Restrict Conservative Management of Renal Artery Thrombosis, case study and review of literature

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Abstract: Renal artery thrombosis is a rare, but serious and often misdiagnosed condition. Emergency physicians, internists and vascular surgeons need to consider this diagnosis in unexplained flank pain, especially in patients with risk factors for this disease. In this case report, the authors review a case of unilateral renal infarction caused by renal artery thrombosis in a patient with risk factors for thrombosis but no previous history of thromboembolism. A review of scholarly articles was performed and the case is discussed in the context of the current knowledge of this condition. Common presenting symptoms, features of the history and risk factors will all be discussed herein. Diagnostic evaluation of flank pain in the setting of the suspicion of renal infarction will be discussed, including the modalities of high-resolution computed tomography, renal angiography, scintography and ultrasound. Acute management and prognosis will also be discussed.

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Introduction

Renal Artery thrombosis is not synonymous with renal infarction, for the later is much more frequently caused by venous thrombosis, which is due to various inflammatory and traumatic lesions affecting the renal vein, acute renal artery thrombosis frequently results in renal infarction. High index of suspicion is required for early diagnosis as timely intervention may prevent the unfortunate consequence which is renal infarction and renal failure. However, multiple small renal arterial infarctions are a common autopsy finding when they were of little clinical significance in the patient's life denoting the underestimated prevalence and misdiagnosis of this emergency vascular event [11].

The most common etiology of renal artery thrombosis is thromboembolism from Atrial Fibrillation [1], atherosclerosis, fibro-muscular dysplasia [2], cocaineabuse [3] or endocarditis [4]. Renal artery thrombosis can also occur in a hypercoagulable states [5], severe blunt trauma, vasculitis, renal transplantation [6], intra-aortic balloon placement [7], oral contraceptives [8], systemic lupus erythematosus [9], or pancreatitis [10]. This diagnosis should be considered in the setting of undiagnosed flank pain or hematuria especially in patients with risk factors for this disease.

Case Report

A 53-year-old male known case of Hypertension and Ischemic Heart Disease, presented to the Emergency Department complaining of epigastric and right flank pain for two days. The patient developed sudden progressive moderate to severe epigastric and right flank pain 7 out of 10 for two days, associated with nausea and two episodes of vomiting of food content.

There was neither history of dysuria, hematuria, diarrhea nor bleeding from any site. Other systemic review was negative. Patient was admitted one year back as Acute coronary syndrome (Non-STEMI) and was discharged on low dose aspirin, clopidogrel, metoprolol and atorvastatin. Initial vital signs were all within normal range. On examination: temperature 37°C, pulse rate of 100 beats/min (irregularly irregular), blood pressure of 160/90 mmHg. He was alert, but appeared in moderate distress due to abdominal pain, his abdominal exam revealed tenderness to palpation all over the abdomen, no guarding or rigidity, the remainder of the exam was unremarkable.

His blood results were as follows: white blood cell (WBC) count, 7,700/µL; hemoglobin, 16.7 g/dL; platelet count, 236,000/µL; blood urea nitrogen 5.7 mmol/L; creatinine (Cr) 1.1 mg/dL; sodium, 132 mEq/L; potassium, 3.7 mEq/L; total protein, 7.1 g/dL; albumin, 3.9 g/dL; lactate dehydrogenase (LDH) 552 U/L; prothrombin time (PT) was found to be 12.8 seconds (international normalized ratio or INR: 1.1, 46.8%) and activated partial thromboplastin time (aPTT) 31 seconds; random blood sugar (RBS) 9

mmol/L; creatine kinase (CK) 165 U/L; Troponin 0.01 ug/L; aspartate aminotransferase (AST) 30 U/L; alanine aminotransferase (ALT) 21 U/L, amylase 54 U/L, Lipase 34 U/L. Urine analysis showed reddish urine and microscopic hematuria with RBCs 20 cell/cc.

Electrocardiography test confirmed Atrial Fibrillation. Pelviabdominal Ultrasound revealed unremarkable study, Abdominal X-ray had shown dilated intestinal loops but no fluid levels could be noticed.

Given the nature of the pain and clinical examination with the new finding of atrial fibrillation on ECG, mesenteric ischemia was strongly considered as cause for this acute pain. Therefore, computerized tomography (CT) scan of the abdomen and pelvis with oral and IV contrast was urgently done, which revealed Right Renal Artery Thrombosis with secondary right renal infarction, Further invasive imaging like renal angiography and scintography were canceled due to clarity of lesions at the contrasted CT (Figure 1), (Figure 2), (Figure 3).

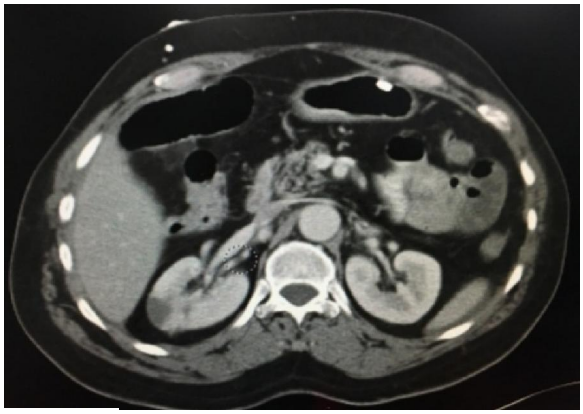

Figure 1: CT scan showing right renal infarction, two thrombi are encircled at the right renal artery

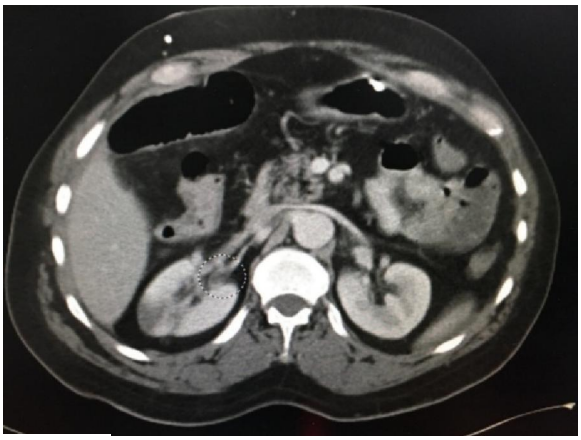

Figure 2: CT scan showing right renal artery distal thrombosis and partial right renal infarction

The urology and vascular surgery consultations were done, and both recommended conservative treatment with anticoagulation. The patient was started immediately on heparin infusion beside IVF and analgesics. Patient started to become anuric, hypokalemic and started to complain of shortness of breath. The patient has developed acute kidney injury (AKI), his creatinine level reached 3.9 mg/dL, patient was admitted to ICU and hemodialysis was initiated, calcium channel blockers and maintained adequate hydration. After the first session of hemodialysis, the patient was still having respiratory distress and furthermore he became desaturated, mechanical ventilation was inevitable. Unfortunately, patient developed *Ventilator-associated pneumonia* (VAP), then after the proper course of antibiotics the patient was extubated successfully. Patient kidney functions gradually improved over 4 weeks of follow up and intermittent four sessions of hemodialysis, and became dialysis independent with average creatinine clearance 55 ml/min/m2.

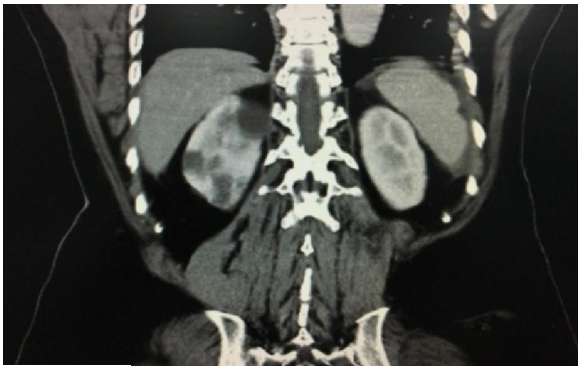

Figure 3: CT scan showing right renal artery thrombosis and segmental right renal infarctions, left kidney at all scans showed normal arterial contrast perfusion.

Transthoracic Echocardiography (TTE) was done during the admission which showed no intracardiac thrombi, Transesophageal echo (TEE) confirmed the TTE negative result. The patient was discharged from the hospital (after a 5 weeks long eventful admission) on lifelong warfarin therapy, calcium channel blockers and follow up at nephrology and cardiology outpatients clinics.

Discussion

Renal artery thrombosis (RAT) is a rare, but serious and often misdiagnosed, condition. In a series of over 14,000 autopsies, about 200 cases of kidney infarction were identified a prevalence of 14/1000.

The largest case series of emergency department patients give a prevalence of 0.02/1000, [11] with <50 patients in each series [15].

RAT is a critical problem requiring rapid diagnosis and treatment. In 94% of patients, systemic emboli commonly originate in the heart. Among contributing cardiac disorders, atrial fibrillation, myocardial infarction (post infarction thrombi) and rheumatic mitral stenosis are the most important ones [11].

Early diagnosis of RAT is difficult. It is not usually diagnosed at the onset of symptoms, and early identification is made in <30% of the patients. The initial differential diagnoses should include: nephrolithiasis, pyelonephritis, acute myocardial infarction and congestive heart failure [15]. Moreover, patients with a right renal artery thromboembolism have been mistakenly diagnosed as having acute cholecystitis, which has led to unnecessary cholecystectomy, or as having renal colic secondary to a calculus. Our patient was initially diagnosed as having an ischemic bowel syndrome based on unexplained abdominal pain and dilated loops of bowel. Right renal artery thromboembolism was found incidentally by contrast - enhanced CT of his abdomen. In our case report the suspicion was supported by an elevation of lactate dehydrogenase (one of the renal enzymes) and acute decline in renal function. Finally, it was clearly confirmed by Contrast enhanced Abdominal CT scan postponing the need for further renal angiography (Figures 1, 2, 3).

Acute renal failure in association with unilateral renal artery thromboembolism as been observed in our patient, is usually ascribed to acute tubular necrosis due to renal hypoperfusion, which often accompanies the vascular catastrophe. Occasionally, contrast nephropathy following angiography may itself lead to acute renal failure. An additional cause has been reported: reflex vasospasm of the contralateral kidney. Such a mechanism for acute renal failure in the setting of unilateral renal artery thromboembolism was originally described by **Levin *et al*** [14]. Accordingly, acute renal failure in our patient secondary to reflex vasospasm of the contralateral kidney is a possibility. However, as renal function did not improve rapidly after therapeutic anticoagulation, contrast nephropathy and prolonged ischemia may have contributed to his prolonged renal failure [18].

Pathogenesis studies of RAT had shown that it is typically caused by blood or cholesterol clots occluding the renal artery or branch vessels. The source of blood clots, typically, is from atrial fibrillation causing thrombogenesis in the left atrium and left atrial appendage [1]. Cholesterol-based emboli cause partial occlusions with a more chronic presentation [11]. In a study of over 600 patients with peripheral arterial thromboembolism, the most common site of peripheral arterial thromboembolism was the extremities (61%), followed by the mesenteric arteries (29%), the pelvic arteries (9%), the aorta (7%) and, followed last, by the renal arteries (2%). In a case series of 27 patients, 41% had obvious cardiac disease, almost all with atrial fibrillation; however, 59% had no discernible structural or arrhythmic cardiac disease. Idiopathic patients are typically younger and have a paucity of thrombogenic risk factors. [12]

Complete infarct (involving entire kidney due to occlusion or interruption of the renal artery) is the rarest, seen typically after trauma or interventions involving the aorta. Most kidney infarction results from emboli caused by atrial fibrillation or endocarditis [11], causing only partial occlusion of the renal artery or a branch. Rare causes reported include spontaneous renal artery dissection, dilated cardiomyopathy, [13] paradoxical embolism and involved multiple organs. Bilateral infarction has also been reported, including bilateral (global) renal infarction subsequent to dissecting aneurysms of the aorta, with septic emboli from endocarditis, lupus vasculitis or antiphospholipid antibody syndrome. or fibro muscular dysplasia of the renal arteries. [2] Reports of other causes associated with renal infarction include trauma, vasculitis, instrumentation, transplant, [6] sepsis, cocaine use [3] and subsequent to carotid artery dissection.

The most common complaints at presentation are flank pain or abdominal pain, usually constant in nature. Other common features include fever, nausea and vomiting. Lumbar and flank tenderness are seen and are even more likely in the idiopathic/younger group. Oliguria is rarely found. New-onset hypertension is uncommon, but can be seen especially if there are underlying renal artery lesions. [14]

The typical patient tends to be older, with an average age of 67 in one series, although significant portions are younger. Reviewing 89 cases from the literature [15,16,17] the mean age at presentation was 65.7 years, with no significant gender predominance or right or left kidney predominance. About 10% of the cases presented with bilateral renal involvement. Previous thromboembolic events in 20/89 (22%) were observed.

The differential diagnosis for this disorder, as with all abdominal pain disorders, is extensive. Emergent conditions that will need to be ruled out include causes of acute surgical abdomen, notably appendicitis, diverticulitis, ruptured abdominal aortic aneurysm, testicular/ovarian torsion, incarcerated hernia, intestinal obstruction and/or perforation. Other non-surgical causes such as mesenteric ischemia, nephrolithiasis and pyelonephritis should also be

considered. Because of the vague clinical presentation, diagnosis is not often made on admission (only 40% of the patients in one case series) [15] and is delayed often up to 2 days or more. However, it is likely that this accuracy will increase with the increasing availability of computed topographic (CT) scans, which are the best way to recognize an infarct.

Urinalysis is recommended, with hematuria being a very common finding, seen in all cases in one study. However, hematuria is not universal, with about one-half of the patients in another study showing no hematuria, [15] and two cases from another center also with no hematuria. [18] In contrast, elevations of lactate dehydrogenase (LDH) are almost universal, with nearly all patients in one study [12] and in all cases in other reports. [17] Proteinuria was seen in 45% of the patients in one retrospective case review. [15] The white blood cell count was often elevated. Serum creatinine was not markedly elevated at presentation, but a small increase was seen at peak in one study and a more marked elevation was seen in another slightly larger case review. C-reactive protein is also often elevated.

Angiography is positive in 100% of the cases (10/10). Renal isotope exam is abnormal in 97%. CT scan is diagnostic in 80% of the cases. Ultrasound is positive in only 3% of the cases. [15] Contrast CT is the diagnostic modality of choice at this time, with the cardinal findings of a wedge-shaped, peripheral, non-enhancing area. The most common finding is a hypoattenuated area with associated mass effect, sometimes accompanied by a cortical rim sign. The cortical rim sign represents opacification of a rim of functioning nephrons supplied via capsular collaterals surrounding an otherwise non-functioning kidney. The cortical rim sign can be especially useful in differentiating ischemia (where it is sometimes seen, especially with global infarcts) vs. pyelonephritis (where it is not seen). Wedge-shaped focal infarcts, global infarcts and multifocal infarcts can also be seen with infarction. In a series of 12 patients, 47% had a cortical rim sign, 21% had a subcapsular fluid collection, 11% had a mass effect and 6% had abnormally thickened renal fascia. [19]

Because of the vague presentation and the lack of easily obtainable definitive imaging, high clinical suspicion will need to be maintained in order to achieve diagnosis. The improvement of the CT technique and increasing utilization will likely improve upon the historical diagnostic accuracy. However, the use of non-contrast-enhanced scan is increasingly thought to be capable of diagnosing not only renal calculi but also appendicitis, diverticulitis, biliary tract disease, some aortic conditions and gynecologic diseases, but is notably unable to detect thromboembolic and other renal vascular disease.

Because non-contrast CT is often the study of choice for fear of kidney function deterioration with contrast, Some general recommendations proposed include the presence of unilateral perinephric stranding without hydrouteronephrosis (suspicious for renal infarction, renal vein thrombosis and pyelonephritis), the presence of significant hypo/hyperdense peri-renal collections (urinoma, hematoma), the presence of a mass or complicated cyst and negative unenhanced CT in a patient with unexplained hematuria [11].

Additionally, even if a contrast-enhanced study is ordered, the sensitivity is only 80%. Therefore, if the patient is at risk for embolic events and has an elevated serum LDH, it is recommended to further image with renal isotope exam (scintography) or with renal angiography if the contrast-enhanced CT is negative.

Because of the infrequent nature of RAT, no large prospective studies have evaluated the optimal treatment modalities regarding the dosing of heparin, the use of low molecular weight heparin or thrombolytic or using medical management vs. surgical management. At this time, there are only recommendations based on the consensus in the literature: -

- Anticoagulation: Start with a heparin bolus with an infusion followed by initiation of coumadin therapy indefinitely, which has been recommended. [11,15] The dosing of initial heparin as well as the target International Normalized Ratio (INR) and the length of coumadin therapy has not been defined. Anticoagulation targets with the usual 2.0–3.0 INR are recommended unless the patient thrombosed while therapeutic, in which case a target of 2.5–3.5 may be more desirable. Many patients will remain on coumadin indefinitely as they have an underlying pro-embolic condition such as atrial fibrillation.
- Antihypertensive: Patients with prior hypertension or with new-onset hypertension from the infarct should be treated with an anti-hypertensive. [13] Because of the insult to the kidney, hypertension often develops and because this is mediated through the increase of renin, it is thought that using angiotensin-converting enzyme inhibitors or an angiotensin receptor blocker may be the most suitable.
- Thrombolysis/thrombectomy: These interventions are currently supported only by case reports, which report successful reperfusion but not uniform improvement in renal outcome. Open surgery is not recommended other than in the case of trauma, where other problems may indicate the need for surgery anyway. In one case report, embolectomy has been performed 30 h after complete bilateral occlusion with complete resolution of kidney failure. [20]

- Local thrombolysis or thrombectomy with minimally invasive percutaneous endovascular therapy for acute occlusions of the main renal artery or significant branch can be considered but, again, no significant clinical evidence supports this intervention. Intra-arterial thrombolytic treatment is an additional therapeutic option in carefully selected cases.

The most common sequel to renal infarction is loss of renal function and persistent hypertension. However, many patients go on to have normal kidney function with no permanent hypertension. A small percent will need dialysis, 8% in one case series**.** [15]

Repeat embolic events have been observed, some with events prior to the renal infarct and some with subsequent events. Because of the lack of prospective study data, it is unknown what the benefit of continuing anticoagulation would be. However, given data regarding other catastrophic thrombotic events, it is likely recommended to continue indefinitely in the setting of atrial fibrillation.

Conclusion:

Renal Artery Thrombosis should be strongly considered when presented with the following triad: persistent abdominal and/or flank pain, elevated serum LDH and/or hematuria and risk of thromboembolic eventandaided by the increased diagnostic accuracy of CT, Restrict conservative treatment in patients with an established diagnosis of Renal Artery Thrombosis to those with absolute contraindications to surgery or angioplasty or to patients who are likely to deteriorate due to other co morbid conditions before advancing to end-stage renal disease. Clinicians must rely on pharmacologic agents (eg, combination of calcium channel blockers to control blood pressure and optimize renal perfusion plus therapeutic anticoagulation), accepting the high probability of deterioration in renal function and shortened survival.

References

1. Kalcik M, Yesin M, Ocal L, et al. A Case Of Acute Thromboembolic Renal Infarction Associated with Paroxysmal Atrial Fibrillation. Journal of Atrial Fibrillation. 2014;7(1):1020. doi:10.4022/jafib.1020.
2. Sinnamon K, McNally D, Harty J. Fibromuscular dysplasia presenting as renal infarction. Kidney Int. 2007;72:1295–1296.
3. Hoefsloot W, de Vries RA, Bruijnen R, Bosch FH. Renal infarction after cocaine abuse: a case report and review. Clin Nephrol. 2009;72:234–236.
4. Liao WB, Bullard MJ, Liaw SJ. Widespread embolism in a patient with infective endocarditis: A case report. Changgeng Yi Xue Za Zhi. 1995;18:82–7.
5. Nishimura M, Shimada J, Ito K, Kawachi H, Nishiyama K. Acute arterial thrombosis with antithrombin III deficiency in nephrotic syndrome: report of a case. Surg Today. 2000;30:663–666.
6. Dimitroulis D, Bokos J, Zavos G, Nikiteas N, Karidis NP, Katsaronis P, et al. Vascular complications in renal transplantation: A single-center experience in 1367 renal transplantations and review of the literature. Transplant Proc. 2009;5:1609–14.
7. Baciewicz FA, Jr, Kaplan BM, Murphy TE, Neiman HL. Bilateral renal artery thrombotic occlusion: A unique complication following removal of a transthoracic intraaortic balloon. Ann Thorac Surg. 1982;33:631–4.
8. Bhargava A, Chopra A, Bernabela L, Chopra T. Oral contraceptive causing renal artery thrombosis. BMJ Case Reports. 2013;2013: bcr2012008055. doi:10.1136/bcr-2012-008055.
9. Tsugawa K, Tanaka H, Kudo M, Nakahata T, Ito E. Renal artery thrombosis in a pediatric case of systemic lupus erythematosus without antiphospholipid antibodies. Pediatr Nephrol. 2005;20:1648–50.
10. Thajudeen B, Budhiraja P, Bracamonte ER. Bilateral renal artery thrombosis secondary to acute necrotizing pancreatitis. Clinical Kidney Journal. 2013;6(5):503-506. doi:10.1093/ckj/sft106.
11. Korzets Z, Plotkin E, Bernheim J, Zissin R. The clinical spectrum of acute renal infarction. Isr Med Assoc J. 2002;10:781–4.
12. Bolderman R, Oyen R, Verrijcken A, Knockaert D, Vanderschueren S. Idiopathic renal infarction. Am J Med. 2006;119:356. e9-12.
13. Nasser NJ, Abadi S, Azzam ZS. Acute renal infarction from a cardiac thrombus. Nat Clin Pract Nephrol. 2007;11:631–5.
14. Levin M, Nakhoul F, Keidar Z, Green J. Acute oligouric renal failure associated with unilateral renal embolism: a successful treatment with iloprost. *Am J Nephrol*1998;18:444–447.
15. Domanovits H, Paulis M, Nikfardjam M, Meron G, Kurkciyan I, Bankier AA. Acute renal infarction. Clinical characteristics of 17 patients. Medicine (Baltimore) 1999;78:386–94.
16. Hazanov H, Somin M, Attali M, Beilinson H, Thaler M, Moulallem M, et al. Acute renal embolism. Forty-four cases of renal infarction in patients with atrial fibrillation. Medicine (Baltimore) 2004;83:292–9.

17. Lessman RK, Johnson SF, Coburn JW, Kaufman JJ. Renal artery embolism: clinical features and long-term follow-up of 17 cases. Ann Intern Med. 1978;89:477–82.
18. Yoshida T, Ikehara N, Miyabe H, Sakata S, Yajima K, Mukai S, et al. Two cases with renal infarction diagnosed in the early course using contrast-enhanced CT. Hypertens Res. 2004;27:523–6.
19. Wong WS, Moss AA, Federle MP, Cochran ST, London SS. Renal infarction: CT diagnosis and correlation between CT findings and etiologies. Radiology. 1984;150:201–5.
20. Morris D, Kisly A, Stoyka CG, Provenzano R. Spontaneous bilateral renal artery occlusion associated with chronic atrial fibrillation. Clin Nephrol. 1993;39:257–9.

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