Posterior Reversible Encephalopathy Syndrome Associated with IVIg in a Child with Guillain-Barré Syndrome: Case Report and Review of the Literature

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Abstract

An 11-year and 7-month-old Chinese boy with Guillain-Barré syndrome (GBS) manifested headaches and seizures after the administration of intravenous immunoglobulin (IVIg). Magnetic resonance imaging revealed posterior reversible encephalopathy syndrome (PRES). Several previous reports described PRES associated with IVIg, but few in children. We suggest that this syndrome should be considered in children with GBS and/or administration of IVIg as a neurologic complication. This report reviews the literature on this unusual association and discusses possible pathophysiological mechanisms.

Key words

Children; Guillain-Barré syndrome; Hypertensive encephalopathy; Posterior reversible encephalopathy syndrome

Introduction

Posterior reversible encephalopathy syndrome (PRES) is characterised by sudden blood pressure fluctuation associated with clinical findings of encephalopathy, seizures, headache, visual changes and neuroimaging findings of reversible vasogenic subcortical oedema. Recent reports described PRES in association with intravenous immunoglobulin (IVIg) in adult patients. Here, we report on a boy with Guillain-Barré syndrome (GBS). We further discuss the possible pathophysiological mechanisms, and review the literature on this rare association.

Case Report

The patient was an 11-year and 7-month-old Chinese boy who manifested acute upper respiratory tract infection with headaches 20 days before admission. Four days before admission, he complained of finger numbness in both hands, followed by progressive gait difficulties two days later. He was hospitalised on August 27, 2011 because of gait and swallowing difficulties. Physical examination revealed blood pressure (BP) 118/68 mmHg, absent gag reflex, muscle strength of MRC grade IV in upper limbs and grade III in lower extremity, and areflexia of his distal extremities without paresthesias. On day 2 of admission, an examination of cerebrospinal fluid (CSF) indicated elevated protein (0.526 g/L) and a normal cell count. He was diagnosed as GBS and treated with IVIg (0.4 g/kg of body weight, daily) for 5 days, ganciclovir antiviral therapy and symptomatic treatment. On day 3 of admission, areflexia and paresthesias of his distal extremities were present. Progressively significant reduction in muscle strength were presented with the minimum of grade I in...
upper limbs and grade 0 in lower extremity. Due to respiratory muscle paralysis, the boy received endotracheal intubation and mechanical ventilation for 8 days till the respiratory muscle function gradually improved. On day 18 after admission, magnetic resonance imaging (MRI) of the brain, and thoracic and cervical spinal cord was normal. However, electromyography findings were suggestive of neuromuscular demyelinating changes. On day 29 after admission, he manifested severe headaches with drowsiness, seizures (twice, grand mal, lasting 7-8 minutes), bilateral divergent strabismus and visual impairment. His BP was 129-152/90-109 mmHg during the period. The examination of CSF indicated elevated proteins (2.92 g/L, reference range: 0.2-0.4 g/L) and a normal cell count. CSF IgG index was elevated to 0.79 (reference range: ≤0.7) with presence of oligoclonal bands. MRI of the brain (Figure 1) on the same day demonstrated an increased intensity in bilateral occipital cortical region, right temporal lobe and under the hanging wall of the bilateral cerebral ventricles on T2-weighted images and fluid-attenuated inversion recovery sequence images (FLAIR). He was diagnosed as the vasogenic oedema of PRES according to above findings. The boy received anti-convulsant (Levetiracetam) and anti-hypertensive drug (Captopril and nimodipine) and neuro nutrition drugs (Citicoline, Vitamin B complex tablet, mouse nerve growth factors). On day 33, he became conscious and manifested normal vision. On day 43, his BP was normal. On day 46, MRI indicated that the abnormal lesions had completely disappeared. On day 49, his eye movement was normal. His dysphagia improved gradually. Six months later, he could walk by himself without seizures, limb muscle strength gradually returned to normal, tendon reflex and electroencephalogram (EEG) were normal.

Discussion

PRES was first described by Hinchey et al., a syndrome characterised by the clinical presence of headache, seizures, encephalopathy, and visual disturbances with radiologic findings of focal reversible vasogenic oedema, best seen on MRI of the brain. Typical lesions are hyperintense on T2-weighted images and hypointense or isointense on diffusion-weighted images, with an increase of the apparent diffusion coefficient, indicating vasogenic rather than cytotoxic oedema. Risk factors are acute hypertension, immunosuppressive therapy, autoimmune diseases, IVIg administration and so on. Treatment of PRES consists of symptomatic treatment and withdrawal of the offending immunosuppressant. The prognosis is generally favourable.

Figure 1    Magnetic resonance imaging of the brain on day 29 of admission demonstrated hyperintensity in bilateral occipital subcortical white matter (arrow) on T2-weighted images (A) and fluid-attenuated inversion recovery sequence images (B).
with complete recovery within a few days; and only a few cases suffering from sequelae, such as epilepsy,2 death3 and so on.

The diagnosis of PRES in our patient was based on a typical clinical presentation of drowsiness, seizures, headaches, visual symptoms with acute hypertension, and a brain MRI demonstrating hyperintense signals in bilateral occipital cortical region, right temporal lobe and under the hanging wall of the bilateral cerebral ventricles on T2-weighted image and FLAIR, which had disappeared on day 46 after admission. The patient recovered with normal vision, muscle strength and EEG after six months.

PRES is now believed to be caused by a breakdown of circulatory autoregulation in the circumstances of acute hypertension. The posterior circulation is particularly susceptible because of sparse sympathetic innervation.4 Probably, the pathophysiology of PRES, although not completely understood, points to two main risk factors: hypertension and autonomic dysfunction. There are two possible etiologies for hypertension and autonomic dysfunction leading to PRES in our patient. First, GBS is occasionally associated with hypertension. Almost two thirds of patients who have GBS have transient hypertension.5 Second, GBS is an inflammatory polyradiculoneuropathy with increased levels of cytokines in serum and CSF.6 This inflammatory process may have a role in PRES by changing capillary permeability. The high percentage of patients with PRES who have autoimmune disorders may support the theory that PRES is in part caused by endothelial dysfunction, a process in which the host autoimmune response is essential.7 Another possible explanation that we cannot rule out for the development of PRES in our patient is IVIg. IVIg has several adverse effects including headache, blood pressure changes and so on. Approximately 30% of patients treated with IVIg complain of headaches, and these patients are sometimes thought to be exhibiting aseptic meningitis, a common adverse effect of IVIg. We postulate role of IVIg in pathogenesis of PRES as that many factors such as hypertension causes temporary damage of the blood brain barrier, leading to temporary cerebral white matter temporary angiooedema. Toxins in the circulation enter through the destroyed blood brain barrier into the brain, causing brain cell oedema, which then lead to PRES. Furthermore, the frequency of headaches caused by exposure to IVIg is thought to be dose-dependent.8

Our patient complained of severe headaches on day 28 after the initial administration of IVIg, and MRI of the brain indicated vasogenic lesions which resolved 17 days later. One previous report of PRES associated with IVIg of a 14-year-old girl with GBS, described development of PRES only 3 days after the initial administration of IVIg, sooner than our patient. And the brain lesion also disappeared sooner by one week.9 This case illustrates that, for GBS, particularly in children, we should be cautious about additional neurologic problems associated with administration of high-dose IVIg, so as not to overlook PRES.

**Conclusion**

Our case illustrates that we should pay attention to additional neurologic signs of central nervous system suggestive of PRES during management of children with GBS and during the administration of high-dose IVIg, so as not to overlook this complication.

**Declaration of Conflicting Interests**

None.

**References**