Segmental arterial mediolysis: a challenging diagnosis in internal medicine

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ABSTRACT

Segmental arterial mediolysis (SAM) is an uncommon, nonatherosclerotic, noninflammatory, large- to medium-sized arteriopathy first described in 1976, affecting splanchnic branches of the aorta. The clinical presentation ranges from asymptomatic to severe, life-threatening intra-abdominal hemorrhage and shock. A healthy 53-year-old woman with abdominal pain was referred to our facility for further management of superior mesenteric artery dissection diagnosed in the emergency room. A computed tomography scan revealed a dissection in both renal arteries, leading to ischemic degeneration in the left apical pole of the kidney. Additionally, three aneurysmatic dilatations, ectasia of intrahepatic vessels, and irregularities in the wall of the iliac arteries were identified. No other pathological lesions were observed. Based on imaging and the absence of inflammatory and autoimmune markers, a diagnosis of SAM was made. Since an endovascular intervention was excluded and both anticoagulation and antiplatelet therapy were initiated, the patient has undergone close clinical and radiological follow-up.

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Introduction

Segmental arterial mediolysis (SAM) is a rare, nonatherosclerotic, noninflammatory, large- to medium-sized arteriopathy affecting splanchnic branches of the aorta, which was first described in 1976. The clinical presentation varies from asymptomatic to severe, life-threatening intra-abdominal hemorrhage and shock.

Case Report

A 53-year-old woman was admitted to the emergency room for abdominal pain that arose abruptly in the epigastric-periumbilical site, without back irradiation, in the absence of vomit, gastrointestinal, or urogenital bleeding.

She had tachycardia (heart rate 100 bpm), hypertension (blood pressure 150/100 mmHg), and normal oxygen saturation without any support (oxygen saturation 97%). The objective assessment of the thorax was negative; it showed a rhythmic heart without pathological tones but abdominal pain at deep palpation in the epigastric zone.

The medical history revealed little data: she worked as a kindergarten teacher, did not smoke, and consumed alcohol moderately. Both her parents passed away from gastric cancer, prompting her to undergo multiple gastroscopies over the years, which led to the discovery of a hiatal herniation treated with proton pump inhibitors (PPI). She is married with one child, delivered naturally, and currently uses oral contraception. She recently found a lipoma on her neck and was waiting for surgical removal.

Initial blood tests revealed normal hemochrome and renal and hepatic function, and mild potassium deficit. Moreover, an abdominal radiography, which excluded an intestinal occlusion or perforation, was performed; the echography did not show anything pathological. Furthermore, the diagnostic investigation was continued with a computed tomography (CT) scan, which showed multiple hypodense

areas of renal parenchyma, more numerous on the left, correlated with hypoperfusion, and an eccentric endoluminal thrombosis with patent residual lumen in the segment of origin of the superior mesenteric artery, with immediate dissection downstream.

The patient went through the evaluation by a general and a vascular surgeon, who agreed on a wait-and-see approach and suggested a continuous endovenous therapy with unfractionated heparin based on the activated partial thromboplastin time levels.

Afterward, she was transferred to the internal medicine ward, where she was hemodynamically stable and asymptomatic, as showed by a continuous monitoring of her vital parameters. First, we decided to implement the anti-hypertensive therapy to better control blood pressure, keeping on levels around 120-80 mmHg. Then, to control the multiple thrombosis, we modified the antithrombotic therapy by switching from unfractionated heparin to low-molecular-weight heparin and also added aspirin to manage arterial dissection. At the same time, gastro-protection was started with PPI. Moreover, the diagnostic investigation was expanded to include the thorax and head, with particular attention to epiaortic and intracranial vessels and coronary arteries.

The results of the CT scans (Figure 1) confirmed the dissection of the superior mesenteric artery, revealing the appearance of multiple flaps with a branched and filamentous aspect of the lumen and the disappearance of thrombotic apposition. Additionally, they showed a focal dissection of the left renal artery and its main branch for the upper pole and a further dissection of the upper branch of the right renal artery, determining tissue ischemia in both kidneys.

Furthermore, aneurysmal dilations of the intrahepatic branches of the arteries were observed without involvement of the hepatic parenchyma. At the level of cerebral and cardiac vessels, no pathological anomalies were detected. In addition, it was performed an echo-color Doppler of epiaortic vessels that confirmed the CT scan results and excluded the presence of atherosclerosis. Moreover, a transthoracic echocardiographic exam was performed to exclude any other cause of thromboembolism without showing any sign of vegetation or aortic atherosclerosis.

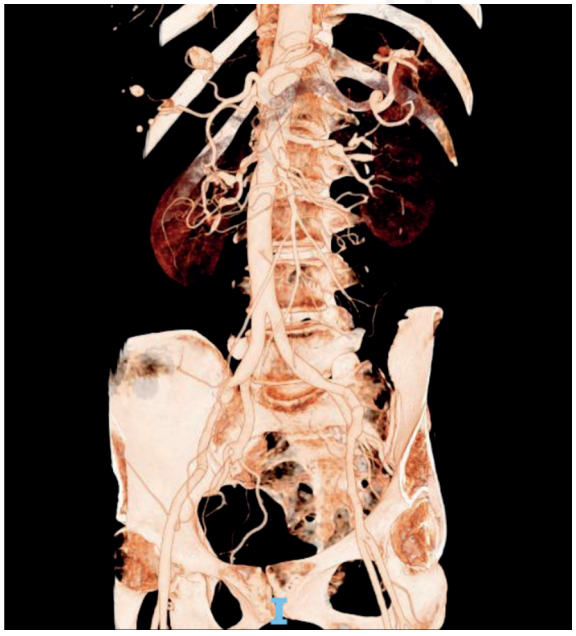

Figure 1. Results of the computed tomography scan.

The patient was then assessed by a vascular surgeon, who found no indication of intervention and recommended continuing conservative therapy.

The case was reported to interventional radiology, who decided it was too risky to proceed with stenting of the superior mesenteric artery or the renal arteries because of the morphology and the location of the lesions, which increased the possibility of a wall rupture.

At that point, considering the impossibility of an interventional approach, which could have benefited from a short-life anticoagulation agent, we decided to modify the therapy, starting the heparin-to-warfarin transition, till the achievement of a correct international normalized ratio range (between 2 and 3), to prevent thrombotic appositions.

At the same time, possible causes of vessel wall weakness were investigated, excluding, through blood tests (Table 1), autoimmune and inflammatory pathologies, or coagulopathy disorders. Autoimmune disease antibodies (antinuclear antibodies and extractable nuclear antigen antibodies) levels were normal, and the thrombophilia blood and genetic tests were negative.

The only abnormal value was a slight hyper-homocysteinemia, correlated with vitamin B12 and folate deficiency, thereby supplemented. The cause of malabsorption of cyanocobalamin, such as celiac disease or other intestinal malabsorption syndromes, was also researched without any results. Moreover, low-density lipoprotein (LDL) cholesterol levels were high compared to a high class of cardiovascular risk, so we started statin therapy, achieving a significant reduction at follow-up examination.

During hospitalization, multiple ultrasounds were performed to monitor the extension of dissections and hepatic aneurysms, observing an improvement in renal perfusion while undergoing therapy.

Given the radiological reports and the absence of significant markers for rheumatological or inflammatory diseases, having achieved good blood pressure control and the correct dosage of anticoagulant with stable hemodynamics, the patient was discharged with a diagnosis of SAM, with instructions to continue the established therapy, characterized by antihypertensive, statin, antiaggregant other than anticoagulant, and PPI, undergoing a close follow-up. At periodic check-ups, the patient has reported a continuous state of well-being, gradually returning to normal daily life, and radiology findings have been substantially stable.

Discussion

SAM is a rare disease characterized by nonatherosclerotic, noninflammatory arterial medial degeneration. Patients may exhibit manifestations such as aneurysm, dissection, stenosis, or visceral and renal artery bleeding.

A retrospective study based on a sample of 117 patients (79 men and 38 women) has shown that the disease arose abruptly with abdominal pain in most people, whereas it is asymptomatic in almost 10% of cases.[1] Furthermore, common manifestations included dissection and aneurysm,

mainly involving the celiac axis, followed by the renal arteries and the superior mesenteric artery, while the involvement of the inferior mesenteric artery is less frequent.

Our case fits the classical manifestation of SAM, considering that the CT scan and the echography study have shown a dissection of the mesenteric artery, extended to hepatic branches, and left and right renal arteries with an ischemic area of both kidneys. The mesenteric dissection was complicated by thrombotic apposition, a less common finding according to the literature.[2]

Usually, the first symptom is acute abdominal pain, like in the reported case, whilst more rarely, SAM may cause hematuria due to focal renal infarcts, ischemic bowel disease, or hemobilia due to erosion of an aneurysm into the biliary tree.[3]

In other, and fortunately rare, cases, the disease could arise with a massive intra-abdominal hemorrhage and consequent hypovolemic shock, as an implication of aneurismatic or vessels' wall rupture.[4] Therefore, a tempestive diagnosis is fundamental to choosing the best treatment and avoiding life-threatening consequences.

A key distinguishing feature is the presence of dissections, the principal morphologic expression of SAM.[4] Nevertheless, artery dissection is a common finding in other noninflammatory conditions, like fibromuscular dysplasia (FMD), or rheumatologic diseases, such as polyarteritis nodosa. From the beginning, it is important to exclude or confirm the presence of a rheumatologic disease to initiate the most appropriate treatment.

A first difficult differential diagnosis must be done between SAM and FMD (Table 2). In fact, as SAM, FMD is a noninflammatory and nonatherosclerotic arterial disease that could involve gastroenterological regions with equally severe complications.[5] FMD generally involves medium- or small-sized arteries, especially renal branches and extracranial carotid and vertebral arteries, usually spared by SAM. Moreover, the involvement of more than one abdominal artery is more frequent in SAM than in FMD.[6] FMD affects young to middle-aged women, is rarely painful, is usually asymptomatic or associated with symptoms of occlusive disease, and rarely ruptures.[4]

In our case, although the patient was a woman in her fifties, we leaned towards SAM for the involvement of multiple abdominal arteries, for aneurismatic and thrombotic manifestations, and for the sudden onset of abdominal pain.

As regards rheumatologic disease, no parameters were

Table 1. Main laboratory results.

Anti-nuclear antibodies	<1:80	<1:80
Extractable nuclear antigen antibodies	<0.5	<10
Anti-gliadin IgA	0.8	<10
Anti-gliadin IgG	<0.4	<10
Anti-transglutaminase IgA	0.3	
Anti-transglutaminase IgG	<0.7 U/mL	
Anti β-2 glycoprotein IgM	<0.7 U/mL	
Anti β-2 glycoprotein IgG	<2.9 U/mL	
Anti-cardiolipin IgM	1.1 U/mL	
Anti-cardiolipin IgG	2.0 U/mL	
Antithrombin III	73%	80-100
Free protein S	84.5%	55-124
Homocysteine	30.50 umol/L	3.20-10.70
Iron	56 ug/dL	33-193
Ferritin	296.0 ng/mL	15.0-150.0
Transferrin	166 mg/dL	200-360
Transferrin saturation	27%	
reticulocytes	72.00	
Folic acid	3.2 ng/mL	3.1-7.5
Vitamin B12	124.0 pg/mL	191.0-663.0
TOT-c	204 mg/dL	
LDL-c	135 mg/dL	
HDL-c	55 mg/dL	
triglycerides	101 mg/dL	
Leiden V factor	Absence of mutation c.1691G>A	
Factor II mutation or prothrombin G20210A	Absence of mutation	
MTHFR mutation	Absence of mutation	
Glycoprotein IIb/IIIa inhibitors	Genotype ND	
Gene PA11-promotor polymorphism 4G/5G	Absence of mutation	

Ig, immunoglobulin; TOT-c, total-cholesterol; LDL-c, low-density lipoprotein-cholesterol; HDL-c, high-density lipoprotein-cholesterol.

Table 2. Main differences between fibromuscular dysplasia and systemic arterial mediolysis.

	Fibromuscular dysplasia	Systemic arterial mediolysis
Mean age of diagnosis	Middle age	Late middle age and elderly
Districts involved	Medium- or small-sized artery Sigle artery Renal, carotid, vertebral coronary and splanchnic arteries	Large- or medium-size vessels More arteries Splanchnic arteries especially medium-size branches of the superior mesenteric artery
Histological findings	Intimal fibroplasia, medial dysplasia and adventitial fibroplasia	Partial or total vacuolization and lysis of the outer arterial media
Imaging findings	Stenosis	Dissection
Onset symptoms	Rarely painful and not associated with hemorrhage	Abdominal pain and hemorrhage

found to sustain such a diagnosis; in particular, the French Vasculitis Study Group diagnostic criteria for polyarteritis nodosa were not fulfilled.[7]

Finally, relying on semeiotic observation, CT scans, and cardiovascular imaging, we could substantially exclude hereditary connective tissue disorders, such as Marfan syndrome, not respecting the diagnostic requirements.[8]

A certain diagnosis of SAM could be made only by a histological analysis of wall vessels' tissue. SAM affects especially the outer layer of the media, with a typical vacuolar degeneration of smooth muscle cells, determining a medial disruption, intramural hemorrhage, and peri-adventitial deposition. Histologically, diagnosis relies on the presence of fibrin and collagen deposits, destruction of smooth muscle cytoplasm in the acute phase, and vessel remodeling in the late phase, with a notable absence of inflammatory cells. In this case, the biopsy was not performed because, as reported in the literature, histological diagnosis is typically only feasible in patients requiring surgical intervention or *post-mortem* examinations for vessels damaged by SAM.[5]

Radiographic criteria include the detection of one or more of six distinct angiographic presentations: arterial dilation, single aneurysm, multiple aneurysms (string of beads), dissecting hematomas, arterial stenosis, and arterial occlusion.[9]

As regards therapy for SAM, there is no standard of treatment in the literature. For patients exhibiting clinical, laboratory, and radiological indications of acute or chronic abdominal bleeding along with radiological evidence suggestive of SAM, minimally invasive endovascular treatment emerges as a safe and secure procedure, and it appears to be the preferred treatment option when feasible.[10]

Given the potentially life-threatening consequences of abdominal bleeding in these cases, prompt diagnosis and endovascular therapy are imperative for addressing visceral vascular alterations associated with SAM.[11] Additionally, it may serve as a temporary solution during the acute phase, offering a bridge until definitive surgical intervention can be pursued at a later stage.[12]

Recently, the development of endovascular interventions has permitted a halving of the mortality rate in the acute phase, which is around 25% nowadays, due to the early management of hemorrhagic emergencies.[2]

The conservative therapy could be practiced with either antiplatelet therapy or anticoagulation if there was evidence of end-organ ischemia or infarction on imaging. In addition, the use of antiplatelets and anticoagulant drugs reduces the risk of thrombus formation in small peripheral arteries due to the turbulent flow of blood through the true and false lumen and aneurismatic formations.

In this case, due to the thromboembolic risk and kidney infarction, we decided to initiate anticoagulation therapy with a vitamin K antagonist, considering the absence of consolidated evidence and guidelines for such a rare disease. Furthermore, vascular surgery guidelines suggest that patients with a thrombotic arterial occlusion should receive the best medical therapy against atherosclerosis, including smoking cessation, statins, and antiplatelet agents.[13]

Finally, considering that the patient was characterized by clinical stability, a low bleeding risk *versus* a higher thromboembolic risk, both anticoagulant and antiplatelet therapy were continued with a close revaluation in the follow-up visits. The therapy will be adjusted based on the follow-up CT images, likely reaching at least 6 months of anticoagulant therapy and continuing the antiplatelet therapy. Antihypertensive agents, such as angiotensin-converting enzyme inhibitors, calcium antagonists, and low dosages of β-blockers, were used for blood pressure control.[9]

A lowering LDL-cholesterol therapy is mandatory to reduce the annual rate of major vascular events, as suggested by more recent guideline.[13] After excluding the inflammatory nature of the condition, the use of corticosteroids is not recommended, considering the risk/benefit ratio.[14] After overcoming the acute phase, the majority of patients achieve stability.[15] In fact, the natural course of the unruptured aneurysm in over two-thirds of patients with SAM is characterized by the stabilization of the lesion during follow-up.[15] Furthermore, the occurrence of regression has been documented in several cases, suggesting a potentially benign prognosis of the disease.

Conclusions

SAM is a rare and complex disease that causes nonatherosclerotic and noninflammatory arterial medial degeneration. It could manifest with aneurysms, dissections, stenosis, and bleeding of several arteries, prevalently involving the celiac artery, superior mesenteric artery, and renal arteries. Abrupt abdominal pain is the most frequent presenting symptom, whereas a small percentage of patients may be asymptomatic. Dissections and aneurysms are common complications, of whom rupture could lead to a massive and life-threatening hemorrhage. Therefore, a tempestive detection and diagnosis of this condition is fundamental to avoid

critical problems and overcome the acute critical phase of the disease.

Imaging findings of SAM overlap with various vasculitis, making differential diagnosis difficult but crucial. The absence of continuous aortic dissection, atherosclerosis, and hereditary connective tissue disorder characteristics are important diagnostic criteria. The certainty of the diagnosis could be achieved only with histological analysis, revealing vacuolar degeneration of smooth muscle cells and medial disruption without inflammatory cells.

There is no standardized treatment for SAM. Minimally invasive endovascular techniques are emerging as the preferred treatment for acute or chronic abdominal bleeding due to SAM, given their safety and efficacy. These techniques may serve as temporary measures before definitive surgical interventions.

Conservative therapy, including antiplatelet and/or anticoagulation therapy other than aortosclerosis agents, may be used, especially in cases with end-organ ischemia or infarction. However, the benefits of these treatments are not fully demonstrated.

Sharing case reports about SAM is fundamental to increasing critical attention about this disease characterized by significant mortality in the acute phase and a challenging differential diagnosis with other more frequent vascular diseases in the medical area. Finally, further research and clinical studies could allow us to establish more definitive treatment protocols and improve patient outcomes.

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