

# Subarachnoid Hemorrhage after an Ischemic Attack Due to a Bacterial Middle Cerebral Artery Dissecting Aneurysm: Case Report and Literature Review

Atsushi SAITO,<sup>1</sup> Tomohiro KAWAGUCHI,<sup>1</sup> Emiko HORI,<sup>1</sup> Masayuki KANAMORI,<sup>1</sup> Shinjitsu NISHIMURA,<sup>1</sup> Seiya SANNOHE,<sup>2</sup> Mitsuomi KAIMORI,<sup>2</sup> Tatsuya SASAKI,<sup>1</sup> and Michiharu NISHIJIMA<sup>1</sup>

*Departments of <sup>1</sup>Neurosurgery and <sup>2</sup>Pathology, Aomori Prefectural Central Hospital, Aomori, Aomori*

## Abstract

A 78-year-old woman suffered sudden-onset left hemiparesis. There were no remarkable infectious findings. Computed tomography (CT) demonstrated a low-intensity area supplied by the right middle cerebral artery (MCA). The diagnosis was cerebral ischemia and she was conservatively treated with hyperosmotic fluids. Two days after the ischemic stroke she suddenly became comatose. CT showed diffuse subarachnoid hemorrhage (SAH) in the basal cistern associated with a right intra-Sylvian and a right frontal subcortical hematoma. Three-dimensional (3D)-CT angiography demonstrated occlusion of the M2 portion of the right MCA. Four days after the ischemic onset she died of brain herniation. Autopsy revealed arterial dissection in the intermediate membrane of the right MCA bifurcation and occlusion of the M2 portion of the thrombosed right MCA. Gram staining showed remarkable bacterial infection in the thrombus. SAH after an ischemic attack due to MCA dissection is extremely rare. We suspect that bacterial infection was involved in the formation of her fragile dissecting aneurysm.

Key words: subarachnoid hemorrhage, cerebral infarction, bacterial aneurysm, dissection

## Introduction

Bacterial aneurysms, also known as infective or microbial aneurysms, are rare inflammatory neurovascular lesions that account for 0.7–6.5% of all intracranial aneurysms.<sup>1,2)</sup> They tend to develop at peripheral arterial branches and result in subarachnoid or subcortical hemorrhage but rarely in ischemic attacks.<sup>3,4)</sup> We report a rare case of subarachnoid hemorrhage (SAH) after an ischemic attack due to a middle cerebral artery (MCA) dissecting aneurysm associated with a bacterial thrombus and present a review of the literature.

## Case Report

This 78-year-old febrile woman was admitted with sudden-onset left hemiparesis with dominance in the upper extremity. She had a long history of treatment for a urinary tract calculus and had repeated urinary infection. She was emergently taken to a near-by clinic.

Echocardiography returned no findings of endocarditis. A computed tomography (CT) scan demonstrated no hemorrhagic lesions (Fig. 1). The diagnosis was cerebral infarction and she was conservatively treated with hyperosmotic fluids. Hematology showed a white blood cell count (WBC) of 13,200 cells/mm<sup>3</sup>; C-reactive protein was 6.67. Two days after onset she suddenly became comatose. CT revealed diffuse SAH associated with intra-Sylvian and intraparenchymal hematomas in the right frontal lobe (Fig. 2). She was introduced to our department. CT showed a low-density lesion in the territory of the right MCA suggesting cerebral infarction associated with SAH (Fig. 2). Three-dimensional (3D)-CT angiography revealed occlusion of the M2 portion of the right MCA (Fig. 3). No severe infectious finding was observed in hematological and urinary data on admission. Her family rejected surgical treatment. Four days after the ischemic onset she died of brain herniation.

Autopsy revealed diffuse SAH and occlusion of the M2 portion due to filling by a thrombus (Fig. 4A–C). Pathological examination showed dense SAH around MCA bifurcation and thrombosed M2 (Fig. 4C). Inflammatory cells such as neutrophils proliferated and infiltrated into

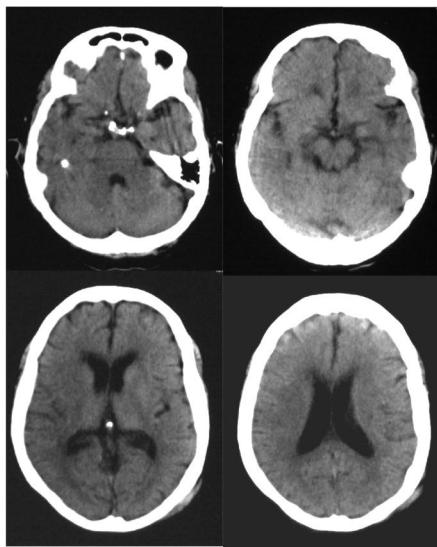


Fig. 1 A computed tomography scan obtained at the time of admission showed no intracranial hemorrhage. Note the faint low-density ischemic lesion in the right middle cerebral artery territory.

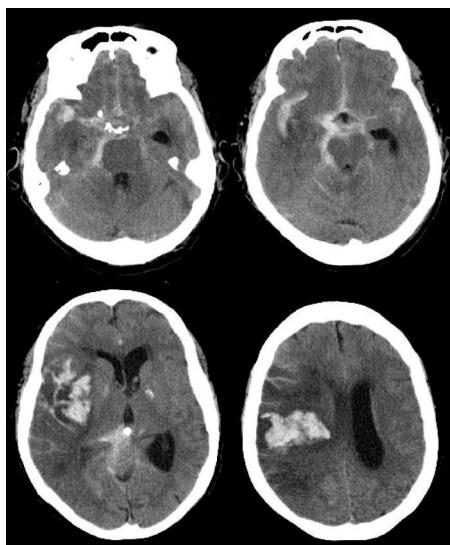


Fig. 2 Computed tomography revealed diffuse subarachnoid hemorrhage associated with intra-Sylvian and intra-parenchymal hematomas in the right frontal lobe. The territory of the right middle cerebral artery is seen as a low-density lesion suggestive of cerebral infarction.

arterial wall around thrombus (Fig. 4C). Gram staining showed remarkable bacterial infection in the thrombus (Fig. 4D). Hematoxylin-eosin stain and Elastica van Gieson stain of serial sections demonstrated that internal elastic membrane partially disrupted and that internal flap and pseudolumen filled with erythrocytes were observed in the right MCA bifurcation (Fig. 5).

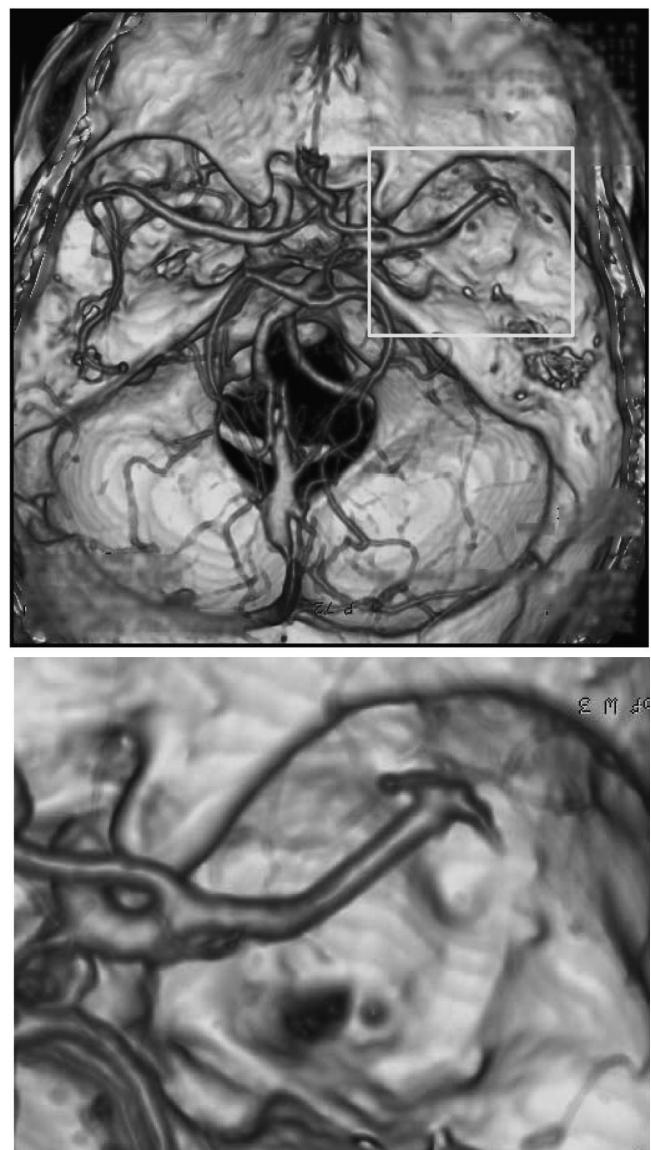


Fig. 3 Three-dimensional computed tomography angiography demonstrated occlusion of M2 portion of the right middle cerebral artery and irregular dilatation at the bifurcation (upper). Lower is higher magnified image of the region of interest on the upper image (square).

## Discussion

Bacterial aneurysms often develop in patients with infectious endocarditis when fragile cardiac vegetation gives rise to septic emboli that lodge in intracranial vessels at branching points and distal branches.<sup>2,5)</sup> The embolic and the more widely accepted *vasa vasorum* hypothesis have been offered to explain the pathogenesis of bacterial aneurysms.<sup>2)</sup> The latter posits afferent progression of inflammation in the disturbed vessel wall. It proposes

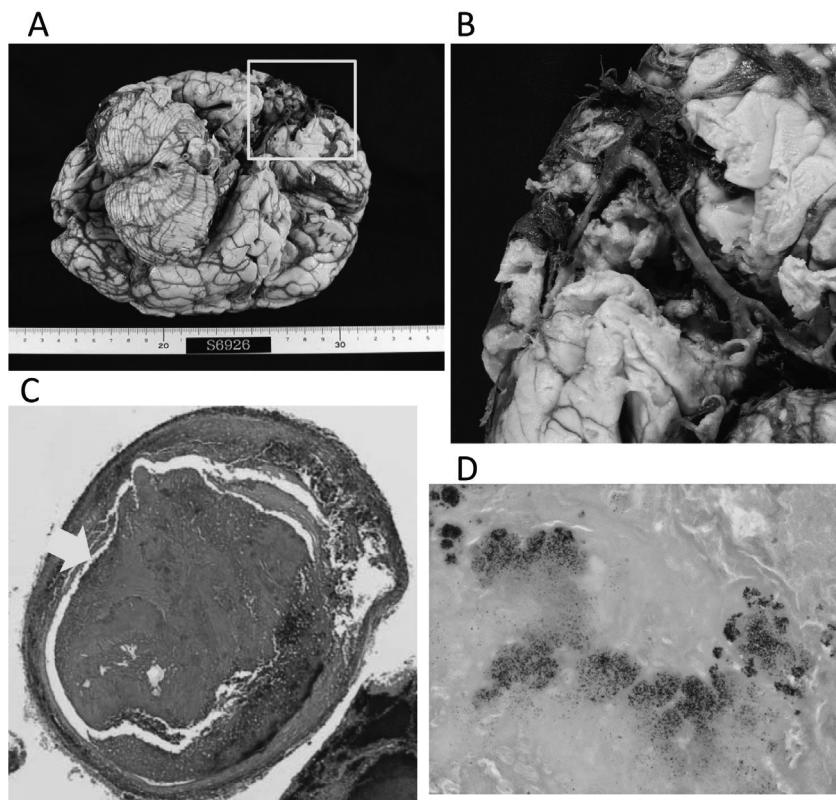


Fig. 4 A: Autopsy specimen of the whole brain. Note the diffuse subarachnoid hemorrhage with an intra-Sylvian hematoma and occlusion by a thrombus of the M2 portion of the right MCA. B: Hematoxylin-eosin staining diagnosed arterial dissection in the intermediate membrane of the right MCA bifurcation and showed a thrombus filling the arterial lumen. C: Gram staining showed a colony of Gram-positive micrococcus involved in bacterial infection in the thrombus located in the occlusive lesion of the M2 portion (D). MCA: middle cerebral artery.

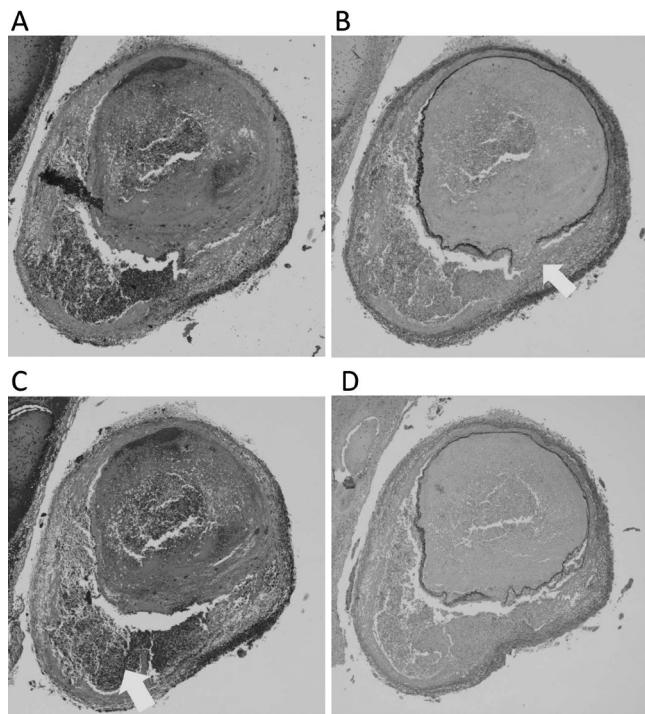


Fig. 5 Hematoxylin-eosin stain (A and C) and Elastica van Gieson stain (B and D) of serial sections demonstrated that internal elastic membrane partially disrupted (arrow in B) and that internal flap and pseudolumen filled with erythrocytes (arrow in C) were observed in the right middle cerebral artery bifurcation.

that bacteria in septic emboli escape through the vasa vasorum, resulting in severe inflammation of the adventitia, and that the infection spreads inwardly.<sup>6)</sup> Arterial pulsation against the weakened vessel wall eventually results in aneurysm formation and enlargement.<sup>7)</sup> The aneurysms are usually fusiform and eccentric, without saccular characteristics, and tend to arise in the anterior circulation.<sup>7)</sup> The embolic hypothesis posits the centrifugal spread of inflammation and proposes that septic emboli occlude the arterial lumen and that destruction spreads outward from the intima to the adventitia.<sup>8)</sup> Histologically, bacterial aneurysms are characterized by acute neutrophil infiltration, marked intimal proliferation, and destruction of the internal elastic lamina; the implicated organisms can be identified by appropriate staining.<sup>1,9)</sup>

Barker (1954) divided the development of bacterial aneurysms into four phases.<sup>10)</sup> The thrombus forms in phase I, in phase II there is aneurysm formation, in phase III the aneurysm ruptures, and in phase IV there is arterial occlusion. Phases I and II are separated by only a very short interval and there are few reports on the radiologic detection of intra-arterial thrombi that develop before the formation of aneurysms in patients with systemic infection.<sup>11)</sup> The clinical detection of thrombus formation is difficult because septic emboli can be small or fragile and patients with embolic stroke can be asymptomatic due to flow compensation by the peripheral collateral circulation. In fact, Wakamoto et al. reported a patient with

early hemorrhage who developed a bacterial aneurysm after a cerebral ischemic attack attributable to a septic embolus.<sup>12)</sup> In their case the interval between aneurysm formation and the ischemic stroke was 3 days, suggesting that aneurysms may form soon after septic embolization. Therefore, we recommend that bacterial aneurysms be assessed thoroughly and addressed soon after a septic embolism is detected.

Several characteristics were rare and clinically important in our case. First, as there were no remarkable infectious findings at the time of her admission, no diagnosis of septic embolism was returned. The patient had past history of repeated urinary infection and might tend to suffer from sepsis. Second, her SAH occurred only two days after the embolic attack. Third, the bacterial embolus that resulted in occlusion of the MCA was pathologically detected at autopsy. Fourth, autopsy revealed arterial dissection and diagnosed inflammation of the arterial wall due to a septic embolus. We discussed the following possibilities related to association of hemorrhagic onset after cerebral ischemia and dissection aneurysm filled with bacterial thrombus: Thrombus embolized in the M2 upper trunk contained Gram-positive bacteria and proliferation of neutrophils and lymphocytes were observed in the adjacent arterial wall, suggesting bacterial inflammation in arterial wall around septic embolus. Septic embolus initially caused embolic infarction in MCA territory and embolized septic embolus caused arterial wall infection. Infectious inflammation made arterial wall fragile, resulting in the rupture of arterial dissection. Obliteration of MCA dissection caused cerebral infarction. Septic embolus occluded MCA and embolized septic embolus caused arterial wall infection. Infectious inflammation made arterial wall fragile, resulting in rupture of arterial dissection. Embolic thrombus occluded MCA and caused hemorrhagic infarction. Septic embolism was associated with embolic infarction and infectious inflammation made arterial wall fragile, resulting in arterial dissection. Although there was no clear evidence of severe systemic infection at the time of admission, her WBC was slightly elevated and she was positive for C-reactive protein. Moreover, she had no past history and no remarkable findings suspecting thrombotic embolism. Together, these clinical and pathological findings suggest that a systemic infectious inflammation led to septic embolization resulting in a cerebral infarct and that local inflammation involving the embolized arterial wall progressed to arterial dissection and rupture.

To our knowledge there have been 4 cases of SAH due to septic embolic infarction (Table 1). All bacterial aneurysms were located in the MCA; they were proximal to M2 in 3 cases. The interval between ischemic onset and rupture was less than 4 days in 3 cases, it was 20 days in one case. These data suggest that septic embolic onset can occasionally be detected before the rupture

**Table 1** Previous reports of subarachnoid hemorrhage due to septic embolic infarction

Author	Age	Gender	Location	Duration	Treatment
Inoue T et al. <sup>3)</sup>	38	M	MCA bifurcation	4 days	Trapping
Yamaguchi S et al. <sup>4)</sup>	56	F	MCA, M2	20 days	Trapping
Wakamoto H et al. <sup>12)</sup>	71	F	MCA, M4	1 day	Trapping
Krapf H et al. <sup>9)</sup>	56	M	MCA, M1	1.5 days	Clipping
Present case	78	F	MCA, bifurcation	2 days	Conservative

Duration: interval between ischemic onset and hemorrhagic event, MCA: middle cerebral artery, SAH: subarachnoid hemorrhage.

of a bacterial aneurysm. However, this is possible only in cases where the ischemic attack exceeds ischemic tolerance. Clinically, focal neurological deficits may be detected depending on the proximity of the occlusion due to septic embolization. The size or fragility of the septic embolus may play an important role in the clinical manifestation of ischemic onset before aneurysmal rupture. Ischemic attack under septic state might be caused by septic embolus and might subsequently cause inflammation into embolized arterial wall to result in aneurysm or dissecting formation. Angiographical evaluation should be useful for prompt diagnosis in acute phase and follow-up.

We document a rare case of SAH followed by ischemic onset due to bacterial arterial dissection. As ischemic onset in the presence of sepsis may alert to subsequent aneurysm formation and rupture, we recommend that affected patients be subjected to thorough examination and follow-up to detect vascular anomalies in the early stage of ischemia to prevent a catastrophic hemorrhagic event.

## Conflicts of Interest Disclosure

The authors report no conflict of interest concerning the case report used in this study or the finding specified in this article.

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*Address reprint requests to:* Atsushi Saito, MD, PhD, Department of Neurosurgery, Aomori Prefectural Central Hospital, 2-1-1 Higashi Tsukurimichi, Aomori, Aomori 030-0910, Japan.  
*e-mail:* satsushi2002@yahoo.co.jp