

Cocaine-Induced Renal Artery Dissection and Thrombosis Leading to Renal Infarction

David A. Edmondson, DO; Jonathan B. Towne, MD; Dennis W. Foley, MD; Majed Abu-Hajir, MD; Mahendr S. Kochar, MD, MS

ABSTRACT

We present the case history of a 40-year-old man who developed renal artery dissection and thrombosis, probably due to cocaine use. The patient underwent exploratory laparotomy and thrombectomy. He remained asymptomatic and cocaine-free, and warfarin was discontinued 9 months after discharge. Approximately 12 months after discharge he returned to the hospital with symptoms very similar to previous episodes. He was found to have recurrent clot formation in the right renal artery. Further workup revealed a double heterozygous methyltetrahydrofolate reductase A1298C/C677T thermolabile polymorphism with an elevated serum homocysteine.

INTRODUCTION

Renal artery dissection is rare and difficult to diagnose. Patients presenting with acute renal infarction typically have severe, persistent abdominal pain along with sudden onset of low back pain. The symptoms of renal dissection and infarction suggest more common diseases including nephrolithiasis, along with other intra-abdominal diseases, musculoskeletal pathology, and angina, thus making this diagnosis difficult to establish.^{1,2} Causes of renal artery dissection include fibromuscular dysplasia, connective tissue disorders including Ehlers-Danlos syndrome, Marfan's syndrome, systemic lupus erythematosus, Behcet's disease, polyarteritis nodosa, trauma and cocaine use.^{1,2} Additionally, iatrogenic causes of renal artery dissection include angiographic

procedures using wires, balloons, stents, and catheters.³ Documented risk factors for renal infarction include atrial fibrillation, valvular heart disease, ischemic heart disease, hereditary clotting disorders, pregnancy, and cocaine use.^{2,4} We present a case of renal artery dissection leading to renal infarction in the setting of recent cocaine use.

CASE REPORT

In September 2002, a 40-year-old man was seen in the emergency department at another facility with severe right abdominal and flank pain. The pain began suddenly, awaking the patient at 3 A.M. The pain was followed by nausea and vomiting. No fevers or chills were noted. The patient stated that he used cocaine the evening prior. The urinalysis was normal with no red blood cells noted. Blood chemistry was blood urea nitrogen 17 mg/dL (6-20 mg/dL) and creatinine 1.3 mg/dL (0.6-1.2 mg/dL). Ultrasound revealed variable attenuation in the right lower pole of the kidney. Computerized tomography of the abdomen revealed a segmental perfusion defect in the lower pole of the right kidney in the distribution of the posterior segment of the renal artery. Urology was consulted and diagnosed the patient with cocaine-induced renal artery spasm resulting in a right renal infarct. No interventions were performed, the patient's pain was controlled, and he was hydrated and discharged home.

Approximately 7 months later, the patient presented to our institution's emergency department complaining of abdominal pain exactly as described above, along with low back pain. He denied chest pain, shortness of breath, dysuria, hematuria, fevers, or chills. The patient reported stopping cocaine use 2 months prior to arrival. Additionally, he denied a family history of thrombosis. At admission time his temperature was 97.0 F, pulse rate 59 regular, blood pressure 119/70 mm Hg, respiratory rate 18 breaths/minute. Physical exam revealed a healthy-appearing male writhing in pain,

All authors are with the Medical College of Wisconsin, Milwaukee, Wis. Doctor Edmondson is a fellow, allergy and immunology; Doctor Towne is a professor of surgery; Doctor Foley is a professor of radiology; Doctor Abu-Hajir is an assistant professor of medicine of hematology and oncology; Doctor Kochar is a professor of medicine and pharmacology and toxicology. Please address correspondence to: Mahendr S. Kochar, MD, Medical College of Wisconsin, 8701 Watertown Plank Rd, Milwaukee, WI 53226; phone 414.456.4575; fax 414.456.6528; e-mail kochar@mcw.edu.

slouched over to his right side. There was significant tenderness to palpation over his right lower quadrant as well as right flank region. Urinalysis was unremarkable for blood, leukocytes, bacteria, and esterases. Urine drug screen was negative for cocaine. Blood chemistry values were blood urea nitrogen 16 mg/dL and creatinine 1.2 mg/dL. The electrocardiogram was unremarkable for arrhythmia, ischemia, or myocardial infarction. Computed tomography of the abdomen revealed multiple infarctions in the right kidney, visible clot in the aorta and right renal artery (Figure 1). The lower pole of the right kidney revealed scarring consistent with previous infarction. The patient was started on intravenous heparin and analgesia and further imaging was obtained. An abdominal aortogram was performed revealing an intraluminal filling defect within the aorta with an extension into the right renal artery. Nephrogram revealed patchy filling defects of the right kidney; additionally the right kidney was notably smaller than the left. A transthoracic echocardiogram revealed a normal ejection fraction, left ventricular function, lack of intracardiac shunt, and no valvular disease; additionally no intracardiac thrombus was visualized. An initial hypercoagulable work up was unremarkable.

The patient subsequently underwent laparotomy. A transverse incision of the aorta was performed and extended to the right renal artery revealing a localized arterial dissection extending from the aorta to the renal artery. A localized endarterectomy of the aorta surrounding the superior mesenteric artery and renal artery was performed. The debris was characteristic of atherosclerotic material. Pathology of the atherosclerotic material revealed tissue consisting of ganglion and nerve.

The patient was discharged home on enoxaparin 1 mg/kg subcutaneously twice daily followed by warfarin. INR was maintained between 2-3. He remained asymptomatic and warfarin was discontinued 9 months after discharge. Approximately 12 months after discharge he returned to the hospital with symptoms very similar to previous episodes. He denied cocaine use within the prior 14 months. He was found to have recurrent clot formation in the right renal artery. A positron emission tomographic (PET) scan, looking for malignant tumors of the blood vessel wall, was negative. Further hypercoagulable workup including factor V Leiden, prothrombin gene mutation, protein C and S deficiency, antithrombin activity, anticardiolipin antibody panel, and lupus anticoagulant revealed a double heterozygous methyltetrahydrofolate reductase (MTHFR) A1298C/C677T thermolabile polymorphism with a mild elevation of serum homocysteine (18 micromol/L) (range 5-

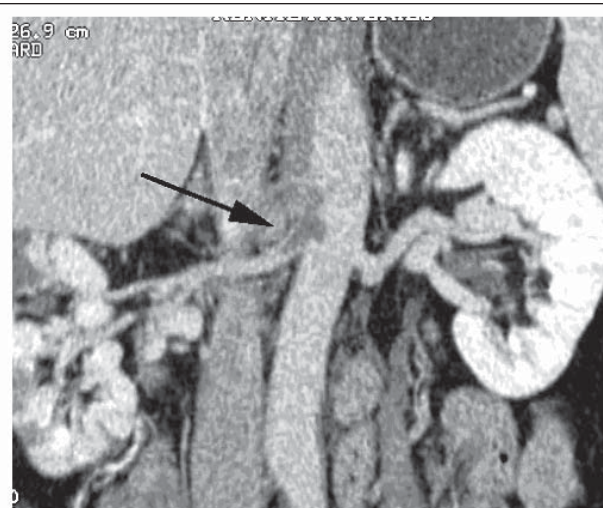


Figure 1. Coronal plane reformation of routine abdominal CT scan. Thrombus attached to right lateral wall of suprarenal aorta and projecting into proximal right renal artery is seen (black arrow). Note relative decreased enhancement of right kidney and multifocal peripheral zones of absent enhancement consistent with multifocal infarction.

14 micromol/L). He was started on oral folic acid 1 mg daily and warfarin was continued, maintaining an INR of 2-3. Following discharge he had no further episodes and his renal function remained normal; a subsequent serum homocysteine level was 12.5 micromol/L.

DISCUSSION

Renal artery dissection leading to infarction is rare. Cocaine-related renal artery dissection is especially rare, which is reflected in the lack of cases reported in the literature. As such, the diagnosis of acute renal artery dissection and renal infarction are often missed. Dissections are usually classified in 2 categories. First, blunt trauma leading to renal artery intimal stretching and tearing. Additionally, intraluminal catheter-induced injury may lead to dissection. Second, there may be spontaneous dissection leading to pseudoaneurysm. Dissections typically occur in healthy men 40-60 years of age, at a rate 10 times that in women. The discrepancy between men and women may be simply activity related.⁵ Spontaneous dissections usually involve the right renal artery, whereas catheter-induced injury usually involves the left renal artery.^{3,5} Dissection propagation may occur due to increased blood viscosity, elevated arterial pressures, and turbulent blood flow.⁵ In many of the cases the etiology of the dissection is unclear.¹ Dissections have been found on autopsy without any prior symptoms. Fibromuscular dysplasia is most frequently associated with renal artery dissection.¹

The use of cocaine is associated with hypertension,

myocardial infarction, hypercoagulability, coronary and peripheral vasospasm, cardiomyopathy, renal infarction, aortic dissection, and stroke.^{4,6,7} Proposed pathophysiological mechanisms of aortic dissection are based on an inherent weakness of the aortic media, possibly caused by chronic hypertension, connective tissue disorders, and sudden and abrupt changes in hemodynamic shear stress.⁷ Hsue et al propose that the delayed uptake of catecholamines in synaptic clefts by cocaine may produce an enhanced adrenergic effect leading to increased heart rate, elevated blood pressure and increased myocardial contractility leading to increased risk of aortic dissection.⁷ Cocaine has been shown to activate platelets and thereby create a prothrombotic environment as well as an association between renal infarction, cocaine use, and latent protein C deficiency.^{4,6,7} The combination of vasoconstriction mediated via endothelin release and hypercoagulability may further weaken the aortic wall due to thrombosis in the vasa vasorum.⁷

Early identification and treatment is paramount to preserving renal function. The signs and symptoms typically associated with acute renal artery dissection and renal infarction are vague and many times attributed to other causes; thus the consideration of renal dissection or infarction is postponed.^{1,2} Most patients with acute dissection may present with accelerated hypertension, back pain, flank pain, ileus, and hematuria.⁵ However, a urinalysis may reveal hematuria in only 20%-35% of patients, and serum creatinine levels above 1.5 mg/dL may occur in only 9%-33% of patients.³ Lactate dehydrogenase (LDH) may be very helpful in diagnosing renal infarction, Domanovits et al reported elevated LDH in 94% of patients on admission and in 100% of patients 24 hours after admission.²

Prompt imaging is essential in making the diagnosis of renal artery dissection. Contrast enhanced computed tomography (CT) is a quick and effective method of diagnosing renal artery dissection or infarction. However, angiography is necessary for confirmation. Signs suggestive of dissection during angiography include luminal irregularity, aneurysmal dilatation, segmental stenoses, and extension of the dissection to first branches of the renal artery.³ Operative intervention is indicated in those with deteriorating renal function and/or severe hypertension. Nephrectomy may be performed in the setting of medically resistant renovascular hypertension.³ Long term follow-up is crucial to assess severe and/or persistent hypertension that may or may not be responsive to medical management. In any event, vascular reconstruction may be seriously considered.³

In this case presentation, the likely etiological culprit

of the renal artery dissection and renal infarction was cocaine-related. The initial insult to the vessel probably occurred in September 2002, with resultant intimal disruption due to elevated arterial pressures, shear forces, vasospasm, platelet activation, renal artery weakening with initiation and propagation of arterial dissection, and local activation of clotting cascades leading to renal infarction. The injured vessel likely has become a thrombogenic nidus with repeated episodes of thrombosis and infarction as evidenced by his readmission to the hospital 1 year later. The hypercoagulable work up was remarkable for a methyltetrahydrofolate reductase (MTHFR) C677T thermolabile polymorphism, which is found in 5%-17% of the general population and predisposes to hyperhomocysteinemia. The compound heterozygous state with the polymorphism of A1298C in the promotor region exaggerates this risk further, and his serum homocysteine levels were slightly elevated.⁸⁻¹⁰ The transthoracic echocardiogram did not reveal the source of a potential thromboembolism, and a transesophageal echocardiogram was not performed. A focused musculoskeletal examination targeting joint hypermobility, laxity as well as skin hyperelasticity, and striae consistent with Ehlers-Danlos or Marfan's Syndrome was negative.

The autosomal recessive inherited thermolabile variant of the MTHFR gene may result in elevated serum homocysteine in homozygotes, especially in the setting of reduced folate levels. However, the presence of the thermolabile MTHFR C677T polymorphism and venous thromboembolism has not yet been established.⁸

The patient had a long history of cocaine use as well as previous evidence of a renal infarct occurring after cocaine use. He did not have hematuria; his renal function was preserved and accelerated hypertension was not observed. However, he had severe abdominal, flank, and back pain very suggestive of renal pathology. The initial contrast-enhanced CT was suggestive of renal artery thrombosis and right renal infarction. He underwent angiography with no clear suggestion of dissection. The only way to clearly differentiate these findings was via endarterectomy. The patient was treated with warfarin, folate, and discharged.

Thus, in a patient with the sudden onset of unremitting severe abdominal, flank, or back pain with risk factors such as atrial fibrillation, valvular heart disease, hypertension, or cocaine use, renal artery dissection or renal infarction should be considered and prompt evaluation via contrast-enhanced CT followed by angiography should be performed.^{1,2} Preservation of renal function is dependent on prompt evaluation, diagnosis and definitive treatment.

REFERENCES

1. Mudrick D, Arepally A, Geschwind JF, Ronsivalle J, Lund G, Scheel P. Spontaneous renal artery dissection: treatment with coil embolization. *J Vasc Interv Radiol.* 2003;14:497-500.
2. Domanovits H, Paulis M, Nikfardjam M, et al. Acute renal infarction: clinical characteristics of 17 patients. *Medicine.* 1999;78:386-394.
3. Yudd M, LLach F. Dissecting aneurysms of the renal artery. In: Brenner BM, ed. *Brenner and Rectors: The Kidney.* Philadelphia: W.B. Saunders Co; 2000:1543-1544.
4. Mochizuki Y, Zhang M, Golestaneh L, Thananart S, Coco M. Acute aortic thrombosis and renal infarction in acute cocaine intoxication: a case report and review of literature. *Clin Nephrol.* 2003;60:130-133.
5. Stanley SC, Henke PK. Dissecting renal artery aneurysms. In: Greenfield LJ, Mulholland MW, Oldham KT, Zelenock GB, Lillemoie KD, eds. *Surgery: Scientific Principles and Practice.* Philadelphia: Lippincot Williams and Wilkins; 2001:1848-1850.
6. Heesch C, Wilhelm C, Ristich J, Adnane J, Bontempo F, Wagner W. Cocaine activates platelets and increases the formation of circulating platelet containing microaggregates in humans. *Heart.* 2000;83:688-695.
7. Hsue P, Salinas C, Bolger A, Benowitz N, Waters D. Acute aortic dissection related to crack cocaine. *Circulation.* 2002;105:1592-1595.
8. Tsai A, Cushman M, Tsai M, et al. Serum homocysteine, thermolabile variant of methylene tetrahydrofolate reductase (MTHFR), and venous thromboembolism: longitudinal investigation of thromboembolism etiology (LITE). *Am J Hematol.* 2003;72:192-200.
9. Den Heijer M. Hyperhomocysteinaemia as a risk factor for venous thrombosis: an update of the current evidence. *Clin Chem Lab Med.* 2003;41:1404-1407.
10. Blom HJ. Genetic determinants of hyperhomocysteinaemia: the roles of cystathionine beta-synthase and 5,10-methylene-tetrahydrofolate reductase. *Eur J Pediatr.* 2000;159:S208-S212.

Wisconsin Medical Journal

The mission of the *Wisconsin Medical Journal* is to provide a vehicle for professional communication and continuing education of Wisconsin physicians.

The *Wisconsin Medical Journal* (ISSN 1098-1861) is the official publication of the Wisconsin Medical Society and is devoted to the interests of the medical profession and health care in Wisconsin. The managing editor is responsible for overseeing the production, business operation and contents of *Wisconsin Medical Journal*. The editorial board, chaired by the medical editor, solicits and peer reviews all scientific articles; it does not screen public health, socioeconomic or organizational articles. Although letters to the editor are reviewed by the medical editor, all signed expressions of opinion belong to the author(s) for which neither the *Wisconsin Medical Journal* nor the Society take responsibility. The *Wisconsin Medical Journal* is indexed in Index Medicus, Hospital Literature Index and Cambridge Scientific Abstracts.

For reprints of this article, contact the *Wisconsin Medical Journal* at 866.442.3800 or e-mail wmj@wismed.org.

© 2004 Wisconsin Medical Society