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Case Report

Segmental arterial mediolysis of the middle colic artery: report of a case with special reference to lesions of small arteries and veins

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Abstract: We report a case of segmental arterial mediolysis (SAM) that involved the middle colic artery, and present some pathologic alterations found in mesenteric small arteries and veins. The patient, a 52-year-old woman, underwent an emergency laparotomy for acute intra-abdominal hemorrhage, and a segment of the transverse colon with hemorrhagic mesocolon was excised. Microscopic examination demonstrated two separate lesions of SAM in the middle colic artery. The involved arterial segments showed a partial to circumferential loss of the media (mediolysis) and intima associated with the formation of a pseudoaneurysm. Smooth muscle cells adjacent to the mediolysis showed various degenerative changes. In addition, we found multiple, tiny foci of degenerative lesions affecting the outer media in the wall of small arteries. Subendothelial vacuoles and nodular intimal proliferation were also noted in small veins. Whereas SAM chiefly affects large or medium-sized arteries, small blood vessels, including veins, are also affected. The present case is unusual in that degeneration of medial smooth muscle cells was clearly observed in the arterial walls, and the small veins were affected by lesions similar to those in arteries. We suspect that a phenotypic modulation of vascular smooth muscle cells induced by some genetic vulnerability plays a role in the pathogenesis of SAM.

Keywords: Degeneration, segmental arterial mediolysis, small artery, smooth muscle cells, vein

Introduction

Segmental arterial mediolysis (SAM) is a rare non-inflammatory vascular disorder of unknown pathogenesis that mainly affects intra-abdominal muscular arteries, especially branches of the celiac artery [1-7]. The patients are predominantly of middle age and often present with acute abdominal symptoms due to rupture of the affected artery. Histopathologically, SAM is characterized by a well-demarcated, segmental, and partial or circumferential loss of the arterial media, which results in formation of a pseudoaneurysm. Although it affects mainly large or medium-sized muscular arteries, small arteries or veins can also be involved [2, 3, 6-8]. Inflammatory changes of the vascular wall are usually absent or mild, and many hypotheses concerning the pathogenesis, such as vascular spasms, an autoimmune mechanism, fibromuscular dysplasia, or modulation of medial smooth muscle cells, have been proposed.

We report a case of SAM that involved the middle colic artery (a branch of the superior mesenteric artery). In addition to typical lesions, we observed degenerative and exudative changes that may represent an incipient stage of the evolution of lesions in the media of small, intramesenteric arterial branches. We also found some pathologic alterations in small intra-mesenteric veins.

Clinical history

The patient, a 52-year-old woman, was transferred to the emergency room of a local hospital for severe abdominal pain of acute onset accompanied by a loss of consciousness. She had suffered from mild abdominal pain and diarrhea for one week previously. Computed

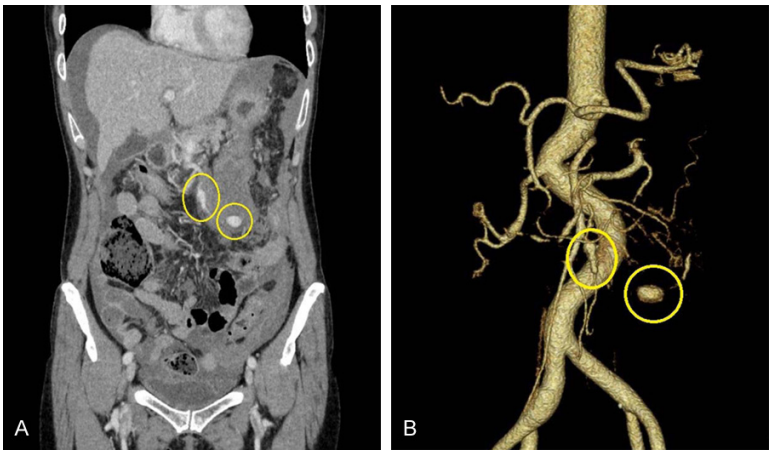

Figure 1. Abdominal CT with contrast enhancement (A) and 3D-magnetic resonance angiogram (MRA) (B). Two aneurysm-like lesions involving the middle colic artery (circled) were demonstrated.

tomography (CT) disclosed intra-abdominal hemorrhage and a mass lesion suggestive of a hematoma adjacent to the greater curvature of the stomach. She was referred to Hikone Municipal Hospital, and CT examination with contrast enhancement and three-dimensional digital subtraction magnetic resonance angiography (3D-MRA) demonstrated two aneurysm-like lesions of the middle colic artery and massive hemorrhage in the transverse mesocolon (**Figure 1A**, **1B**). Marked anemia (hemoglobin: 6.5 mg/dL) was noted. Serological tests for syphilis were positive, but she had no personal or family history suggestive of collagen-vascular diseases. She was a non-smoker and had no history of diabetes mellitus or hypertension.

Emergency laparotomy disclosed massive intra-abdominal hemorrhage (1,180 mL) with diffuse hemorrhage in the transverse mesocolon, which was partly lacerated. A short segment of the transverse colon with the mesocolon was excised. The postoperative course was uneventful, and the patient was discharged on the tenth postoperative day. Systemic imaging studies of the cardiovascular system, including the carotid, vertebral, and renal arteries, did not demonstrate any abnormalities.

Pathologic findings

The excised segment of the colon did not show any ischemic changes. Massive and diffuse hemorrhage was found in the transverse mesocolon, and on step sectioning, two separate, aneurysm-like, segmental lesions involving the middle colic artery embedded within the hemorrhagic adipose tissue were observed (**Figure 2A**).

On histopathologic examination, the two arterial lesions showed a similar appearance characteristic of SAM. In the involved areas, the arterial media completely disappeared (mediolysis) together with the intima over one half to almost the entirety of the arterial circumference, and outward bulging of the arterial wall (pseudoaneurysm) was formed (**Figure 2B**). The lumen of the pseudoaneurysm was filled with a fresh thrombus, and the residual external elastic lamina formed the outermost layer of the pseudoaneurysm (**Figure 2C**). The localized defect of the media was clearly defined, and in the media adjacent to the defect, derangement of muscle fibers, deposition of acid mucopolysaccharide in the interstitium, fragmentation of elastic fibers, and degenerative changes of smooth muscle cells, such as an irregularity of the nuclear contours, nuclear enlargement with hyperchromasia, and homogenization of the cytoplasm, were observed (**Figure 2D**). Mild vacuolar degeneration of muscle cells was occasionally observed, but fibroblastic proliferation with collagen deposition was minimal in the arterial wall. Mesenteric adipose tissue surrounding the artery showed fibroblastic proliferation and the infiltration of neutrophils and eosinophils, representing a response to rupture of the pseudoaneurysm. The mediolytic lesions respectively undermined the adjacent media longitudinally and produced a gap between the media and adventitia, which was filled with blood and associated with linear fibrin deposition along the adventitia (**Figure 2E**, **2F**). The intima of the affected artery showed multifocal and eccentric fibromuscular proliferation.

In addition to these typical lesions of SAM, some small arteries and veins in the mesocolon showed pathologic alterations. The lesions of small arteries consisted of very small, local-

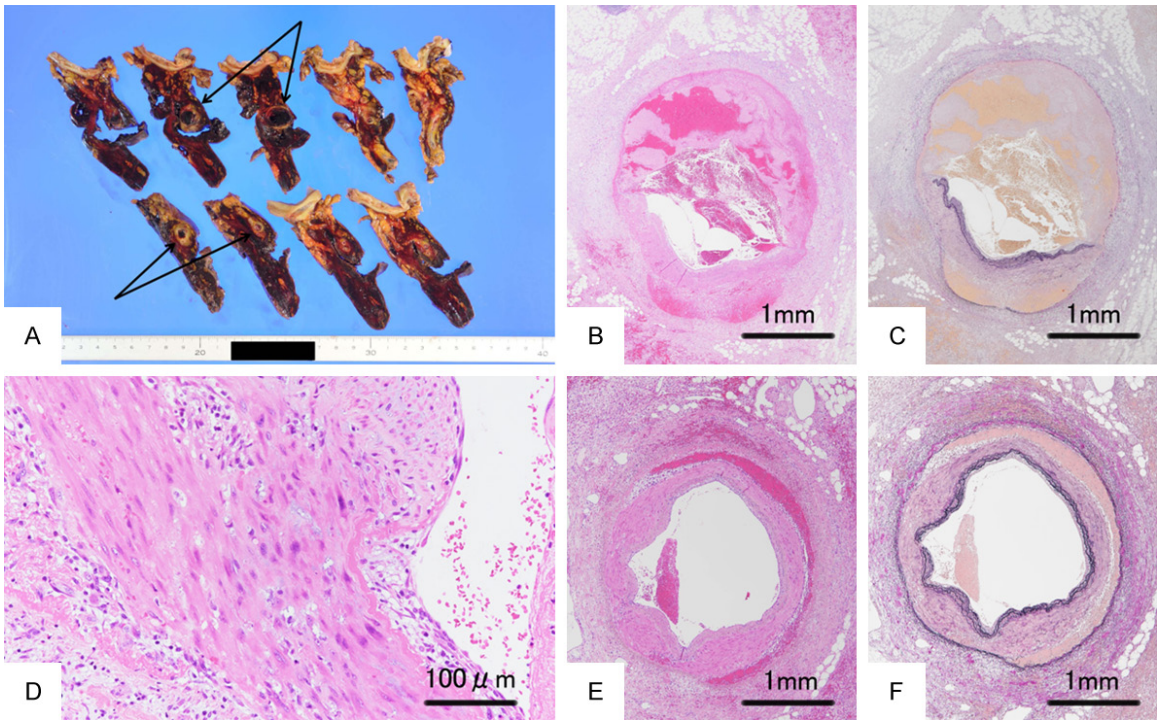

Figure 2. Gross appearance (A) and histopathologic findings (B-F). (A) Step sections of the excised transverse colon and mesocolon. Two separate, aneurysm-like lesions due to SAM (arrows) were found embedded within hemorrhagic adipose tissue of the mesocolon. (B, C) Typical appearance of an SAM lesion, consisting of a defect of the media (mediolysis) and intima over half of the arterial circumference associated with pseudoaneurysm formation and a fresh thrombus. The residual external elastic lamina formed the outermost layer of the pseudoaneurysm (C). (B: H&E stain, C: Elastica-van Gieson stain, ×20, scale bars 1 mm). (D) Smooth muscle cells adjacent to the mediolysis showed various degenerative changes, such as a derangement of muscle fibers, nuclear enlargement with hyperchromasia, and interstitial deposition of acid mucopolysaccharide. (H&E stain, ×200, scale bar 100 μm). (E, F) Gap formation between the media and adventitia that was filled with blood. Inflammatory changes and fibrosis were seen in adipose tissue surrounding the affected artery (E: H&E stain, F: Elastica-van Gieson stain, ×20, scale bars 1 mm).

ized degenerative foci in the outer media, which were associated with local exudation of fibrin-like material (**Figure 3A**). The lesions of small veins consisted of subendothelial vacuole formation (**Figure 3B**), the deposition of acid mucoppolysaccharide in the wall (**Figure 3C**), and small foci of nodular intimal proliferation (**Figure 3D**, **3E**).

Discussion

Segmental arterial mediolysis (SAM) was first reported by Slavin and Gonzalez-Vitale under the term “segmental mediolytic arteritis” [1]. Because inflammatory changes of the involved arteries are usually absent or mild, the term SAM [3, 9] or “segmental mediolytic arteriopathy” [5] has been more commonly used in recent years. No systemic findings suggestive of collagen-vascular disorders are noted in most cases.

The pathogenesis of SAM still remains obscure. Many investigators advocate vasospasm as the cause, mainly based on the finding of vacuolar degeneration of smooth muscle cells of the affected arteries [2, 3, 5, 6, 9], and local dysfunction of the endothelial paracrine system mediated by endothelin-1 was considered to play a role in the pathogenesis of SAM [3, 9]. De Sa, in a study of coronary arterial lesions in stillbirths and infants, argued that acute elevation of the blood pressure as a response to hypoxia during the perinatal period brings about rupture of capillaries in the adventitia, which in turn causes medial necrosis [10]. However, histopathologic findings corresponding to the radiological findings of vascular spasm are controversial, and in most reported cases of SAM, patients did not have clinical conditions that would increase the likelihood of local vasospasm. One of the pathologic characteristics of SAM is that lesions in different phas-

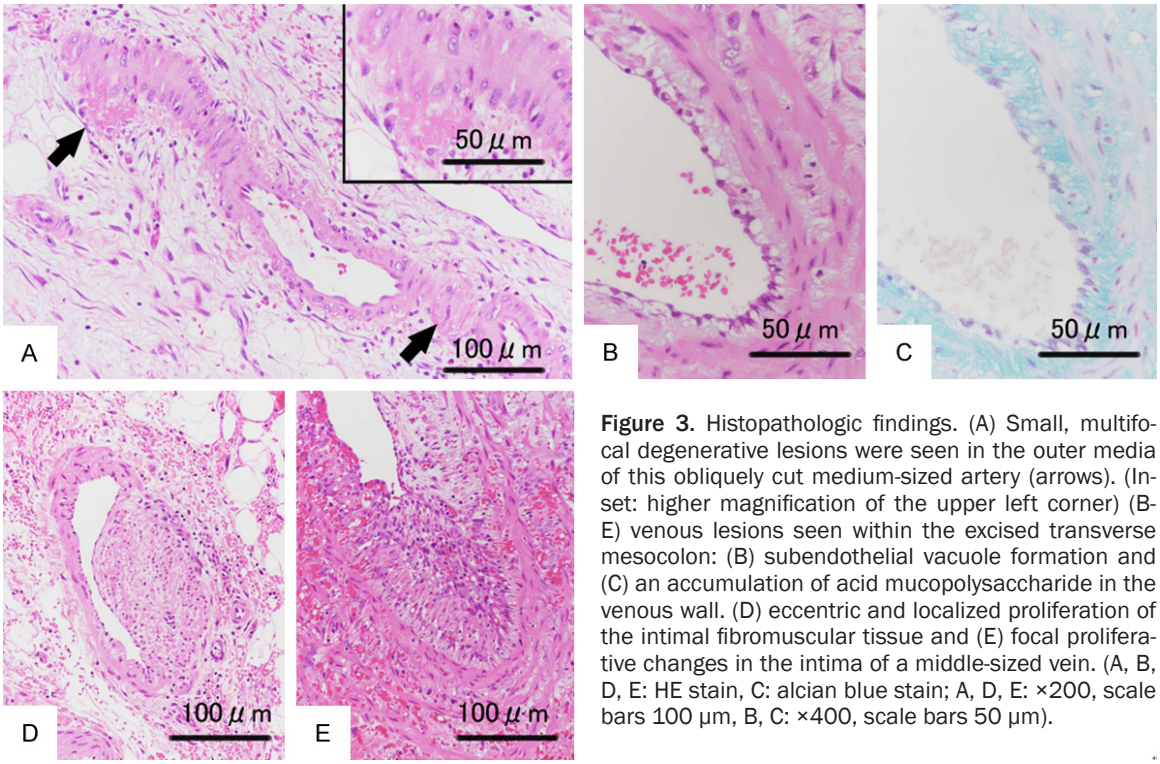

Figure 3. Histopathologic findings. (A) Small, multifocal degenerative lesions were seen in the outer media of this obliquely cut medium-sized artery (arrows). (Inset: higher magnification of the upper left corner) (B-E) venous lesions seen within the excised transverse mesocolon: (B) subendothelial vacuole formation and (C) an accumulation of acid mucopolysaccharide in the venous wall. (D) eccentric and localized proliferation of the intimal fibromuscular tissue and (E) focal proliferative changes in the intima of a middle-sized vein. (A, B, D, E: HE stain, C: alcian blue stain; A, D, E: ×200, scale bars 100 μm, B, C: ×400, scale bars 50 μm).

es of disease progression can be seen in the same patient [1-3, 5, 9], a fact that is difficult to explain on the basis of the vasospasm theory. In an experiment of vasoconstriction induced by the local application of epinephrine to the mesenteric arteries of dogs, whereas nuclear deformities and irregularity of cellular arrangement were observed in medial smooth muscle cells, no mediolysis was observed [11]. Mediolysis seen in SAM is different from ordinary coagulation necrosis of smooth muscle cells [2], and apoptotic cells are not found in mediolytic lesions [6]. Cell death seen in the arterial media in SAM may represent a special form of primary degenerative change [6] or liquefaction necrosis of arterial smooth muscle cells.

Other investigators suggested the involvement of an autoimmune mechanism mediated by immune complexes [1, 12]. A rare association of SAM with systemic lupus erythematosus [12] or microscopic polyarteritis nodosa [13] has been reported, and the deposition of immunoglobulins and complements was demonstrated in the arterial lesions of a few cases [4, 14]. However, the complication of autoimmune or collagen-vascular diseases is not seen in most patients, and SAM does not respond to immunosuppressive therapy [3].

Lie suggested that SAM was a variant of fibromuscular dysplasia (FMD) [15]. FMD is a noninflammatory disorder affecting muscular arteries, such as carotid, vertebral, and renal arteries [15, 16]. It is characterized by the deposition of collagen fibers (fibroplasia) associated with hypertrophy or hyperplasia of smooth muscle cells [16]. In the present case, we observed some degenerative changes of smooth muscle cells in media adjacent to mediolytic lesions. They consisted of a derangement of muscle fibers, interstitial deposition of acid mucopolysaccharide, an irregularity of the nuclear contours, nuclear enlargement with hyperchromasia, and homogenization of the cytoplasm. We consider that they represent primary lesions, which may suggest an association between SAM and FMD. Similar degenerative changes of the arterial wall in SAM have been reported by some investigators [4, 9]. In most cases of SAM, in which surgical intervention is performed in the early stage of disease progression, fibroplasia in the media is minimal. However, in the late, reparative, or organized stage, SAM transforms into lesions that closely resemble those seen in some types of FMD [3, 8, 9]. However, FMD is basically a developmental vascular anomaly, and its clinicopathological features are as a whole different from those of SAM [9, 16]. FMD character-

istically causes stenosis of the arterial lumina, only infrequently affects the intra-abdominal arteries, and the formation of pseudoaneurysms is rare [7].

Smooth muscle cells in the arterial wall are considered multifunctional mesenchymal cells [17, 18]. Hartman and Eftychiadis stated that changes of the media seen in cystic medionecrosis of the aorta represent a sequence of the differentiation of contractile smooth muscle cells into collagen-producing cells [18]. According to them, smooth muscle cells in the arterial wall differentiate into proliferating cells showing a synthetic phenotype, and the fragmentation of elastic fibers, production of proteoglycan, and mediolysis can be explained as functional activities of these modulated smooth muscle cells [18]. Deposition of acid mucopolysaccharide was observed in the lesional areas of arterial and venous walls of our case, and it may be an expression of the phenotypic modulation of vascular smooth muscle cells. This hypothesis of "smooth muscle cell modulation" [17] might provide a clue to explain the pathogenesis of SAM. It is conceivable that some genetic controls of the metabolism of arterial smooth muscle cells are deranged in SAM.

SAM typically affects large or medium-sized muscular arteries, but small arteries, especially small branches of the affected arteries, are also involved [2, 3, 6-9]. The simultaneous, multifocal occurrence of small arterial lesions is frequently seen [2, 7]. We found some lesions that probably represent an incipient stage of the disease in small arteries. They consisted of small degenerative foci in the outer media associated with local exudation of fibrin-like material. However, vacuolar degeneration was not noted in these lesions.

We also noted some pathologic alterations in small or medium-sized veins. They consisted of subendothelial vacuole formation, the deposition of acid mucopolysaccharides in the wall, and small foci of a nodular proliferation of intimal cells and elastic fibers. These lesions suggest that not only arteries but also veins are affected in SAM. Inada et al. described some pathologic changes involving veins ("venous angiopathy") [3, 8]. According to them, the venous lesions affect large or medium-sized veins adjacent to arteries with SAM lesions and show pathologic alterations, such as intimal edema with fibrosis, dispersion of smooth muscle fibers, vacuole formation, and patchy loss of smooth muscle cells [3, 8]. They hypothesized the effects of vasoactive substances produced by injured cells in the arterial wall and stated that venous lesions are secondarily induced [8].

Acknowledgements

The study followed the policies of the institutional review board, and informed consent to use both clinical data and pathologic material was obtained in accordance with the Declaration of Helsinki.

Disclosure of conflict of interest

None.

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