Thrombotic thrombocytopenic purpura-induced posterior leukoencephalopathy in a patient without significant renal or hypertensive complications

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ABSTRACT

A 40-year-old male with recent-onset idiopathic thrombotic thrombocytopenic purpura (TTP) developed focal transient neurological findings lasting for several hours, remitting, then recurring in a different pattern. Brain magnetic resonance imaging (MRI) was consistent with a posterior leukoencephalopathy and electroencephalography demonstrated lateralized slowing during an episode. No acute ischemic changes were found on diffusion-weighted imaging. Close monitoring in an intensive care setting revealed no significant hypertensive episodes. The patient’s condition resolved with plasmapheresis and immunoglobulin therapy. The relation of TTP to reversible posterior leukoencephalopathy syndromes is discussed. Clinical features of this case suggest a mechanism for TTP-induced leukoencephalopathy independent of hypertension and renal failure.

KEY WORDS: Purpura, thrombotic thrombocytopenic; encephalopathy, hypertensive; brain oedema

Thrombotic thrombocytopenic purpura (TTP) is a form of haemolytic anaemia with neurological abnormality as a salient feature. Serial neuroimaging studies of patients with neurological dysfunction and TTP suggest an association with reversible posterior leukoencephalopathy syndrome (RPLS). Acute hypertensive events and renal failure have been postulated as the likely underlying aetiology to this radiographic finding. In contrast to this hypothesis, we report a patient with TTP having neurological dysfunction and neuroimaging consistent with posterior leukoencephalopathy syndrome despite the absence of significant hypertension or clinical nephropathy.

Case History

A previously healthy 40-year-old man was seen in the Emergency Department for the rapid onset of right upper and lower extremity weakness of an hour’s duration. During evaluation by the consulting neurologist, the patient developed difficulty in speaking. Language examination was characterized by non-fluent speech with severely impaired naming but intact comprehension and repetition. Visual fields were full to confrontation. He had a right hemiparesis without brisk reflexes. Tactile sensation and coordination were intact. A CT scan of the head was normal. Investigations showed a hematocrit of 41% and platelets of 178,000/mm³. He was normotensive but had a mild fever of 100.4°F. The patient was admitted to intensive care for further monitoring. Three hours after the initial examination, his speech had returned to baseline and he had normal strength.

The day after admission, he developed left upper extremity weakness and confusion with impaired attention but largely normal language. He did not appear to have a hemineglect. An electroencephalogram obtained during this episode depicted marked slowing in the posterior right hemisphere without evidence of epileptiform activity. A brain MRI showed no acute changes on diffusion weighted imaging, but T2 signal attenuation was seen in the posterior periventricular white matter, greater on the right, consistent with vasogenic oedema (Figure 1). Brain MR Angiography was normal. A lumbar puncture had unremarkable results. A human immunovirus (HIV) test was negative and blood cultures had no bacterial or fungal growth.

His confusion and attentional difficulties persisted with slow improvement over two weeks with the initiation of daily plasma exchange and intravenous gammaglobulin beginning on hospital Day two. He remained in intensive care for one week and was transferred to the medicine ward after his platelet count and hematocrit had normalized. Brain MRI obtained eight months later showed nearly complete resolution of the T2 signal changes seen on the first MRI (Figure 2).

He was on a cardiac monitor with frequent blood pressure monitoring throughout his ICU stay, with recorded mean arterial pressures between 90mm and 110mm Hg. Daily serum creatinine did not exceed 1.0 mg/dl. He had no other stigmata of hypertension or renal dysfunction.
Discussion

TTP is a thrombotic microangiopathy with Coombs’ negative haemolytic anaemia and thrombocytopenia. The clinical presentation is characterized by the pentad of signs and symptoms of renal failure, fever, microangiopathic haemolytic anaemia (MAHA), thrombocytopenia, and neurological dysfunction. The diagnosis is strongly suggested by the presence of elevated lactate dehydrogenase and schistocytes. Neurological abnormality is present in 50 to 60% of patients during the acute phase of illness.

TTP-related end-organ dysfunction is related primarily to microangiopathic disturbances. Damage to endothelial cells within the blood vessel wall accelerates the formation of platelet-rich microthrombi which can cause microinfarctions of affected tissue. This coagulopathy can lead to serious neurological compromise from stroke or haemorrhage, but case series with MRI and CT implicate altered cerebrovascular autoregulation as a mechanism. A posterior leukoencephalopathy is posited on the basis of these studies. Normalization of follow-up imaging with clinical resolution of neurological abnormality makes infarction unlikely.

Reversible posterior leukoencephalopathy syndrome (RPLS), is seen in several conditions which share acute hypertension as a significant feature. Chronic hypertension, renal insufficiency and eclampsia are associated with acute elevations in systemic blood pressure that can alter the permeability of cerebral vessels, resulting in petechial haemorrhage and fluid transudation through a disrupted blood-brain barrier. RPLS in the setting of TTP is thought to share this mechanism of hypertensive encephalopathy. In a neuroimaging analysis of 12 patients with TTP, six presented with cerebral oedema associated with hypertension and renal failure. Only one of the twelve had cerebral oedema with normal creatinine and a maximum blood pressure of 140/85.

Patients with RPLS present with confusion and lethargy. Visual disturbances can occur with occipital lobe involvement. Seizures have also been reported. Asymmetric hemiparesis can occur despite relatively symmetric lesions. The symptoms are highly variable and may largely be dependent on the extent of cerebral vasogenic oedema.

We present a patient with TTP, normal to slightly elevated blood pressure with normal renal function who had posterior predominant vasogenic oedema on brain MRI consistent with posterior leukoencephalopathy. We attribute his confusion and inattention to this lesion. The absence of seizures and visual obscurations may be secondary to lack of cortical involvement. Furthermore, this patient demonstrated that renal dysfunction and subsequent hypertension, while present in many TTP patients, are not necessary prerequisites to RPLS. We postulate that TTP alters endothelial function whereby increased permeability of the blood-brain barrier creates a lower threshold for formation of brain oedema.

This case shows the importance of the prompt recognition and treatment of patients with TTP. The classic pentad of findings is not present in all cases, and failure to diagnose can lead to a lethal outcome. However, neurological impairment with TTP occurs in the majority of patients, making the role of the neurologist potentially invaluable. With proper treatment 90% of
patients survive an episode of TTP, generally without permanent organ damage. This case illustrates that cerebral oedema can occur in TTP with only minor perturbations in blood pressure and normal renal function. Careful observation of the patient’s neurological condition may be a clue toward the diagnosis and management of this hazardous illness.

References


