A Patient with Acute Kidney Pain and High Blood Pressure

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Abstract
This case presented challenging diagnostic and management issues in a young healthy man who presented with abdominal pain and new-onset hypertension. The differential diagnosis evolved over the course of the clinical presentation. The patient had severe vascular involvement of his renal and basal cerebral arteries that initially was assumed to be due to a vasculitic process or hypercoagulable state. Finally it became apparent that the patient did not have a systemic illness but rather a localized vascular disease most likely due to segmental arterial mediolysis, a rare, under-recognized condition that can potentially be fatal. This condition is often difficult to distinguish from fibromuscular dysplasia. It is important to recognize and correctly diagnose the condition, particularly in the acute phase of the disease, because delay in diagnosis can contribute to morbidity and mortality.


Introduction
A previously healthy 32-year-old man presented with sudden-onset right flank pain. He reported no fever, hematuria, dysuria, or history of kidney stones. Pain was not related to trauma. He was not taking any medications. He had no known allergies. He reported that he did not smoke tobacco but did drink alcohol socially and used marijuana occasionally. Family history was notable for a history of well controlled hypertension in his father and type 2 diabetes. The patient’s mother also had well controlled hypertension. His sister had gestational hypertension that resolved after her pregnancy. The patient was single and worked as a chef.

On examination the patient was alert and in moderate distress with diaphoresis. He was afebrile, with a respiratory rate of 24 breaths/min a BP of 178/104 mmHg, and a heart rate of 112 beats/min. Pulse oximetry reading was 100% on room air. Pupils were equal and reactive to light. Mucous membranes were moist. Jugular venous distention was not elevated. The patient’s neck was supple, and no lymphadenopathy was present. No carotid bruits were detected. The cardiac, pulmonary, and neurologic examinations were within normal limits. The abdomen was tender in right upper quadrant and soft, with no rebound tenderness. No epigastric bruising or organomegaly was noted, and bowel sounds were present. The patient’s right flank was tender. The patient had no edema, normal peripheral pulses, no clubbing, and no cyanosis was present. No skin rash or vasculitic lesions were present.

Initial laboratory results were as follows: creatinine, 0.9 mg/dL; glucose, 101 mg/dL; sodium, 138 mEq/L; potassium, 4.0 mEq/L; bicarbonate, 27 mEq/L; alanine aminotransferase, 85 U/L; aspartate aminotransferase, 36 U/L; hemoglobin, 14.2 g/dL; white blood count, 9.9 THO/uL; platelet count, 277 THO/uL; prothrombin time (PT) and partial thromboplastin time (PTT), normal; troponins, normal; lactate, 1.3 mmol/L; lipase, 41 U/L. Urine results were as follows: no proteinuria, 1+ red blood cells, no white blood cells, no crystals, few epithelial cell casts, no red blood cell casts. Electrocardiography showed normal sinus rhythm with no other abnormalities. Chest radiography showed no acute abnormality.

What Is the Differential Diagnosis for Flank Pain and Hypertension in a Young, Previously Healthy Man?
The differential diagnosis would include kidney stones, vasculitis, localized trauma with a Page kidney (hypertension caused by activation of the renin-angiotensin system after long-standing compression of the renal parenchyma by a subcapsular hematoma), renal infarct, and acute GN. Kidney stones and renal infarct are possibilities that could both present with red blood cells seen on urinalysis, but further imaging would be needed to confirm either of these diagnoses. Patient reported no prior trauma. Vasculitis was a possibility, and various serologic tests were performed to determine whether vasculitis was present. Urinalysis showed no red blood cell casts, which would indicate acute GN or possible vasculitis with renal involvement. No rash was present, which may be present in certain vasculitic lesions, such as cryoglobulinemia, microscopic polyangiitis, or Henoch–Schönlein purpura. Acute GN is unlikely, but diseases such as Henoch–Schönlein purpura could have this clinical presentation.

Initial Hospital Course
Computed tomography (CT) of the abdomen was performed and showed a right renal infarct and right renal artery dissection (Figure 1, A and B). The patients began receiving systemic anticoagulation on the assumption that he had an underlying vasculitic process or hypercoagulable state. He subsequently had a work-up for a...
hypercoagulable state, including PT, PTT, factor V Leiden, antiphospholipid antibodies, lupus anticoagulant, and prothrombin mutation, all of which were within normal limits or negative. Laboratory tests were also performed for erythrocyte sedimentation rate, C-reactive protein, antinuclear antibody, complement levels, and rheumatoid factor, all of which were normal or negative. The patient was discharged with a prescription for warfarin, antihypertensive medications (amlodipine, 10 mg daily, and carvedilol, 25 mg twice daily), and pain control.

Subsequent Clinical Course
The patient presented 2 weeks later to the emergency department with acute-onset left flank pain that he felt was more severe than his prior pain on the right side 2 weeks previously. Again, pain was not precipitated by trauma. He reported no fevers or hematuria. On examination he was alert and in moderate distress with diaphoresis. The patient was afebrile, with a respiratory rate of 20 breaths/min, BP of 164/104 mmHg, and heart rate of 96 beats/min. Pulse oximetry reading was 100% on room air. Pupils were equal and reactive to light. Jugular venous distention was not elevated. Neck was supple, and no lymphadenopathy was present. No carotid bruits were detected. Findings on cardiac, pulmonary, and neurologic examinations were within normal limits. The abdomen was soft; it was tender in both upper quadrants, with greater tenderness on the left side. There was no rebound tenderness, no organomegaly, and no epigastric bruit. Bowel sounds were present. Left and right flank tenderness was present, with the left side being more predominant. No edema, clubbing, or cyanosis was present. Peripheral pulses were normal. The patient had no skin rash or vasculitic lesions.

Results of repeat laboratory studies included the following: creatinine, 1.13 mg/dl; glucose, 101 mg/dl; sodium, 130 mEq/L; potassium, 4.6 mEq/L; bicarbonate, 27 mEq/L; alanine aminotransferase, 80 U/L; aspartate aminotransferase, 34 U/L; hemoglobin, 13.2 g/dl; white blood count, 9.0; platelet count, 288; PT, 21.8 seconds; international normalized ratio, 2.0; and PTT, 48.4 seconds. Complements, cytoplasmic ANCA, and perinuclear ANCA were normal. Tests for hepatitis virus B and C, HIV, Lyme IgM, and tuberculosis (quantitative assay) were negative. B2 glycoprotein was <20 SAU, anticardiolipin antibody IgG was <15 GPL, and IgM was <12.5 MPL; a urine drug screen was positive for opiates and benzodiazepines.

Repeat electrocardiography and chest radiography showed no acute abnormalities. He underwent the following imaging studies: (1) CT of the abdomen with contrast medium, which showed two new infarcts at the upper and lower poles of the left kidney (Figure 1C), no change in previous right renal artery abnormalities, and slight decrease in previous right renal infarct, and (2) abdominal aortography, which showed complex abnormalities involving three of the four renal arteries, including dissections with tandem segments of narrowing and dilation extending from the origins to the renal hilum.

To summarize, at this point we had a 32-year-old, previously healthy man with a right-sided renal infarct with new-onset hypertension who 2 weeks later presented with new left-sided renal infarcts despite receiving anticoagulation. The patient also had complex dissections of three of four of his dual renal arteries without flow-limiting lesions. BP was elevated despite being treated with antihypertensive medications. His work-up for vasculitis and rheumatologic disorders, as well as a hypercoagulable state, was negative.

Figure 1. | Angiographic and computed tomographic findings. (A) Maximum-intensity projection from diagnostic computed tomographic angiogram at time of initial presentation depicting two right renal arteries with alternating dissections and fusiform aneurysms (arrows). (B) Coronal multiplanar reconstruction depicting segmental infarction in the medial lower pole of the right kidney (arrows). (C) Single-phase contrast-enhanced diagnostic computed tomographic scan obtained 1 week later depicts new infarcts in the left upper and lower poles (arrows).

Differential Diagnosis
The differential diagnosis had now shifted with the clinical presentation to include spontaneous bilateral renal infarcts with renal artery dissection and new-onset hypertension in a healthy young man. This refocused the differential diagnosis on vascular diseases that predominantly affect the renal vasculature, including atherosclerosis, fibromuscular dysplasia (FMD), segmental arterial mediolysis (SAM), infection
(mycotic aneurysm and endocarditis), connective tissue diseases (Behçet disease, polyarteritis nodosa, neurofibromatosis, and inherited defects in vessel wall structural proteins (such as type IV Ehlers-Danlos syndrome and Marfan syndrome, although the latter usually affects the aorta with cystic medial necrosis). The patient did not have a coagulation disorder, and results on all serologic tests were negative, making an autoimmune vasculitic procedure very unlikely. He was relatively young and was unlikely to have atherosclerosis. This appeared to be a localized process and not a systemic process. The most likely diagnosis at this point was FMD or SAM.

At this point the patient was transferred to our tertiary care center for further management. On arrival he reported severe left flank pain. His BP was 180/108 mmHg, with a heart rate of 112 beats/min. He was admitted directly to the medical intensive care unit. He began receiving nicardipine and esmolol infusions. He now also reported pain in the neck when turning and a severe headache. Because the patient was symptomatic and cerebral involvement is known to occur in both SAM and FMD, imaging of the cerebral vessels was scheduled. Anticoagulation was stopped because of the possibility of SAM, as patients with SAM are prone to aneurysm rupture with catastrophic bleeding. Pertinent laboratory findings on admission to the intensive care unit were as follows: Urinalysis showed trace protein, no hematuria, and no cellular casts; thyroid-stimulating hormone level was 1.68 mIU/L; the C-reactive protein level was 2.4 mg/L; the erythrocyte sedimentation rate was 36 mm/hr, and results for rheumatoid factor and antinuclear antibody were negative.

CT angiographic images of the renal arteries from the referral hospital were reviewed by the attending interventional radiologist (M.S.). He will review the images in detail and discuss the decision process that was undertaken to proceed with an interventional procedure at this point.

CT Angiographic Findings

Dr. Soulen: Digital subtraction angiography showed bilateral accessory renal arteries originating from the aorta immediately inferior to the main renal arteries. Selective mesenteric angiography was performed to look for additional abnormalities that might indicate segmental arterial mediolysis; findings were normal. Selective right renal angiography (Figure 2A) demonstrated tandem >50% stenosis of the proximal portion of this vessel; a dissection flap with fusiform dilation was seen within its inferior branch. Diagnostic arteriography of the accessory right renal artery demonstrated a patent appearance of the vessel with multiple sausage link-type stenosis (Figure 2B). Diagnostic arteriography of the left renal arteries demonstrated no significant stenosis of the main left renal artery but severe segmental stenosis of the proximal accessory left renal artery (Figure 2, C and D).

After angioplasty, arteriography showed no significant residual stenoses, but residual mural irregularity and dissection flaps remained (Figure 3). In summary, angioplasty in three of the four renal arteries was performed successfully.

BP was much improved after the angioplasty procedures, and nicardipine drip was weaned. The patient remained on esmolol infusion. He had continued headaches and pain upon turning his neck. The patient then underwent CT angiography of the cerebral vessels. This examination demonstrated a distal left cervical internal carotid artery pseudoaneurysm and right vertebral artery pseudoaneurysm (distal right V2 segment), with diffuse luminal irregularity of the right V1 and V2 segments concerning for diffuse dissection (Figure 4).

These findings were confirmed on magnetic resonance angiography, which showed a focal outpouching of the distal cervical segment of left internal carotid artery without corresponding signal abnormality on T1-weighted images. This finding possibly represented a sequela of prior dissection with pseudoaneurysm formation. Crescentic high signal along the V2 segment of right vertebral artery was present within the transverse foramen of C2 without flow-limiting stenosis.

Hospital Course

The neurology service was consulted, and they recommended starting low-dose aspirin with no further intervention. They recommended reimaging the neck vasculature in 3 months. The patient tolerated the renal angioplasty procedures well without any major complications. After angioplasty, BP control improved and was within 118–134/68–84 mm Hg; the patient’s heart rate ranged from 60 to 72 beats/min. The patient was discharged with a prescription for amlopidine, 10 mg daily; aspirin, 81 mg daily; carvedilol, 50 mg twice daily; and cyclobenzaprine, 5 mg daily. The patient began receiving a β-blocker intentionally to maintain a low heart rate, with the purpose of lowering the risk of rupture of any unstable vascular lesions, and a dihydroxypridine calcium channel blocker (amlodipine) because this is an effective antihypertensive that does not affect renal function. Aspirin was added to decrease platelet aggregation, in particular for the cerebral vascular lesions.

What Is SAM?

SAM is a rare, noninflammatory, nonatherosclerotic vasculopathy of unknown etiology that affects medium-sized arteries (1). The condition was first described in 1976 by Slavin and Gonzalez-Vitale, who reported three autopsy cases of ruptured aneurysms resulting in massive hemorrhage and death (2). Since then approximately 85 cases have been reported in the literature, increasing understanding of the disease course, sequelae, and prognosis (3). The prevalence of the disease is probably underestimated because of lack of recognition of the disease, but awareness of the disease has increased, particularly among radiologists and pathologists.

The condition is characterized by disruption of the arterial medial layer of medium-sized vessels, resulting in increased susceptibility to vessel dissection, hemorrhage, and ischemia (4). The condition can affect patients of any age but usually presents between the ages of 40 and 60 years; there is no sex or ethnic predisposition. No genetic mutation has been identified as being specifically associated with SAM. The abdominal visceral arteries are most frequently involved, but any vessel may be affected, including the retroperitoneal, renal, intracranial, and coronary arteries. Cardiac vessel involvement is more frequent in utero and in neonates and young adults; basal cerebral artery involvement is also more frequent in young adults (5).

Clinical presentation can vary from vessel rupture (with a mortality of up to 50%) to acute abdominal pain,
severe acute onset hypertension, hematuria, hemobilia, severe headache, or any symptoms attributable to organ ischemia. Patients may also be asymptomatic. SAM is not a systemic disease and presents with single or multiregional vascular involvement. Patients have a negative work-up for hypercoagulable states, rheumatologic disorders, and systemic inflammatory disorders.

Histopathology

The histopathologic changes begin with vacuolar degeneration of smooth muscle cells in the arterial media, followed by fibrin deposition at the medial-adventitial junction. This predisposes to dissecting aneurysms. Vascular alterations of SAM stem from two separate lesions: (1) mediolysis and (2) a tear that separates the outer medial muscle layer from the adventitia (5). This initial injury phase of SAM exhibits one or both of these lesions. The degree, extent, and subsequent evolution in the repair phase create the diversity of lesions responsible for the angiographic findings seen in SAM. Mediolysis is caused by disruption of smooth muscle cell membranes by cytoplasmic vacuoles of various sizes and usually begins in the outer media. However, it can also involve the entire medial muscle, with preservation of the intima and internal elastic

Figure 2. | Angiographic and arteriographic findings. (A) Selective right renal angiography demonstrated tandem >50% stenosis of the proximal portion of this vessel, with a dissection flap with fusiform dilation seen within its interior branch (arrows). (B) Diagnostic arteriography of the accessory right renal artery demonstrated multiple sausage link-type stenoses (arrows). (C and D) Diagnostic arteriography of left renal arteries demonstrated no significant stenosis of the main left renal artery but did show severe segmental stenosis of the proximal accessory left renal artery.
lamina. It can occur in a section of the arterial circumference or its entirety but most frequently exhibits segmental distribution. The variable loss of the supporting muscular wall results in angiographic arterial dilatation observed at the onset of SAM (5). The medial defects in this lesion are rapidly repaired by granulation tissue to create a healed artery, which will appear on angiography as a stenosed lesion and may evolve into FMD. The disease appears to be an acute process and is usually limited to a specific anatomic site: the abdomen, the base of the brain, or the heart. An example of the pathologic changes that result from SAM in a vertebral artery is shown in Figure 5 (6).

**Diagnosis of SAM**

SAM is predominantly an angiographic diagnosis after exclusion of a systemic vasculitic process. The angiographic appearance of SAM ranges from arterial dilatation to single or multiple aneurysm formations to stenosis or occlusion with frequent dissections (5,7). The gold standard for diagnosing SAM is to obtain a histopathologic diagnosis, but this usually occurs only in a postmortem setting or, rarely, when surgery is performed. It is not safe to pursue a vessel biopsy in these patients; because of their very friable vessels they are already at increased risk of spontaneous hemorrhage.

**Management**

Immunosuppressive agents and steroids have no role in SAM. Use of aspirin and anticoagulation is controversial but is probably best avoided because patients are prone to catastrophic fatal aneurysmal rupture. In patients presenting with massive hemorrhage, endovascular procedures...
have been successfully used; mortality rates with an endovascular approach have been lower than those with open procedures (3). For renal artery involvement, angiographic intervention with balloon angioplasty must be done with extreme caution if deemed necessary in patients who have severe uncontrolled hypertension or ischemia. Vessels are extremely friable and should never be stented. For most patients who do not present with catastrophic bleeding, management is often conservative and most lesions will undergo a reparative process in 30–45 days. Most lesions will fibrose and will not require intervention.

**Prognosis**

Prognosis is uncertain because the literature reports are more likely to include the most severe presentations of this disease. The mortality rate associated with intra-abdominal hemorrhage approaches 50% (4), but for most patients the long-term prognosis after treatment of the acute presentation is good.

A recent systematic review of the literature covered SAM cases between 1976 and 2012 and focused on arterial involvement, diagnostic imaging modalities, mortality and morbidity rates, and treatment outcomes with open versus endovascular intervention (3). Sixty-two studies reporting on 85 cases of SAM were reviewed. Sixty-nine percent of cases were diagnosed histologically (24% at autopsy). Angiography was the most common form of diagnostic imaging modality in 56% of cases. Arterial involvement was largely abdominal or cranial, with splenic arterial involvement being the most prevalent (29% of cases). The total SAM-related mortality rate was 26%. Endovascular intervention, most commonly in the form of coil embolization of aneurysmal vessels, was successful in 88% of cases where attempted; no mortality was reported. In contrast, the mortality rate was 9% when open surgery was attempted. This review, however, was heavily weighted toward cases of catastrophic rupture, which did not occur in our patient. Another reason that this condition is frequently not recognized may be the publication of reports of only the more severe presentations of the disease. Most presentations of SAM are self-limited, are often not associated with hypertension, and resolve over time with no sustained loss of renal function.

**How Do You Distinguish SAM from FMD, and Are These Different Diseases or Varying Spectrums of the Same Disease?**

SAM is often difficult to distinguish from FMD, as in this particular patient. There is much debate in the literature about whether these are two different conditions or different...
parts on the spectrum of the same condition. Slavin et al. have postulated that arteries that originally present as isolated aneurysms and dissecting hematomas may evolve into FMD (5). Two reports described follow-up lesions that were initially diagnosed as SAM but on follow-up imaging had evolved into lesions that would be considered more likely to be FMD (8,9). Classically, FMD presents more commonly in middle-aged women and has a predisposition for the renal arteries, thereby causing premature hypertension (10). SAM may be a subclinical process, and silent cases with small or absent gaps and no dissection may evolve into FMD because fibrosis of the reparative granulation tissue can metamorphose into lesions identical to medial fibroplasia or perimedial dysplasia (the two most common forms of FMD) (11,12). The frequent involvement of renal arteries in SAM may be congruent with the notion that this is an evolving process in which patients initially present with vascular lesions with aneurysms and dissections consistent with SAM and that these lesions evolve and become fibrotic and stenosed over time, which is more consistent with FMD.

Although our patient had lesions on both the renal arteries and the carotid arteries, which could be consistent with SAM or FMD, we believe he had SAM. However, the diagnosis could be verified only with a tissue diagnosis, which was not practical in this patient. Our patient was also younger than the median age at presentation among patients with SAM, but the angiographic and clinical features were consistent with the diagnosis.

**Patient Follow-up**

The patient was seen at a follow-up visit 1 month after discharge in the complex hypertension clinic at our institution. He was doing well overall, with systolic BP in the range of 104–116 mmHg and heart rate of 60–70 beats/min. He had no further headaches and reported no chest pain, palpitations, dyspnea, orthopnea, paroxysmal nocturnal dyspnea, or peripheral edema. The patient was feeling tired. He continued receiving amlodipine, 10 mg daily; aspirin, 81 mg daily; and carvedilol, 50 mg twice daily. Recent laboratory studies included the following: creatinine, 0.94 mg/dl; potassium, 3.8 mg/dl; calcium, 9.3 mg/dl; and hemoglobin, 10.8 mg/dl.

Renal angiography performed 6 months after the initial presentation showed patent aorta; celiac, superior, and inferior mesenteric arteries; and common, external, and internal iliac arteries. The bilateral accessory renal arteries were patent. No renal artery dissection or aneurysm was identified. The beaded appearance of the renal arteries seen on angiography 6 months earlier was markedly improved. Cortical scarring in the bilateral kidneys related to prior infarcts was seen again, unchanged from prior imaging. No evidence of acute renal infarct was seen.

The carvedilol dose was reduced to 25 mg twice daily, and the amlodipine dose was reduced to 5 mg daily. BP was well controlled in the range of 110–120/60–70 mm Hg, and heart rate was maintained at 60–70 beats/min.

**Patient follow-up after resolution of the acute condition is not well defined because of the rarity of the condition. We would suggest frequent follow-up initially, with a goal of keeping BP in a lower range of around 110–120/60–70 mmHg and a heart rate of 60–70 beats/min to avoid any excessive risk of rupture of the friable vessels. These renal lesions may progress to FMD, so follow-up is needed. This would include BP monitoring and imaging. There are no guidelines for imaging, but we would suggest imaging 3 months after the acute event, every 6 months for the first year, and annually thereafter. How long to continue imaging is not clear, but our practice has been to image with magnetic resonance angiography to avoid radiation exposure annually or biannually. No data are available on the most appropriate choice of antihypertensive agents in this population; however, we feel it is worthwhile to use a β-blocker to maintain a lower heart rate. Addition of a renin-angiotensionaldosterone system inhibitor for possible long-term benefit of vascular remodeling can be considered. There are also no data on statin use. Because these lesions are not atheromatous, regular guidelines for statin use should be followed.**

**Disclosures**

None.

**References**


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