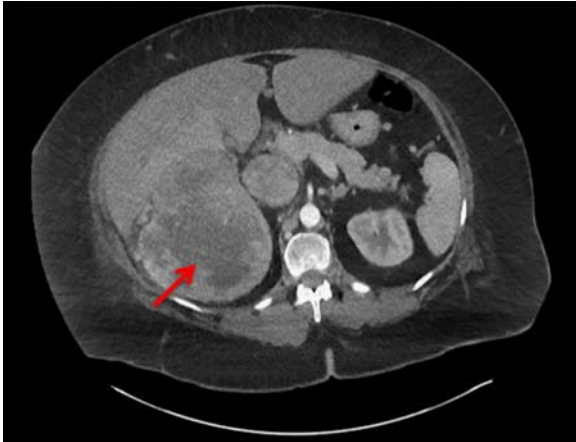


FIGURE 2. Axial abdominal computerized tomography images showing a solid, extensive right renal mass (red arrow) with heterogeneous contrast enhancement and areas of central necrosis.

CASE REPORT

A 55-year-old woman was transferred to our facility for a higher level of care of a newly diagnosed right-sided renal mass and extensive thrombus in her IVC. She had no significant medical history other than arterial hypertension and obesity. About 2 months before the presentation, she had started to complain of bilateral leg swelling and weakness, shortness of breath, and palpitations. Laboratory testing at an urgent care facility had been notable for anemia. An electrocardiogram and chest x-ray were unrevealing and a lower extremity ultrasound did not reveal deep venous thrombosis.

She was initially treated with diuretics and iron tablets, however, her condition continued to deteriorate. One and a half weeks before her transfer, she was seen at a local emergency department with worsening dyspnea and palpitations. An echocardiogram demonstrated an intracardiac thrombus, prompting admission to the local hospital. She subsequently underwent a computerized tomography (CT) scan of the chest to rule out pulmonary embolism, which confirmed a right atrial thrombus (Fig. 1). A CT angiogram of the chest, abdomen, and pelvis showed an 18-cm mass of the right kidney with extensive tumor thrombus ranging from her IVC to the right atrium (Figs. 2, 3). In addition, retroperitoneal lymphadenopathy and a heterogeneous nodule of the right thyroid were noted. A 2.3-cm mass in the left kidney likely represented a complex cyst, however, malignancy could not be ruled

out. Three to 4 days before the transfer, she was started on anticoagulation with therapeutic doses of subcutaneous enoxaparin.

After the transfer, she was evaluated by an interdisciplinary team that included urology, cardiology, vascular surgery, and cardiothoracic surgery services. She underwent preoperative medical evaluation including transthoracic echocardiogram, CT coronary angiography, and pulmonary function tests and was cleared for surgery. On day 6 of the hospitalization, the patient underwent right open radical nephrectomy and regional lymph node dissection, IVC, and right atrial tumor thrombectomy and resection of the infrahepatic vena cava. Access was obtained through a combination of a subcostal and midline incision and a median sternotomy. Cardiopulmonary bypass commenced after administration of 35,000 units of intravenous heparin, and the patient was cooled to $\sim 32^{\circ}\text{C}$. However, ultimately it was felt by the operating teams that hypothermic circulatory arrest would not be required and the patient was rewarmed. Two applications of the Pringle maneuver, that is, clamping of the hepatoduodenal ligament to reduce intraoperative blood loss, were performed resulting in a total Pringle time of 20 minutes. The total cardiopulmonary bypass time was 46 minutes.

The dissection of the renal mass and exposure of the vena cava was complicated by extensive bleeding from parasitic blood vessels and the sheer size of the tumor. Intraoperatively it was noted that the tumor thrombus completely occluded the intrapelvic iliac veins, as well as the left and right renal veins up to the intrahepatic vena cava. Unfortunately, there was an invasion of the tumor into the IVC throughout its extent. Intraoperative transesophageal echocardiogram (TEE) showed the large tumor thrombus filling the entire circumference of the IVC, extending into the right atrium and prolapsing across the tricuspid valve into the right ventricle during diastole. A PFO was noted. Most of the thrombus could be resected en bloc along with the mass. A smaller portion of thrombus, however, had to be removed manually and the cardiac surgery team had to milk parts of the thrombus from the right ventricle into the vena cava. Subsequently, the rest of the tumor mass was removed from the right atrium. After completion of the resection, there was no identifiable residual tumor mass on inspection of the right atrium, tricuspid valve, right ventricle, and vena cava. The infrahepatic IVC was transected and removed in its entirety. TEE confirmed the complete removal of the tumor thrombus from the IVC and right atrium with postbypass left ventricular ejection fraction of 65%. The patient in total received 6 units of packed red blood cells and 6 units of fresh frozen plasma. Postoperatively, she was transferred immediately to the intensive care unit for further management.

Upon weaning off sedation the patient was noted to be agitated and showed signs of dense left hemiplegia. When the neurology team arrived at the bedside, the patient had already been resedated. Neurological examination was notable for no movement in left arm and leg and a left extensor plantar response. Her National Institutes of Health Stroke Scale was 30 and Glasgow Coma Scale was 6. An emergent



FIGURE 3. Coronal (A) and sagittal (B) abdominal computerized tomography images showing a solid mass in the right kidney extending into the right renal vein with a diffuse inferior vena cava tumor thrombus extending above the diaphragm into the right atrium (red arrows).

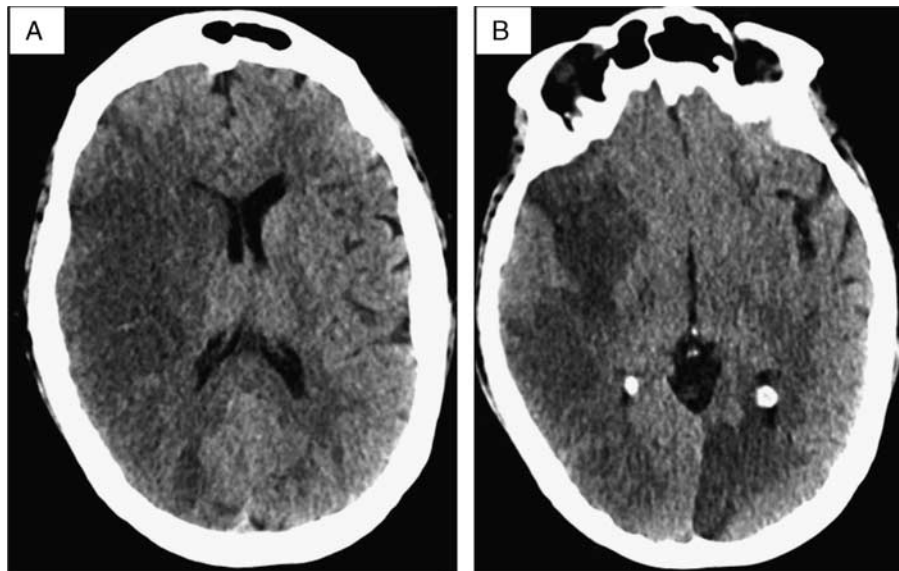


FIGURE 4. Axial noncontrast brain computerized tomography scan images showing a large right middle cerebral artery stroke, moderately effaced right lateral ventricle, right-to-left midline shift (A) and a left paramedian occipital stroke (B).

noncontrast head CT showed extensive acute infarction in the territory of the right middle and left posterior cerebral arteries (Fig. 4). CT angiogram showed occlusion of a distal branch of the left posterior cerebral artery and otherwise patent vasculature. There was moderate effacement of the right lateral ventricle with 5 mm of right-to-left midline shift and no sign of hemorrhage. The patient was not a candidate for the administration of tissue plasminogen activator (t-PA) or endovascular mechanical thrombectomy. In an emergent meeting with the patient's family, it was decided not to pursue further invasive interventions. The patient was initiated on comfort care measures and died on the postoperative day 7.

The final pathology of the resected renal tumor revealed RCC, clear cell type, with 30% necrosis and 5% rhabdoid features, International Society for Urological Pathology (ISUP) grade 4, extending into the IVC with the involvement of the vessel wall. Metastatic carcinoma was also found in 4 of 6 resected lymph nodes.

DISCUSSION

Here we report the first case of acute ischemic stroke caused by intraoperative paradoxical embolism in the setting of RCC with cavoatrial extension and PFO. Venous involvement in RCC is common and typically demands aggressive surgical management. Acute ischemic stroke caused by paradoxical venous thromboembolism through a PFO has been well described in the general population and the benefit of PFO closure has been demonstrated for selected patients.^{10–13} Stroke seems to be a rare perioperative complication in RCC. A recent case series from Weill Medical College in New York evaluated 25 patients with intra-abdominal malignancies with the cavoatrial extension (mostly RCC) and reported a 4% perioperative rate of stroke.¹⁴ Another recent case series of 41 patients reported perioperative stroke in 1 patient.¹⁵ No strokes were reported in the Mayo Clinic case series.⁶

On the basis of a comprehensive search of the bibliographic databases of published biomedical research, only 3 reports of paradoxical embolism as a cause of acute ischemic stroke in the setting of RCC were retrieved. Schwamm et al¹⁶ reported a case of acute ischemic stroke caused by paradoxical embolism through a PFO in a patient with May-Thurner syndrome and occult RCC. Dumont et al¹⁷ described a case of paradoxical cerebral emboli through a PFO from cardiac

metastasis 5 years after resection of a primary RCC. In addition, Gonzalez et al¹⁸ described the case of metastatic growth after cerebral infarctions traced to paradoxical emboli in the setting of PFO and RCC metastasis of the IVC and right atrium, 2 years after complete resection of the primary tumor. Finally, Hamirani et al¹⁹ reported a case of impending paradoxical embolism 1.5 years after RCC resection, with a thrombus extending across a PFO into the left ventricle. Other reported cases of ischemic stroke in RCC have been attributed to polycythemia, metastatic invasion of the pulmonary veins, or the use of tyrosine kinase inhibitors.^{20–22}

Our case suggests that patients undergoing radical surgery for RCC with venous involvement might be at an increased risk for cerebrovascular accidents in the presence of a PFO. We, therefore, propose that vigorous screening for PFO, including transthoracic echocardiogram with agitated saline injection, transcranial Doppler to detect right-left shunt, and TEE, be a component of the preoperative workup for RCC with venous involvement. In the event a PFO is discovered preoperatively, its closure should be contemplated in this population.

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