Slowly Progressive Ischemic Stroke as First Manifestation of Essential Thrombocythemia

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We report a case of essential thrombocythemia, the only clinical manifestation of which consisted of neurologic symptoms, including anomic aphasia, tactile and painful hypesthesia in the right hand, headache, and Gerstmann syndrome, with a relatively benign and slowly progressive clinical course. Neuroradiologic examination disclosed a large ischemic area in the left temporo-parietal region. Cerebral angiography revealed an occlusion of the cortical branches of the left middle cerebral artery with total sparing of the carotid vessel. These findings are discussed in relation to the possible pathogenetic mechanisms of the vascular occlusion due to abnormal platelet function in essential thrombocythemia.

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Essential thrombocythemia is a myeloproliferative disease associated with persistent increased platelet count and megakaryocytic hyperplasia in the bone marrow in the absence of other identifiable causes of thrombocythemia. Abnormal platelet function can usually be demonstrated. The main clinical features are recurrent spontaneous hemorrhage and/or thrombotic phenomena involving both the arterial and venous circulations. Central nervous system complications include transient ischemic attack or stroke, in both the carotid and vertebrobasilar distributions, intracranial bleeding, headache, and, less commonly, seizures or vertigo. Neurologic symptoms can appear at any time during the clinical course of the disease but are rarely reported as the only presenting features.

We describe a patient whose only clinical expression of essential thrombocythemia consisted of cerebrovascular occlusion in the middle cerebral artery (MCA) territory and an unusual clinical course.

Case Report

T.O., a 30-year-old right-handed man and smoker, was admitted to our hospital in December 1987 because of speech difficulties, headache, and seizure. Since age 28 years he had gradually begun to experience difficulty in finding the correct words while speaking and, occasionally, his speech was punctuated by phonemic paraphasic errors. This disturbance was mild and progressed very gradually over months. A similar difficulty was noted in writing. During this period, T.O. developed impaired sensation and difficulty in using his right hand. Three months before admission, he experienced several episodes of transient visual disturbances consisting of a moving shimmering light over the entire visual field. Furthermore, he complained of a slight, constant, and dull headache that persisted, unabated, until the time of admission. During the previous month, three brief episodes with interruption of ongoing activities, immobility, and loss of contact were reported by colleagues at work. He did not consider these symptoms incapacitating, and he continued to perform his occupational activities until admission.

On neurologic examination, the major abnormalities were anomic aphasia and literal paraphasia; slight tactile and painful hypesthesia in the right hand; and right-left confusion, acalculia, and digital agnosia (Gerstmann syndrome). General physical examination was normal except for a palpable spleen protruding 4 cm below the left costal margin.

The leukocyte count was 15,000/μl with 76% neutrophils, 20% lymphocytes, 2% eosinophils, 1% monocytes, and 1% basophils. The erythrocyte count was 5,780,000/μl, hematocrit 48.6%, and hemoglobin 15.6 g/100 ml. Serum iron level and total iron binding capacity were normal. The platelet count was 1,100,000/μl and platelet function assessed by Born's method was abnormal after adenosine diphosphate, epinephrine, and collagen stimulation. Peripheral blood analysis failed to reveal morphologic changes in erythrocytes or platelets, and no immature neutrophils were detected. Bone marrow biopsy
revealed a megakaryocytic hyperplasia and a slightly increased amount of reticulin fibers without morphologic evidence of impaired platelet formation.

Computed tomography showed a large hypodense area in the left temporoparietal region, unmodified after administration of contrast material, and enlargement of the occipital horn of the left lateral ventricle. Magnetic resonance imaging confirmed an abnormal signal on T1- and T2-weighted images, suggesting a parenchymal ischemic alteration in the left temporoparietal region. Left carotid angiography showed an absence of injection of the terminal branches of the left MCA in the postinsular tract.

On the basis of these results, we diagnosed essential thrombocythemia with ischemia in the vascular territory of the terminal branches of the left MCA.

Cyclic treatment with busulfan led to remission of T.O.'s thrombocythemia. A platelet antiaggregating agent and an antiepileptic drug (carbamazepine) were also administered. The patient's seizures were controlled, but other neurologic symptoms remained unchanged at follow-up.

Discussion

Cerebral ischemic events are a well recognized complication of essential thrombocythemia.6-10 This case presents neuroradiologic evidence of a cerebral infarct due to occlusion of the cortical branches of the left MCA and an insidious, slowly progressive clinical course that closely simulates an expanding lesion. Similar findings have been reported in three cases of primary polycythemia11 and, more recently, in a case with cigarette and oral contraceptive use.12

The pathogenetic mechanism of the vascular occlusion in essential thrombocythemia has been analyzed in several studies. Elevated platelet count and marked abnormalities of platelet function are associated with a high risk of thrombotic complications.2

A causal relation between platelet hyperaggregability and vascular occlusion has been demonstrated,3 with the platelet aggregates involving mainly the microvascular district and small arteries.5,13

In this case, we speculate that small recurrent infarcts in the cortical territory of the left MCA were secondary to spontaneous platelet aggregation occurring over months, with resulting gradual occlusion of the vessels. Thus, the pathophysiology of the stroke syndrome of this case seems to differ from that of a classical stroke. Although the abnormal tendency to thrombosis is the single most important factor determining vascular occlusion in essential thrombocythemia, other mechanisms may play a role. In the erythromelalgic syndrome associated with essential thrombocythemia, arteriolar inflammation, fibromuscular intimal proliferation, and vascular occlusion have been histopathologically demonstrated.13,14 Thus, an inflammatory-occlusive disease due to platelet aggregation and activation, with release of prostaglandins and thromboxanes, is considered the most likely pathogenetic mechanism of the peripheral vascular complication of essential thrombocythemia. The importance of this vascular lesion mechanism in cerebral ischemic events has never been established. However, on the basis of the long-lasting, monofocal, and progressive symptoms of our case, we speculate that a localized arteriolar disease similar to that demonstrated in the erythromelalgic syndrome occurred at the level of the MCA branches.

References


Key Words • arterial occlusive diseases • cerebral ischemia • thrombocythemia, hemorrhagic
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