Segmental arterial mediolysis: a vasculitis mimicker. A single-centre experience

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ABSTRACT

Objective. *Segmental arterial mediolysis (SAM) is a rare vasculopathy of unknown aetiology. It is non-atherosclerotic, non-inflammatory, non-hereditary, non-infectious, large to medium-sized arteriopathy. SAM is a condition which in some circumstances behaves as a vasculitis mimicker and should be recognised in order to provide appropriate treatment and avoid unnecessary immune-suppressive therapy.*

Methods. *We report a single-centre experience of 6 consecutive SAM cases (3 males and 3 females). A literature search of cases reported with SAM was performed and data summarised.*

Results. *Abdominal or flank pain was the presenting symptom in 5 of the 6 patients. CT angiography (CTA) was the method of diagnosis in all 6 patients. 3 patients underwent therapeutic angiography; 2 with angiographic embolisation because of bleeding, and one patient needed a stent insertion because of left renal infarction. 2 patients underwent FDG-PET to rule out vasculitis. Serological tests were negative in all case, but C-reactive protein was elevated in 4 of them. 2 patients were treated with angiographic embolisation due to bleeding, 2 treated with anti-platelet therapy, one with stent insertion, and one with antihypertensive treatment.*

A medical literature review of 160 additional cases shows that abdominal or flank pain was the chief complaint in the vast majority of the cases. Renal and abdominal medium-sized arteries were the most commonly involved. CTA was the preferred method of diagnosis.

Conclusion. *SAM should be suspected in cases presenting with abdominal or flank pain. Angiographic features should be carefully studied by experienced radiologists to rule out vasculitis.*

Introduction

Segmental arterial mediolysis (SAM) is a rare vasculopathy of unknown aetiology. It is a non-atherosclerotic, non-inflammatory, non-herediatary, non-infectious, large to medium-sized arteriopathy. First described as "segmental mediolytic arteritis" by Slavin and Gonzales-Vitale in 1976 (1), this disease has been renamed "segmental arterial mediolysis" due to absence of inflammatory changes (2).

Slavin *et al.* reported 3 autopsy cases of ruptured aneurysms resulting in massive haemorrhage and death (1). Some authors consider the report of Gruenwald regarding arterial medial necrosis in the coronary arteries of newborns in 1949 as the first description of this entity (3).

The main histological characteristic of this disorder is the disruption of the arterial medial layer, with resultant susceptibility to vessel dissection, haemorrhage and ischaemia (4). The affected arteries manifest with aneurysms and/or dissections, sometimes associated with serious intra-abdominal or intracerebral haemorrhages (1, 5).

The pathophysiology of this disorder is still undiscovered. Repeated vasoconstrictive stimuli is considered to be a possible inciting event leading to arterial injury as it causes degeneration of smooth muscle cells in the media (6). A histological pattern similar to SAM was induced by an epinephrine analogue in a canine model (7). Some authors propose that SAM is a precursor of fibromuscular dysplasia (FMD), an angiopathy that affects medium-sized arteries predominantly in young women of childbearing age (2). Pathologically, alteration of the media occurs with collagen replacement of smooth muscle cells (8). Stenotic lesions are common in FMD, while aneurysmatic changes and vessel dissections are less frequently seen (9).

Computed tomographic angiography (CTA) provides useful information as it can evaluate vessel wall thickening, dissection, perivascular changes and small

aneurysms. Diagnosis of SAM is based on imaging studies. Although MRI lacks ionising radiation, its detailing and spatial resolution are suboptimal compared with CTA, particularly when small-branch disease is evaluated (10).
We report 6 cases of SAM that were diagnosed at our medical centre, and review the relevant medical literature.

Case 1
A 40-year-old healthy man presented to our emergency room complaining of severe sharp epigastric pain. A similar previous episode was less severe and resolved spontaneously. These episodes were not incited by meals or exertion. His physical examination revealed soft abdomen with no tenderness, the rest of the physical examination was unremarkable. An electrocardiogram (ECG) revealed normal sinus rhythm without ischaemic changes. Complete blood counts, lactate and troponin levels were normal, CRP was elevated, 2mg/dl (normal <0.5). Antinuclear antibodies (ANA), antineutrophil cytoplasmic antibodies (ANCA), complement (C3, C4), rheumatoid factor (RF) and anticardiolipin antibodies were negative. CTA of the abdomen revealed unremarkable coeliac artery origin. A significant focal stenosis 1.5 cm distant to the origin, with post-stenotic aneurismatic dilation measured 1*1.2 cm with fat opacity. Treatment with 100 mg aspirin was initiated. A follow-up CTA 2 weeks later showed expansion in the aneurysm. The patient is under follow-up treated with aspirin with no further progression of his condition.

Case 2
A 46 year-old man with hyperlipidaemia and prediabetes presented with epigastric pain and one episode of vomiting. On physical examination the abdomen was soft and without tenderness, the rest of the physical examination was also unremarkable. Blood counts were normal, CRP was slightly elevated, 1.15mg/dl. ANA, ANCA, complement (C3, C4) and RF were negative.
CTA of abdomen revealed significant wall thickening of the coeliac artery and its branches. Irregularity and sever stenosis of the hepatic and gastro-duodenal arteries. A presumptive diagnosis of SAM was made based on the CT findings. Dual antiplatelet therapy was initiated and the patient is under regular outpatient follow-up, with no further episodes of epigastric pain.

Case 3
A 63-year-old woman with a past medical history of Glucose 6 Phosphate Dehydrogenase (G6PD) deficiency and cholelithiasis presented with abdominal pain accompanied by vomiting and melena. Laboratory tests showed slight anaemia with Hgb 11.3 mg/dl, unconjugated hyperbilirubinaemia (total bilirubin 9.2 mg/dl, direct 1.6 mg/dl), and significant liver function tests abnormalities. A diagnosis of gangrenous cholecystitis was established based on abdominal CT scan and cholecystectomy was performed. A Doppler test of the abdominal vessels showed enhancement of flow within the SMA. CTA showed hepatic and coeliac artery aneurysms, and gastroscopy demonstrated haemobilia. Polyarteritis nodosa (PAN) was suspected and steroid therapy was initiated. The pathology specimen showed severe chronic acute necrotising cholecystitis, but no vasculitis was demonstrated. A diagnosis of SAM was considered, and steroid therapy was discontinued. The patient was lost at follow-up. (Fig. 1-4).

Case 4
A 53-year-old woman presented with abdominal pain, vomiting and syncope. Her physical examination showed diffuse abdominal tenderness, but the rest of the physical examination was unremarkable. Laboratory examination: normal blood counts, lactate 5, CRP 0.2 mg/dl, troponin was normal. ANA, ANCA, complement (C3, C4), and RF were negative. CT scan revealed a peripancreatic haematoma with suspected pseudoaneurysm of the inferior pancreatoduodenal artery. The patient's haemoglobin had dropped from 13.4 mg/dl to 11 mg/dl and angiography showed a pseudoaneurysm arising from the inferior pancreatoduodenal branch and multiple small-vessel aneurysms and stenoses of the pancreatoduodenal branches. A fluorodeoxyglucose (FDG)-positron emission tomography (PET) showed no abnormal uptake. Embolisation was performed with discontinuation of the bleeding. A follow-up CTA performed 3 months later showed 2 small aneurysms without any changes in comparison with the first CTA. A repeated CTA was recommended within one year.

Case 5
A 25-year-old young woman was recently diagnosed with hypertension. A Doppler study performed for further investigation of her hypertension revealed left renal artery stenosis. A CTA showed stenosis of the distal aorta.
Magnetic resonance angiography (MRA) showed left subclavian artery stenosis, left renal artery stenosis, bilateral carotid and vertebral artery stenoses and stenosis of the superior mesenteric artery. Blood counts were normal, CRP 0.37mg/dl; a diagnosis of SAM was considered, no immunosuppressive therapy was initiated.

Case 6
A 48-year-old man with past medical history of coeliac disease was presented with left flank pain and fever. Physical examination showed left costovertebral tenderness, but the rest of the physical examination was unremarkable. Blood counts were normal, CRP was elevated 4.9, but ESR was normal 21mm/h, creatinine 0.94 mg/dl, and unremarkable urine sediment. ANA, ANCA, complement (C3, C4), RF and anticardiolipin antibodies were negative. CT showed renal infarction in the upper pole of the left kidney and irregularity in the lamina of the left renal artery. Angiography revealed segmental stenosis in the left renal artery with 3 aneurysms, the largest was 11 mm. Glucocorticoids and enoxaparin were recommended for a presumed diagnosis of PAN, and further work-up was recommended. The patient declined immunosuppressive therapy. FDG-PET scan showed no sign of vasculitis. A diagnosis of SAM was considered, and therapeutic angiography with stent insertion to the left renal artery was performed. Dual antiplatelet therapy with clopidogrel 150 mg and aspirin 100 mg a day were ini-

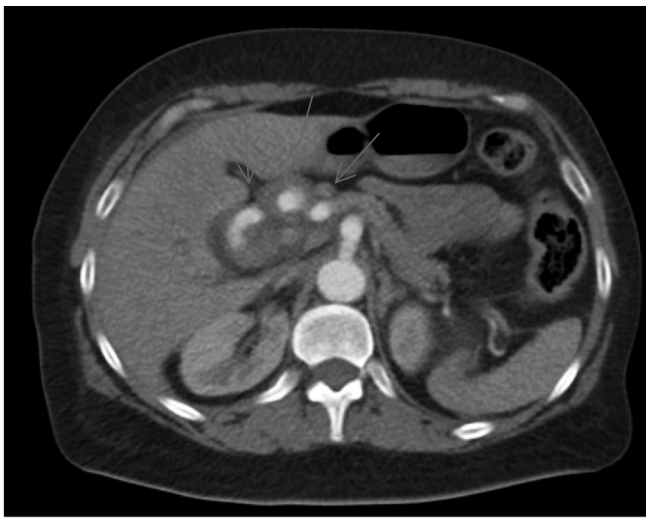

Fig. 1. Axial contrast enhanced CT scan of the abdomen demonstrating aneurysm formation within the common hepatic artery (arrows).

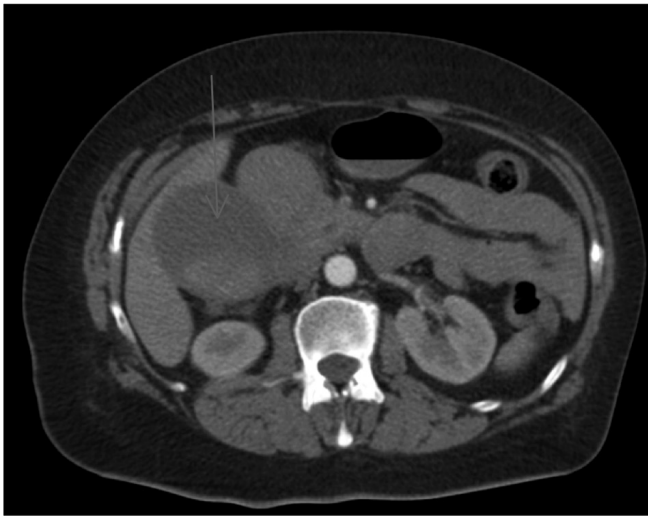

Fig. 2. Axial contrast enhanced CT scan of the abdomen demonstrating high attenuation fluid (arrow) within the gallbladder lumen suggestive of acute haemorrhage.

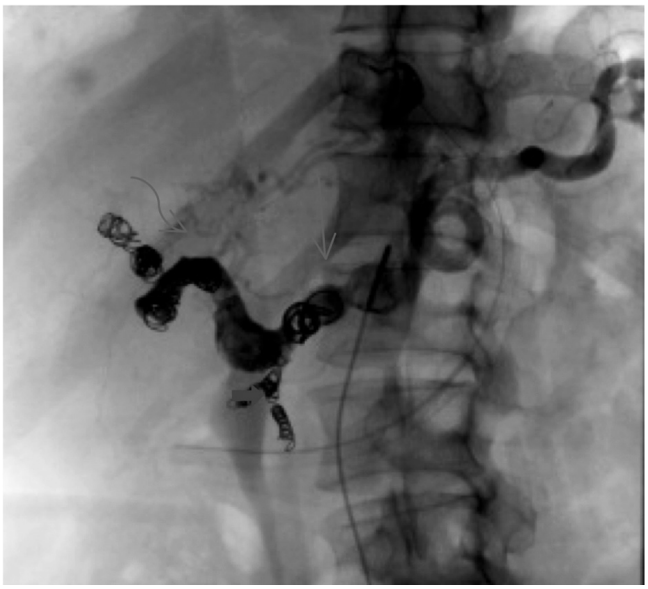

Fig. 3. Selective coeliac artery angiogram after embolisation of the common hepatic (arrows), proper hepatic (curved arrow), and gastroduodenal arteries with platinum coils (arrowhead).

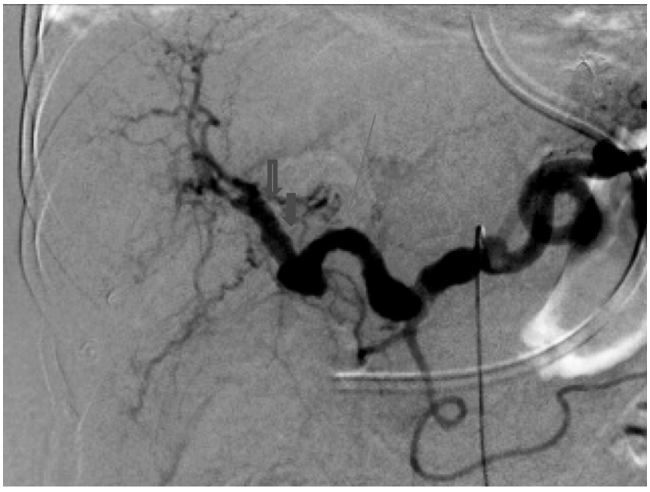

Fig. 4. Selective coeliac artery angiogram demonstrating aneurysm formation within the common hepatic (arrows) and proper hepatic (arrowheads) arteries.

tiated. Inflammatory markers returned to normal ranges. On follow-up the patients was doing well with no evidence of residual disease (Fig. 5-8).

Discussion

Criteria for non-invasive diagnosis of SAM were developed by Kalva *et al*. (8) and then used as institutional guidelines for the diagnosis.

Clinical criteria were absence of congenital predisposition for dissection (Ehlers-Danlos, Marfan or Loeys-Dietz syndrome), absence of FMD, collagen vascular disorder or arteritis, acute presentation, such as abdominal or flank pain, back pain, chest pain, hypotension, haematuria or stroke, and/or chronic presentation such as abdominal pain, hypertension, haematuria orasymptomatic.

Imaging criteria were the presence of dissection, fusiformaneurysm, occlusion, beaded appearance, wall thickening of the mesenteric or renal arteries with or without organ infarction, absence of associated contiguous aortic dissection or atherosclerosis.

Serologic criteria were absence of inflammatory/serological markers such as ANA, ANCA, ESR and CRP, and normal complement levels. It should be noted that in some cases tissue ischaemia or necrosis could increase ESR and CRP levels.

All 6 patients met the diagnostic criteria, 3 patients were female (50%), the mean age was 45.8±12.9 years. Three patients had past medical history (hyperlipidaemia, prediabetes and coeliac disease), the other 3 patients were in good health prior to SAM diagnosis.

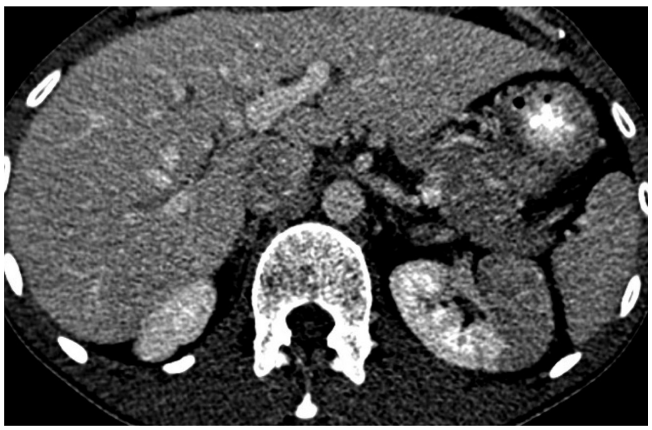

Fig. 5. Axial contrast enhanced CT scan demonstrating hypoperfusion of the left renal parenchyma, suggesting pyelonephritis or renal infarct.

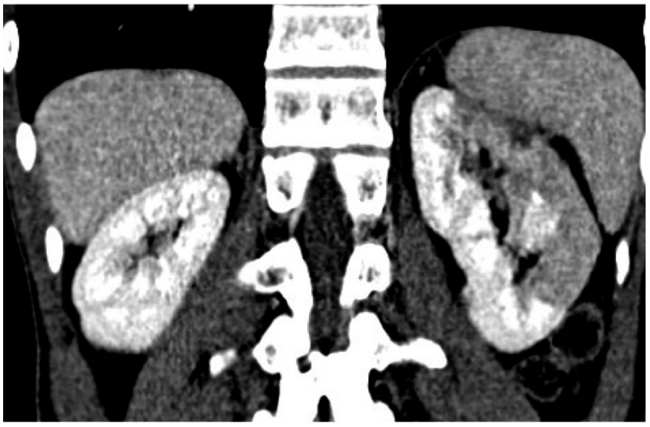

Fig. 6. Coronal contrast enhanced CT scan demonstrating hypoperfusion of the left renal parenchyma, suggesting pyelonephritis or renal infarct.

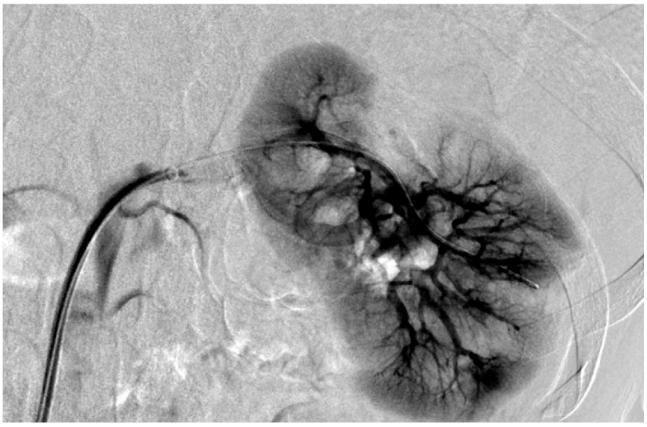

Fig. 7. Selective left renal angiogram after covered stent (arrow) placement in segmental left renal artery with exclusion of renal artery dissection and aneurysm.

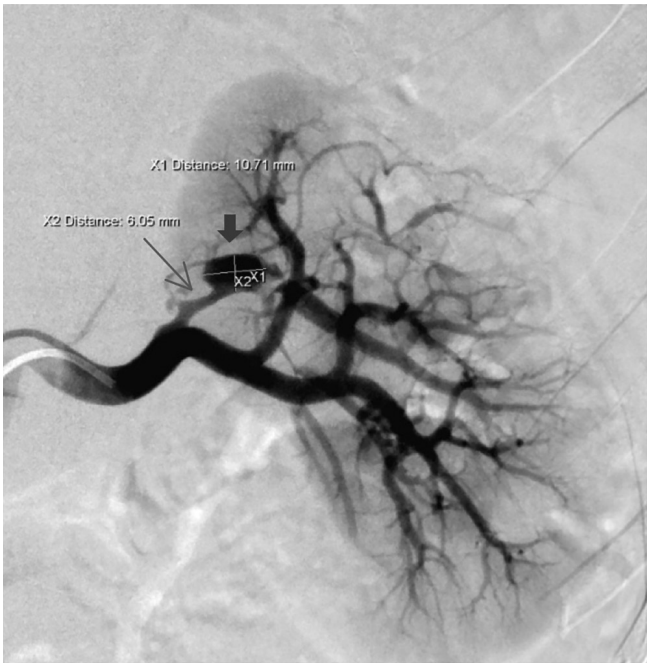

Fig. 8. Selective left renal angiogram demonstrating segmental dissection (arrow) and aneurysm (arrowhead) formation. →

None of the patients was on antihypertensive medications at the time of diagnosis. The most common presentation was abdominal or flank pain (5 patients). One patient was asymptomatic, and SAM was diagnosed following work-up for early-onset hypertension. None had family history or clinical signs to suggest an alternative diagnosis (*e.g.* Marfan syndrome, Ehlers-Danlos syndromes, FMD, collagen vascular disease and arteritis).

Serologic markers such as ANA, ANCA, complement (C3, C4) and RF were assayed in 5 patients and were all negative or in normal ranges, in patient 3 only ANCA was assayed and it was negative. C-reactive protein (CRP) was tested in all patients and was found to be mildly increased in 4 patients with mean 2.4±2.5 mg/dl, erythrocyte sedimentation ratio (ESR) was tested in 3 patients and was found to be elevated only in one. These cases had evidence of tissue necrosis or ischaemia.

CTA was the initial method of diagnosis in all 6 patients, 3 patients (4, 5, 6) underwent therapeutic angiography; 2 patients had angiographic embolisation because of bleeding, the third patient needed a stent insertion because of significant left renal artery involvement leading to infarction. Two patients (4, 6) underwent FDG-PET scan to rule out vasculitis, and only one patient underwent an MRI. No evidence supporting a diagnosis of vasculitis was shown by these imaging modalities (Table I). Two patients (1, 4) underwent a follow-up CTA. Patient 1 was referred to our emergency room complaining of abdominal pain, a CTA was performed and showed no changes in the aneurysms. Patient 4 underwent the CT scan 3 month after the diagnosis as was scheduled; the scan did not reveal any progression of the aneurysms.

CTA identified several arterial lesions. The coeliac artery was involved in 3 patients (1, 2, 3), 2 patients had renal artery stenosis (5, 6), one patient (2) had a pseudoaneurysm of the hepatic artery, and one patient (4) had multiple lesions in the pancreatoduodenal artery and its

Table I. Patients characteristics, clinical and imaging finding at presentation.

No	Age/Gender	Clinical presentation	Serologic and inflammatory markers	Treatment
1	40/ Male	Abdominal pain	Negative ANA, ANCA and RF, normal C3, C4, Elevated CRP	Aspirin
2	46/ Male	Abdominal pain	Negative ANA, ANCA and RF, normal C3, C4, Elevated CRP	Dual antiplatelet therapy
3	63/ Female	Abdominal pain Upper GI Bleeding	Negative ANCA Elevated ESR and CRP	Angiographic embolization
4	53/ Female	Abdominal pain	Negative ANA, ANCA and RF, normal C3, C4, normal IgM, IgG, IgA, normal CRP	Angiographic embolization
5	25/ Female	Early-onset hypertension	Negative ANA, ANCA and RF, normal C3, C4, CRP and ESR	Antihypertensives
6	48/ Male	Flank pain	Negative ANA, ANCA and RF, normal C3, C4, elevated CRP and normal ESR	Left renal artery stent insertion

ANA: antinuclear antibodies; ANCA: antineutrophil cytoplasmic antibodies; C3, C4: complement; RF: rheumatoid factor; CRP: C-reactive protein; ESR: erythrocyte sedimentation rate.

Table II. Imaging findings, arteries involved and methods used in diagnosis.

No	Lesions	Involved arteries	Imaging methods	Follow-up
1	Coeliac artery stenosis with post stenotic dilatation	Coeliac artery	CTA	7 months
2	Thickening of coeliac artery wall and its branches. Hepatic artery stenosis.	Coeliac artery, hepatic artery	CTA	No follow-up with imaging
3	Fusiform aneurysm of the hepatic artery, 2 big aneurysms of intrahepatic arteries. Dilation of the coeliac artery. superior mesenteric artery stenosis with suspected dissection.	Coeliac artery, hepatic artery, intrahepatic arteries, superior mesenteric artery	CTA Angiography	One month
4	Pseudoaneurysm of inferior pancreatoduodenal branch. Multiple small-vessel aneurysms and stenoses of the pancreatico-duodenal branches.	Inferior pancreatico-duodenal artery	CTA Angiography	4 months
5	Left subclavian artery stenosis Renal artery stenosis	Subclavian artery, renal artery	CTA MRA Doppler of carotid and vertebral arteries	No follow-up with imaging
6	Luminal irregularity of left renal artery with renal infarction	Renal artery	CTA Angiography	21 months

CTA: computed tomographic angiography; MRA: magnetic resonance angiography; FDG/PET: fluorodeoxyglucose - positron emission tomography.

branches. The lesions varied from wall thickening, aneurysms, artery dilation, stenosis and infarction (Table II).

The clinical presentation and arterial involvement were similar to those reported in larger-scale studies (Table III). Naidu *et al*. retrospectively identified a large cohort of 111 patients with SAM. Abdominal pain was the most common complain (74%), followed by flank pain (21%). The renal artery was the most commonly affected (47%) followed by superior mesenteric artery (46%), coeliac artery (46%), hepatic artery (23%), iliac arteries (18%), and splenic artery (14%) (11).

A systematic review by Kim *et al*. reported 101 cases of SAM from 76 studies published between 1976 and 2015: most patients presented with abdominal pain (68%), where 8 patients were asymptomatic. The most commonly involved arteries were the splenic artery (28%), common hepatic artery and branches), coeliac trunk and renal arteries (12).

The imaging findings of our study showed stenosis to be the most common imaging finding (40%), followed by aneurysms (26%). In contrast, dissection was the most common imaging finding in Nadiu and Kalva reviews, 86% and 71%, respectively. But similar to our report, aneurysms were the second most common imaging finding.

The diagnosis of SAM is challenging because it can mimic vasculitis, especially PAN. At times it might be difficult to distinguish between them initially, as happened in patients 3 and 6. FMD should be considered in the differential diagnosis as it shares histologic and imaging findings with SAM. Table IV, comparing clinical, laboratory and imaging features of SAM and other mimickers might help in distinguishing between them. A group of connective vascular disorders with predisposition

Table III. Summary of recent studies of SAM cases.

Author (year)	Number of patients	Median age, years	Females, no. (%)	Clinical presentation, most common feature (%)	Commonly involved vessels (%)
Inada (2007)	27	60.5	10 (37)	Abdominal pain (100)	Colic arteries (57)
Backer-LePain (2010)	2	38	1 (50)	Abdominal pain (100)	Hepatic artery (100)
Kalva (2011)	14	53	5 (36)	Abdominal pain (50)	Coeliac artery (50) SMA (36) Renal artery (36) Hepatic artery (21)
Kim (2016)	8	62.8	4 (50)	Abdominal pain (100)	SMA (50) Coeliac artery (37) Hepatic artery (25)
Nadiu (2018)	111	51	32 (29)	Abdominal pain (74)	Renal artery (47) SMA (46) Coeliac artery (46) Hepatic artery (23) Iliac arteries (18) Splenic artery (14)
Current study	6	45.8	3 (50)	Abdominal pain (66)	Coeliac artery (50) Renal artery (33)

SMA: superior mesenteric artery.

Table IV. Differential diagnosis of SAM.

PAN	FMD	Collagen vascular disease	Marfan syndrome	Ehrler-Danlos syndrome	Loeys-Dietz syndrome
+	-	+	±	+	+
+	-	+	-	-	-
+	-	-	-	-	-
+	-	+	-	-	-
+	-	+	-	-	-
+	-	-	-	-	+
+	+	+	-	-	-
Uncommon	+	-	-	-	-
+	-*	+	-	-	-
+	-	+	-	-	-
+	+	+	-	-	-
+ (uncommon)	-	-	-	-	-
-	-	-	-	-	-
	Involvement of renal and extracranial carotid and vertebral arteries.		Involvement of the ascending aorta. Dissection.	Involvement of the aorta and it's branches. Arterial rupture, arteriovenous fistulae.	Involvement of aorta and it's branches. Aneurysm and tortousity.
	Arteriography		Involvement of mesenteric, hepatic and renal arteries. Stenosis, dissection, aneurysms/pseudoaneurysms, infarction, bleeding.	Involvement of mesenteric, renal, subcutaneous and cutaneous arteries. Aneurysms, stenosis or occlusion, infarction.	Stenosis, aneurysms, dissection.

*May be mildly elevated in cases of bleeding or tissue necrosis.
SAM: segmental arterial mediolysis; PAN: polyarteritis nodosa; BP: blood pressure; CNS: central nervous system; ESR: elevated sedimentation rate; CRP: C reactive protein; BUN: blood urea nitrogen; ANCA: anti-neutrophil cytoplasmic antibodies.

for dissection such as (Ehlers-Danlos, Marfan or Loeys-Dietz syndrome) should be included in the differential, however it exhibits a distinct clinical features. Ehlers-Danlos syndrome is a congenital disorder characterised by joint hypermobility, skin laxity and lens subluxations. It involves the large-sized arteries such as aorta and its branches

causing dissection or rupture. It has a genetic mutation in the COL5A genes (15). Cystic medial necrosis is an arteriopathy associated with Marfan syndrome which is characterised by FNB1 gene (chromosome 15) mutation (16). Loeys-Dietz syndrome is an autosomal dominant genetic connective tissue disorder resulted from mutations in the genes encoding transforming growth factor beta receptor and it is marked by aneurysms in the aorta (17). Systemic vasculitis are heterogeneous, complex disorders with an inflammatory nature different than SAM but may be confusing. (18).

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