Case Report

Thrombolysis in Ischemic Stroke Patients with Isolate Pulmonary Arteriovenous Malformations

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Pulmonary arteriovenous malformations are rare cause for ischemic stroke. British Thoracic Society Clinical Statement considered insufficient evidence of safety or clinical benefit to recommend thrombolysis for stroke with pulmonary arteriovenous malformations. For pulmonary arteriovenous malformations with hereditary hemorrhagic telangiectasia, bleeding risk after thrombolysis is high, while for isolate pulmonary arteriovenous malformations, bleeding risk is much lower. We here present 2 cases of ischemic stroke with isolate pulmonary arteriovenous malformations treated with thrombolysis. Right-to-left shunt was found by contrast-enhanced transcranial Doppler in these 2 patients and pulmonary arteriovenous malformations were confirmed by contrast-transthoracic echocardiography and thoracic computed tomography angiography. Neurological signs improved after intravenous thrombolysis without bleeding complication.

Key Words: Thrombolysis—stroke—pulmonary arteriovenous malformations—right-to-left shunt

Pulmonary arteriovenous malformations (PAVMs) are rare disorders with an incidence of 2-3 per 10,000.[1] British Thoracic Society Clinical Statement did not recommend thrombolysis for ischemic stroke with PAVMs because of insufficient clinical evidence.[2] Most PAVMs are found in patients of hereditary hemorrhagic telangiectasia (HHT), for whom thrombolysis may be accompanied by a high risk of bleeding. But for isolate PAVMs, bleeding risk is much lower. We report 2 ischemic stroke patients caused by isolate PAVMs who were treated with intravenous thrombolysis and achieved good outcomes.

Case Reports

Case 1

A 68-year-old female was admitted to our hospital for numbness of right extremities and dysarthria. She had no history of hypertension, diabetes mellitus, nor atrial fibrillation. No symptom of epistaxis and gastrointestinal bleeding occurred before. Neurological examination showed hypoalgesia of right extremities and blur speech with National Institute of Health stroke scale (NIHSS) of 3. Prothrombin time was 11.2 seconds and D-dimer was 1720 μg/L. Thrombolysis with 0.9 mg/kg alteplase was administered 110 minutes after symptom onset. Dysarthria alleviated and numbness disappeared 2 hours after thrombolysis. Twenty four hours later, 200 mg Asprin was given every day. Focal hyperintense lesion of left hemisphere was noticed on diffuse weighted imaging (Fig 1, A). Cranial computed tomography angiography showed no stenosis of large arteries. No atrial fibrillation was detected on a Holter monitor. Curtain form of microbubbles was detected by contrast-enhanced transcranial Doppler (Fig 1, B). Then contrast-transthoracic echocardiography showed extensive opacity of right

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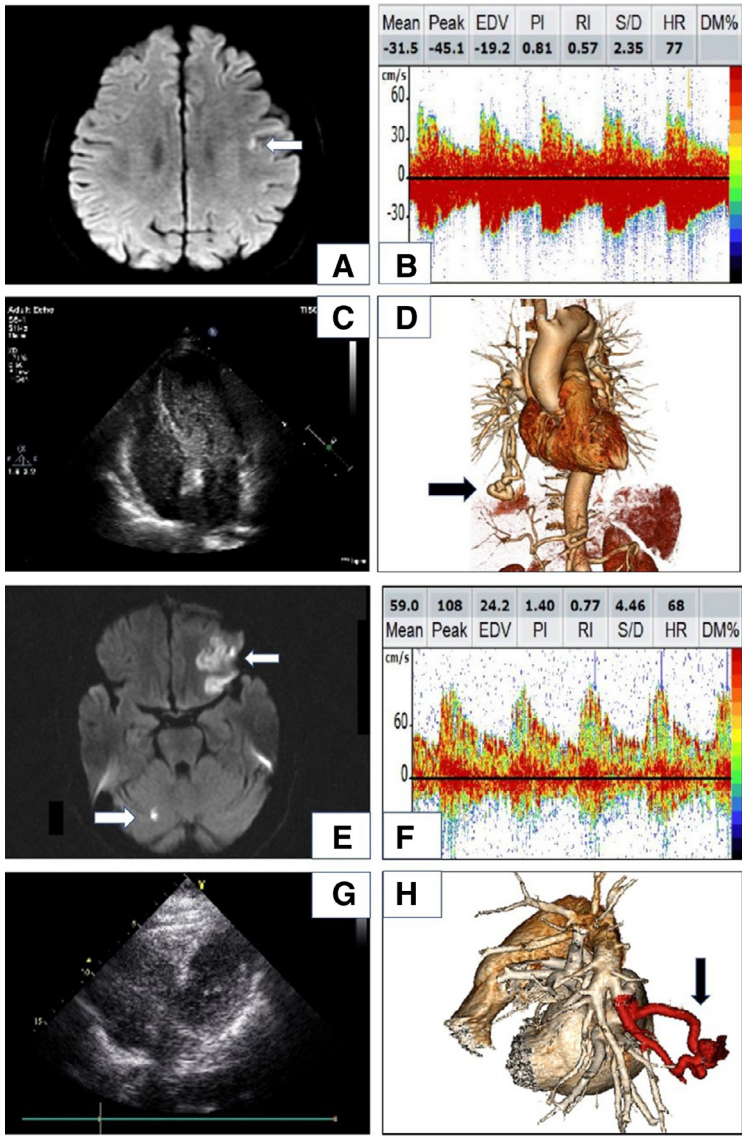

Figure 1. *Case 1. Hight intensity on the cortex of left hemisphere on diffuse weighted imaging (arrow) (A). Curtain form of microbubbles were detected in the right middle cerebral artery on cTCD (B). Extensive opacity of right ventricle shown on cTTE (C). PAVM in the lower lobe of the right lung confirmed by thoracic CTA (arrow) (D). Case 2. Multiple infarcts in the right frontal lobe and right cerebellum on diffuse weighted imaging (arrow) (E). Curtain form of microbubbles were detected in the right vertebral artery on cTCD (F). Microbubbles in the left atrium shown on cTTE (G). Thoracic CTA confirmed PAVM in the lower lobe of the left lung (H).* Abbreviation: *CTA, computed tomography angiography; cTCD, contrast-enhanced transcranial Doppler; cTTE, contrast-transthoracic echocardiography; PAVM, pulmonary arteriovenous malformations. (Color version of figure is available online.)*

ventricle without outlining the endocardium 4 cardiac cycles after agitated saline injection (Fig 1, C). Thoracic computed tomography angiography confirmed a simple PAVM in the lower lobe of the right lung (Fig 1, D). No deep venous thrombosis was found by venous ultrasound in both lower extremities. Embolotherapy was not administered because of financial reason, and aspirin 100 per day was given to the patient after discharge. No sequela existed and no stroke recurred on follow-up 6 months later.

Case 2

A 73-year-old female was sent to the emergency department because of hemiplegia of the right side and global aphasia. Right side gaze palsy and right hemianopia were found on neurological examination and NIHSS scale was 27. Prothrombin time was 10.9 seconds and D-dimer was 750 μg/L. Thrombolysis with 0.9mg/kg alteplase was given after contraindication was ruled out and onset to needle time was 3 hours. Then angiography showed no obstruction or stenosis of large cerebral arteries. 200mg aspirin per day was given 24 hours after thrombolysis. 2 days later, infarction was found on left middle cerebral artery territory and right cerebellum (Fig 1, E). Holter monitor showed sinus rhythm and transesophageal echocardiography found no proof of patent foramen ovale. Curtain form of microbubbles was found in middle cerebral arteries during the

examination of contrast-enhanced transcranial Doppler (Fig 1, F). More than 10 microbubbles were founded in the left atrium during 5 cardiac cycles on contrast-transthoracic echocardiography (Fig 1, G). Isolate pulmonary arteriovenous malformation was confirmed by CT angiography (Fig 1, H). Deep vein thrombosis was not found in venous ultrasound of the lower extremities. Though we recommended embolotherapy, the patient chose conservative therapy. Neurological signs improved and NIHSS was 4 when discharged from the hospital. The neurological symptom was stable and modified Rankin Scale was 3 when followed-up 6 months later.

Discussion

PAVMs are pulmonary vascular anomalies consisting of supply arteries, sacs, and drainage veins.[3] Through the direct communication, thrombi from the pulmonary artery can reach the left atrium without filtration of capillary vessels. Thus, important neurological complications including stroke, brain abscesses, and migraine can be caused.[4] As a rare etiology, thrombi from the right side of the heart can travel to the left atrium through right-to-left shunt causing ischemic stroke.

There are some researches concerning the relationship between the number of PAVMs and stroke. The results are inconsistent. Moussouttas et al found a greater number of malformations were associated with more radiologic evidence of cerebral ischemia.[5] On the contrary Shovlin et al found that risk of clinical strokes was not associated with the number of PAVMs. He also found the diameter of feeding artery $\leq$3 mm had no relationship with the incidence of ischemic stroke.[6] Thus, till now, all radiologically visible PAVMs were recommended to be considered for interventional therapy to reduce risks from paradoxical emboli.[2]

Because PAVMs are rare causes for stroke, the literature about medical therapy in the acute stage of stroke is lacking and the safety of thrombolysis for PAVMs-related stroke is not established.[2] About 80%-90% of PAVMs are diagnosed in patients with HHT.[7] Clinical diagnostic criteria for HHT include epistaxis, mucocutaneous telangiectasia, visceral AVMs, and family history.[8] There are some case reports on thrombolysis for HHT patient. Kane et al gave thrombolysis to a patient of right posterior artery occlusion with HHT. A good neurological recovery was obtained without bleeding complication.[9] McGrath et al treated a patient with HHT misdiagnosed as pulmonary embolism who was treated with anticoagulation and thrombolysis, resulting in upper gastrointestinal hemorrhage afterwards.[10] However, to the best of our knowledge, no reports of thrombolysis for isolate PAVMs-related stroke have been published before. Our 2 patients were diagnosed with isolate PAVMs as they did not meet the criteria of HTT. Good results were achieved after intravenous thrombolysis without any bleeding complication. Thus, we consider thrombolysis may be a choice for isolate PAVMs-related stroke within the time window, while thrombolysis may be cautious based on the haemorrhagic diathesis due to HTT. Careful inquiring of case history for HTT symptom such as epistaxis and gastrointestinal bleeding is important before thrombolysis.

Similar to the patent foramen ovale, the mechanism of PAVMs-induced ischemic stroke is paradoxical embolism. No thrombosis was found in femoral and popliteal veins by ultrasound in our 2 patients. The embolus might originate from the pelvic vein, hemorrhoid vein, or other locations upstream of PAVM. Based on the experience in the treatment of patent foramen ovale, we chose antiplatelet therapy for secondary prevention and no recurrence of stroke was found on 6-month follow-up.

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