

## Lacunar Syndrome Associated with Paradoxical Brain Embolism

Yoshiomi Shimizu<sup>1</sup>, Ryuzo Fukunaga<sup>1</sup>, Makoto Kinoshita<sup>2</sup>, Shiro Yamamoto<sup>2</sup>,  
Kouji Kajiyama<sup>2</sup> and Takenori Yamaguchi<sup>2</sup>

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### Abstract

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We report a patient who developed lacunar syndrome due to left upper pons infarction after performing leg exercises associated with paradoxical brain embolism. A 32-year-old man developed right arm weakness and moderate dysarthria following leg exercise. Brain MRI showed a paramedian pontine infarction of the left upper pons, and contrast transesophageal echocardiographic examination indicated that the patent foramen ovale was the embolic source. Simultaneous RI venography examination of the lower limbs identified deep venous thrombosis in the right leg as a paradoxical emboligenic source. We concluded that the presence of lacunar syndrome suggests that this mechanism was responsible for the paradoxical brain embolism.

**Key words:** patent foramen ovale, paradoxical embolism, lacunar syndrome, transesophageal echocardiography

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### Introduction

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The current consensus is that cardiogenic brain embolism is a common cause of large vessel occlusion and massive cortical infarction. Recently, Steiner et al (1) who investigated paradoxical brain embolism, which is one form of cardiogenic brain embolism, among patients with patent foramen ovale (PFO), suggested that it also might affect supratentorial large vessel occlusion and occipital and infratentorial infarction. However, the relationships between small vessel occlusion, so-called brain-perforating artery occlusion, and paradoxical brain embolism have not yet been fully clarified (1, 2). In order to contribute to a better understanding of these relationships, we herein report the highly relevant case of a patient who, after performing leg exercises, developed lacunar syndrome due to small paramedian pontine infarction of the left upper pons associated with paradoxical brain embolism.

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### Case Report

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A 32-year-old man developed right-sided motor weakness

immediately after performing three hours of aerobic leg exercises, and his temporal profile was the sudden onset type suggestive of embolism. He also had apparent right-sided leg pain since admission. Neurological examination showed right arm weakness and moderate dysarthria. There were no other cranial nerve symptoms, and intelligence and consciousness were normal.

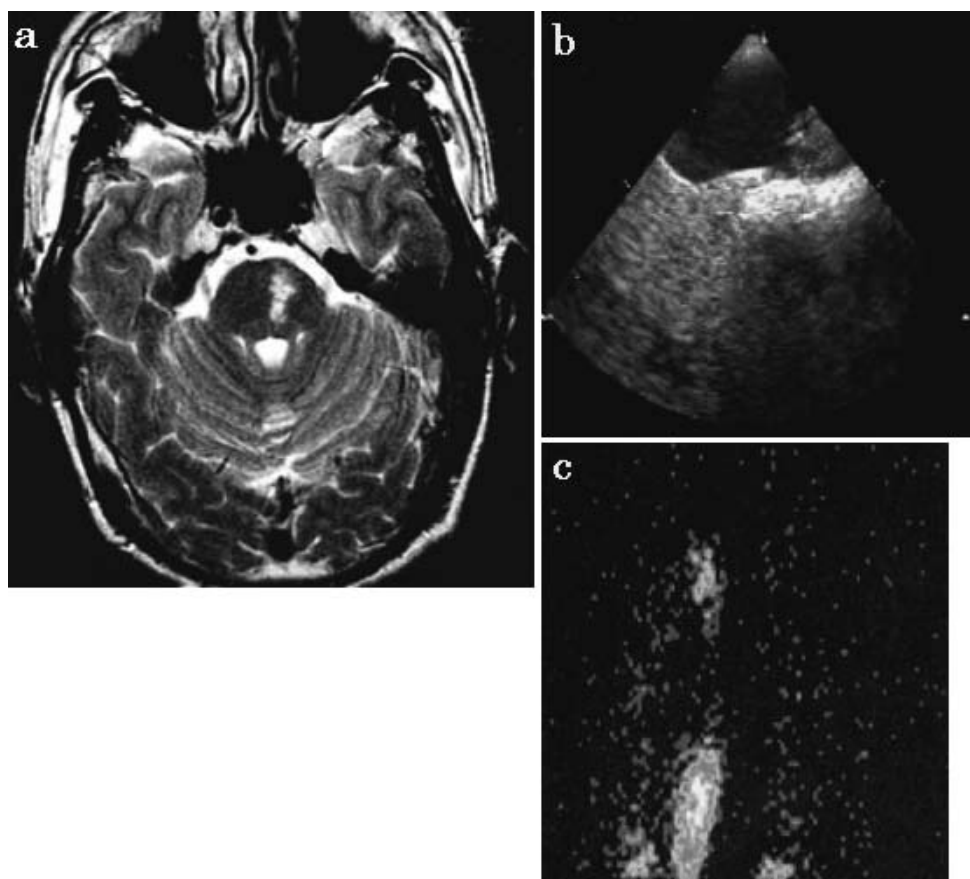
The initial NIH stroke scale was 3 points. Thus, we diagnosed this patient as having lacunar syndrome (dysarthria-clumsy-hand syndrome). Following admission, initial cerebral brain CT and CT angiography did not show any apparent abnormal lesions. Hematological studies including tests for coagulopathy (protein C and protein S deficiency, antithrombin III deficiency, and antiphospholipid antibody syndrome), serum homocysteine and Lp(a) concentration, and the antibody titer of collagen disease (ANA, P-ANCA, and C-ANCA) were all normal. Results of carotid ultrasound and transthoracic echocardiography were also normal. On 24-hour Holter electrocardiogram, there were no signs of atrial fibrillation. The patient had a history of thrombophlebitis in the lower limb related to bone fracture of the right leg. Since the patient had no traditional atherosclerotic risk factors such as hypertension, diabetes mellitus, hypercholes-

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<sup>1</sup> Department of Internal Medicine, Hoshigaoka Kouseinenkin Hospital, Hirakata and <sup>2</sup> Department of Neurology, Japan Labour Health and Welfare Organization, Kansai Rosai Hospital, Amagasaki

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Correspondence to Dr. Yoshiomi Shimizu, hoshim1010@hotmail.co.jp



**Figure 1.** a: Magnetic resonance imaging (T2-weighted) of the brain showing left paramedian pontine infarction. b: Contrast transesophageal echocardiography shows right-to-left shunt via the patent foramen ovale. Agitated microbubbles are seen in the right atrium. c: RI venography examination of the late phase of the lower limbs identified deep venous thrombosis of the right leg.

terolemia, and smoking habit, we suspected this brain stem infarction involving the pons to be cryptogenic stroke. Antiplatelet treatment was administered for two weeks to facilitate recovery from neurological impairment. Brain MRI performed on the day after treatment was started indicated the presence of an apparent infarction of the left upper pons, which accounted for the proximal occlusion of the paramedian pontine artery originating from the basilar artery (Fig. 1a). However, there was no evidence of any intracranial stenotic lesion in the vertebrobasilar artery on MR angiographic imaging findings. Because we suspected that this cryptogenic ischemic stroke was associated with right-to-left shunt from the PFO, contrast transesophageal echocardiography (TEE) combined with a previously reported contrast microbubble method was used for PFO detection (3). Contrast TEE examination identified the apparent large PFO (maximal diameter: 3 mm) as an embolic source (Fig. 1b). However, there were no other embolic sources seen on TEE examination in the ascending aorta and aortic arch which could cause cryptogenic stroke. Simultaneous RI venography examination of the lower limbs identified deep venous thrombosis (DVT) in the right leg as a paradoxical emboligenic source (Fig. 1c). However, there was no pulmonary infarction on pulmonary V/Q scintigram. We finally con-

cluded that the small infarction of the left upper pons was associated with PFO and DVT. One month later, after oral anticoagulation treatment for the treatment of DVT and secondary stroke prevention as well as stroke rehabilitation, the patient had recovered completely and was discharged from our hospital (4).

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## Discussion

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This is an interesting case report of a paradoxical brain embolism of a small brain stem-perforating artery. We are reasonably confident that the lesion seen on MRI was a paradoxical embolization into the basilar perforator artery, rather than a manifestation of atherosclerotic small vessel occlusion based on the patient's clinical history (young age, history of thrombophlebitis, sudden onset during exercise suggesting PFO route, and absence of atherosclerotic risk factors), and thought that this cryptogenic stroke being induced by a cerebral embolism associated with PFO was highly doubtful.

It has often been considered difficult to prove the mechanism of paradoxical embolism because the diagnostic criteria are not generalized and the causal relationships between stroke and PFO remain controversial (5-7). Meister et al

suggested that the diagnostic criteria for paradoxical brain embolism were: systemic or cerebral embolism in the absence of a left-sided cardiac origin, apparent right-to-left cardiac shunt, elevated right heart pressure, and apparent DVT (8). Although not all cases meet these diagnostic criteria, our case met all.

There have been only a few studies on the prevalence of DVT in stroke patients with PFO because the rate of identification of DVT in embolic stroke patients is very low (9, 10). Yasaka et al (10) suggested that only 3.2% of cryptogenic stroke among patients with PFO fit their criteria for definite paradoxical brain embolism on imaging findings using ultrasonography and/or RI scintigraphy for the detection of DVT. These findings also indicate that the present case is rare.

To date, the relationships between lacunar syndrome and paradoxical brain embolism associated with PFO have not been fully investigated and are not even considered very interesting because lacunar syndrome was considered to be due to characteristic atherosclerotic vascular lesions (11). Moreover, several previous case studies demonstrated the relationship between the roles of PFO and stroke subtypes. These studies have demonstrated that the role of PFO was not so important because, in patients with lacunar infarction and/or lacunar syndrome, detection of the cardiac source of embolism usually represents an incidental finding (2, 12, 13). However, several studies have emphasized that a variety of etiologies can cause small vessel occlusions, and currently, approximately 10% of typical small vessel occlusion are related to cardiogenic embolism (14, 15). In particular, Toyoda et al (16) suggested that the etiology of a pontine infarction such as that visualized on our MRI is attributable to different mechanisms, such as cardioembolism, artery-to-artery embolism, or atherosclerosis of the basilar artery af-

fecting pontine branches. In the present case, a small paramedian pontine infarction of unknown etiology was associated with the presence of PFO. This would constitute a rare but important cause of lacunar syndrome. A practicing physician might diagnose patients carefully in individual cases if the occult cardiac source of an embolism such as PFO is detected in patients with lacunar syndrome.

Although the pulmonary V/Q scintigram and brain MRI we conducted did not reveal pulmonary infarction or other supratentorial or superficial cortical multiple infarctions, which are important complications of systemic embolism due to paradoxical embolism, it remains unknown why small emboli migrate to and reach only the small branch or penetrating artery via PFO. Patient age, the circumstances surrounding onset, and degree of DVT may be related to the size of the infarction.

One possible mechanism which may help to explain our case was recently reported, whereby Ueno et al (17) suggested the relationship between lacunar stroke and PFO. They reported that PFO was more frequently detected in lacunar stroke patients without hypertension and diabetes mellitus. They emphasized that increasing pressure in the left ventricle may prevent right-to-left shunt via PFO. This might partly explain the mechanism of paradoxical embolism into the small perforator artery. However, several questions still remain regarding the explanation of the whole mechanism. Further studies are needed to identify the stroke mechanism in such cases.

In summary, we describe a case of lacunar syndrome occurring as a result of paradoxical brain embolism due to PFO as a potential embolic source. Physicians should note that this mechanism may account for the etiology of small vessel occlusive disease in young persons.

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