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Educational Case Report

Case Report: Segmental Arterial Mediolysis, a Rare Cause of Hypertension

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Abstract

Rationale: The differential diagnosis for hypertension with elevated plasma renin is broad. This case illustrates one of the rarer, and therefore underrecognized, causes of high renin hypertension.

Presenting concerns of the patient: A 41-year-old man with a medical history significant for multiple ischemic strokes and dyslipidemia presented for assessment of decreased renal function and resistant hypertension. His initial workup for secondary causes of hypertension was remarkable for an elevated plasma renin and normal aldosterone. Further investigation with computed tomography (CT) angiography was performed, which demonstrated multiple bilateral renal aneurysms and infarcts.

Diagnoses: After ruling out other potential causes of bilateral renal aneurysms and infarcts, a diagnosis of segmental arterial mediolysis (SAM) was made.

Interventions: Optimization of antihypertensive regimen, counseling regarding regular home blood pressure monitoring, and smoking cessation.

Outcomes: The patient achieved excellent blood pressure control, stable renal function, and had no further strokes or other vascular events.

Teaching points: Our case demonstrates the importance of considering SAM in the diagnosis of hypertension with elevated plasma renin and as a vasculitis mimic. It also highlights the importance of considering renal vascular imaging in the workup of resistant hypertension.

Abrégé

Justification: Le diagnostic différentiel de l'hypertension avec élévation des concentrations plasmatiques de rénine est vaste. Le cas présenté illustre une des causes les plus rares et les moins connues de cette forme d'hypertension.

Présentation du cas: Un patient de 41 ans dont les antécédents médicaux montraient des dyslipidémies et des accidents ischémiques cérébraux multiples s'est présenté pour une réduction de la fonction rénale et une hypertension résistante. Le premier bilan des causes secondaires de l'hypertension se distinguait par une concentration plasmatique élevée de rénine et une aldostérone normale. L'angiographie par tomodensitométrie a révélé de multiples anévrismes et infarctus rénaux bilatéraux.

Diagnostic: Après avoir écarté les autres causes potentielles d'anévrismes et d'infarctus rénaux bilatéraux, un diagnostic de médiolyse artérielle segmentaire a été posé.

Interventions: Optimisation du traitement antihypertenseur, encadrement quant à la surveillance régulière de la pression artérielle à domicile et abandon du tabac.

Résultats: Le patient a réussi à contrôler sa pression artérielle, sa fonction rénale s'est stabilisée et aucun autre événement vasculaire n'est survenu.

Leçons tirées: Ce cas souligne l'importance d'envisager la médiolyse artérielle segmentaire comme affection analogue de la vascularite, et d'en tenir compte dans le diagnostic de l'hypertension avec élévation de la concentration plasmatique de rénine. Ce cas insiste également sur l'importance de considérer l'imagerie vasculaire rénale dans l'étude de l'hypertension résistante.

Keywords

segmental arterial mediolysis, secondary hypertension, renovascular hypertension, renin, renal infarcts

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Introduction

A diagnosis of secondary hypertension is suspected in patients with early, severe, or sudden onset of hypertension, resistant hypertension, absence of predisposing comorbidites, or evidence of end-organ damage.[1-3] In younger patients with secondary hypertension, one of the most common causes is renal parenchymal or renovascular disease.[4] In this case report, we describe a patient with segmental arterial mediolysis (SAM), a rare renovascular cause of secondary hypertension.

Presenting Concerns

A 41-year-old Caucasian man with a medical history significant for hypertension, dyslipidemia, and multiple cerebrovascular events was referred for evaluation of decreased renal function (estimated glomerular filtration rate [eGFR] 58 mL/min/1.73 m^2 via the CKD-EPI equation). His first presentation to medical attention was 7 years previously with ataxia and binocular diplopia. He presented 2 months later, and this time was assessed by the Neurology service. He was found to have an intranuclear ophthalmoplegia with imaging evidence of a small right midbrain stroke. During this assessment, he was found to be hypertensive with a blood pressure (BP) of 164/92 mm Hg. He presented again on 3 separate occasions (7, 4, and 2 years prior) with vertigo, ataxia, blurred vision, vision loss, and other neurological symptoms, which were thought to represent additional cerebrovascular events (see timeline, Figure 1). His history was otherwise unremarkable, and he felt systemically well with no constitutional symptoms, oral ulcers, rashes, arthralgias, or previous episodes of hematuria, severe abdominal pain, or back pain. Medications at the time were amlodipine 10 mg po daily, metoprolol 50 mg po qam and 25 mg po qhs, perindopril 8 mg po daily, chlorthalidone 25 mg po daily, rosuvastatin 40 mg po daily, and clopidogrel 75 mg po daily, with no known drug allergies.

Clinical Findings

The patient had a 20 pack-year smoking history and occasional use of marijuana. Family history was positive only for a paternal grandfather who had chronic kidney disease (CKD) of unknown etiology requiring dialysis, and who suffered 2 strokes in the fifth decade of his life.

Physical examination revealed a well-appearing man who appeared his stated age with a normal body habitus (body mass index [BMI] 22). His BP via BP Tru was 131/91 mm Hg, with no significant BP difference between arms, and a heart rate of 59 beats/min. His neurological, cardiopulmonary, and abdominal exams were unremarkable. Specifically, there were bilaterally symmetric radial pulses, no abdominal or costovertebral angle tenderness, no renal bruits, and no rashes, joint effusions, or erythema.

Timeline

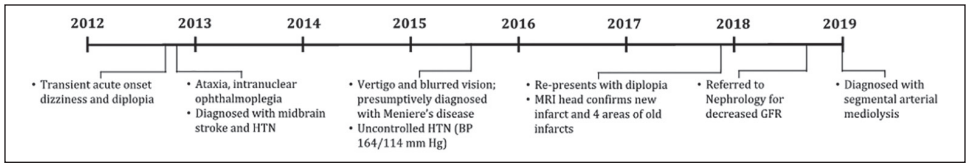

Figure 1. Timeline of patient's symptoms, diagnoses, and investigations.
Note. BP = blood pressure; HTN = hypertension; GFR = glomerular filtration rate.

Diagnostic Focus and Assessment

His initial bloodwork demonstrated sodium 141 mM, potassium 4.2 mM, bicarbonate 30 mM, urea 8.1 mM, and creatinine 152 μM with eGFR 48.3 mL/min/1.73 m^2 via CKD-EPI. His urinalysis was negative for blood and protein, with a urine albumin-creatinine ratio (ACR) 0.9 mg/mmol and protein-creatinine ratio (PCR) 18 mg/mmol. Previous investigations for the etiology of his strokes, including Holter monitor and transthoracic echocardiogram with bubble study did not reveal abnormalities. Serial computed tomography (CT)/CT angiography (CTA) and magnetic resonance imaging (MRIs) of head and neck over a 6-year time span demonstrated multiple infarcts at the genu and anterior aspect of the corpus callosum, medial left basal ganglia, internal capsule, and the area

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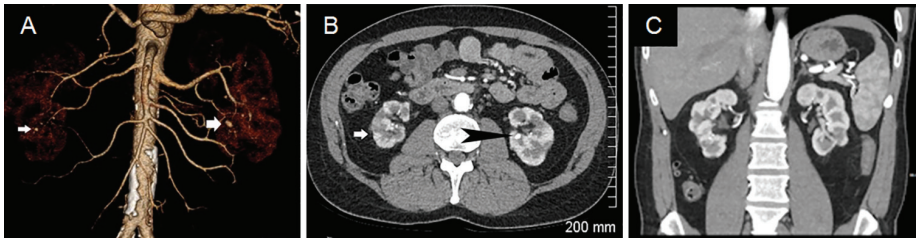

Figure 2. Computed tomography angiogram of the abdomen and pelvis showing (A) renal artery branch microaneurysms (white arrows); (B) axial image showing renal infarct on the right (white arrow) and microaneurysm on the left kidney (black arrow); (C) coronal image showing bilateral small kidneys with lobulation in the renal cortices consistent with multiple renal infarcts.

posterior to the third ventricle and medial to the left thalamus. However, imaging did not reveal evidence of arterial stenosis, aneurysm, dissection, arteriovenous malformations (AVMs), or other vascular abnormalities.

Workup for secondary causes of hypertension, including plasma thyroid stimulating hormone (TSH), and 24-hour urine levels of cortisol, metanephrines, and normetanephrines were unremarkable. The plasma renin was elevated (43.5 ng/L; ref 2.6-26.7 ng/L), and plasma aldosterone was high-normal (968 pmol/L; ref 61-978 pmol/L). A 24-hour ambulatory BP monitoring test showed mild diastolic hypertension, with a mean awake BP of 128/87 mm Hg, and demonstrated the normal pattern of nocturnal dip (asleep BP 112/76 mm Hg).

Because of hyperreninemia, abdominal CTA was performed to assess the renal vasculature, which notably demonstrated bilateral renal artery microaneurysms, 4 to 5 on the left and 1 on the right, in addition to 4 to 5 infarcts in each kidney and 1 microaneurysm in the left hepatic artery (Figure 2).

Further investigations to determine the etiology of his renal artery aneurysms and infarcts were conducted. Infectious serology tests, including HIV, Hepatitis B, and Hepatitis C, were negative, and there was no evidence of past or recent endocarditis. The anti-nuclear antibody (ANA) was strongly positive 7 years previously (1:2560), but on repeat at that time was 1:320 with a negative anti-double stranded (ds) DNA, and was considered of uncertain clinical significance. His C-reactive protein (CRP) was mildly elevated at 27.6 mg/L (ref <10 mg/L). No erythrocyte sedimentation rate (ESR) was performed at the time; however, 7 years earlier, his ESR was 14 mm/h (ref 0-6 mm/h) with a CRP of 34.5 mg/L. The remainder of his autoimmune and coagulopathy workup was negative, including extractable nuclear antibody (ENA), antineutrophil cytoplasmic antibodies (ANCA), rheumatoid factor (RF), complements 3 and 4, prothrombin time/international normalized ratio, partial thromboplastin time, thrombin time, β2-microglobulin, lupus anticoagulant, anti-cardiolipin antibody, protein C, and activated protein C.

The patient was referred to the Rheumatology service for further assessment, and the lack of systemic symptoms and otherwise negative rheumatological workup was felt to be inconsistent with a diagnosis of vasculitis.

Based on the location and appearance of the renal aneurysms, a diagnosis of SAM was made. This accounts for his hyperreninemic state, hypertension, and mild CKD. The etiology of his strokes was unclear, however, as there were no obvious structural intracranial vascular changes on CT and MRI head.

Therapeutic Focus and Assessment

The patient's antihypertensive regimen was reviewed and modified slightly as he developed symptoms of orthostatic hypotension. He remained consistently on angiotensin-converting enzyme inhibitors throughout his treatment regimen. He was counseled regarding biweekly home BP monitoring, dietary sodium restriction, and smoking cessation.

Follow-up and Outcomes

In the year since initial presentation, his BP has remained consistently below office target of <140/90 mm Hg, renal function has remained stable, and he has not sustained further cerebrovascular events. The patient has been adherent to medication therapy, as per interviews at visits and pharmacy records of prescription renewals, and he has reported no adverse effects.

Discussion

The differential diagnosis for renal artery aneurysms associated with infarcts includes atherosclerosis, fibromuscular dysplasia, and phakomatoses, as well as infectious, autoimmune, and connective tissue disorders such as Marfan's and Ehlers-Danlos syndromes.[5,6] Although our patient did have several risk factors for atherosclerosis such as dyslipidemia, hypertension, and smoking, his vascular imaging did not demonstrate significant disease burden. Similarly, in the absence of visible vascular beading, a diagnosis of fibromuscular dysplasia (FMD) was not favored. The lack of clinical infectious features and negative infectious serologies also made infectious vasculitis and mycotic aneurysms less likely as the cause of his aneurysms. Furthermore, the patient did

not have the classic neurological, ocular, and skin findings compatible with a diagnosis of neurocutaneous or connective tissue syndromes. Although the initial appearance of his CT angiogram was suggestive of polyarteritis nodosa or other medium-vessel vasculitis, the patient had no clinical features of vasculitis on history or physical examination, and hepatitis B screening was negative. In the absence of a clinical correlation and largely negative rheumatological workup, his positive ANA is likely of no clinical significance.

SAM is a noninflammatory, nonatherosclerotic vascular disease with unclear etiology and pathogenesis, although it is postulated that vasospasm and endothelin-1 play a role in its development.[7] SAM affects the medial layer of arteries, causing lysis and disruption of the vessel wall, leading to subsequent aneurysm, dissection, hemorrhage, and ischemia.[8,9] Commonly affected vascular territories are the celiac, mesenteric, and renal arteries, although central nervous system presentations have also been reported.[10,11] Epidemiological data indicate that there is a slight male preponderance, with presentation typically between the fifth to sixth decades of life.[10] However, as patients may sustain silent infarcts or have asymptomatic disease progression, SAM may in fact have an earlier age of onset. Presentations of SAM vary depending on the affected vascular territories, as well as the extent of involvement. Accordingly, SAM can present as abdominal, flank or chest pain, hematuria, or stroke.[10,12] The radiologic appearance of SAM can be virtually indistinguishable from that of a medium-vessel vasculitis. Common appearance on CT angiogram includes arterial dissection, aneurysm, beading, and occlusion.[10,12] Although the gold standard for diagnosis is histologic confirmation, in many cases (including this patient), biopsy is relatively contraindicated due to the associated high risk of bleeding. Cases confirmed with histological evidence often involve biopsies during surgical procedures or at autopsy. In the absence of histologic evidence, a clinical diagnosis of SAM can be made based on presentation, angiographic pattern of infarcts and aneurysms, as well as the exclusion of other potential diagnoses such as vasculitides, connective tissue disorders, or atherosclerosis.[12]

The natural history of SAM is unclear. Based on longitudinal studies with serial imaging of patients with SAM, there appear to be two potential disease courses.[10,12,13] Most commonly, imaging studies have shown remission and few clinical symptoms. However, in a small proportion of cases, the disease becomes fulminant and causes significant morbidity and mortality. Given the low incidence of this disease and limited clinical data, the cause for the wide range of outcomes is unclear. It is also uncertain whether SAM and FMD are variations of the same disease process or represent distinct entities. Demographically, SAM and FMD appear to affect different populations, with FMD affecting younger, female patients while SAM is more frequently diagnosed in middle-aged, male patients.[10,12] In addition, the presentation of FMD is more indolent and often discovered in the workup for secondary causes of hypertension, while SAM tends to present more acutely as a result of infarct or aneurysm rupture. The incidence of disease at separate vascular sites is also different, with FMD having a preponderance for renal arteries. In contrast, SAM tends to affect other intraabdominal vasculature as well, most commonly the splenic, celiac, hepatic, as well as renal arteries.[13,14] Thus, these conditions may represent disparate pathologic processes. Nevertheless, histologic evidence demonstrates that there are many similarities between SAM and FMD. It has been postulated that SAM could represent a rarer variant of FMD, or the reparative fibrotic phase of SAM may mimic the appearance of FMD.[15] Accordingly, the natural history of this disease and its possible pathophysiologic or temporal relationship to FMD continues to be elucidated.

There are no guidelines regarding optimal treatment and follow-up for patients with SAM. Often, treatment is on a case-by-case basis and depends on features of the initial presentation and presence of dissection, aneurysm, or ischemia.[16] Fulminant cases of aneurysm rupture often require surgical or endovascular intervention, whereas infarcts may be treated with antiplatelets or anticoagulants, and hypertension is managed as per guidelines with standard antihypertensive agents.

A limitation of our case study is the absence of detailed information regarding the patient's BP control in the 7 years (and earlier) preceding his presentation for nephrology consultation. Whether uncontrolled hypertension alone induced his stroke events remains unclear. In this regard, although prior CT angiography showed no evidence of cerebral aneurysms, we acknowledge the possibility that SAM may have affected the cerebral circulation and contributed to his adverse neurologic events. In the 1.5 years since maintaining optimal BP control, he has not suffered further complications from SAM.

In summary, our case highlights the importance of working up secondary hypertension in younger patients, especially those who have already sustained serious vascular events. The case also illustrates the importance of renovascular imaging in the workup for hypertension associated with hyperreninemia. Although rare, in patients with suggestive clinical and imaging findings and no alternative diagnoses, SAM should be considered in the differential diagnosis of renal artery aneurysms and infarcts.

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Ethics Approval and Consent to Participate

Institutional ethics approval was not sought for this case report. The patient provided informed written consent for participation in the report.

Consent for Publication

Informed written consent was provided by the patient for publication of this anonymized case report, including anonymized diagnostic images.

Availability of Data and Materials

Anonymized data and materials regarding this case report are available by contacting the corresponding author (KDB).

Declaration of Conflicting Interests

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