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Clinically Suspected Segmental Arterial Mediolytic of the Splanchnic Arteries: A Report of 2 Rare Cases

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 Statistical Analysis C
 Data Interpretation D
 Manuscript Preparation E
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Conflict of interest: None declared

Case series

Patients: Female, 89-year-old • Male, 52-year-old
Final Diagnosis: Segmental arterial mediolysis
Symptoms: Abdominal pain • bleeding
Medication: —
Clinical Procedure: —
Specialty: Radiology

Objective: Rare disease

Background: Segmental arterial mediolysis (SAM) is an uncommon vascular pathology characterized by arteriopathy, mainly of medium-sized abdominal splanchnic vessels, without an atherosclerotic, inflammatory, infectious, or auto-immune underlying etiology. Segmental arterial mediolysis is clinically heterogeneous and symptoms may be completely nonspecific. The knowledge of radiological features of segmental arterial mediolysis and the exclusion of other pathologies should direct early diagnosis and refer patients for correct treatment.

Case Report: In the last 2 years, we treated 2 different adult patients (an 89-year-old woman and a 52-year-old man) with spontaneous visceral bleeding, admitted to the Emergency Department due to acute onset of abdominal pain, anemia, and computed tomographic angiography (CTA) evidence of aneurysmatic, and stenotic alterations of splanchnic arteries. Based on clinical, laboratory, and radiological features, segmental arterial mediolysis was suspected. These 2 patients were referred to our Interventional Radiology Department and treated with super-selective transcatheter arterial embolization (TAE), performed by a minimally invasive approach, allowing an immediate clinical improvement with regression of symptoms and avoiding major surgical treatment.

Conclusions: In patients with clinical, laboratory, and radiological signs of acute and/or chronic abdominal bleeding and radiological findings suggesting segmental arterial mediolysis, mini-invasive endovascular treatment is a safe, extremely reliable, and secure procedure and appears to be the first-choice treatment when available. Since abdominal bleeding could have fatal consequences in these patients, timely diagnosis and endovascular therapy are essential to treat visceral vascular alterations due to segmental arterial mediolysis.

Keywords: Aneurysm, False • Angiography, Digital Subtraction • Embolization, Therapeutic • Radiology, Interventional • Tomography Scanners, X-Ray Computed

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Background

Segmental arterial mediolysis (SAM) is a rare vascular disease of the medium-sized and large-sized abdominal splanchnic arteries, characterized by stenoses, fusiform aneurysm, dissections, and occlusions of the vessels involved [1]. SAM is a vascular pathology affecting mainly middle-aged and elderly patients, with an incidence of 1 out of 100 000 inhabitants per year. From the first cases described by Gruenwald in 1949 in a newborn with coronary arteries involvement [2], Slavin and Gonzales-Vitale in 1976 studied artery histopathologic features of patients with abdominal muscular arteritis, dissecting aneurysms and arterial luminal occlusion, defining a new histopathological entity in segmental arterial mediolysis [3]. Today, more than 100 cases have been reported in the literature [4]. However, the prevalence of SAM may be higher due to increased use of computed tomographic angiography (CTA) and magnetic resonance imaging (MRI) in recent years [5]. This allows early detection of vascular morphological alterations of the vessels affected and guides the correct management of this rare pathology, mainly in asymptomatic patients. Pathophysiology

and histological alterations begin with the “mediolysis process” which consists of non-inflammatory degeneration and lysis of the smooth muscle layer of the outer media of the arterial wall. The etiology of SAM is unknown, but an association with episodes of splanchnic hypoxia and vasoconstriction observed in multiple medical conditions such as shock, trauma, recent major surgery, vasopressor infusion drugs, has been described [6]. Recent studies also reported dysregulation of the peripheral nervous system and stimulation of adrenergic receptors, mainly in young patients [1]. SAM is an uncommon cause of spontaneous intra-abdominal bleeding in middle-aged patients. However, the broad spectrum of symptoms varies from asymptomatic forms (often diagnosed incidentally after CT or MRI) to catastrophic clinical presentations mainly due to aneurysmal rupture and subsequent massive hemorrhage [7]. Bleeding may occur into the peritoneum or the bowel lumen, and related symptoms include abdominal and flank pain, which are the most common symptoms, often associated with hematochezia or vomiting and diarrhea. Signs and symptoms of hypovolemic or hemorrhagic shock with a drop of hemoglobin and hematocrit levels are typical of severe forms. Bowel

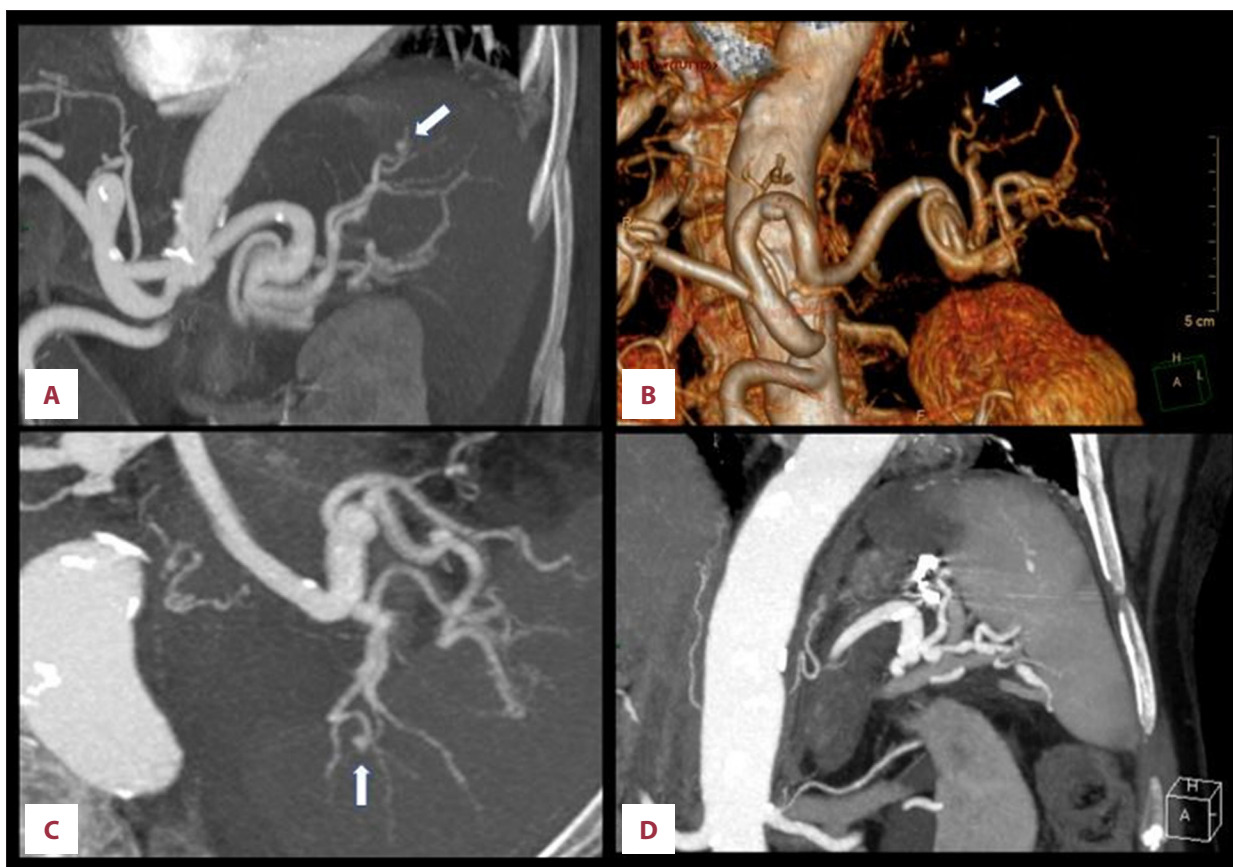


Figure 1. Case 1. (A-C) Coronal-CT, three-dimensional reconstruction, and axial-CT images show pseudoaneurysmatic dilations involved a distal branch of the splenic artery (white arrow) with an axial dimension of 6 mm. (D) Coronal-CT image after angiographic treatment with coil embolization reveals the presence of an area of infarction in the upper pole of the spleen, without clinical and laboratory sequelae.

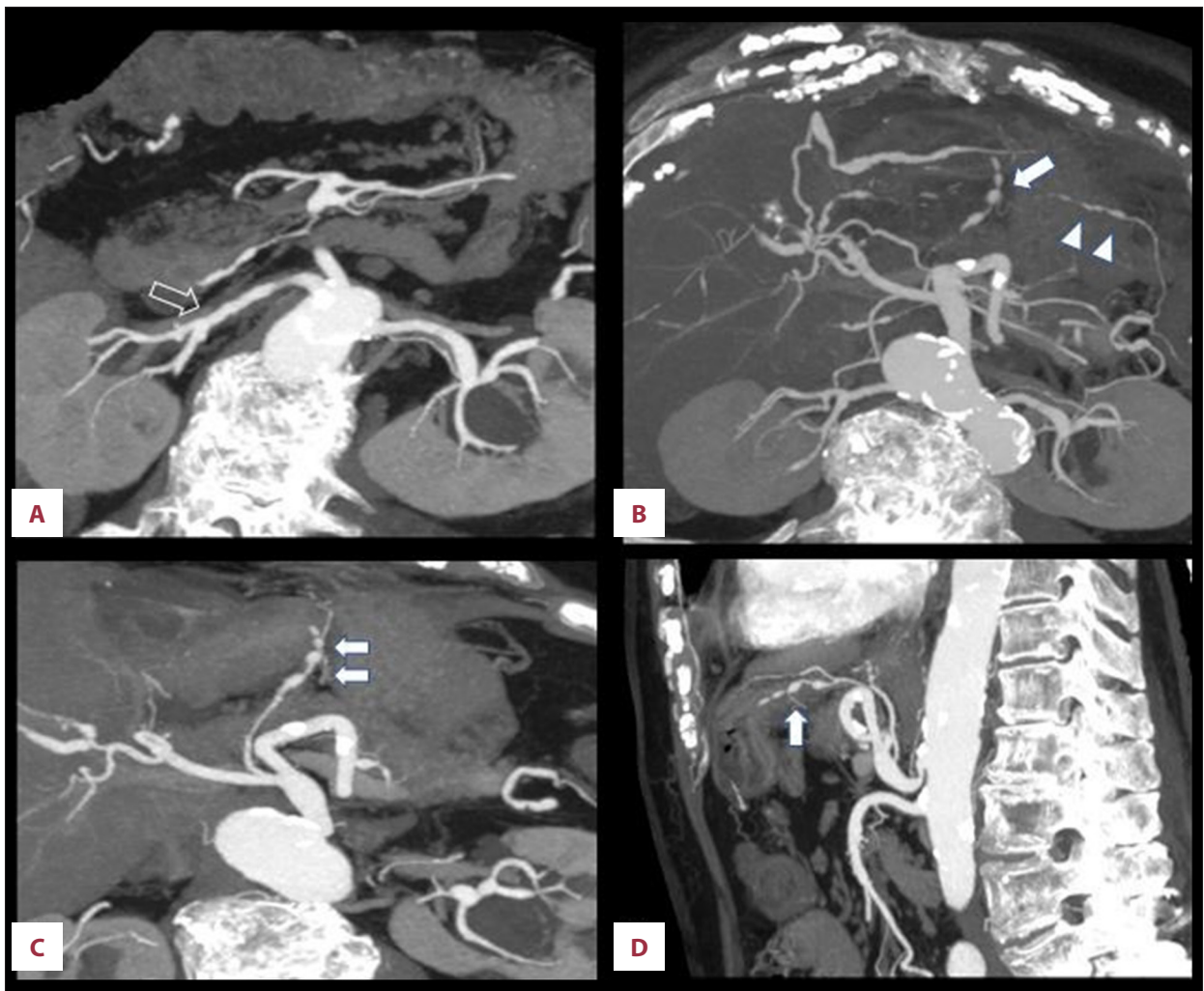


Figure 2. Case 1. (A-D) Multiplanar-CT reconstructions (MPR) show multiple alterations of splanchnic vessels, such as a right renal artery mimic a fibromuscular dysplasia aspect (open arrow in **A**), a 'string of beads' appearance of the left gastric artery (white arrow in **B-D**), right gastroepiploic artery, and anastomotic arcades of the middle colic artery and left colic artery and ileal and jejunal branches from the superior mesenteric artery (white arrowheads).

ischemia, renal involvement with hematuria, headaches, and stroke symptoms and coronary artery diseases are also reported [8,9]. The suspicion of SAM is also based on the exclusion of other clinical conditions, such as traumatic, infectious, inflammatory, or systemic diseases and genetic disorders. SAM has a mortality rate as high as 50% when a rupture of a visceral artery aneurysm occurs [10]; therefore, early diagnosis and treatment are mandatory to improve the outcome and survival of these patients. We present 2 different cases admitted to the Emergency Department due to acute onset of abdominal pain in patients with a drop in hemoglobin levels and CTA evidence of aneurysmatic and stenotic alterations of splanchnic arteries. The patients were treated with super-selective transcatheter arterial embolization (TAE). For these 2 case reports, we used noninvasive diagnostic criteria for the diagnosis of SAM based on clinical evaluation (absence of genetic,

inflammatory, infectious or atherosclerotic disorders), radiological features (presence of arterial dissection, fusiform aneurysm, arterial wall thickening, focal stenosis), laboratory findings (absence of high antibody values, antinuclear antibodies, antineutrophil cytoplasmic antibodies, inflammatory markers) and exclusion of other medical conditions.

Case Report

Case 1

An 89-year-old woman affected by cholelithiasis, vascular dementia, and hypertension (treated with hypotensive drugs – Ca⁺⁺-blockers) was admitted to the Emergency Department due to an episode of lipothymia, fatigue, and acute onset of

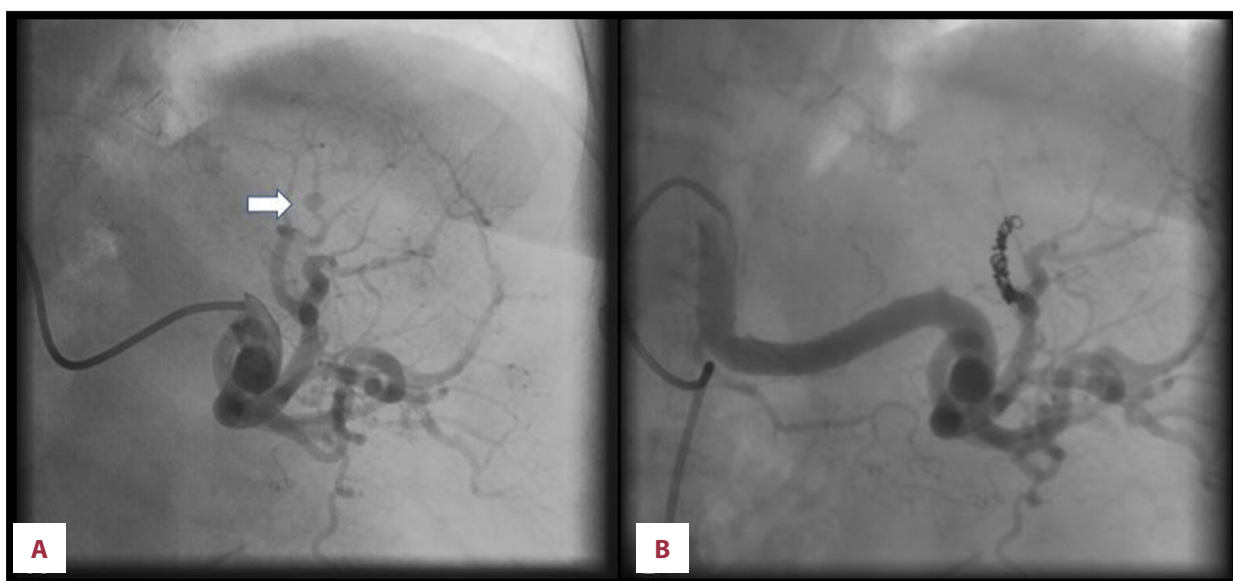


Figure 3. Case 1. Catheter angiogram of the splenic artery via the coeliac axis shows a distal pseudo-aneurysm marked in (A) by white arrow. (B) Catheter angiogram post-coil embolization: the pseudo-aneurysm was successfully occluded.

abdominal pain for 6 h. Clinical examination revealed hyposthenia of the upper left arm, fever (38°C), vomiting, abdominal tenderness in the upper quadrants, with associated pain during deep palpation. Cardiovascular parameters were altered, with hypotension (blood pressure values: 100/60 mmHg), heart rate of 95 bpm, and drop of laboratory hemoglobin values (Hb 10.5 gr/dl). Hyperglycemia (Hemo Gluco Test: 190 mg/dl) was also present. Oxygen saturation was normal (95%). There were no clinical features of infection. CTA revealed direct signs of active bleeding fed by the gastroduodenal artery and splenic artery, with peritoneal blood collection (hemoperitoneum) in the posterior right subhepatic space (Morison pouch), perisplenic space, and rectouterine space (pouch of Douglas). Multiple alterations of splanchnic vessels were also detected. CTA showed stenosis of the origin of the celiac trunk. Furthermore, aneurysmatic dilatations involved a distal branch of the splenic artery (axial dimension of 6 mm), right renal artery, right gastroepiploic artery (axial dimension of 8 mm), and the anastomotic arcades of the middle colic artery and left colic artery (Riolan's arch). These vessels on CTA showed a 'string of beads' appearance (Figures 1, 2). Thus, the patient was urgently referred for endovascular treatment to our interventional unit (a University second-level hospital) after the failure of medical therapy. Vital parameters were in the normal range and the patient was transferred to the angiographic room. Superficial anesthesia with lidocaine hydrochloride (1-2%) was performed and vascular access was achieved through the right common femoral artery under ultrasound guidance and using a 5-Fr sheath. Then, a hydrophilic wire (Terumo 180 cm) and a Cobra C2-5 Fr shaped catheter, 80 cm in length, were inserted coaxially and the celiac trunk was catheterized. Diagnostic angiography documented stenosis of the celiac trunk with post-stenotic tract

dilatation and aneurysmatic dilatation of an intraparenchymal branch of the splenic artery. Then, using a microcatheter-microwire system (Boston Scientific Direxion Transed System 0.021 inch×130 cm×165 cm), the splenic artery was negotiated and a superior polar branch was embolized with 3 detachable micro-coils (2 micro-coils of 3 mm×8 cm – Azur CX 18 Detachable – and 1 micro-coil of 4 mm×13 cm – Azur CX 18 Detachable). After coil embolization, occlusion of the pathological vessels was achieved (Figure 3). After the endovascular procedure, clinical parameters (hemoglobin values, heart rate, oxygen saturation, blood pressure) and patient performance status improved and were maintained throughout her hospital stay. Four days later, subsequent radiological controls with CTA revealed the presence of an area of infarction of the upper pole of the spleen without clinical sequelae. Then, the patient was discharged in good clinical condition.

Case 2

A 52-year-old man, with a remote pathological diagnosis of hypertension treated with hypotensive drugs, was admitted to our Emergency Department for asthenia, sudden onset of abdominal pain, and diarrhea. The clinical examination revealed abdominal tenderness associated with pain during palpation, mainly in the upper abdominal quadrants. Blood pressure was 110/70 mmHg, heart rate was 90 bpm, and laboratory hemoglobin values revealed anemia (Hb 9.8 gr/dl). Oxygen saturation was normal (95%). There were no clinical features of infection. A CTA was acquired, showing fat stranding in the peripancreatic space and vascular injury, with direct signs of active bleeding due to inferior pancreaticoduodenal artery pseudo-aneurysm formation. In this patient we observed an

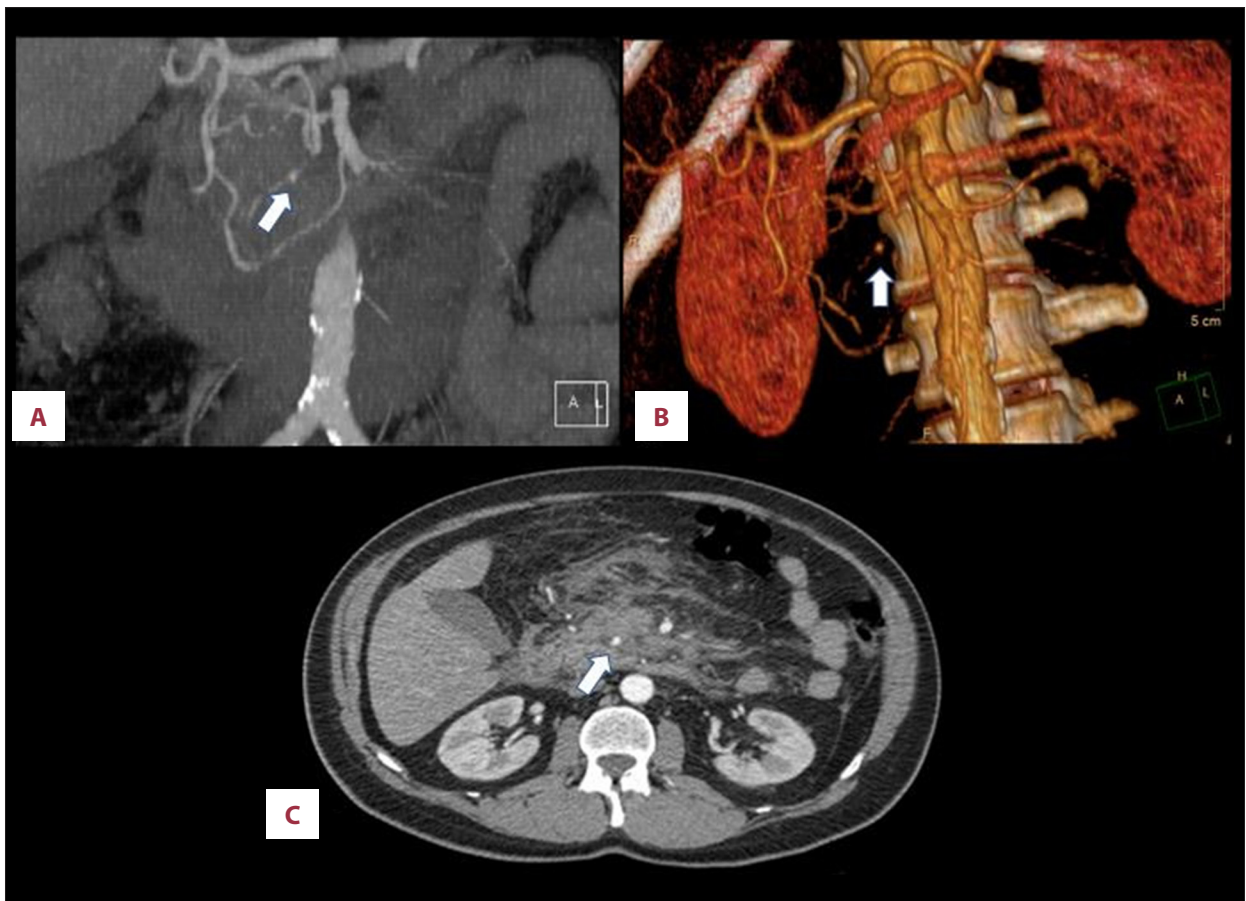


Figure 4. Case 2. (A-C) Coronal-CT, three-dimensional reconstruction and axial-CT images show an inferior pancreaticoduodenal artery pseudo-aneurysm formation (white arrow) and fat stranding in the peripancreatic space, with an anatomical variant subtype consisting of an inferior pancreaticoduodenal artery (IPA) originating from an accessory right hepatic artery from the superior mesenteric artery (SMA).

anatomical variant subtype with the inferior pancreaticoduodenal artery (IPA) originating from an accessory right hepatic artery from the superior mesenteric artery (SMA) (Figure 4). The patient, without evidence of hemodynamic instability, was transferred to our Radiology Department; right common femoral artery access was achieved using a 5-Fr introducer sheath and the SMA was selectively catheterized using a Cobra C2 5-F shaped catheter, 100 cm in length and a hydrophilic wire system (Terumo 260 cm). Digital subtraction angiography (DSA) of the SMA was performed, detecting a pseudo-aneurysmatic formation with active bleeding of the IPA. A microcatheter-microwire system (Boston Scientific Direxion Transend 0.021 inch×130 cm×165 cm) was inserted coaxially and the IPA was super-selectively catheterized and embolized with 2 detachable micro-coils (2 mm×4 cm, Azur CX 18 Detachable). The final angiographic check demonstrated total occlusion of the target vessel. Two days later, a second arteriography was necessary due to the drop of hemoglobin values of the patient. DSA, performed through super-selective arteriography using a microcatheter-microwire system (Boston Scientific Direxion

Hi-Flo 0.021 inch×155 cm), showed further active bleeding from a branch of the inferior pancreaticoduodenal artery, distally to the previously embolized area (Figure 5). The target vessel was treated by placing another detachable micro-coil (2 mm×4 cm, Azur CX 18 Detachable). After the procedure, clinical parameters and laboratory values improved, with no further evidence of anemia.

In these 2 cases, total occlusion of the target vessel at final angiographic control during procedures was considered a technical success. Clinical success was evaluated by clinical, laboratory, and radiological findings for several hours after the procedure. We also evaluated the hemoglobin levels for 48 h after the procedure. Discontinuation of vasopressor medications, normalization of blood pressure and heart rate, and stabilization of serum hemoglobin values suggested that active bleeding had clinically ceased. Procedure-related minor and major complications were analyzed and compared according to the Society of Interventional Radiology (SIR) classification [11]. In addition, blood and stool cultures were negative, as well as



Figure 5. Case 2. (A, B) Two days later, the first embolization multiplanar-CT reconstructions (MPR) demonstrating the presence of a direct sign of bleeding (blush) from a branch of the inferior pancreaticoduodenal artery, distally to the embolized region (white arrow) with surrounding hematoma (asterisk). (C) Super-selective arteriography confirmed the pathological vessel, which was treated using another detachable micro-coil (white arrow).

systemic features suggesting a vasculitic process (anti-neutrophil cytoplasmic antibody, antinuclear antibody, double-stranded DNA, rheumatoid factor, and antiphospholipid panel). The radiological and clinical findings argued against a diagnosis of Marfan, Gsell-Erdheim syndrome, and polyarteritis nodosa (exclusion of American Rheumatology Association's criteria). Then, the patients were managed with a strict clinical check-up and imaging follow-up with CTA at 6 and 12 months for the first year and then surveillance at 12-month intervals. The patients gave written informed consent for the publication of their case data and details.

Discussion

Although the first case was described 70 years ago, SAM is a little-known and often misdiagnosed pathology of the blood vessels, with a broad spectrum of clinical presentations varying

from asymptomatic forms to life-threatening conditions. The exact etiology of SAM is still unknown; however, its histological features are widely described. Medium-sized arteries are the main structures involved, with a dynamic pathological process, called mediolysis, leading to irreversible alterations of the medial layer of the arterial wall. The mediolysis pathological process leads to progressive loss of the external elastic lamina, resulting in separation of the outer medial muscle layer from the adventitia in a focal area or in the entire circumference of the vessel. The breach between the internal elastic lamina and the intima layer causes an area of weakness where blood can enter and determines aneurysmatic alterations and vessel dissection with subsequent intramural hematoma [12,13]. The dissecting hematoma may also compromise the vessel lumen and cause repair process and fibrosis. These alterations lead to stenoses and thrombosis of the arteries, resulting in ischemic manifestations. The most commonly involved vessels are the celiac trunk and its branches (in about 70-80% of

cases), the superior and inferior mesenteric arteries and their branches (in about 10-15% of cases), and other visceral arteries (in about 5% of cases) [1,15]. The natural history is unpredictable and SAM can evolve over time, remain stable for several months, or suddenly deteriorate with the extension of the pathology to other vascular segments. The early detection of SAM is important to improve the prognosis after the first occurrence [16]. Diagnosis and management of SAM are very complex since the heterogeneous clinical forms of presentation with multiple visceral arteries involvement and parenchymal alterations make it a challenge for physicians. Histological examination of lesions is the criterion standard for diagnosis, but it is usually too invasive for patients. Furthermore, interventional therapy does not allow collecting tissue during the same endovascular procedure. Histological tissue samples in other anatomical regions (superficial arteries) are often not examined because the patient's condition does not allow a more invasive diagnostic procedure. Given the characteristic discontinuity of vascular lesions, the risk of obtaining a nondiagnostic tissue sample in other vascular areas is high. Kalva et al used noninvasive diagnostic criteria derived from a literature review, considering that it was too invasive to obtain pathologic tissue with high clinical suspicion of SAM and after ruling out alternative diagnoses [17,18]. However, laboratory data are often normal and not specific for the pathology. Patients often have no signs of inflammatory conditions, and blood and stool cultures are negative for infectious diseases. Then, a correct clinical and radiological examination and the exclusion of other causes of arteriopathies, such as systemic diseases and genetic disorders, are the key points to guide the correct diagnosis and management of this disease. CTA is the criterion standard to assess splanchnic arteries and parenchymal-related alterations and it reveals patterns compatible with SAM [19]. Furthermore, CTA provides high spatial resolution and shows the detailed anatomy of vessels and their alterations. Naidu et al showed the importance of using CTA to assess radiological findings and disease progression in a review of 111 patients with SAM [20]. The main radiological characteristics are dissecting aneurysms (distribution tends to spare bifurcations), and patients often have CT scans showing intraperitoneal hemorrhage; radiological findings also include a 'string of beads' pattern, characterized by arterial dilations, single or multiple visceral aneurysms, arterial stenosis, or arterial occlusions. The absence of vessel inflammation is typical of SAM. Due to the nonspecific clinical presentation, SAM can mimic different pathologies and conditions, including atherosclerosis alterations, systemic inflammatory vasculitis such as granulomatosis with polyangiitis, polyarteritis nodosa, eosinophilic granulomatosis with polyangiitis, Kawasaki disease or Takayasu's arteritis, mycotic aneurysm, cystic medial necrosis (in patients with Marfan Syndrome), fibromuscular dysplasia, and infectious processes. Epidemiological, laboratory, histology, and radiological findings need to be carefully

analyzed and integrated to obtain the correct diagnosis and to guide the treatment [21,22]. The natural history of SAM is unpredictable and requires continued surveillance over several years. SAM can be a life-threatening condition if the clinical presentation is severe (a hemorrhage can lead to significant mortality) and if treatment is delayed. However, no formal guidelines and standardized clinical practices exist for the treatment of SAM. The management depends mainly on clinical symptoms and severity and extent of the alterations of vessels involved. Conservative medical therapy may be the first choice in patients with no symptoms and without signs of rapid evolution of pathology. In these patients, blood pressure control, lifestyle modifications, and conservative medical therapy with antiplatelet and hypotensive drugs are recommended. Close monitoring of vessel alterations with CTA is strongly recommended based on the literature. The monitoring of aneurysms is also necessary, and elective angiographic intervention should be considered based on the dimensions and radiological signs of immediate rupture of vascular aneurysms. In the literature, patients with SAM and with clinical presentation of acute intra-abdominal spontaneous bleeding and drastic degradation of clinical performance were treated with 2 different therapeutic approaches: surgical treatment and endovascular therapy [23,24]. When possible, TAE should be the first choice in patients with SAM. Endovascular management is a mini-invasive procedure with a low rate of periprocedural complications and lower procedural time with improved survival in the acute presentations of segmental artery mediolysis. Surgery should be considered when TAE is not available or is contraindicated, or for the management of extensive occlusive or hemorrhagic events that cannot be readily treated with a mini-invasive approach.

Conclusions

Segmental arterial mediolysis is an uncommon condition in which endovascular therapy is a minimally invasive, safe, and reliable treatment. In these 2 rare cases, interventional radiologists played a crucial role in performing timely super-selective transcatheter arterial embolization of pathological vessels resolving intra-abdominal active bleeding. In this condition, patients who are not promptly treated may experience severe clinical complications, with a poor prognosis. Furthermore, patients with clinical and radiological characteristics of SAM are often elderly and have comorbidities that make invasive surgical therapy technically difficult or contraindicated. Therefore, considering the heterogeneity of vessels involvement leading to intra-abdominal bleeding in SAM patients, a minimally invasive endovascular management should be the first choice when available and in the absence of contraindications to resolve a potential life-threatening medical condition.

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