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Single Case

Catastrophic Fibromuscular Dysplasia Presenting with Concomitant Bilateral Renal Infarction, Vertebral Artery Dissection, and Mesenteric Ischaemia

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Keywords
Fibromuscular dysplasia · Renal infarction · Acute kidney injury · Vertebral artery dissection

Abstract
Fibromuscular dysplasia (FMD) is a non-atherosclerotic, non-inflammatory disorder of the arterial wall muscular layer which can lead to arterial stenosis, occlusion, and dissection. Clinical presentations of FMD vary depending on the arterial territories involved, often leading to diagnostic challenges. This case report describes an exceptionally unusual presentation of FMD, not previously described, affecting a previously fit and well 37-year-old female presenting with bilateral renal infarction, sequential vertebral artery dissections, mesenteric ischaemia, and the requirement for continued renal replacement. This report highlights how unusual presentations of FMD can mask the underlying diagnosis. Early consideration of FMD in a differential diagnosis can guide an effective management strategy, including appropriate imaging and multi-speciality involvement.

Introduction

Fibromuscular dysplasia (FMD) is a non-atherosclerotic, non-inflammatory disorder affecting the arterial wall smooth muscle layer and predisposing to arterial stenosis, occlusion, and dissection [1]. The underlying pathogenesis of FMD is poorly understood, although a

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potential genetic component has been described [2]. Although FMD typically affects the renal, extracranial carotid, and vertebral arteries [1], cases have been observed in all arterial territories [3]. Approximately two-thirds of patients diagnosed with FMD have multiple arteries involved [1]. Clinical presentations differ depending on the distribution and severity of arterial lesions and the underlying mechanism of vascular pathology such as stenosis, dissection, and aneurysms. FMD can be classified based on the arterial layer affected. Medial fibroplasia causes the classical "string of beads" appearance on renal angiography. Ninety percent of adult cases are in females; however, FMD is increasingly recognized and diagnosed in all age groups [4].

Case presentation

A 37-year-old female non-smoker, prescribed the combined oral contraceptive pill, presented with sudden-onset severe left-sided flank pain following a similar, self-limiting, right-sided episode 1 week prior. She was apyrexial and hypertensive (180/90 mm Hg). Pulses were intact and capillary refill time was normal. The abdomen was tender to palpation in both renal angles. No skin changes were noted. Electrocardiography demonstrated normal sinus rhythm and echocardiography revealed normal ventricular function without vegetations or thrombi. Urinalysis was positive for protein only which was the same on repeat testing. Acute kidney injury was evident (serum creatinine 155 μmol/L). C-reactive protein (CRP) was 21 mg/L and white cell count 9.9×10^9/L. The following tests were negative or within normal ranges: cytoplasmic and perinuclear anti-neutrophil cytoplasmic antibodies; myeloperoxidase and proteinase 3 antibodies; complement C3 and C4; anti-nuclear antibodies; serum immunoglobulins and electrophoresis; anti-cardiolipin and anti-glomerular basement membrane antibodies. A midstream urine taken 24 h after the admission returned no growth. Lactate dehydrogenase was elevated at 850 iu/L. A computed tomography (CT) scan, performed without contrast, demonstrated renal asymmetry with an enlarged left kidney but no calculi.

Intravenous pivmecillinam/tazobactam was commenced to cover infection and specifically pyelonephritis and oral amlodipine was administered for hypertension. Over the following days, the patient developed fevers and the CRP rose to 326 mg/L. She became oligo-anuric and serum creatinine rose to 491 μmol/L. Renal Doppler ultrasound demonstrated good cortical perfusion bilaterally. On day 4, the patient reported left-sided neck pain in keeping with carotidynia and subsequently developed tonic-clonic seizures.

Cerebral CT angiography showed a left vertebral artery dissection (shown in Fig. 1), abnormal irregular appearances of the right vertebral artery (shown in Fig. 2), internal carotid artery, and a small acute cortical infarct in the right occipital lobe. Renal CT angiography (performed 5 days after the non-contrast CT) showed two 90% stenosis of the right renal artery (Fig. 3) and multiple stenoses on the left which were up to 70% (Fig. 4). Both kidneys showed extensive branched vessel stenoses. The right kidney measured 9.8 cm in length (9.5 cm on first CT) compared to the left which measured 12.9 cm (12.3 cm on first CT). The slight interval increase in size of both kidneys likely represents oedematous change. Wedge-shaped opacities in the left kidney were considered indicative of acute infarcts. Acute haemodialysis was commenced via a femoral venous catheter.

The degree of parenchymal infarction was so extensive that it was considered that risks of angioplasty to the left renal artery outweighed the potential benefits. Methylprednisolone 500 mg was administered intravenously for 5 days followed by oral prednisolone. This was tapered and discontinued following a CT aortogram and fluorodeoxyglucose positron emission tomography as neither revealed evidence of medium- or large-vessel vasculitis, although the former did demonstrate features of ischaemia in the ascending colon. Anticoagulation with

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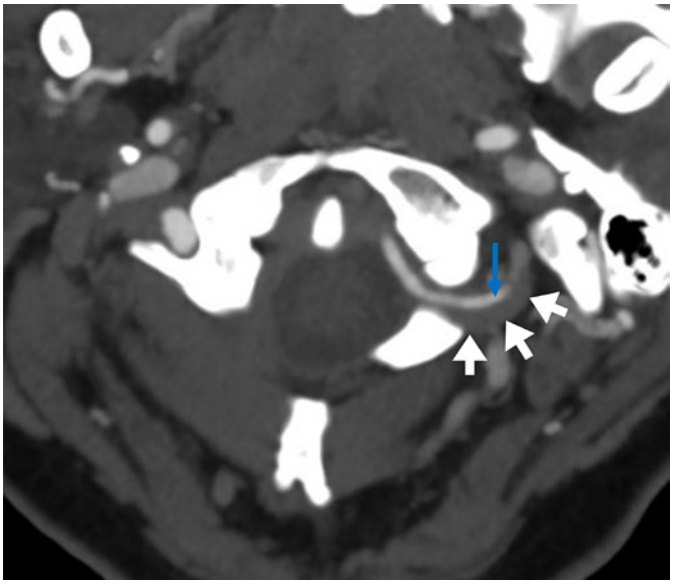

Fig. 1. Thick-walled dissected left vertebral artery. The contrast-filled stenosed lumen can be seen (blue arrow) with the outer wall of the thickened artery marked with short white arrows.

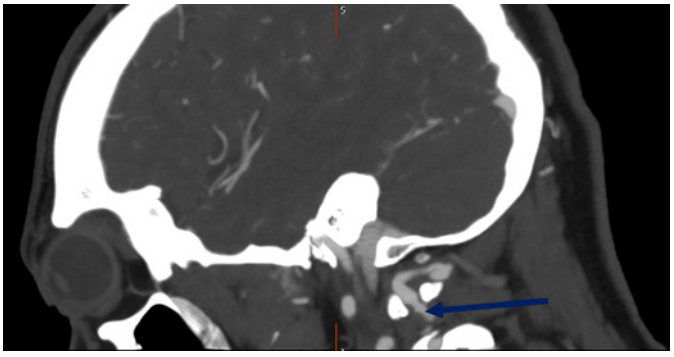

Fig. 2. Beading of right vertebral artery (blue arrow).

low molecular weight heparin was commenced. Further carotidynia occurred 3 weeks after admission, and a right vertebral artery dissection was diagnosed on CT angiography. Anticoagulation was later switched to warfarin and subsequently clopidogrel. Peritoneal dialysis was commenced and excellent blood pressure control was established on 5 mg ramipril daily. The patient remains well on peritoneal dialysis, 1 year after presentation, and is being considered for renal transplantation.

Discussion

Flank pain has several differential diagnoses including pyelonephritis, renal colic, and renal infarction. The latter is uncommon, accounting for just 0.007% of all emergency department attendances [5]. Presentation of FMD is heterogeneous; only 15% patients present with abdominal/flank pain [6], and typically delayed diagnosis results in missed treatment opportunities and is associated with poorer outcomes.

Our case, in which the constellation of flank pain markedly elevated CRP and features suggestive of pyelonephritis on non-contrast CT and Doppler ultrasonography led to pyelonephritis being the initial diagnosis, highlights several important points for clinicians. Firstly,

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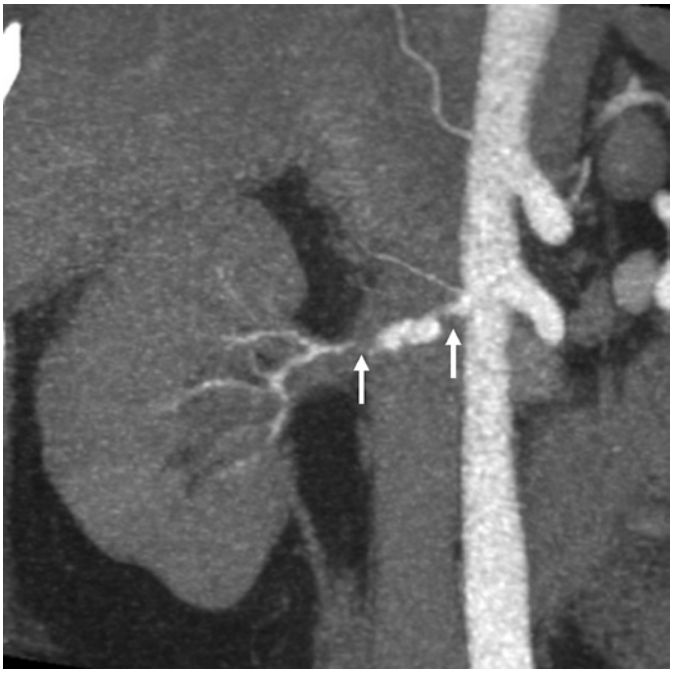

Fig. 3. Renal angiogram of the right renal artery showing multiple short stenoses (white arrows) in addition to the right kidney which shows globally poor enhancement.

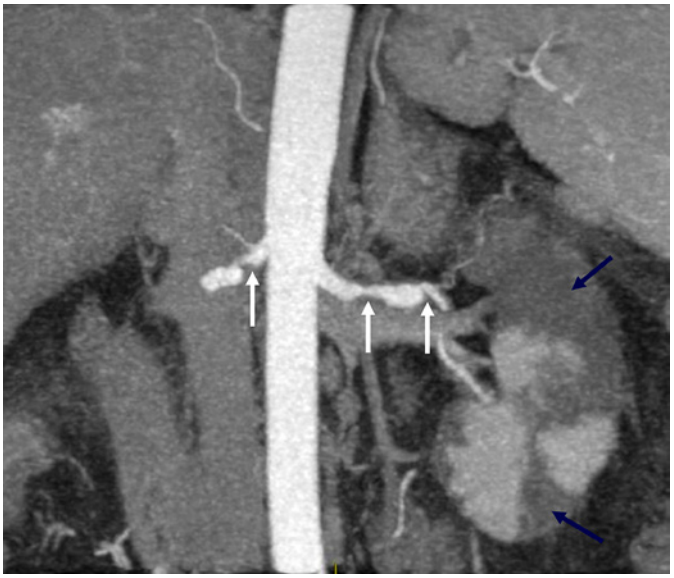

Fig. 4. Renal angiogram of the left renal artery, and first part of the right renal artery showing multiple stenoses (white arrows). In addition, the left kidney with multiple non-enhancing infarcted segments can be seen (blue arrows).

hypertension is not a feature of pyelonephritis and should prompt consideration of renal infarction in patients with flank pain. Secondly, fever is present in about 20% of patients with renal infarction and should not preclude this diagnosis [7]. Thirdly, the diagnosis of renal infarction cannot be excluded with non-contrast CT, and Doppler ultrasonography is highly operator dependent and potentially unreliable. Furthermore, the findings on urinalysis are variable in renal infarction [8], and reassurance cannot be taken from the absence of haematuria. Our case demonstrates that renal infarction must be considered in patients with loin pain and especially in cases of suspected pyelonephritis with no growth on midstream urine. An elevated lactate dehydrogenase in the setting of normal transaminases is a non-specific

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but characteristic laboratory finding in renal infarction [8, 9]. This case illustrates the difficulty of reaching this diagnosis in centres without full access to imaging facilities.

The diagnosis of renal infarction should in turn prompt consideration of the aetiology. Thromboembolic disease, secondary to arrhythmias, hypercoagulable states, or complicating medical procedures, should be excluded [10]. Vascular injuries including inflammatory vasculitides or FMD are responsible for about 7.5% of those with renal infarction [8]. Therefore, a multisystem inflammatory condition such as a large- or medium-vessel vasculitis must be considered, and this is particularly important in patients with multiple affected vascular territories and raised inflammatory markers.

Multi-territory disease is evident on imaging in approximately two-thirds of patients with FMD at presentation [1, 11]. However, it is uncommon for patients to present with symptoms representing widespread disease involvement and, as such, it is recommended that the diagnosis of FMD is followed by head-to-pelvis imaging with CT and magnetic resonance angiography (which has superseded invasive angiography).

Although renal involvement is common in FMD, affecting 75–80% of patients [6], infarction is rare (being seen in only 0.9% of cases). Bilateral renal infarction has only been reported in a small number of case reports [12]. The ARCADIA study imaged 469 patients with FMD, of whom 66.3% had multi-vessel FMD. Cerebrovascular disease was more common in patients with bilateral renal involvement but not infarction [11]. A review of the published cases of bilateral renal infarction secondary to FMD reported that no patients with bilateral renal infarction had cerebral involvement [12]. Chronic kidney disease may occur with renal artery dissection or renal infarction, but progression to end-stage renal disease from FMD alone is rare [6, 13, 14].

The catastrophic nature of this case presentation, in which the patient had widespread disease resulting in dialysis-dependent acute kidney injury, cerebral infarction, and bowel ischaemia, is extremely unusual and to our knowledge has not previously been described. The case serves to underline the importance of considering FMD in multi-territory acute vascular disease when an inflammatory condition may seem more likely.

Conclusion

We report an exceptionally rare case of FMD in which the patient developed bilateral renal infarction, resulting in the requirement for renal replacement therapy, with simultaneous cranial involvement. The case highlights the importance of considering FMD early, especially when features (e.g., hypertension) are inconsistent with more common diagnoses causing flank pain (such as pyelonephritis). Due to the potential for involvement of multiple vascular beds, and the inherent limitations of certain imaging modalities, head-to-toe cross-sectional imaging should be an early consideration and inflammatory conditions should be carefully excluded.

Statement of Ethics

Written informed consent for the publication was obtained by the patient, including for the use of images. As per the NHS Research Ethics Committee guidelines, where research has not taken place, as in this case, no study approval or Ethics Committee involvement is required and therefore was not sought for the publication of this case study. The patient was already seen, and the case report was written in retrospect with no alteration in the patients care due to the report.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

Nicholas Martin Gourd and Hannah Elizabeth Jenkins were responsible for writing the main body of the text and were involved in the clinical care of the patient. Adrienne Lee was responsible for contributing towards the main body of the text, obtaining and formatting the radiological images and was involved in the clinical care of the patient. Andrew Connor was the senior clinician responsible for the care of the patient and contributed to writing and editing the main body of the text. Richard Miles was responsible for contributing insight and information for the manuscript with respect to radiological aspects of the case and editing of the text and was involved in the clinical care of the patient. Professor Justin Mason contributed insight and information regarding rheumatological aspects of the case and to editing of the text and was involved in the clinical care of the patient.

Data Availability Statement

All data used in the writing of this case report are included within the article.

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