

Multiple Cerebral Infarctions Due to Patent Foramen Ovale in a Patient with Eosinophilic Granulomatosis with Polyangiitis

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A 51-year-old man was diagnosed with eosinophilic granulomatosis with polyangiitis 6 years ago due to asthma, sinusitis, hypereosinophilia, and peripheral neuropathy based on the diagnostic criteria of American College of Rheumatology, and corticosteroid therapy achieved a remission. One year ago, he was hospitalized due to deep venous thrombosis (DVT) and pulmonary embolism, and rivaroxaban was administered. He was admitted to our hospital for acute onset of diplopia and right hemiparesis. Peripheral blood examinations disclosed leukocytosis with hypereosinophilia. Perinuclear anti-neutrophil cytoplasmic antibodies were positive. Diffusion-weighted imaging showed multiple fresh ischemic lesions. Chronic ischemic lesions were seen in subcortical cerebral region. No stenosis or occlusion was shown in extracranial and intracranial arteries on magnetic resonance angiography. Ultrasonography of leg vein showed DVT. Right-to-left shunt through patent foramen ovale after Valsalva maneuver was seen on transesophageal echocardiography. Treatment with corticosteroid and cyclophosphamide alleviated clinical deterioration. Rivaroxaban was changed to warfarin. Diplopia and muscle strength of right limbs were improved. This is a first case of multiple cerebral infarction caused by paradoxical embolism due to patent foramen ovale with DVT based on hypercoagulable state of hypereosinophilia. Overall this case illustrates that eosinophilic granulomatosis with polyangiitis can be a risk factor for multiple cerebral infarction in the systemic phase and that transesophageal echocardiography and ultrasonography of leg vein should be conducted in stroke patient with eosinophilic granulomatosis with polyangiitis.

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Case Report

A 51-year-old man with concomitant asthma, sinusitis, hypereosinophilia, and peripheral neuropathy was diagnosed with eosinophilic granulomatosis with polyangiitis (EGPA) based on the diagnostic criteria of American College of Rheumatology 6 years previously; corticosteroid therapy achieved remission. One year previously, he was hospitalized because of deep venous thrombosis (DVT) and pulmonary embolism; rivaroxaban was administered. He was hospitalized for acute onset diplopia due to

oculomotor nerve palsy and right hemiparesis (medical research council grading for muscle power, 4).

Peripheral blood examinations revealed leukocytosis with hypereosinophilia (white blood cell, 12200/ μ L; eosinophils, 33.5%). Prothrombin, activated partial thromboplastin times, protein C, protein S, anti-thrombin III, creatine kinase and troponin were normal. D-dimer (1.50 μ g/mL), thrombin-antithrombin complex (26.4 ng/mL), C-reactive protein (5.4 mg/dL), erythrocyte sedimentation rate (1 h, 41 mm; 2 h, 54 mm), and IgE (1072 IU/L) were elevated. Perinuclear anti-neutrophil cytoplasmic antibodies were positive. Antiphospholipid-antibodies and tumor markers (CEA, CA19-9, SCC and PSA) were negative.

Diffusion-weighted imaging revealed multiple fresh ischemic lesions (Fig 1A). Chronic ischemic lesions were observed in the subcortical cerebral region (Fig 1B). Magnetic resonance angiography revealed no stenosis or occlusion in the extracranial and intracranial arteries. Electrocardiography revealed normal sinus rhythm. Transthoracic echocardiography was normal. Leg vein ultrasonography revealed DVT (Fig 1C). Transesophageal echocardiography revealed right-to-left shunt through the patent foramen ovale after the Valsalva maneuver (Fig 1D). There was no plaque in aorta.

He was administrated intravenous methylprednisolone (500 mg/day for 3 days) that was replaced by oral prednisolone (30 mg) and cyclophosphamide (50 mg/day). Rivaroxaban (15 mg/day) was changed to warfarin (2.5 mg/day). At discharge, oral prednisolone, cyclophosphamide, and warfarin were continued. Diplopia and muscle strength of the right limbs were improved (medical research council grading, 5). At the fourth month follow-up, ESR and total eosinophil counts were normal.

Discussion

Multiple ischemic cerebral infarctions are rare in patients with EGPA.^{1,2} Cardioembolism due to eosinophilic endomyocarditis is the underlying etiology of multiple ischemic cerebral infarctions in EGPA.^{1,3-5} Eosinophilic infiltration produced extensive endomyocardial fibrosis and overlying thrombosis. In a recent report, thrombus on the aorta wall caused multiple cerebral infarctions.⁶ DVT frequency was higher in EGPA than in other anti-neutrophil cytoplasmic antibodies-associated vasculitis.⁷ Eosinophilic cationic protein may promote fibrinogenesis and endothelial cell activation, consequently developing ischemic stroke.⁸

He was diagnosed with paradoxical embolism due to patent foramen ovale with DVT on the basis of the hypercoagulable state of hypereosinophilia. Thus, transesophageal echocardiography and leg vein ultrasonography should be performed in stroke patients with EGPA.

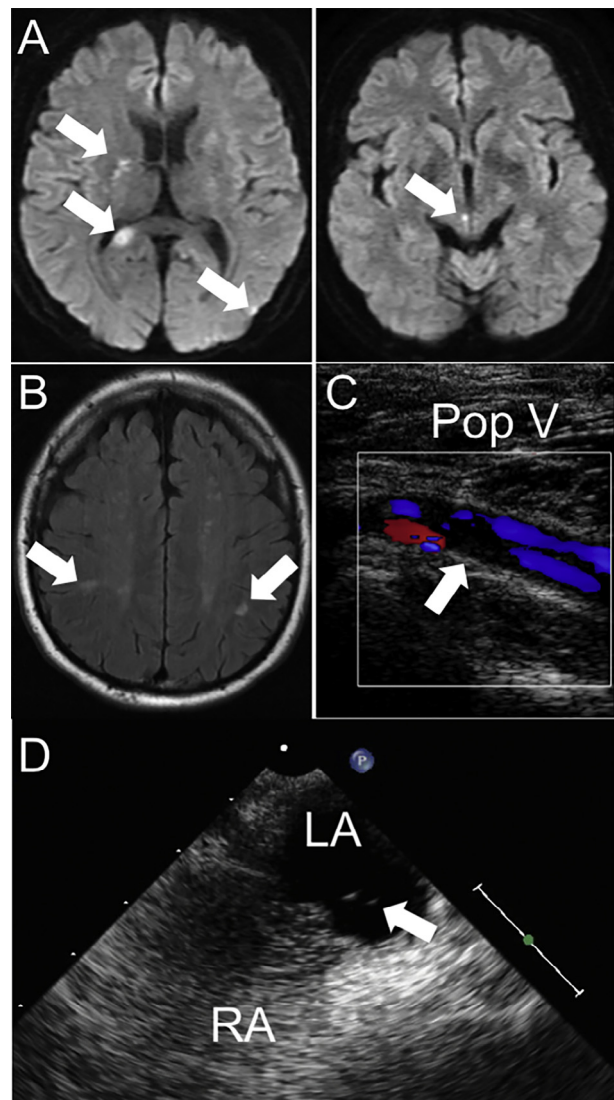


Figure 1. Pop V: Popliteal vein, RA: Right atrium, LA: Left atrium. (A) Diffusion-weighted imaging showed multiple ischemic lesions in bilateral thalamus, left radiate crown, midbrain, and left parietal lobe. (B) Fluid attenuated inversion recovery revealed chronic ischemic lesions in subcortical cerebral region. (C) Ultrasoundsonography of leg vein showed deep venous thrombosis in right popliteal vein. (D) Microbubble test on transesophageal echocardiography demonstrated right-to-left shunt through patent foramen ovale after Valsalva maneuver.

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