Deterioration of Vascular Dementia Caused by Recurrent Multiple Small Emboli from Thoracic Aortic Atheroma

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Abstract

We report a case of a 77-year-old man with deteriorating dementia caused by repeated multiple small cerebral embolisms from a thoracic aortic atheroma. Multiple small embolisms were confirmed by diffusion-weighted magnetic resonance imaging (DWI). The patient ultimately died due to aortic dissection. Pathological examinations revealed that no causative embolic source for multiple embolisms could be detected other than severe atheromatous ulcer in thoracic aorta. This case demonstrates that severe aortic atheroma has the potential to precipitate deterioration of vascular dementia. (Internal Medicine 43: 607–611, 2004)

Key words: multiple emboli, aortic atheroma, vascular dementia, DWI, cerebral infarction

Introduction

Vascular dementia is common in Japan and the prevalence is nearly equal to that of Alzheimer’s disease and most of the vascular dementia seen in Japan is due to multiple lacunar infarctions or Binswanger disease (1). The underlying mechanism of these disorders is believed to be severe small vessel disease. Thus, vascular dementia in Japan differs from that commonly seen in the USA and Europe, where common etiology is cortical infarction caused by large blood vessel occlusion or cardioembolism (1).

Diffusion-weighted MRI (DWI) is a sensitive method for detecting early and very slight ischemic changes (2). We can differentiate acute ischemic lesions from chronic ones, because ischemic lesions detected by DWI are diminished and nearly undetectable in the late stage (2). When two or more acute ischemic lesions are detected by DWI, it is conceivable that they have occurred simultaneously or within a brief time period. With wider use of DWI, reports of multiple small cerebral ischemic lesions have increased (3–5). According to these reports, multiple small acute ischemic lesions in different vascular territories are associated with cardiac embolism or artery-to-artery embolism, because it is unlikely that small vessel disease (arteriolsclerosis or arterionecrosis) would induce multiple lacunar-sized ischemic lesions almost simultaneously.

This report describes a patient with vascular dementia, whose cognitive function deteriorated due to recurrent multiple small embolisms from an atheromatous ulcer in the ascending aorta. These recurrent multiple small embolisms were confirmed by DWI.

Case Report

A 77-year-old Japanese man was admitted to hospital on August 16, 2000, with worsening dysphasia, dysarthria, cognitive dysfunction, and gait disturbance. He had been a postal worker until retirement. He had no history of atrial fibrillation (AF), diabetes mellitus, or smoking, but he had consumed as much as 180 ml of Japanese sake daily (average drinker). He had been treated with antihypertensive drugs since the age of 43. Although he had a history of lacunar infarction of the right lenticulostriate artery 10 years earlier, antiplatelet therapy with aspirin had been continued and he had remained almost symptom free for 8 years. His family noted that he became forgetful 2 years before admission, but there had been no abnormal behavior or failure to recognize family and friends. He showed progressive gait disturbance and lost the ability to walk without assistance. In July 2000, he suffered from dysphasia and dysarthria. In
August 2000, he became mute to his family. On physical examination at admission, his temperature was 37.5°C, blood pressure was 178/100 mmHg, and heart rate was 84 bpm, with a regular rhythm. There were no neck bruits. The radial and femoral pulses were palpable on both sides. Lung and heart auscultation was normal. His consciousness was clear. Neurological examination revealed dementia, with a Mini-Mental State Examination (MMSE) score of 12/30, dysarthria, and mild muscle weakness of the left arm and both legs. He had no meningeal irritation signs, papilledema, visual field defects, sensory disturbance, or unilateral neglect. The deep tendon reflexes were normal and pathological reflexes were absent. On laboratory examination, urinalysis showed white blood cells (>100/HPF). The complete blood cell count showed a white blood cell count of 8,900/μl (86.3% neutrophils, 2.9% eosinophils, 0.3% basophils, 4.9% monocytes, and 5.6% lymphocytes), a red blood cell (RBC) count of 3.98×10¹²/μl, hemoglobin of 11.4 g/dl, and a platelet count of 252×10¹³/μl. Liver and renal function tests were normal. The serum fasting plasma glucose, HbA1c, total cholesterol, and triglycerides were normal. C-reactive protein (CRP) was increased, at 7.4 mg/dl. Antinuclear antibody and rheumatoid factor were negative. The prothrombin time (PT) and activated partial thromboplastin time (APTT) were normal. Fibrinogen was 599 mg/dl; fibrin degradation products (FDP) were 8.2 μg/ml; D-dimer was 7.7 μg/ml; and thrombin-antithrombin complex was 13.0 ng/ml. Thyroid function tests were normal. A serological test for syphilis was negative. Arterial blood gas analysis showed a pH of 7.45, a partial pressure of carbon dioxide (Pa CO₂) of 33.1 mmHg, and partial pressure of oxygen (P a O₂) of 68.2 mmHg. Blood cultures were negative, while urine cultures yielded *Escherichia coli* at 10⁷ CFU/ml. The ECG revealed sinus rhythm, left ventricular hypertrophy, and a mild negative T wave in leads V4, V5, and V6. Rhythmic theta waves without spikes were seen in the background of the electroencephalogram. The cardiothoracic ratio (CTR) was 60% on the chest radiograph. Ultrasonography of the abdomen was normal. The CT scan of the chest revealed dilatation of the thoracic artery suggestive of a thoracic fusiform aneurysm and a small nodule (diameter 1 cm) in the right upper lobe of the lung, but no infiltrating shadow suggestive of pneumonia. Emergency T2-weighted MRI showed periventricular hyperintensity and multiple small chronic infarctions in both basal ganglia (Fig. 1). MR angiography showed no apparent stenosis or occlusion of the main arteries in the anterior or posterior circulation. Diffusion-weighted MRI (DWI) showed multiple small ischemic lesions in the territories of the cortical and perforating arteries (Fig. 2).

Diagnoses of multiple small acute cerebral infarctions and urinary tract infection were made. The patient was treated with sodium ozagrel (thromboxane A2 inhibitor) and antibiotics. Although he became able to take food orally a few days after admission, he became relatively mute and remained bedridden and incontinent, requiring constant nursing care. The low-grade fever and CRP gradually fell to normal. When the patient became clinically stable, he was discharged and returned to home on September 13, 2000, with a prescription for cilostazol (phosphodiesterase inhibitor, 100 mg, once per day). On September 25, 2000, he was readmitted to hospital with worsening dysphasia and slight drowsiness. The platelet count was 223×10¹³/μl, and the PT and APTT were normal. Fibrinogen was 505 mg/dl. DWI showed multiple new small lesions in the left cerebellum, left occipital cortex, bilateral frontal cortices, left white matter, and right parietal cortex (Fig. 3). His level of consciousness improved with hydration therapy, but the next day, his condition deteriorated with an MMSE score of 2/30. He had

![Figure 1](image1.png)

**Figure 1.** Horizontal section of T2-weighted MRI at first admission. T2-weighted MRI showed severe periventricular hyperintensity (arrowheads) and multiple small chronic infarctions in both basal ganglia (arrows).

![Figure 2](image2.png)

**Figure 2.** Horizontal section of DWI at first admission (August 16, 2000). DWI showed multiple small acute ischemic lesions (arrows) in the territory of the cortical arteries and the perforating artery.
a sudden cardiopulmonary arrest 1 week after readmission. Despite cardiopulmonary resuscitation efforts, he died.

At autopsy, macroscopic pathological examination revealed that the cause of sudden death was dissection of the thoracic aorta (Stanford A type or DeBakey IIIa type). The left pleural cavity was filled with 1,300 cc of blood, and cardiac tamponade was present. The length of dissection was 8 cm. There was a severe atheroma with irregular ulceration from the arch to the thoracic aorta (Fig. 4). The histological findings in the brain showed cholesterol emboli in the small cortical arteries of the right frontal and occipital lobes (Fig. 5); however, there was no infarction in the territories of these two arteries. Multiple old to subacute infarctions the size of rice grains were seen in the right frontal and occipital lobes, bilateral basal ganglia, and pons; there were micro-infarctions in the cerebellum. Old small infarctions and arteriosclerosis were also seen in the bilateral basal ganglia and thalamus, although there were no ischemic lesions in the hippocampus. No obvious ischemic lesions were detected in the lungs, spleen, or kidneys, but cholesterol emboli were present in the arcuate arteries or interlobular arteries in the kidneys. There were a few senile plaques and neurofibrillary tangles in the brain. However, atherosclerosis of the bilateral common carotid and internal carotid arteries was minimal; the bilateral vertebral, basilar, bilateral renal, and coronal arteries showed moderate to severe atherosclerosis. A small lesion (soybean-size) in the right upper lobe of the lung detected on chest CT was a primary lung cancer (moderately differentiated papillary adenocarcinoma). In addition to this lesion, a small poorly differentiated adenocarcinoma and slight metastasis to the lymph nodes, which were not detected in the chest CT, were also seen.
emboli in the brain; 2) the postmortem examination did not reveal any heart disease that would have induced cardioembolism, such as valve abnormalities or endocarditis; and 3) the patient had no history of atrial fibrillation. A common source of cholesterol emboli is thought to be the rupture of atherosclerotic plaques (20). In this case, the ruptured plaques were located only in the thoracic aorta. Comparing the small, scattered, ischemic lesions seen on DWI with the findings in the brain at autopsy, we found relatively few emboli or new or subacute infarctions. However, our explorations might have been insufficient; very small ischemic lesions do not always become infarcted and small cholesterol or other embolisms might disappear due to phagocytosis by endothelial cells, neutrophils, or macrophages. It was supported by the fact that most of the very small ischemic lesions seen on DWI at the patient’s first admission did not appear in the FLAIR or T2-weighted images taken at the second admission.

Autopsy also showed that the patient had two small nodules of lung cancer. Malignancy sometimes induces disseminated intravascular coagulation (DIC), and DIC induces multiple embolisms via non-bacterial thrombotic endocarditis (NBTE). In this case, we thought that the lung cancer and DIC did not play an important role in the production of multiple microemboli because each lung mass was very small and the DIC was not severe (no clinical signs of DIC; FDP and D-dimer were only slightly elevated on the first admission, and the PT, APTT, and platelet count were normal on both admissions). Although Singh et al reported that multiple embolisms caused by NBTE induced both small and large ischemic lesions detectable with DWI (6), the DWI in our case showed only small multiple ischemic lesions, which differed from the image pattern caused by NBTE.

Approximately 30% of patients display a persistent cognitive decline in verbal memory and language 1 month after coronary artery bypass grafting (21). A possible cause of the cognitive dysfunction after cardiac surgery is thought to be microembolism from aortic arch atheromas, secondary to mechanical manipulation. Intraoperative transcranial Doppler studies demonstrate the release of microemboli when the aortic clamp is removed (22), and the presence of emboli correlates with cognitive impairment (22, 23).

Although primary and secondary preventive treatment for artery-to-artery embolism from large vessels has not yet been established in large randomized trials, a glycoprotein IIb/IIIa receptor antagonist (24) or 3-hydroxy-3-methylglutaryl coenzyme-A reductase inhibitors (statins) (25) may be effective. The former agents inhibit platelet aggregation, and statins not only reduce cholesterol levels, but also stabilize atheromas (26). We speculate that these drugs have the potential to prevent the progression of dementia in some vascular dementia patients with severe aortic arch atheroma.

The majority of vascular dementia seen in elderly Japanese patients is due to multiple lacunar infarctions orBinswanger disease (1). Although the mechanism underlying vascular dementia in Japan is generally considered to be repeated attacks of small vessel disease, our case suggests that

Discussion

Multiple cerebral embolisms can occur with several conditions, such as atrial fibrillation (4), endocarditis (6), vasculitis (7, 8), severe atherosclerosis of the major vessels (3, 4), as a complication of heart surgery (9) or cerebral angiography (10), and in coagulopathy (6, 11). Common conditions that induce multiple acute cerebral embolisms include artery-to-artery embolism caused by severe atherosclerosis or cardiac embolism (3–5). Moreover, patients with vasculitis have multiple ischemic strokes in more than one arterial circulation (7, 8). Vasculitic strokes are usually located in the deep arterial territories, rather than in the cortical or border zone territories (7).

Several authors have described thoracic aortic atheroma as associated with an increased risk of cerebral infarction because of the potential for cerebral embolism (12–14). Transesophageal echocardiography (TEE) is a useful technique for detecting aortic arch atheromas, and transcranial Doppler ultrasound (TCD) is also capable of detecting microembolic material in the arteries of the circle of Willis by recording high-intensity transient signals (HITS). TEE and TCD can be conducted noninvasively. Although the microemboli detected by TCD do not always induce ischemic lesions of the brain, many authors have reported that HITS are associated with an increased risk of symptomatic ischemic stroke, especially among ischemic patients with carotid artery stenosis (15–17) or a cardiac embolic source (16, 18). Rundek et al detected HITS in 70% of elderly patients with a large (>4 mm thick) aortic atheroma and no other cardiac embolic sources (19). She also reported that atheromas with ulceration or mobile components (complex atheromas) were associated with a higher frequency of HITS than were noncomplex atheromas. In the present case, DWI detected microemboli in the anterior and posterior circulation. Based on this, we considered the embolic source in this case to be either the heart or the aortic atheroma. We finally concluded that the source of the embolism was the thoracic aortic atheroma because 1) the postmortem examination revealed severe atheroma of the thoracic aorta and cholesterol emboli in the brain; 2) the postmortem examination did not
we must pay attention not only to small vessel disease, but also to artery-to-artery embolism from large vessel atheroma in elderly patients with vascular dementia. If necessary, we should examine DWI, TTE or TCD and implement an appropriate preventive strategy.

References