

Posterior reversible encephalopathy syndrome with essential thrombocythemia

A case report

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Abstract

Rationale: Posterior reversible encephalopathy syndrome (PRES) is a rare neurological disease of the posterior subcortical white matter that manifests as headache, seizures, visual impairment, disturbance of consciousness, and changes in mental state. While PRES is associated with specific imaging findings involving the posterior circulation area of the brain. In the present study, we report the first case of PRES associated with essential thrombocythemia (ET).

Patient concerns: A 49-year-old man suddenly experienced headache, followed by the gradual appearance of consciousness disorders and mental behavior abnormalities. Neurological tests showed that the patient had a Glasgow Coma Scale score of 12, normal muscle strength and tension of the limbs, and was negative for meningeal irritation.

Diagnosis: Magnetic resonance imaging of the brain showed extensive vasogenic edema in the deep white matter of the right cerebellum and the left occipital and temporal lobes and a diagnosis of PRES was considered. Routine blood test showed that his platelet count was markedly increased, and the JAK2 V617F mutation analysis with allele-specific real-time polymerase chain reaction was positive. The bone marrow biopsy indicated an increasing number of megakaryocytes. These findings indicated ET.

Interventions: PRES was treated with a dehydrating agent and supportive and symptomatic treatments. Aspirin tablets were prescribed to address the patient's ET.

Outcome: After treatment, the abnormal findings on head imaging were completely reversed. His neurological symptoms were completely relieved.

Lessons: PRES may be correlated with ET; specifically, ET may trigger PRES and be a risk factor for the acute onset of neurological deficits.

Abbreviations: ET = essential thrombocythemia, PRES = posterior reversible encephalopathy syndrome.

Keywords: essential thrombocythemia, posterior reversible encephalopathy syndrome, neurological disease

1. Introduction

Posterior reversible encephalopathy syndrome (PRES) is an acute neurological disease first introduced by Hinchey et al in 1996.^[1]

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It is characterized by changes in mental state (stupor and confusion), headache, epilepsy, cortical blindness or other visual changes, and cerebellar ataxia.^[2] Indicated by unique neuroimaging manifestations of white matter tractography abnormalities, PRES is usually induced by malignant hypertension or eclampsia, severe kidney disease, chemotherapy for malignant tumors, and immunosuppressive therapy following organ transplantation. Advances in magnetic resonance imaging (MRI) approaches have improved the detection of PRES. Consequently, the prognosis of the disease is usually satisfactory, and most patients can make a full recovery.^[1]

Essential thrombocythemia (ET) is a chronic myeloproliferative disease characterized by the abnormal proliferation of megakaryocytes in the bone marrow and significant increases in platelet counts.^[3–5] ET manifests as bleeding and thrombophilia and is associated with a high risk of thrombotic events.^[3–5] Here we present a case of PRES with ET and discuss the possible association between the 2 diseases.

2. Case presentation

A 49-year-old Chinese man presented with a 5-day history of headache. On the 5th day, he was admitted to a local clinic where he underwent head computed tomography, which showed a low-density shadow in the left temporal lobe. His condition generally worsened over the following week. He began to experience

obvious unresponsiveness, irritability, and communication difficulties with family members and became increasingly unable to perform requested actions. Therefore, the patient was admitted to the inpatient department for further emergency treatment.

The patient had no history of hypertension; diabetes; coronary heart disease; or infectious diseases, such as hepatitis, tuberculosis, and typhoid. The physical examination revealed a relatively low blood pressure (130/80 mmHg) and a body temperature of 36.8°C. The patient was somnolent and unresponsive. His abilities to understand, calculate, recall, and orient himself had significantly diminished. Neurological tests showed that he had a Glasgow Coma Scale score of 12 and normal limb strength and muscle tension with no signs of meningeal irritation. Cerebrospinal fluid examination findings excluded a diagnosis of intracranial infection. Routine biochemical tests showed normal levels of electrolytes and blood sugar, and electroencephalography revealed no abnormalities. MRI showed long T1 and T2 signal in the right cerebellum as well as in the subcortical white matter of the left occipital and temporal lobes (Fig. 1). A fluid-attenuated inversion recovery (FLAIR) sequence showed high signal in the same brain area. Head magnetic resonance angiography showed no obvious abnormalities in the blood vessels. Routine blood tests revealed a platelet count of $896 \times 10^9/L$, white blood cell count of $15.97 \times 10^9/L$, red blood cell count of $4.48 \times 10^{12}/L$, and hemoglobin count of 134 g/L. C-reactive protein levels and erythrocyte sedimentation rates were normal. The thrombocytosis persisted during hospitalization. A bone marrow biopsy showed that the megakaryocytes in the bone marrow tissue were focally distributed and partially dispersed.

While the morphology of megakaryocytes was diverse, most were abundant in the cytoplasm. Genetic analysis with allele-specific, real-time polymerase chain reaction was positive for the JAK2 V617F mutation and negative for the BCR-ABL1 or MPL W515L/K mutations and a diagnosis of ET was considered.

The patient was orally administered low doses of aspirin (100 mg/d) to treat the ET. Mannitol, furosemide, and supportive and symptomatic treatments were used to treat the brain edema. The patient recovered quickly after treatment. On the 9th day of hospitalization, the patient's consciousness gradually returned to normal, and he was able to communicate normally. Neurological tests yielded a Glasgow Coma Scale score of 15. The second MRI examination revealed a significant reduction of leukoencephalopathy (Fig. 2). The patient's condition had occurred suddenly and manifested clinically as headache and changes in his mental state. Head MRI revealed abnormal signals in the white matter of the occipital and temporal lobes and the cerebellum. Treatment significantly relieved the clinical symptoms of the patient. The second head MRI examination showed that the extent of the white matter edema was significantly reduced relative to that observed on the previous MRI. A diagnosis of PRES was considered. An additional MRI conducted in December 2015—the 34th day following admission—showed no abnormalities (Fig. 3). After discharge, the patient continued taking the prescribed aspirin at doses of 100 mg/d. Routine blood tests and assessments of coagulation function were conducted at 1-month intervals during the following 26 months of follow-up. No bleeding or vascular embolism was observed after discharge. Across follow-up, the patient had a platelet count of

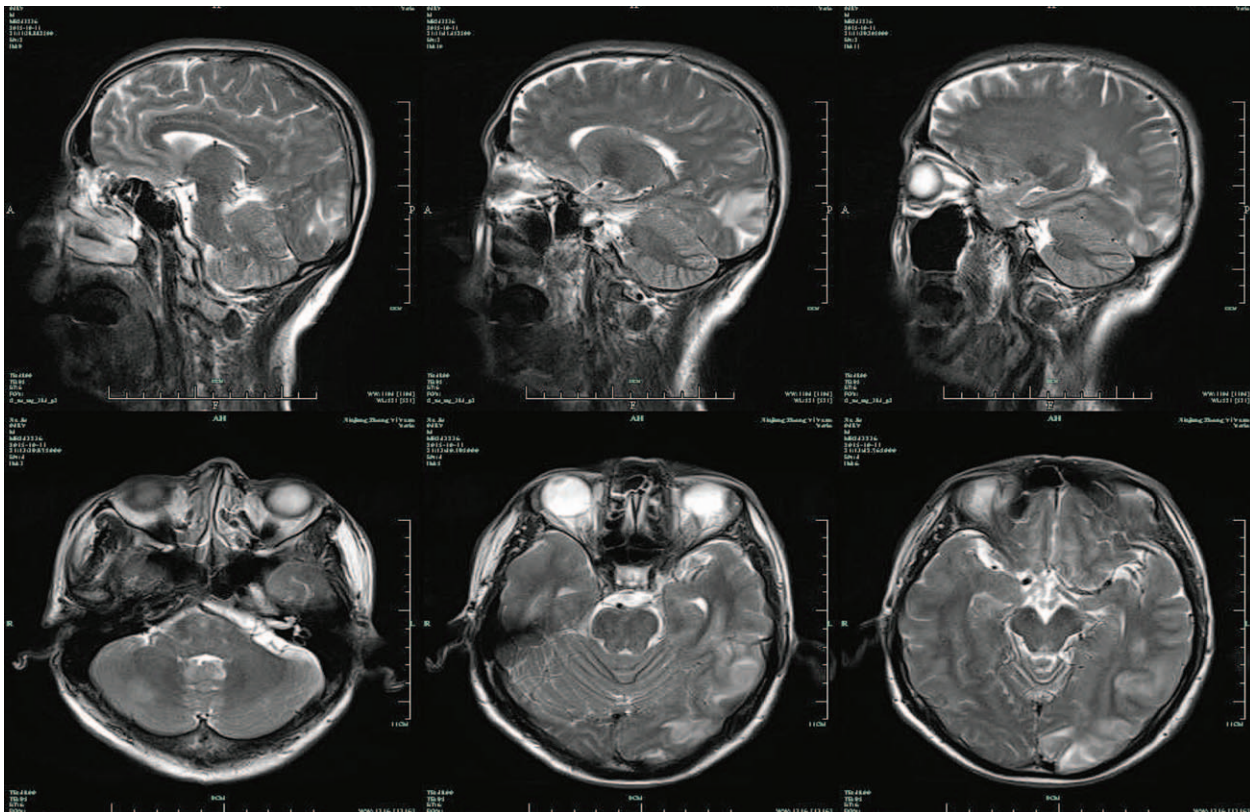


Figure 1. The brain MRI images obtained on admission. The images confirmed extensive hyperintense lesions on the T2 sequence (vasogenic edema) with the involvement of the occipital and temporal lobes, as well as the cerebellum. MRI=magnetic resonance imaging.

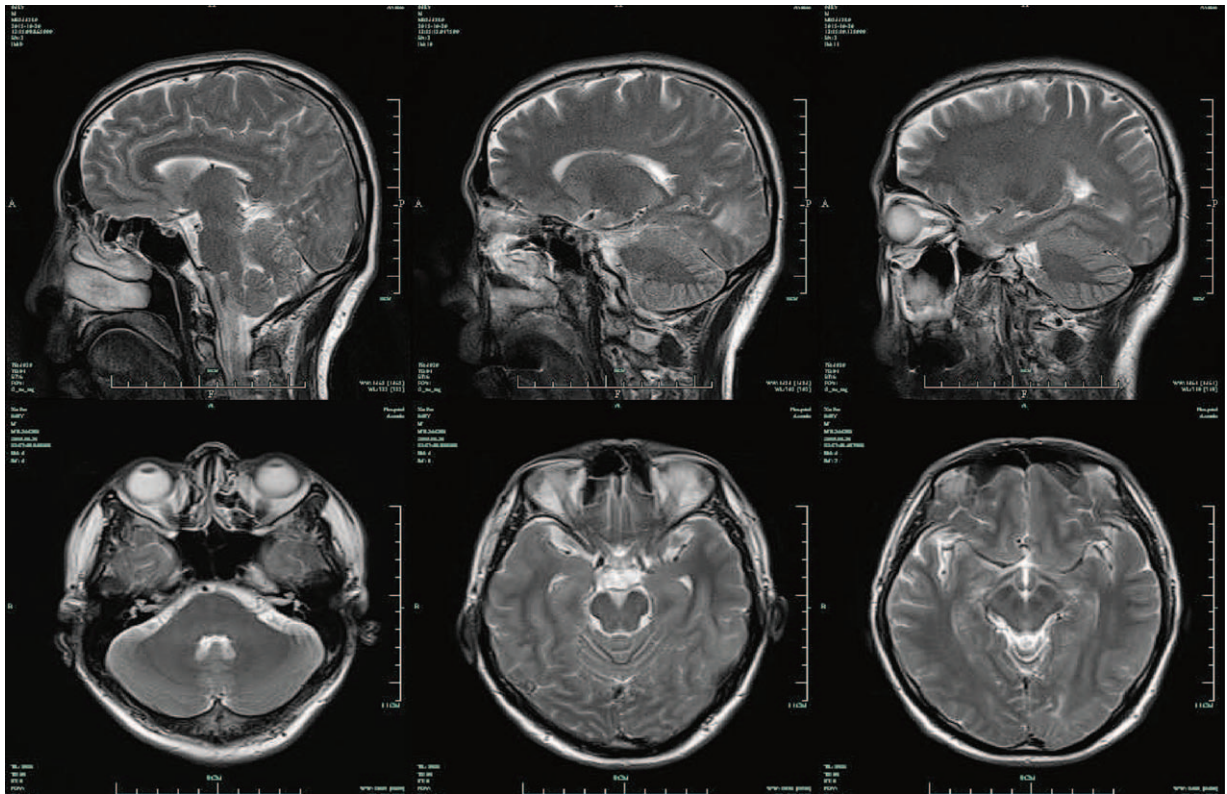


Figure 2. The brain MRI images obtained on day 9 of hospitalization. MRI=magnetic resonance imaging.

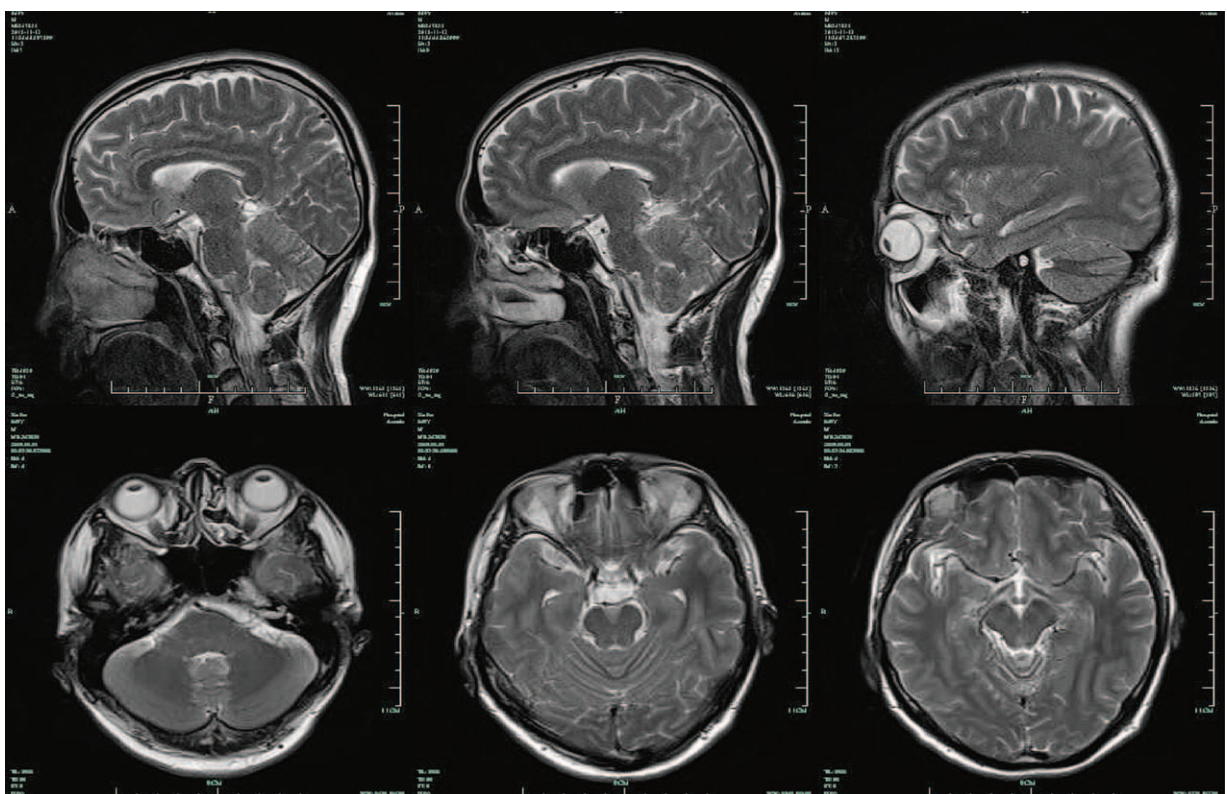


Figure 3. The brain MRI images obtained on day 34 of hospitalization. MRI=magnetic resonance imaging.

approximately 300 to $700 \times 10^9/L$. The last recorded platelet count was $465 \times 10^9/L$ on December 6, 2018.

3. Discussion

To the best of our knowledge, this report is the first to document a case of PRES and ET. Hyperintense abnormalities in the left occipital and temporal lobes were observed on FLAIR. Hyperintensities in the right cerebellum were also observed on T2 and ADC. These neuroimaging findings indicated vasogenic edema. After treatment, the abnormal signal intensities in the left occipital and temporal lobes were significantly reduced, and the right cerebellar lesions disappeared. These outcomes were similar to those previously reported. While we suspect a direct relationship between PRES and hypertension,^[1] patients with PRES can reportedly present without hypertension.^[6–8] However, unlike previous reports of PRES, our patient was diagnosed with essential thrombocythemia (ET) during his hospitalization. The patient's platelet count continued to exceed $450 \times 10^9/L$ during his hospitalization. The bone marrow biopsy indicated an increasing number of megakaryocytes. The patient's not having the BCR-ABL1 mutation could exclude a diagnosis of human chronic myeloid leukemia and acute lymphoblastic leukemia. The patient's levels of C-reactive protein were normal. As the patient was determined to be positive for JAK2 V617F, a diagnosis of reactive thrombocytopenia was excluded. The lack of anemia and abnormalities in red blood cell count or hemoglobin excluded primary myelofibrosis and polycythemia vera.

ET is a chronic myeloproliferative disorder characterized by a relatively benign clinical process.^[9,10] However, the pathogenesis of ET remains unclear. Previous studies have reported that a point mutation on exon 14 of the JAK2 gene causes the formation of the JAK2 V617F transcript, which is closely related to the incidence of ET.^[11] Middle-aged patients are more commonly afflicted with ET. Most of the patients have normal life expectancies, and a few patients develop acute leukemia.^[9,10] Despite the lack of prospective data concerning ET, aspirin is recommended to reduce the enhanced vascular risk.^[12,13]

The relationship between PRES and ET has not been previously reported or explored. While ET might increase the risk of stroke (acute ischemic stroke and hemorrhagic strokes),^[5,14] whether and how ET influences PRES is unclear. Although the pathophysiological changes induced by PRES remain poorly understood, endothelial dysfunction has been implicated in PRES.^[15] Previous studies have found that the activation of endothelial cells is enhanced in ET and is more common in patients with JAK2 mutations.^[16,17] Endothelial cells appear to respond to the pathological condition of patients with ET; since platelets have been shown to stimulate the endothelial-cell-mediated synthesis of PA1 via transforming growth factor- β ,^[18–21] the endothelium itself can be impaired in patients with myeloproliferative neoplasms. Indeed, previous studies demonstrating high circulating levels of vascular endothelial growth factor have shown that patients with ET exhibit impaired angiogenesis.^[22] ET is also reportedly associated with the activated neutrophil-mediated release of proteolytic enzymes (i.e., elastase and cathepsin G) and reactive oxygen species that can change endothelial functions.^[23–25] Hence, ET may trigger PRES, and ET should be considered a risk factor for the acute onset of neurological deficits. The question of whether PRES is the result or complication of ET requires investigation by large-scale animal studies and clinical trials. However, because the

incidence of ET and PRES is low, no mature animal models of these 2 diseases exist at present.

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