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CASE REPORT

Bilateral spontaneous renal artery dissection and antiphospholipid antibodies

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Introduction

Renal arteries are the most common site of dissection involving visceral vessels [1]. Generally, rupture occurs as an extension of aortic dissection or secondary to trauma [2], more rarely arises spontaneously. Spontaneous renal artery dissection (SRAD) is a rare disorder with a prevalence of 0.005% and a predilection for males (M:F ranging from 4:1 to 10:1), for smokers and in the fourth to sixth decades of life. Bilateral SRAD is seen in about 12–18% of all cases [2]. SRAD was first reported by Bumpus [3], and 29 cases of bilateral SRAD have been previously described. Here, we report a review of the literature and the 30th case of a 46-year-old man with bilateral SRAD and repeatedly positive IgM anti-cardiolipin antibodies (aCL).

Case report

A 46-year-old man was admitted to our emergency department due to a sudden abdominal pain prevalently localized to right hypochondrium. The pain started in the morning and was followed by diarrhoea. Physical examination of the abdomen showed diffuse tenderness at palpation. Bowel sounds were present. Vital parameters were within normal limits. The pain was of intensity 7.5 on a scale ranging from 0 to 10. His past medical history was unremarkable, with the exception of smoking, and he was not taking any medication.

Blood analysis showed a neutrophil leucocytosis, whereas anti-thrombin, homocysteine, lactate hydrogenase, creatinine, urea and 24-h proteinuria were within normal limits. Fibrinogen, IgM aCL, C-reactive protein (CRP) and D-dimer levels were also increased (Table 1). Fluoresence flow cytometry showed low CD3+ve cells at 0.37×10^6/ml (reference range 0.96–2.5), normal CD3/CD8+ve cells at 0.17×10^6/ml (0.27–0.93), low CD3/CD4 + cells at 0.2×10^6/ml (0.5–1.7), low CD4/CD8 ratio 1.14 (1.5–3.0), low CD19+ve/CD45+ve cells at 0.029×10^6/ml (0.12–0.63), borderline low CD3-ve/CD16+ve/CD56+ve/CD45+ve cells at 0.02×10^6/ml (0.02–0.74).

Total body computed tomography (CT) scan revealed a large infarct involving superior and medial poles of the right kidney. Echocolourdoppler ultrasound of the renal artery did not show significant stenosis. Selective arteriography of the right renal artery demonstrated a dissection of the anterior branch of the right renal artery, leading to a lack of vascularization at superior and medial kidney portions. Anticoagulation with subcutaneous low-weight heparin was started.

In the week that followed, a complete metabolic profile, coagulation tests and laboratory markers of systemic autoimmunity were performed. Protein C (94%, reference range 70–130%), protein S (70%, reference range 64–129%), anti-nuclear antibodies, anti-neutrophil cytoplasmic antibodies, anti-smooth muscle cell antibodies, rheumatoid factors, antibodies to extractable nuclear antigens, anti-β2glycoprotein1 antibodies and lupus anti-coagulant were all normal or negative. On genetic screening for inherited connective tissue disease, Factor V Leiden was absent, prothrombin G2021A was normal and methylenetetrahydrofolate reductase C677T and A1298T variants were both negative. HIV test was negative. To complete the diagnostic work-up, a transthoracic echocardiography was carried out showing a slight increase of aortic root. Cerebral angio-MRI showed no abnormalities, whereas 24 h monitoring of arterial blood pressure demonstrated a grade 1 hypertension [4] so that a treatment with beta-blockers and calcium antagonists was started.

During hospitalization, certain blood tests and a total body CT scan were repeated, the latter revealing a bilateral dissection of the renal artery with consensual areas of renal infarction in both the kidneys (Figure 1). Blood analyses normalized although IgM aCL was still high. The vascular surgeon was in

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Table 1. Laboratory data.

	Admission	1 week	1 month	6 months	Reference range
White blood cell count (10^6/ml)	18.3	7.65	7.45	7.2	4.3–10.8
Neutrophils (10^6/ml)	14.3	4.4	4.0	4.5	1.8–7.5
Lymphocytes (10^6/ml)	1.6	1.1	2.2	1.9	1.2–4.0
Fibrinogen (mg/dL)	702	638	304	289	200–400
d-Dimer (mg/dL)	604	394	92	102	<243
Anti-thrombin (%)	98%	97%	97%	–	83–118
Homocysteine (mmol/L)	7.3	–	–	5.3	5–12
Urea (mmol/L)	1.5	1.8	3.0	2.7	0.8–4.2
Creatinine (µmol/L)	75	77	83	76	62–110
24-h proteinuria (mg/24 h)	108	–	–	103	<150
CRP (mg/dL)	23.2	6.1	0.5	0.1	0–0.5
ESR (mm/h)	–	49	14	6	2–25
LDH (U/L)	229	405	199		125–220
Anti-CL IgM (MPL)	45	–	58	33	<20
Anti-β2GPI IgM (CU)	–	–	7.5	14	<10

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; LDH: lactate dehydrogenase; CL: anti-cardiolipin; GPI: β-2-glycoprotein-1.

agreement with the interventional radiologist, considering well-controlled values of blood pressure, normal creatinine and urea levels and risk of extending dissection by percutaneous intervention on renal artery suggested an instrumental follow-up and conservative management. The patient was discharged with oral anticoagulation, beta-blockers and calcium antagonists, and he was advised to monitor his blood pressure and renal function.

After a six-month follow-up, the patient was in good general conditions, renal function remained within the normal limits and arterial blood values were well controlled by treatment. aCL IgM persisted at medium titres (Table 1). Total body CT scan demonstrated the persistence of a focal dissection of the anterior branch of the right renal artery with the regular flow after the dissected tract and a reduction of the extension of the ischaemic area in the superior pole of the kidney. Moreover, a slight reduction of the calibre of the left renal artery with a sign of partial revascularization in the medial pole of the left kidney was found (Figure 2). In view of stable clinical, laboratorial and instrumental tests, further invasive interventions were excluded, and medical treatment was continued.

This study was conducted in accordance with the World Medical Association Declaration of Helsinki. The patient gave his written informed consent to publish his case.

Discussion

A PubMed search using keywords ‘spontaneous bilateral renal artery dissection’ and ‘spontaneous renal artery dissection’ was performed. We found 29 cases of bilateral SRAD.

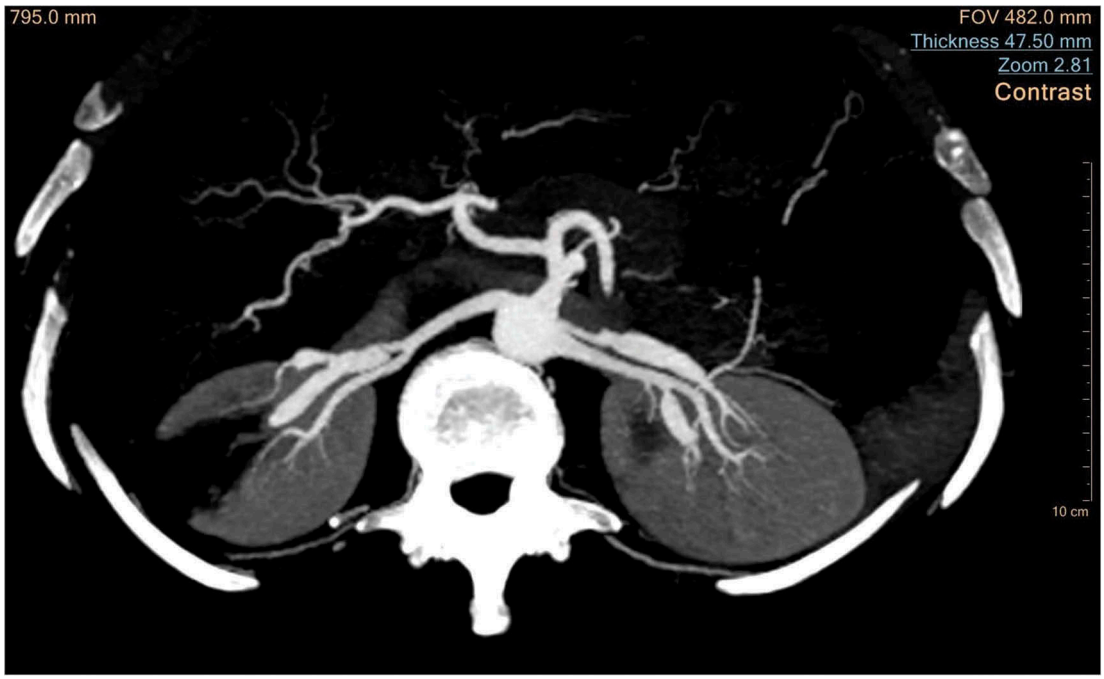

Figure 1. Angio-CT scan with axial MIP reformat shows, on the *right* side, at the origin of the anterior branch, a stenotic tract with contextual dissection and a post-stenotic dilation. On the *left*, a long stenotic tract with associated downstream dilation.

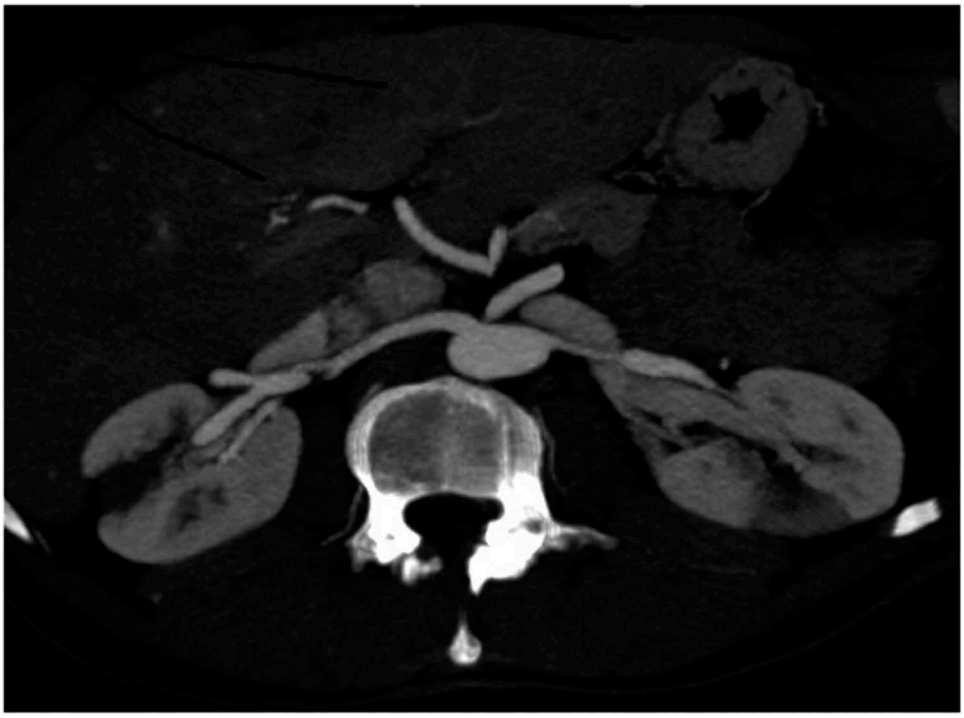

Figure 2. Six-week follow-up Angio CT scan. A stable bilateral arterial pathological condition with more defined ischaemic areas.

Bilateral SRAD is a rare disease of unknown aetiology [5]. SRAD can occur chronically, and since its symptoms are non-specific, more than half of the patients with SRAD will already have had renal infarction at diagnosis. Lumbar or abdominal pain represents the onset clinical presentation in 77% of the cases. Moreover, severe arterial blood hypertension, poorly responsive to anti-hypertensive treatments, can develop because of renal ischaemia. Nausea, vomiting, dysuria, renal failure, haematuria and testicular and/or groin pain can also occur [5,6]. Clinical features of SRAD not distinguishable from those occurring in the most common diseases involving abdomen and urogenital tract such as infections, trauma and nephrolithiasis are presented. A new-onset arterial hypertension can represent a signal of an underlying SRAD, mainly when associated with abdominal pain.

SRAD has been mostly associated with atherosclerosis and fibromuscular dysplasia. However, no inflammatory, no atherosclerotic segmental arterial mediolysis (SAM), trauma or inherited tissue connective diseases (such as Marfan and Ehlers–Danlos syndromes) predispose the renal artery to dissection [5,6]. Moreover, in one patient with SRAD, positive antiphospholipid antibodies (aPLs) have been found [7]. In this case, renal artery dissection was related to aPLs both throughout a direct effect on endothelium and by their pro-thrombotic actions [7]. Also in our patient, repeatedly positive aCL IgM antibodies at medium titres were found, suggesting a possible relationship between aPLs and SRAD. It is well known that thrombotic complications of aPLs syndrome (APS) can affect renal arteries and veins, intrarenal arteries and arterioles and glomerular capillaries [8]. Accordingly, renal vasculopathy is included among APS classification criteria [9] and comprises a wide spectrum of vascular diseases ranging from large renal vessel occlusion to thrombotic microangiopathy [8,9]. Renal infarction represents a possible complication of APS related to ischaemic kidney damage. Patients typically present with sudden-onset or uncontrolled systemic hypertension or the diffuse abdominal or flank pain in the cases of renal infarct. Recently, renal artery stenosis without evidence of thrombosis has been described in the context of APS [10], suggesting that vascular features of renal APS can be wider than expected. Interestingly, in our patent, left renal artery dissection evolved towards a vascular stenosis as demonstrated by abdomen CT scan. The hypothesis of a relationship between aPLs and bilateral SRAD is attractive, mainly considering that in our patient, other causes potentially related to renal artery dissection and renal ischaemia such as vasculitis, cardiogenic embolism, atrial fibrillation, cardiomyopathy, valvular heart disease, endocarditis, thrombo-embolism, haematologic disorders, renal artery injury by trauma or angiographic procedures were excluded. Atherosclerosis, fibromuscular dysplasia and SAM were also excluded because of epidemiological feature and no evidence of atherosclerotic lesions at any arterial site. Moreover, arteriography was not consistent with the radiological features of fibromuscular dysplasia SMA [1]. However, considering that positive aPLs have been evaluated in only two patients affected by SRAD, including our case, we can only suggest a possible relationship between positive aPLs and SRAD.

Further confirming the role of the immune system in arterial wall weakening, in our case, a marked decrease

of peripheral blood T and B subpopulations was observed, suggesting that in SRAD immune response undergoes peculiar modifications, that have also been described in Stanford-A acute aortic dissection (AAD) [11]. It is well known, indeed, that a depletion of cells related to acquired immunity with a prevalent neutrophil and macrophage natural response occurs in the peripheral blood and within aortic wall of patients with AAD [11]. Such pattern of immune response favours pro-inflammatory cytokine and metalloproteinase release, which, in turn, leads to matrix degradation and arterial wall rupture [12,13]. In agreement, in our case, the transient increase of neutrophils, platelet, CRP, erythrocyte sedimentation rate and fibrinogen levels were observed, confirming that a systemic pro-inflammatory environment occurs also in acute phases of SRAD [14] (Table 1).

Management options of SRAD include a wide spectrum of alternatives ranging from medical treatment to endovascular intervention or surgical revascularization [1,8]. Patients require a close follow-up for monitoring arterial blood pressure, creatinine values, urinalysis and appearance of spontaneous dissection at other vascular sites. Invasive therapeutic approaches are recommended only when arterial hypertension becomes uncontrollable or renal function worsens since several case reports demonstrated successful conservative management [15]. Moreover, angioplasty and stenting can be dangerous in the acute phases of dissection since vessels are extremely friable. In our patient, preserved renal function, well-controlled arterial hypertension and evidence of revascularization at imaging discouraged further invasive interventions, whereas standard oral anticoagulation was continued since aCL IgM antibodies were still positive.

In conclusion, we suggest considering bilateral SRAD as a differential diagnosis in young/middle-aged men with abdominal pain and new-onset arterial hypertension. Prevalence of SRAD, can be underestimated, whereas a well-timed therapeutic approach is fundamental to prevent the onset of potential life-threatening complications such as uncontrolled arterial hypertension and renal insufficiency.

Disclosure statement

No potential conflict of interest was reported by the authors.

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References

[1] Onteddu NK, Hindi Z, Rajashekar G, et al. Segmental arterial mediolysis presenting as spontaneous bilateral renal artery dissection. Radiol Case Rep. 2018;13:495–498.
[2] Araki T, Nakamura M, Imamura T, et al. Bilateral spontaneous renal artery dissection. J Cardiol Cases. 2011;8:e101–e105.
[3] Bumpus HJ. A case of renal hypertension. J Urol. 1944;52:295–299.
[4] Williams B, Mancia G, Spiering W, et al. 2018 ESC/ESH guidelines for the management of arterial hypertension. Eur Heart J. 2018;39:3021–3104.
[5] Katz-Summercorn AC, Borg CM, Harris PL. Spontaneous renal artery dissection complicated by renal infarction: a case report and review of the literature. Int J Surg Case Rep. 2012;3:257–259.
[6] Miyamotto M, Okabe MC, Neumann PRP, et al. Spontaneous dissection of the renal artery: case report. J Vasc Bras. 2018;17:156–159.
[7] Santhosh GJ, Pillai U, Vaidan PB, et al. Spontaneous renal artery dissection. Missouri Med. 2010;107:124–126.
[8] Tektonidou MG. Antiphospholipid syndrome nephropathy: from pathogenesis to treatment. Front Immunol. 2018;31:1181.
[9] Miyaks S, Lockshin MD, Atsumi T, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid antibodies syndrome (APS). J Thromb Haemost. 2006;4:295–306.
[10] Sangle SR, D'Cruz DP, Jan W, et al. Renal artery stenosis in the antiphospholipid (Hughes) syndrome and hypertension. Ann Rheum Dis. 1990;49:184–187.
[11] Del Porto F, Proietta M, Tritapepe L, et al. Inflammation and immune response in acute aortic dissection. Ann Med. 2010;42:622–629.
[12] Del Porto F, Cifani N, Proietta M, et al. MMP-12 and TIMP behaviour in symptomatic and asymptomatic critical carotid artery stenosis. J Stroke Cerebrovasc Dis. 2017;26:334–338.
[13] Del Porto F, Cifani N, Proietta M, et al. Regulatory T CD4 + CD25+ lymphocytes increase in symptomatic carotid artery stenosis. Ann Med. 2017;49:283–290.
[14] Aliberti G, Proietta M, Pulignano I, et al. Association between fibrinogen plasma levels and platelet counts in an outpatient population and in patients with coronary heart disease. Blood Coagul Fibrinolysis. 2010;21:216–220.
[15] Tandon G, Sukhija R. Isolated spontaneous renal artery dissection: a case report and review. Int J Angiol. 2012;21:99–102.