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Case Report

Unexpected intraabdominal hemorrhage due to segmental arterial mediolysis following subarachnoid hemorrhage: A case of ruptured intracranial and intraabdominal aneurysms

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Abstract

Background: Segmental arterial mediolysis (SAM) is an uncommon vascular disease, which manifests as catastrophic intraabdominal hemorrhage caused by rupture of visceral dissecting aneurysms in most cases. The etiology of SAM is still unclear, but SAM may be a vasospastic disorder and the responsible pressor agent is norepinephrine. Recently, abdominal SAM coexisting with intracranial dissecting aneurysms has been reported, but the relationship between intraabdominal and intracranial aneurysms in SAM remains unclear, as no cases of concomitant abdominal SAM and ruptured intracranial saccular aneurysm have been reported.

Case Description: A 49-year-old woman underwent emergent clipping for a ruptured saccular aneurysm at the left C1 portion of the internal carotid artery. Intraoperatively, norepinephrine was continuously administered intravenously under general anesthesia. Four days after the subarachnoid hemorrhage (SAH), the patient suddenly developed shock due to massive hematoma in the abdominal cavity. Imaging showed multiple aneurysms involving the splenic artery, gastroduodenal artery, common hepatic artery, and superior mesenteric artery. Coil embolization of the splenic artery was performed immediately to prevent bleeding. Subsequent treatment for cerebral vasospasm following SAH was performed with prevention of hypertension, and the patient recovered with left temporal lobe infarction. The diagnosis was abdominal SAM based on the clinical, imaging, and laboratory findings.

Conclusion: Norepinephrine release induced by SAH and/or iatrogenic administration of norepinephrine may have promoted abdominal SAM in this case.

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Abdominal SAM may occur subsequent to rupture of ordinary saccular aneurysm, and may provoke catastrophic abdominal hemorrhage in the spasm stage after SAH.

Key Words: Internal carotid artery, intraabdominal aneurysm, norepinephrine, segmental arterial mediolysis, subarachnoid hemorrhage

INTRODUCTION

Segmental arterial mediolysis (SAM) is an uncommon nonatherosclerotic, noninflammatory vascular disease.[18] SAM is characterized by vacuolization and lysis of the outer arterial media, severing of the adventitia from the outer media, and formation of arterial gaps, which result in dissecting aneurysm.[18] SAM manifests as catastrophic intraabdominal hemorrhage caused by rupture of visceral aneurysms in most cases, but any vessel may be involved, including the intracranial and coronary arteries.[18] SAM is characterized by multiple lesions occurring at different times.[5,7] The etiology of SAM is still unclear, but SAM may be a vasospastic disorder and the responsible pressor agent may be norepinephrine.[17–19] Recently, abdominal SAM coexisting with intracranial dissecting aneurysms has been reported in a few cases,[2,4,8,10,12,14] but the relationship between intraabdominal and intracranial aneurysms in SAM remains unclear. Moreover, concomitant abdominal SAM and ruptured intracranial saccular aneurysm have not been reported previously. We describe a rare case of abdominal SAM in which massive intraabdominal hemorrhage occurred during the acute stage of subarachnoid hemorrhage (SAH) caused by the sequential rupture of both visceral and intracranial saccular aneurysms. In this case, the etiologies of the intraabdominal and intracranial aneurysms were thought to be different, but the occurrence of the intraabdominal aneurysms was suspected to be related to SAH. The possibility of abdominal hemorrhage due to SAM should be considered during the period following SAH caused by rupture of typical saccular aneurysm.

CASE REPORT

A 49-year-old woman consulted our hospital because of sudden onset of headache and vomiting. Physical examination found the World Federation of Neurosurgical Societies grade II with systolic blood pressure of 152 mm Hg. No morphological features were identified suggesting congenital structural vascular disease such as Ehlers–Danlos syndrome or Marfan's syndrome. Her past history and family history were unremarkable, and systemic evaluation demonstrated no abnormality. Most laboratory data on admission were unremarkable including white blood cell count of 11.3 × 10^3/mm^3, C-reactive protein level of 0.3 mg/dL, and negative findings for human immunodeficiency virus and syphilis. She smoked 10 cigarettes per day and occasionally consumed alcohol. Computed tomography (CT) of the head revealed SAH [Figure 1a] and cerebral angiography showed a saccular aneurysm at the C1 portion of the left internal carotid artery (ICA) [Figure 1b].

The patient underwent emergent clipping of the typical saccular aneurysm which had no features of dissection [Figure 2]. Norepinephrine was continuously administered intravenously between 1.8 to 4.8 μg/min during the operation under general anesthesia to prevent any decrease in blood pressure caused by increased remifentanil hydrochloride dose. The postoperative course was uneventful without neurological deficits. Postoperative natural hypertension was permitted and systolic blood pressure was controlled between 130 to 160 mm Hg without continuous intravenous administration of norepinephrine. However, 4 days after the SAH, the patient suddenly developed shock after severe abdominal pain. CT of the abdomen revealed massive hematoma in the abdominal cavity around a splenic artery aneurysm, suggestive of the origin of bleeding [Figure 3a]. In addition to this lesion, three-dimensional CT angiography of the abdomen showed multiple aneurysms involving the gastroduodenal artery, common hepatic artery, and superior mesenteric artery [Figure 3b]. Blood transfusion for shock and coil embolization of the splenic artery to prevent bleeding were performed immediately. Extensive laboratory analysis was performed with negative myeloperoxidase-anti-neutrophil cytoplasmic antibody, proteinase 3-anti-neutrophil cytoplasmic antibody, and anti-nuclear antibody. The diagnosis of abdominal lesions was compatible with SAM based on the combination of

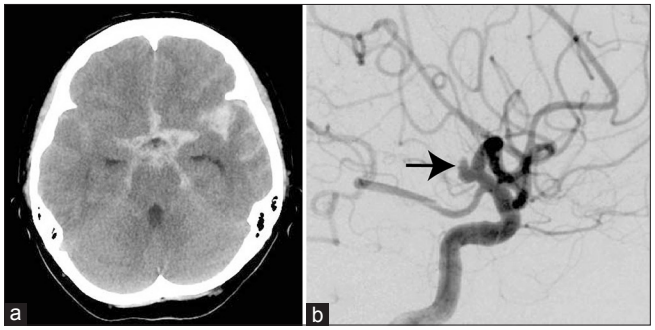

Figure 1: (a) Computed tomography scan of the head demonstrating subarachnoid hemorrhage mainly in the left sylvian fissure. (b) Left carotid angiogram showing a saccular aneurysm (arrow) at the C1 portion of the left internal carotid artery without the typical angiographic appearance of dissecting aneurysm such as focal irregularity of the vessel wall and fusiform dilatation

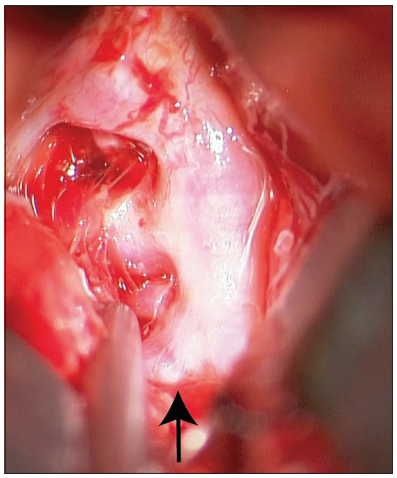

Figure 2: Intraoperative photograph showing a saccular aneurysm (arrow) in the left internal carotid artery without the features of dissecting aneurysm

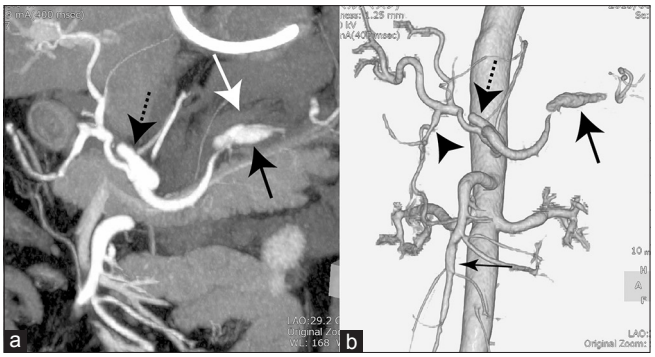

Figure 3: (a) Oblique coronal maximum intensity projection image of the abdomen demonstrating intraabdominal hematoma (white arrow) around the splenic artery aneurysm (black arrow) and common hepatic artery aneurysm (dotted arrow). (b) Three-dimensional computed tomography angiogram of the abdomen showing multiple aneurysms with the characteristics of dissection of the splenic artery (large arrow), gastroduodenal artery (arrowhead), common hepatic artery (dotted arrow), and superior mesenteric artery (small arrow)

clinical and imaging findings and absence of laboratory findings indicating infection or inflammatory etiology.

Treatment for cerebral vasospasm following SAH was performed with prevention of hypertension, which might be contraindicated in the presence of abdominal lesions. She was given oral and continuous intravenous administration of calcium antagonist to maintain a systolic blood pressure of 100–140 mm Hg. Left temporal lobe infarction was detected, but the patient was discharged after 1 month hospitalization with mild aphasia which recovered completely afterward. The patient remained asymptomatic for 34 months after SAH and CT angiography of the head and abdomen demonstrated no recurrence of the aneurysms in both visceral and intracranial arteries.

DISCUSSION

The differential diagnosis of SAM includes atherosclerosis, fibromuscular dysplasia (FMD), Behçet's disease, polyarteritis nodosa, neurofibromatosis, Ehlers–Danlos syndrome type IV, Marfan's syndrome, and mycotic aneurysms.[1,18] Dissections and aneurysms are common in Ehlers–Danlos syndrome and Marfan's syndrome, but involvement of the splanchnic vasculature is less common.[1,7] The absence of physical signs and symptoms, and laboratory indicators of systemic inflammation are helpful to distinguish SAM from inflammatory vasculitides.[1] SAM typically involves the medium and large abdominal muscular arteries, and the natural history of the arterial lesions can be divided into the injurious phase followed by the reparative phase. In the injurious stage, arterial gaps are created by transmedial mediolysis and loss of the internal elastica and intima putatively caused by disruption and loss of musculostromal connection.[18] In the reparative phase, proliferation of granulation tissue repairs medial defects and so obliterates small gaps and fortifies arterial aneurysms. SAM may be the precursor of FMD based on the morphological appearance of SAM in the reparative phase.[18] However, FMD is not caused only by SAM but also represents a group of arterial disorders with diverse etiologies.[18] The clinical presentations of these two disorders differ, as SAM manifests as profuse bleeding from the abdominal intestinal arteries whereas FMD manifests as ischemic changes causing hypertension or strokes derived from renal artery alterations in the former and ICA changes in the latter.[18] Definitive diagnosis of SAM requires histopathological evaluation of the arterial lesions, but endovascular treatment of abdominal aneurysms in SAM has been reported recently.[13] The clinical non-pathological guidelines for the diagnosis of abdominal SAM consist of absence of congenital predisposition for dissections, absence of more plausible diagnosis such as FMD or arteritis, abdominal or flank pain, vascular lesions such as dissection of the mesenteric or renal arteries, and absence of inflammatory markers.[7] Our case satisfied these criteria for abdominal lesions, so abdominal SAM was indicated despite the absence of pathological findings.

SAM was first described as a distinct pathological entity in 1976,[15] and initially named segmental mediolytic arteritis since SAM was suspected to represent an immune-mediated arteritis.[15,18] However, this hypothesis was negated by the findings of inconstant inflammatory changes and absence of laboratory evidence of immunological or infectious assault.[16,18,19] Subsequently, SAM was suspected to be the result of an inappropriate vasospastic response expressed in a splanchnic vascular bed undergoing vasoconstriction as a response to shock or severe hypoxemia.[16] The etiology of SAM is still unclear. However, similar pathological findings were induced in an experimental model by administering ractopamine, a beta-2 adrenergic agonist, which suggested that SAM

is a vasospastic disorder and that the responsible pressor agent is norepinephrine.[17–19] Moreover, SAM may be a disorder principally caused by iatrogenic or accidental exposure to alpha-1 adrenergic receptor agonists or beta-2 agonists which can induce release of norepinephrine from the peripheral nervous system.[17,18] The release of norepinephrine from varicosities of the efferent nerves of the splanchnic arteries stimulates the alpha-1 receptor on the cell membrane of the medial smooth muscle to cause either transient intense vasoconstriction followed by apoptosis or direct initiation of apoptosis caused by shearing separation of the adventitia from the media.[17,19] The quantity of released norepinephrine is important in determining the extent of mediolysis.[19] SAM develops very rapidly after exposure to such agents, within 1–4 days, and results in the formation of apoptotic lesions.[17]

Recently, abdominal SAM coexisting with intracranial dissecting aneurysms has been reported. Locations of the intracranial aneurysm included the ICA, basilar artery, vertebral artery (VA), and anterior cerebral artery.[2,4,8,10,12,14] An autopsy case of SAM with both intraabdominal and intracranial VA dissections indicated that medial defects, which resemble the vascular lesions found in patients with SAM, are very important in the occurrence of intracranial VA dissections.[10,11] However, pathological findings of intracranial aneurysm are difficult to obtain except for autopsy cases, so the relationship between intraabdominal and intracranial lesions in SAM is unclear, especially whether the intracranial aneurysm is caused by SAM or not. Moreover, in our case, the cause of sequential rupture of the intracranial and intraabdominal aneurysms was also unclear, but patients with SAH show approximately 3-fold increase in total body norepinephrine spillover into the plasma within 48 h after insult, compared with healthy subjects.[9] This sympathetic activation persists for 7–10 days. Such marked elevation in norepinephrine spillover shows no association with the Hunt and Hess score, Fisher score, or location of the aneurysm.[9] Therefore, whether the intracranial aneurysm is caused by SAM or not, norepinephrine release induced by SAH and/or iatrogenic administration of norepinephrine may have promoted the occurrence of abdominal SAM and rupture of visceral aneurysm in the acute stage of SAH.

The intracranial aneurysm of our patient seemed not to be related to SAM in contrast to the abdominal lesions because of the absence of dissection, but occurred as a typical saccular aneurysm. The limitation of this case is the absence of histopathological evidence of abdominal SAM, but it is important to be aware of the possibility that abdominal SAM may occur subsequent to rupture of ordinary saccular aneurysm, and may provoke catastrophic abdominal hemorrhage in the spasm stage after SAH. The different etiologies of the intracranial and intraabdominal aneurysms in this case may indicate that intracranial dissecting aneurysms coexisting with abdominal SAM are not necessarily caused by SAM and the concomitance of abdominal SAM and SAH is not rare.

Ten cases of coexisting SAH and visceral aneurysm have been reported.[2–4,6,8,12,14,20–22] Table 1 presents the characteristics of the patients, of whom only six also

Table 1: Reported cases of subarachnoid hemorrhage concomitant with visceral aneurysm

Authors, year	Age (years), sex	WFNS grade	Location and type of neurovascular aneurysm	Treatment for neurovascular aneurysm	Abdominal hemorrhage following SAH	Diagnosis of abdominal SAM	Outcome	Follow-up period (mos)
Isla *et al*., 1988[6]	68, female	II	AcomA saccular	Clipping	1 month after operation	No	Improved	NA
Fuse *et al*., 1996[3]	56, female	II	Left ICA saccular, right MCA saccular	Clipping	16 days after SAH	No	Improved	NA
Sakata *et al*., 2002[12]	48, male	V	Right VA dissection, left ICA dissection	No	NA	Pathological	Dead	
Soga *et al*., 2009[20]	73, female	V	NA	No	No	Pathological	Dead	
Matsuda *et al*., 2012[8]	59, male	I	Right A1 dissection, distal right ACA, left VA	Coating	No	Non-pathological	Improved	12
Stetler *et al*., 2012[21]	59, female	NA	Right PcomA saccular	Coiling	Postoperative day 3	No	Improved	6
Cooke *et al*., 2013[2]	4555, male	V	Left VA dissection	Coiling	No	Non-pathological	Improved	NA
Shinoda *et al*., 2016[14]	47, male	V	Left VA dissection	Coiling	8 days after SAH	Pathological	Improved	1
Welch *et al*., 2017[22]	61, s male	NA	Posterior spinal artery pseudoaneurysm	Embolization	Simultaneous	Non-pathological	Improved	10
Hellstern *et al*., 2017[4]	30, male	IV	BA dissection, both ICA dissection	Coiling and flow diverter	Simultaneous	Pathological	Improved	11
Present case	49, female	II	Left ICA saccular	Clipping	4 days after SAH	non-pathological	Improved	34

ACA: Anterior cerebral artery, AcomA: Anterior communicating artery, BA: Basilar artery, ICA: Internal carotid artery, MCA: Middle cerebral artery, NA: Not available, PcomA: Posterior communicating artery, SAH: Subarachnoid hemorrhage, SAM: Segmental arterial mediolysis, VA: Vertebral artery, WFNS: World Federation of Neurosurgical Societies

suffered from abdominal bleeding caused by rupture of visceral aneurysm, as in our patient.[3,4,6,14,21,22] Only three of the six cases were diagnosed as abdominal SAM,[4,14,22] but all resembled our case in clinical features, that is, the abdominal bleeding occurred within several days in most cases to 1 month in one case of the onset of SAH, and the intracranial aneurysms were not all dissections but also included saccular types. Abdominal SAM could not be excluded in the abdominal lesions of three cases with saccular intracranial aneurysms.[3,6,21] The occurrence of abdominal SAM may be underestimated and more common than suggested by the few reported cases.

The postoperative hypertensive state to counteract cerebral vasospasm following SAH may have also influenced the abdominal bleeding of SAM in this case, but the ideal management strategies for vasospasm in the presence of abdominal SAM have not yet been established because of the rarity of SAM following SAH. The catastrophic abdominal bleeding due to SAM during the acute stage of SAH prevents safe treatment for vasospasm following SAH, so blood transfusion and hemostasis of abdominal bleeding should be ensured immediately as the first step for such hemorrhagic shock. Moreover, it is important to recognize the causative abdominal lesions as SAM, because the resultant shock should not be treated by adrenergic agents which could intensify SAM and generate additional lesions.[18] Surgical treatment for abdominal SAM generally consists of surgical ligation or resection of the aneurysm, but advanced endovascular techniques are increasingly used to manage SAM without the need for major surgery.[13] Endovascular treatment of the visceral aneurysms is a suitable and less invasive treatment modality, especially for patients in the vasospasm stage after SAH.

CONCLUSION

Norepinephrine release induced by SAH and/or iatrogenic administration of norepinephrine may have promoted abdominal SAM in this case. Little is known about the association of increased levels of norepinephrine with SAM after SAH, in spite of the risk that SAM may induce sudden visceral hemorrhage in the unstable cerebral circulation stage of vasospasm, which is likely to result in death and needs prompt diagnosis and treatment. Neurosurgeons should be aware of the possibility of unexpected abdominal hemorrhage caused by SAM within several days following SAH. Early recognition of SAM and management can lead to significant reduction in subsequent complications and mortality. The different etiologies of the intracranial and intraabdominal aneurysms in this case may indicate that intracranial dissecting aneurysms coexisting with abdominal SAM are not necessarily caused by SAM and the concomitance of abdominal SAM and SAH is not rare. The natural history of SAM is poorly understood, so we continue to follow up our patients regularly.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. The form specifies that the patient (s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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