

Repeated Episodes of Ischemic Stroke over a Short Period in a Patient with Essential Thrombocythemia on Anticoagulant Therapy

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A 69-year-old man who had essential thrombocythemia, for which he was taking no medications, suddenly developed aphasia and right hemiplegia and was admitted to the hospital. He was thought to have had an embolic stroke and was initially treated with warfarin. Although the international normalized ratio was in the therapeutic range, he had 3 additional ischemic stroke episodes with the same symptoms after the index stroke. Magnetic resonance angiographic examinations revealed serial changes in middle cerebral artery stenosis. After administration of an antiplatelet agent and hydroxyurea, he had no additional strokes. **Key Words:** Anticoagulant—antiplatelet—embolic stroke—essential thrombocythemia—stroke—magnetic resonance angiography.
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Essential thrombocythemia (ET) is a myeloproliferative disease with a high incidence of thrombotic complications. Ischemic stroke (IS) caused by ET accounts for 0.25% to 0.54% of all cases of IS.^{1,2} ET is a rare cause of strokes, and the distinctive characteristics of strokes associated with ET have not been well documented. We present a patient who had repeated IS events and had serial changes in middle cerebral artery (MCA) stenosis.

Case Report

A 69-year-old man who suddenly developed severe global aphasia, right unilateral spatial neglect, and right

hemiplegia—symptoms that led to a score of 24 on the National Institutes of Health Stroke Scale (NIHSS)—was admitted to our affiliated hospital. He had a history of hypertension, and after being transferred to our hospital was found to have ET. He was taking no medications at the time of admission. His laboratory data at admission revealed high white blood cell ($19,300/\text{mm}^3$) and platelet ($87.4 \times 10^4/\text{mm}^3$) counts and a normal red blood cell count ($472 \times 10^4/\text{mm}^3$). He had high levels of D-dimer (2.3 $\mu\text{g}/\text{mL}$) and fibrin fibrinogen degradation products (6.6 $\mu\text{g}/\text{mL}$) and normal fibrinogen (220 mg/dL) and antithrombin (100%) levels. Initial diffusion-weighted magnetic resonance imaging (DWMRI) scans revealed vast ischemic changes in the middle cerebral artery (MCA) area (Fig 1A), and magnetic resonance angiography revealed diffuse stenosis of the left MCA (Fig 1C). During the first couple of days after admission, his neurologic deficits improved to slight aphasia and slight right hemiparesis, corresponding to an NIHSS score of 3 (Fig 1B). Although the detailed examinations showed no evidence of embolic sources, he was treated with warfarin because of the high D-dimer and FDP levels. Although he was appropriately treated with

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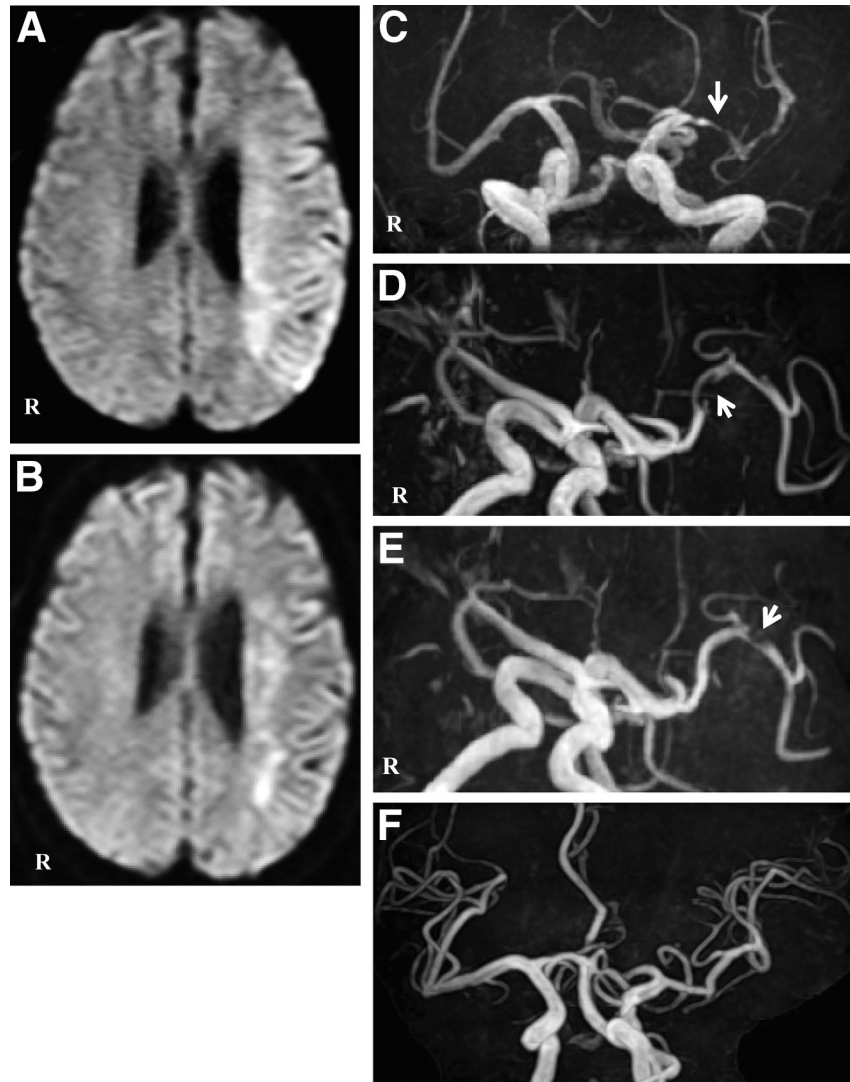
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Figure 1. Diffusion-weighted magnetic resonance imaging and magnetic resonance angiography. (A) Diffusion-weighted magnetic resonance imaging on day 1 reveals vast ischemic change in the area of the left middle cerebral artery (MCA), including the cerebral cortex. (B) Diffusion-weighted magnetic resonance imaging on day 16 reveals only white matter changes. Magnetic resonance angiography performed on days 1 (C), 16 (D), and 18 (E) reveals stenosis of the left MCA migrating distally with time. Magnetic resonance angiography performed on day 32 (F) shows no stenosis. Arrows (C-E) indicate the stenosis in the left MCA.



warfarin (INR \sim 2.0), he had 3 additional similar episodes of transient aphasia and right hemiplegia, worsening on days 16, 25, and 32. Follow-up MRI scans revealed stenosis migrating to the distal MCA (Fig 1D-F). After 4 IS episodes, he was transferred to our hospital and started on cilostazol and hydroxyurea after being referred to a hematologist. He had no additional stroke episodes over 1 year of follow-up.

Discussion

Patients with ET tend to have the embolic type of stroke, and one mechanism of stroke is the formation of thrombi in arteries.^{1,3} The precise mechanism of thrombus formation is unclear, but activation of platelet and coagulation systems and vascular endothelial damage might be involved. In ET patients, plasma protein C and protein S levels are decreased, and soluble P-selectin and soluble CD40 ligand, which are released from the activated platelets, are

increased.^{4,5} Plasma concentrations of thrombomodulin and von Willebrand factor, which are markers of endothelial cell damage, are significantly elevated.⁶ The stroke in the present patient might have been caused by intramural thrombus that formed on the damaged endothelium of the MCA. In addition, the migration of thrombus from the proximal to the distal MCA might have led to the recurrence of stroke.

Hydroxyurea and low-dose aspirin are effective in the prevention of thromboses.^{7,8} Anticoagulant therapy has been anecdotally effective,⁹ but it sometimes fails to prevent recurrent thrombosis.¹⁰ Clinicians should pay attention to high platelet counts and consider additional therapies after the first recurrence.

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