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Case Report

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Acute Renal Infarction Pathogenesis and Atrial Fibrillation: Case Report and Literature Review

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Abstract

Kidney infarction is an uncommon thromboembolic complication of atrial fibrillation (AF). Diagnosis of this condition can be challenging due to its rarity and the fact that its presentation is associated with a multitude of other pathologies. No treatment guidelines have been established so far; however, multiple modalities have been employed, including systemic thrombolytics, intra-arterial thrombolytics and anticoagulants. In this article, we review acute renal infarction pathogenesis with a focus on AF as an important etiology.

Keywords: Acute renal infarction; Atrial fibrillation; Pathogenesis

Introduction

Once thought to be a rare disease, acute renal infarction (ARI) is now being diagnosed more frequently due to the increased prevalence of patients with atrial fibrillation (AF) who are at an increased risk for thromboembolic phenomenon. It is still an under-diagnosed cause of kidney dysfunction and is often missed because its symptoms are misleading and can mimic renal colic, pyelonephritis or other conditions [1, 2]. Hence, early diagnosis is important, as renal function can be restored with revascularization of the occluded vessel [3].

Case Report

A 71-year-old Caucasian woman with a past medical history of hypertension and peripheral arterial disease presented to the hospital complaining of right-sided flank pain and hematuria. The patient did not have a history of AF. The onset of her flank pain was sudden, one day prior to admission and associated with nausea vomiting and abdominal distension. She denied dysuria or increase in urinary frequency or diminished urine flow or volume. Her home medications were aspirin, metoprolol twice daily and rosuvastatin.

On presentation, her blood pressure was 165/77 mm Hg and her heart rate was 67 bpm. Her physical examination revealed regular rate and rhythm, no cardiac murmurs or gallop, diminished lower extremity pulses, and right upper quadrant tenderness with bilateral costovertebral angle tenderness.

Her initial evaluation showed a normal TSH level, a microscopic hematuria with few RBCs in the urine and a creatinine of 1.26 mg/dL up from her baseline of 0.72 mg/dL. Her initial electrocardiogram (EKG) showed unchanged left bundle branch block with normal sinus rhythm.

She had a non-contrast abdominal computed tomography (CT) scan that showed right-sided kidney infarct as well as small left-sided kidney infarcts (Fig. 1). A CT angiogram of the chest and abdomen revealed no aortic pathology but did confirm bilateral kidney infarcts. She had a transthoracic echo that showed moderate left atrial enlargement without any clots and a normal left ventricular ejection fraction.

On the second day of hospitalization, her telemetry monitor showed an abnormal rhythm suggesting AF that was confirmed by an urgent EKG. A diagnosis of paroxysmal AF was made. Her CHA2DS2-VASc score was 6 which put her at a very high risk for thromboembolic events. The patient was anticoagulated appropriately with intravenous heparin in addition to warfarin and was also continued on a beta-blocker regimen for AF rate control. Due to the high CHA2DS2-VASc score, she was placed on lifelong anticoagulation.

The patient's creatinine improved and went back to the baseline of 0.8 mg/dl within a week.

Discussion

Renal vasculature anatomy

The abdominal aorta gives rise to the renal arteries at the level of L1 or L2. In the majority of individuals, the renal artery gives off branches that become the anterior and posterior divi-

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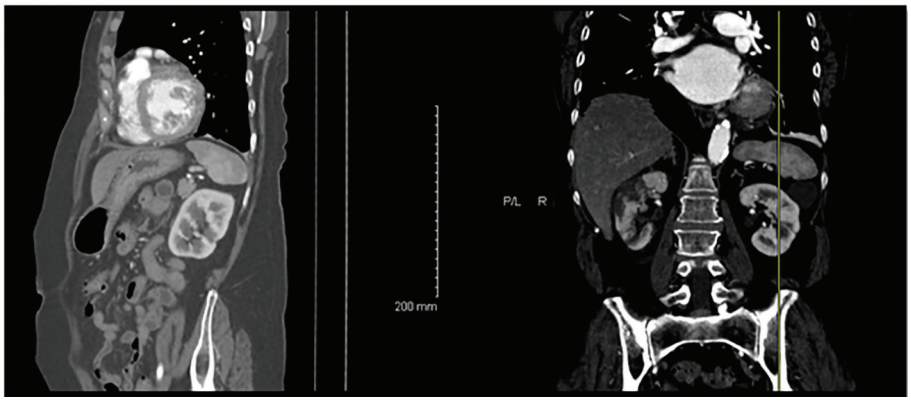

Figure 1. CT scan of the abdomen showing bilateral kidney infarctions.

sions, and inside the hilum the anterior renal artery will give rise to the apical, anterior and inferior segmental branches. The segmental vessels branch deeper into the renal parenchyma to finally reach the capillaries and glomeruli [4] (Fig. 2). It is believed that the renal circulation is the final resting place for up to 2.3% of systemic arterial embolizations [5] (Figs. 3-5).

ARI presentation and diagnosis

Renal infarction is often misdiagnosed since other disorders such as renal calculi and acute pyelonephritis could have a similar presentation [2].

Most patients with ARI are in their 60s and present with flank pain and hematuria with no predominance towards the right or left kidney. Acutely elevated blood pressure is thought to be secondary to renin-angiotensin-aldosterone related mechanisms. Other nonspecific signs and symptoms may include fever, nausea and vomiting. On the other hand, kidney infarctions may be completely asymptomatic and could be detected incidentally on CTs scan [1, 6, 7]. It has been estimated that renal infarction has an incidence of 1.4% based on an autopsy series study [8].

Elevations of white cell counts may be seen along with other serum markers which have been found to be inconsistently elevated including: alkaline phosphatase, fibrinogen, C-reactive protein and aspartate aminotransferases. The most sensitive marker is serum lactate dehydrogenase, however it is not specific for ARI diagnosis [1, 9]. Renal angiography can virtually diagnose all cases but computed tomography (CT) imaging is key for diagnosing renal artery occlusion and has good sensitivity in detecting renal infarction [10].

ARI pathogenesis

There are several mechanisms for renal infarction with the thromboembolic phenomenon being the most common. This and other etiologies are discussed below.

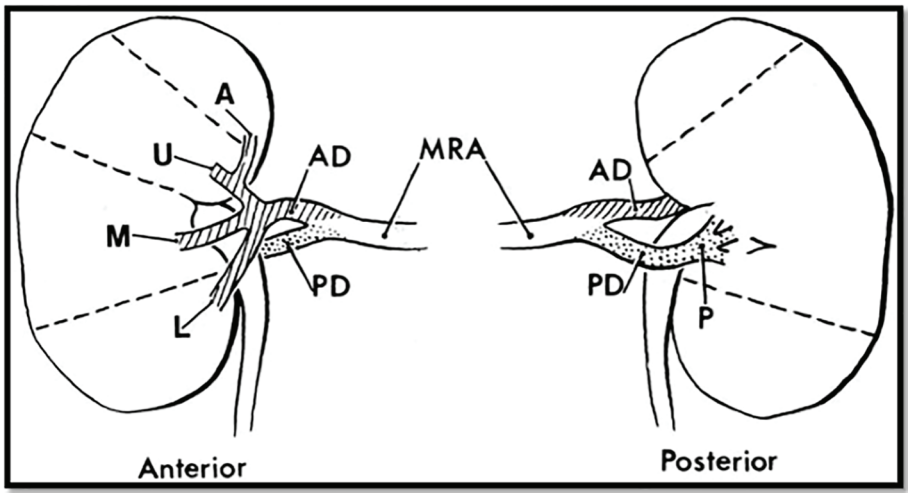

Figure 2. A diagram of the most common pattern of arterial supply to the kidneys demonstrating the main renal artery, anterior and posterior branches, and five segmental arteries. MRA: main renal artery; PD: posterior division; AD: anterior division. Segmental arteries are indicated by A (apical), U (upper), M (middle), L (lower), and P (posterior). Modified from Graves FT. The anatomy of the intrarenal arteries and its application to segmental resection of the kidney. Br J Surg 1954;42:132.

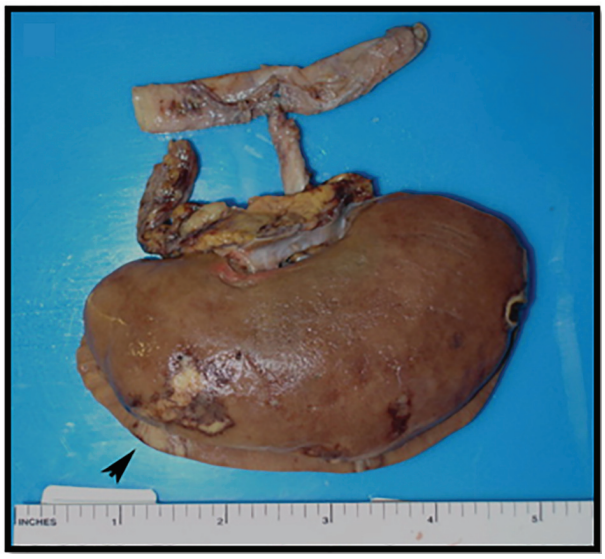

Figure 3. An allograft kidney from a 58-year-old obese man with a past medical history of hypertension and diabetes mellitus, who expired due to acute myocardial infarction and was found to have ARI on autopsy.

Thromboembolic phenomenon

AF, previous embolic phenomenon, ischemic and valvular diseases put the patient at an increased risk for kidney infraction from a thromboembolic phenomenon [11]. The embolic pathogenesis involves the occlusion of a renal artery or branch vessel by cholesterol or blood clots [12, 13]. AF is the most common etiology for kidney infarction and thromboembolic phenomena [8].

AF is one of the most common arrhythmias accounting for more than 467,000 admissions annually in the United States. It has been estimated that 2% of Americans under 65 and up to 9% over 65 years of age have AF. AF increases the risk of stroke and/or peripheral thromboembolism due to thrombi formation in the atrium and especially in the left atrial appendage. Thrombus formation in AF is classically attributed to blood flow stasis but it is now becoming apparent that thrombogenesis in AF is multifactorial. Loss of coordinated left atrial systole along

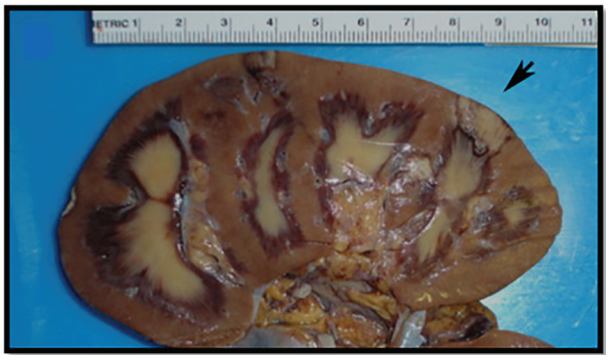

Figure 4. Gross image of the bivalved kidney with cortical infarcts secondary to arterial thrombus, largest infarct (black arrow pointing to the tip of the infarction) measuring 5.0 cm in greatest dimension.

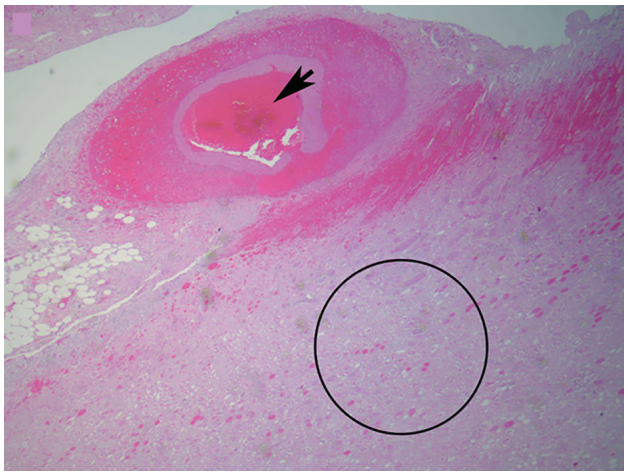

Figure 5. Microscopic image of an arterial thrombus showing a vessel completely occluded by the thrombus (black arrow) and the resulting renal infarct (in and around the circle) (from Fig. 4) (H&E, × 2.5).

with atrial dilation leads to atrial blood flow stasis. Anatomical changes seen in AF including endocardial denudation and even edematous and fibrinous changes may also play a role. Increased levels of prothrombin, prothrombin fragments 1 and 2, tissue factor and vWF are seen and there has been recent interest in the roles of IL-6 and growth factors (e.g. VGEF) as contributors to thrombus formation. Both IL-6 and VGEF can increase tissue factor production and are both increased in AF [14].

The CHA2DS2-VASc score is used in non-valvular AF to calculate the yearly stroke risk and is composed of congestive heart failure (one point), hypertension (one point), age ≥ 75 (two points), diabetes (one point), prior stroke, transient ischemic attack (TIA) or thromboembolism (two points), vascular disease (one point), age 65 - 74 (one point), and female sex (one point). Increase in a patient's CHA2DS2-VASc score is associated with a considerably high incidence of yearly thromboembolic complications [14].

Korzets and colleagues evaluated 11 patients admitted with kidney infarctions between the years of 1997 and 2000. The prevalence in that review was thought to be 0.007% in one center with 60% of the cases identifying AF as the cause. In all the cases reported, the diagnosis was delayed because ARI was not initially part of the differential diagnosis. Ten out of 11 patients with ARI had recovery of their renal function [7].

Hazanov and colleagues described 44 patients with ARI between 1948 and 2002, among which 40 patients (90%) had a history of AF and four (10%) presented with AF with rapid ventricular response. Two (4%) of these patients were on warfarin and had therapeutic INR and yet they suffered ARI. The outcome for the renal function was available in 38 patients. Sixty-one percent had a normal kidney function on follow-up, while 18% and 8% ended up with renal failure (creatinine > 2 mg/dL) and end-stage renal disease, respectively. Two (4%) of these case had bilateral kidney involvement [15].

In a Danish study conducted by Frost and colleagues, 14,917 men and 14,945 women diagnosed with AF were followed up from diagnosis to first thromboembolic event, death or to the end of the year 1993. From this group, 2% were found

to develop renal artery thromboembolic events [16].

An emergency department retrospective study done by Antopolsky and colleagues looked at 38 patients seen in the ED that were diagnosed with renal infarction during a 10-year period. Patients in whom infarction was due to trauma, coronary PCI, recent vascular surgery were excluded from the study. In this group, AF was the most common etiology (n = 14, 37%). Other etiologies included hypercoagulation (n = 6, 16%), endocarditis (n = 3, 8%), others (n = 10, 26%), and idiopathic (n = 5, 13%) [10].

Hereditary and acquired clotting factors diathesis

Hypercoagulable disorders are a rare cause of kidney infarction. Amongst these antiphospholipid syndrome (APS), antithrombin III deficiency, factor V Leiden, protein C and S deficiencies, hyperhomocysteinemia and polycythemia vera play an important role [17, 18]. APS can cause both arterial and venous thrombotic events and while these events mostly involve lower limb deep veins and cerebral arteries, the renal circulation can also be targeted. Renal infarction can be a sequela of the above as well as renal artery thrombosis or emboli from cardiac or other arterial sources [19]. The rarity of antithrombin III deficiency as a causative factor of ARI is demonstrated by the fact that there is only a single reported case in the literature of a 47-year-old male with antithrombin III deficiency and heterozygosity for prothrombin (G20210A) gene mutation who presented with bilateral renal infarcts [20].

Vessel anomalies

Fibro-muscular dysplasia (FMD) and renal artery aneurysm have been reported to cause kidney infarction. It has been reported in an otherwise healthy individual who presented with acute bilateral flank pain in which ARI and bilateral FMD were found. In such cases, treatment is with stent placement leading to a complete resolution of kidney function [21].

Trauma

Kidney infarction has been reported with penetrating and blunt trauma to the abdomen with complete recovery of kidney function after conservative therapy with anticoagulation. The kidney dysfunction secondary to trauma can be divided into five grades, with grade 5 being the worst. The kidney injury secondary to trauma usually occurs when there is an intimal injury and thrombus formation in the renal artery. Sometimes kidney injury could be caused by severe retroperitoneal hemorrhage. Severe renal artery spasm causing decreased renal perfusion with trauma has also been reported [9, 22].

Idiopathic

Idiopathic etiology is an important cause for ARI. In some case series, it has been estimated that up to 60% of kidney infarction cases were idiopathic. These patients were younger and more likely to be cigarette smokers. However, this idiopathic etiology could have been overestimated as there are a significant number of these patients with a hypercoagulable state like hyperhomocysteinemia, antithrombin deficiency and protein S and C deficiency [18].

Less common causes

Kidney infarction has been reported with the use of cocaine and was attributed to cocaine-induced vasoconstriction, oxidative stress and increased atherogenicity [23]. Kidney infarction was also reported with mucormycosis infection when the infection involves the kidneys [18].

Treatment

Even though treatment guidelines have not been established, conservative therapy with thrombolysis or anticoagulation, as in our case, appears to be effective. Similarly to our case where creatinine returned to baseline within several days, recovery of renal function is achieved in most cases of renal infarction. This underlies the importance of always keeping ARI in the differential diagnosis when a patient presents with flank pain and hematuria for prompt identification and treatment.

Conflict of Interest

The authors of this manuscript declare no conflict of interest.

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