A Case of Multiple Cerebral Infarction Preceding Acute Exacerbation of Idiopathic Thrombocytopenic Purpura

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Background: Although it was suggested that idiopathic thromobocytopenic purpura (ITP) can be a paradoxical cause of cerebral infarction, previous reports indicate that cerebral infarction associated with ITP occurs when thrombocytopenia is already evident at the onset of cerebral infarction. *Case report:* We report a case of multiple cerebral infarction that preceded acute exacerbation of ITP. An 80-year-old woman with a history of ITP presented with tetraplegia, and brain magnetic resonance imaging revealed multiple infarction in bilateral cerebral and cerebellar hemispheres. For ITP, she was treated with oral prednisolone and subcutaneous injection of thrombopoietin receptor agonists. Her platelet count was within the normal range at the onset of cerebral infarction. Medical work-up did not reveal the obvious causes of her multiple cerebral infarction. On day 10 of hospitalization, she showed melena and oral hemorrhage and her platelet count markedly decreased. Her platelet-associated IgG level was elevated and a diagnosis of acute exacerbation of ITP was made. She was treated with intravenous immunoglobulin and her platelet count increased moderately. However, her neurological symptoms and cerebral infarction on magnetic resonance imaging deteriorated accompanied by hemorrhagic transformation. Finally, she died of respiratory failure. *Conclusions:* Our case suggests that thrombophilia accompanied by ITP can precede actual exacerbation of ITP and we have to consider ITP as a possible cause of multiple cerebral infarction, even when the platelet count is within the normal range at the onset of cerebral infarction.

Key Words: Multiple cerebral infarction—idiopathic thrombocytopenic purpura (ITP)—acute exacerbation—platelet-associated IgG—platelet microparticles

Case Report

Although idiopathic thromobocytopenic purpura (ITP) is usually associated with severe bleeding,[1] it may also be associated with cerebral infarction. Previous reports suggest that cerebral infarction associated with ITP occurs, when thrombocytopenia is already evident at the onset of cerebral infarction.[2-7] Herein, we report a case of multiple cerebral infarction preceding acute exacerbation of ITP.

An 80-year-old woman was admitted to our hospital for sudden-onset tetraplegia. Three years before, she was diagnosed as having ITP and treated with oral prednisolone and subcutaneous injection of a thrombopoietin receptor agonist (romiplostim), which maintained her platelet count within 150-250 $\times$ 10^9/L. Brain magnetic resonance imaging (MRI) showed multiple high-intensity lesions on diffusion-weighted images, which are indicative of acute cerebral infarction (Fig 1, A and B). MR

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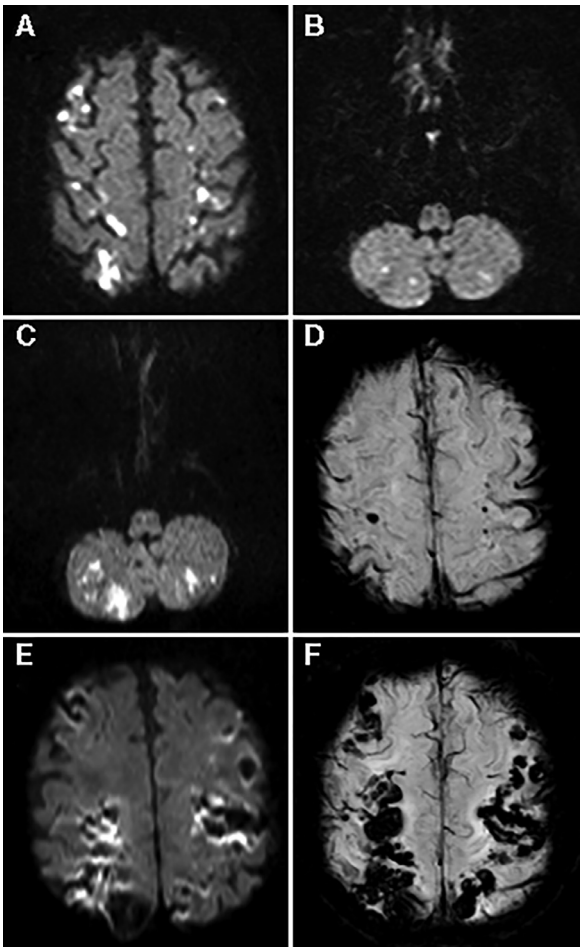

Figure 1. *(A, B) Brain magnetic resonance imaging (MRI) on admission. Diffusion-weighted (DW) images showing acute multiple infarction in bilateral cerebral (A) and cerebellar (B) hemispheres. (C, D) Brain MRI on day 3. DW image showing recurrence of cerebellar infarction (C). Susceptibility-weighted (SW) image showing hemorrhagic infarction (D). (E, F) Brain MRI on day 22. DW (E) and SW (F) images showing deterioration of hemorrhagic infarction.*

angiography showed no abnormalities. A blood test showed a normal platelet count (167×10^9/L) and a slightly elevated D-dimer level (1.57 μg/mL; normal, <1.0 μg/mL). Her electrocardiogram showed a normal sinus rhythm pattern and no paroxysmal atrial fibrillation was detected by electrocardiogram monitoring. Her transthoracic echocardiogram showed no remarkable abnormalities. Contrast-enhanced whole-body computed tomography scans showed no evidence of malignancy and the levels of tumor biomarkers such as carcinoembryonic antigen (CEA), CA19-9, and the soluble interleukin-2 receptor were not elevated. The levels of coagulation factors including protein S and protein C were normal and no autoantibodies such as antineutrophil cytoplasmic antibodies were detected. In particular, although the coexistence of antiphospholipid syndrome with ITP is associated with thrombosis in ITP,[8] no antiphospholipid antibodies including lupus anticoagulants, anticardiolipin antibodies, and anti-β2-glycoprotein I antibodies were detected. Although the cause of cerebral infarction was unclear, heparin sodium was administered by constant intravenous infusion to prevent recurrence of cerebral infarction. However, brain MRI on day 3 revealed a recurrence of cerebral infarction (Fig 1, C). Since hemorrhagic infarction was observed, heparin sodium was discontinued (Fig 1, D). On day 10 of hospitalization, she showed melena and oral hemorrhage. Her platelet count decreased to 1×10^9/L from 171×10^9/L on day 5. Her platelet-associated immunoglobulin G level was elevated (926.1 ng/10^7 cells; normal, .0-30.2 ng/10^7 cells), and a diagnosis of acute exacerbation of ITP was made. She was treated with intravenous immunoglobulin (total 2 g/kg) and her platelet count increased (82×10^9/L). However, her hemorrhagic infarction (Fig 1, E and F) and neurological symptoms deteriorated. On day 33, she died of respiratory failure. No autopsy was performed.

To the best of our knowledge, this is the first case report of multiple cerebral infarction preceding acute exacerbation of ITP. Although the causal relationship between cerebral infarction and ITP in this case is not definitely established, we speculated that cerebral infarction was associated with ITP, since there were no obvious causes of recurrent cerebral infarction other than ITP in this case. It was previously theorized that paradoxical thrombosis caused by ITP may be associated with platelet microparticles, which are produced subsequently to the activation and destruction of platelets and can lead to activation of thrombin and other coagulation factors.[6-9] If this theory is correct, in our patient, platelet microparticles might have been produced already before thrombocytopenia was evident, which could lead to cerebral infarction. This case suggests that ITP should be considered as a possible cause of cerebral infarction with unknown etiology, even when the platelet count is within the normal range at the onset.

Conflict of interest

None.

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