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Clinical Report

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Bilateral renal infarction: an uncommon presentation of fibromuscular dysplasia

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Abstract
While fibromuscular dysplasia (FMD) is an established cause of secondary hypertension, its association with renal infarction is less well recognized. We report a middle-aged man who presented with complaints of loin pain and severe hypertension. Computed tomography angiography of the abdomen revealed bilateral renal infarction with multiple short-segment arterial dissection compatible with FMD in the absence of systemic vasculitis and other risk factors for thromboembolic events. Bilateral renal infarction complicating FMD is extremely rare and has so far been reported only in a handful of cases. Physicians encountering cases of otherwise unexplained renal infarction/ischemia need to be aware of this complication.

Keywords: fibromuscular dysplasia; hypertension; renal infarction

Introduction

Fibromuscular dysplasia (FMD) represents a group of non-atherosclerotic and non-inflammatory arterial diseases that most commonly involve the renal and carotid arteries [1]. They often present with signs and symptoms related to reduced downstream perfusion (e.g. cerebral ischemia). While FMD of the renal arteries is an established cause of secondary hypertension, its association with renal infarction, which often has a subtle presentation, is very rare and less well recognized. Here, we report a case of FMD presenting with bilateral renal infarcts as well as severe hypertension, and briefly review the clinical, laboratory and imaging findings of the patient. We also provide an overview of the previous reports to help identify common characteristics that can be used to facilitate the diagnosis.

Case

A 53-year-old Caucasian man with no major past medical history except for squamous cell carcinoma of the neck presented with sudden onset right loin pain associated with nausea. His physical examination was remarkable for a blood pressure of 194/129 mmHg, regular heart rate of 87 bpm and right lower quadrant abdominal tenderness without any skin lesions. Laboratory studies showed a serum creatinine level of 1.20 mg/dL (106.08 μmol/L), mild leukocytosis with WBC of 13 800/mm^3, hematuria and leukocyturia. Computed tomography (CT) angiography of the abdomen was performed to further explore the etiology of abdominal pain; it revealed several wedge-shaped renal infarcts bilaterally (Figure 1) as well as multiple short-segment dissections of the middle colic, right renal, left renal and left external iliac arteries. C-reactive protein was elevated at 193.7 mg/L (reference range: 0–4.9 mg/L). A comprehensive immunologic workup including antinuclear antibody, antineutrophil cytoplasmic antibodies, serum and urine protein electrophoresis as well as serum complement levels was normal. Thrombophilia tests including protein C, protein S, anticardiolipin antibody, anti-β2 microglobulin antibody and factor V Leiden were all negative. Echocardiogram did not show any thrombus or vegetation.

In light of imaging evidence of short-segment dissections and downstream ischemia of multiple arteries associated with the lack of any evidence of an ongoing immunologic process, cutaneous lesions or hypercoagulability state, the diagnosis of FMD was made. Supportive therapy, including analgesics and intravenous antihypertensive agents that were subsequently switched to oral medicines, was followed by improvement in symptoms and adequate control of blood pressure; the follow-up CT angiography a few weeks later demonstrated stabilization of the renal lesions. Interestingly, a subsequent CT angiography that was performed 8 months later could further identify several clinically silent microaneurysms.

Discussion

The incidence of renal infarction (RI) has been estimated to be as low as 0.007%, but it should be noted that it remains undiagnosed in a significant subset of patients [1]. Although RI typically presents with flank or abdominal pain, fever, nausea and vomiting, its only presentation can

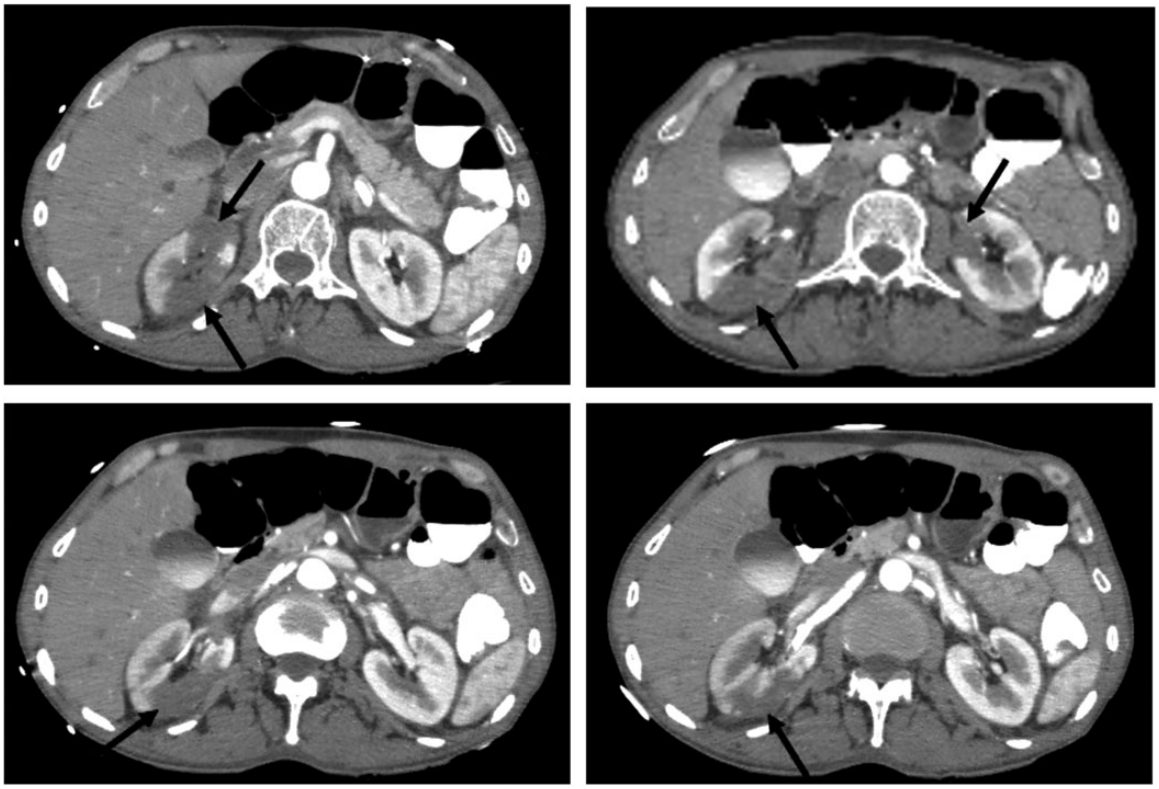

Fig. 1. CT angiogram of the abdomen reveals bilateral renal infarcts (arrows) that are predominant on the right side.

be acute severe hypertension. Laboratory studies reveal hematuria in most instances, and the blood levels of lactate dehydrogenase and C-reactive protein are frequently elevated [2, 3].

Renal infarction commonly results from thromboembolism related to cardiac arrhythmia or structural disease. Vegetations in infective endocarditis and heart tumors are other potential cardiac sources of emboli, while hypercoagulability, autoimmune disorders, sickle cell disease and aortic interventions comprise the main non-cardiac etiologies. Diseases associated with interruption of the renal arterial endothelium such as vasculitis, Marfan syndrome and FMD are among less common causes of RI [1, 2]. In our patient, once the renal infarcts were identified, cardiac echography was performed to explore a potential cardiac source for emboli. Similarly, a comprehensive workup for vasculitis and hypercoagulability that was carried out in search for more common identifiable causes of renal infarct was negative.

FMD is a non-inflammatory vascular disease that primarily affects small- and medium-sized arteries. It is most common in the renal and internal carotid arteries, but involvement of almost every arterial bed in the body has been described. The clinical presentation of FMD varies widely from an asymptomatic condition to a multisystem disease depending on the anatomic distribution, extent of vascular involvement and the type of FMD [1]. Approximately two-thirds of patients have multiple arteries involved. Renal arteries are the most commonly involved vascular bed in FMD. It is bilateral in 35–50% of cases; nearly half of the patients with bilateral renal arterial FMD will have extra-renal involvement [1]. Hypertension is the most common clinical presentation. While various degrees of renal dysfunction are reported in up to 63% of patients, overt renal failure is uncommon in this setting [3]. Our case presented with slight elevation of serum creatinine and acute onset of severe hypertension. Due to bilateral involvement of the renal arteries, a Doppler ultrasound of the carotid arteries was performed that was unremarkable.

Renal infarction is seen in only 0.9% of the patients with FMD; bilateral renal infarction is extremely rare and has so far been reported only in a handful of cases [4–9]. Previously reported cases of renal infarction complicating FMD are summarized in Table 1. Interestingly, while FMD as a cause of renal artery stenosis is more common in young females, cases of associated renal infarction seem to have an equal distribution in both genders with a median age of 39. It is also noteworthy that the majority of the patients whose renal arterial damage due to FMD has been severe enough to result in infarction (including those with involvement of bilateral renal arteries) did not present with extra-renal manifestations. This could potentially represent a challenging aspect of the diagnosis of FMD in acute cases. Moreover, renal function was reported to be normal or close to normal in most cases, although all patients except for one presented with hypertension. Our patient's serum creatinine that was slightly elevated at the time of admission decreased to 0.9 mg/dL (79.5 mmol/L) at discharge; after 8 months of follow-up his renal function remained normal.

In the past, the gold standard for the diagnosis of renal artery FMD was considered to be digital subtraction angiography (DSA). Currently, there are several non-invasive imaging modalities that are available for the diagnosis of FMD; Doppler ultrasound, contrast-enhanced CT scan angiography (CTA) and magnetic resonance angiography (MRA) [1]. Two retrospective studies have reported a high

Table 1. Reported cases of renal infarction complicating FMD

Case	Age/ Gender	Presenting symptoms	Blood pressure	Renal function	Renal infarction	Extra-renal manifestation	FMD diagnosis	Management
Van den Driessche *et al.* [10]	44 M	Right loin pain	191/106	eGFR 71 mL/min	Unilateral, right	None	Angiography	Medical
Connor and Mathieson [11]	28 F	Left loin pain, vomiting and fever	154/80	NS	Unilateral, left	Probable involvement of hepatic artery	Angiography	Medical
Sinnamon *et al.* [12]	39 F	Right iliac fossa pain and fever	140/90	NS	Unilateral, right	None	MRA and angiography	PTA
Shlomai *et al.* [13]	56 F	Abdominal pain, vomiting	124/75	NS	Unilateral, right	None	MRA	Medical
González-Moreno *et al.* [4]	38 F	Asymptomatic	210/110	NS	Bilateral	None	Angiography	Medical
Niizuma *et al.* [5]	27 F	Asymptomatic	150/90	NS	Bilateral	Hepatic artery aneurysm	Angiography	Medical
Doody *et al.* [6]	34 M	Bilateral loin pain and fever	160/95	NS	Bilateral	None	Angiography and MD-CTA	PTA
Salifu *et al.* [7]	40 M	Bilateral flank pain and fever	200/103	Cr 1.6 mg/dL (141 µmol/L)	Bilateral	None	MRA and angiography	Medical
Dursun *et al.* [8]	37 M	Bilateral flank pain and fever	160/100	Cr 3.3 mg/dL (292 µmol/L)	Bilateral	None	MRA and angiography	PTA
Basile *et al.* [9]	43 M	Bilateral flank pain	150/100	Cr 1.8 mg/dL (159 µmol/L)	Bilateral	None	CT angiography and SRA	Medical
Present case	53 M	Right loin pain, nausea	194/129	Cr 1.2 mg/dL (106 µmol/L)	Bilateral	Multiple arterial involvement in the abdomen	CT angiography	Medical

NS, not specified (mentioned as normal); PTA, percutaneous transluminal angioplasty; MRA, magnetic resonance angiography; MD-CTA, multi-detector CT angiography; SRA, selective renal arteriography; eGFR, estimated glomerular filtration rate.

sensitivity for CTA and MRA in this setting, which is comparable for the two modalities [14, 15]. Therefore, CTA or MRA should be initially considered in the diagnosis of FMD, and DSA be reserved for those cases where the findings of these imaging studies are inconsistent in the presence of high clinical suspicion. In our patient, the diagnosis was made by CTA that confirmed the presence of multiple arterial bed involvement characteristic of FMD, including several microaneurysms that were identified on a subsequent CT scan several months later.

The main impetus in management of patients with renal FMD is control of hypertension. In most patients, it can be primarily managed medically; the principles of drug therapy are based on the presence of renal artery stenosis and renal hypoperfusion [16]. In patients with unilateral renovascular FMD, activation of renin–angiotensin–aldosterone system (RAAS) with its downstream effects is considered the primary mechanism of hypertension. In these cases, the contralateral kidney maintains adequate natriuresis, thus avoiding aldosterone-mediated sodium and fluid retention. RAAS blockade is, therefore, the initial target in unilateral renovascular FMD. In cases of bilateral disease, natriuresis cannot occur leading to sodium and volume overload and portending an additive impact on RAAS-mediated hypertension [17]. RAAS blockers could lead to significant perturbation in renal hemodynamics in these cases; close monitoring of renal function is warranted. Diuretics can be used as a second-line therapy in unilateral disease and possibly as first line in cases of bilateral disease. Our patient's blood pressure has remained under tight control with an angiotensin-converting enzyme inhibitor as well as a beta blocker. He has shown no clinical evidence of fluid retention.

Revascularization is reserved for patients with resistant hypertension, poor tolerance or non-compliance with medications, and progressive deterioration in renal function from ischemic nephropathy [2]. Percutaneous transluminal angioplasty has largely replaced surgery as the preferred treatment of renal arterial FMD. Over the years, the technical success rate of the procedure has approached 100%, and it leads to cure or improvement of hypertension in a high percentage of patients with FMD. Surgery is generally reserved for treating macroaneurysms or complex lesions [3].

Since the underlying mechanism for the renal infarct in FMD is not entirely clear, evidence is lacking regarding the benefit of anticoagulation for patients with ischemia/infarction secondary to FMD. Nevertheless, some authors have recommended the use of aspirin [3]. Our patient initially received anticoagulation with heparin due to extensive infarction; it was subsequently stopped once thromboembolic etiologies were eliminated. He has been receiving low-dose aspirin since then.

Conclusion

This case, coupled with previous reports, illustrates the high variability of the presentation of FMD ranging from asymptomatic disease to extensive infarcts and acute severe symptoms. FMD is a clinical diagnosis that should be considered in those patients presenting with otherwise unexplained renal ischemia or infarction and involvement of multiple arteries, particularly in the context of new-onset or severe hypertension.

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