Posterior Reversible Encephalopathy Syndrome and Guillain-Barré Syndrome after Head Injury: Case Report

Satoru YONEKURA,[1] Takayuki ANNO,[1] and Nobuyuki KOBAYASHI[1]

[1]*Department of Neurosurgery, Tochigi Medical Center Shimotsuga, Tochigi, Tochigi, Japan*

Abstract

We report a case of head injury with posterior reversible encephalopathy syndrome (PRES), followed by Guillain-Barré syndrome (GBS). A 74-year-old man was brought to our hospital after a fall. Computed tomography revealed intracranial hemorrhage. Magnetic resonance imaging showed bilateral reversible intensities with features of vasogenic edema in parietooccipital areas, suggesting PRES. After admission, weakness and areflexia of extremities and respiratory muscles developed gradually, which favored a diagnosis of GBS. Common etiologies of PRES were absent. Concurrent occurrence of PRES and GBS is rare. Given that PRES can be an initial manifestation of GBS, GBS must be considered in head trauma patients with PRES.

Key words: posterior reversible encephalopathy syndrome, Guillain-Barré syndrome, magnetic resonance imaging, head injuary

Introduction

Posterior reversible encephalopathy syndrome (PRES) is a neurotoxic state that presents with unique features on computed tomography (CT) or magnetic resonance (MR) imaging. The characteristic MR imaging findings of PRES mainly consist of altered intense areas in the parietooccipital lobes with features of vasogenic edema. Etiologies of PRES include hypertensive emergency, preeclampsia or eclampsia, cytotoxic medications, sepsis, multiple organ dysfunction, triple-H (hypertension, hemodilution, and hypervolume) therapy for vasospasm after subarachnoid hemorrhage (SAH), and autoimmune diseases.[1] In contrast, Guillain-Barré syndrome (GBS) is typically triggered by infection. We describe a rare case of PRES followed by weakness of extremities with areflexia and bulbar palsy resembling GBS after head trauma in the absence of any of the common etiologies of PRES and GBS. The purpose of this case report is to suggest the importance of a potential association between PRES and GBS in a patient with head trauma.

Case Report

Admission due to head trauma and appearance of altered intensities in bilateral parietooccipital areas on MR imaging

A 74-year-old Japanese man was brought to our emergency department 1 day after falling on a mountain. He had no headaches, seizures, or visual disorders, but many painful bruises were present on his arms and legs. He had a medical history of dementia. There was no history of any infection.

On clinical assessment, his Glasgow Coma Scale was evaluated as 13/15 (E3V4M6). His heart rate was normal at 94 beats per minute, his blood pressure was 149/75 mmHg, and his temperature was 37.9°C, remaining at approximately 38°C for about 2 weeks after admission. A physical examination showed an abrasion wound on the head, several bruises on the chest and upper abdomen, and severe tenderness in his right lower leg. Results of manual muscle testing (MMT) were significant for four-fifths of the right lower leg. Results of laboratory analyses were as follows: hemoglobin 13.5 mg/dL, leukocyte count 19,200 cells/μL, neutrophil count 15,398 cells/μL, urea 25 mmol/L, creatinine 0.76 mg/dL, potassium 3.8 mmol/L, sodium 141 mmol/L, chloride 108 mmol/L, creatine kinase 20,518 IU/L, and C-reactive protein 13.43 mg/dL. A tetanus vaccine was administered for prevention of tetanus due to

injuries. Intravenous administration of tazobactam/piperacillin hydrate (18 g/day) was performed from 6th to 20th day after admission.

A plain X-ray revealed no fractures on the upper limbs, lower limbs, or pelvis. A CT scan of his head showed SAH, acute subdural hematoma, and hypodense lesions in the bilateral parietooccipital areas with no fractures of cranial bones (Fig. 1). Lung and abdominal CT scans revealed no abnormalities. MR angiography revealed no carotid stenosis, brain aneurysm, or vasospasm. Brain MR imaging showed cortical and subcortical altered intensities in the bilateral parietooccipital areas. There were hyperintense regions on T2-weighted imaging (T2WI), fluid attenuated inversion recovery (FLAIR), diffusion-weighted images (DWI), and apparent diffusion coefficient (ADC) (Fig. 2A). Spinal cord MR imaging results were normal.

Clinical diagnosis of Guillain-Barré syndrome

Two days after admission, ascending weakness in the muscles of the extremities and bulbar weakness developed gradually. Twelve days after admission, physical examination revealed complete quadriplegia, bulbar palsy, and weakness of respiratory muscles with lower oxygen saturation, resulting in respiratory intubation with mechanical ventilation. Deep tendon reflexes (DTR) were absent. Sensory loss was not clear due to sedation during intubation. The clinical symptoms raised a possibility

Fig. 1 Head CT shows subarachnoid hemorrhage, acute subdural hematoma, and bilateral hypodense lesions in parietooccipital areas with no fractures of cranial bones.

of GBS. Intravenous immunoglobulin (IVIg) was administered. While leukocyte count was 12,700 cells/μL, C-reactive protein decreased to 3.50 mg/dL and creatine kinase was within normal limits. Laboratory analysis revealed neither anti-GM1 nor anti-GQ1b antibodies. Blood and cerebrospinal fluid (CSF) cultures were negative. IgGs of viruses such as Epstein–Barr virus, herpes simplex, and cytomegalovirus were not detected in the CSF. Analysis of the CSF revealed 92 mg/dL protein and a cell count of 8/mmc. An electrophysiological analysis was not performed at that time due to the limitations of our facility. Brain MR imaging showed increased signals of hyperintensity on T2WI, FLAIR, DWI, and ADC (Fig. 2B).

Resolution of Guillain-Barré syndrome and radiographical diagnosis of PRES

Twenty-four days after admission, the patient was extubated, with improved MMTs of limbs and brisk DTR. Brain MR imaging showed almost complete disappearance of the T2WI, FLAIR, DWI, and ADC hyperintensities, which are consistent with the characteristic images of PRES (Fig. 2C). Fifty-five days after admission, the patient was sent to a rehabilitation hospital.

Discussion

This was a rare case of concurrence of PRES and GBS after head trauma. PRES is a disorder of reversible subcortical vasogenic brain edema.[1,2] Underlying pathophysiological mechanism of PRES is the breakdown of blood-brain barrier (BBB).[2] Brain imaging usually shows vasogenic edematous lesions predominantly involving parietooccipital regions.[1,2] The patient showed characteristic imaging patterns of PRES. The imaging differential diagnosis of symmetrical edema of the parietooccipital lobes includes cerebral venous sinus thrombosis, posterior circulation stroke, primary central nervous system vasculitis, infective encephalitis, autoimmune encephalitis, osmotic demyelination syndrome, and metabolic/toxic encephalopathy such as carbon monoxide (CO) intoxication.[2,3] In this case, both the complete resolution of radiological findings that showed symmetrical edema of the parietooccipital lobes on MR imaging and MR angiography were not indicative of stroke. The results of physical examination, laboratory data, blood cultures, and CSF analysis were not suggestive of infection, encephalitis and metabolic/toxic encephalopathy. Brain imaging showed no lesions of basal ganglia lesions that can be often found in CO poisoning. The patient received no rapid normalization of
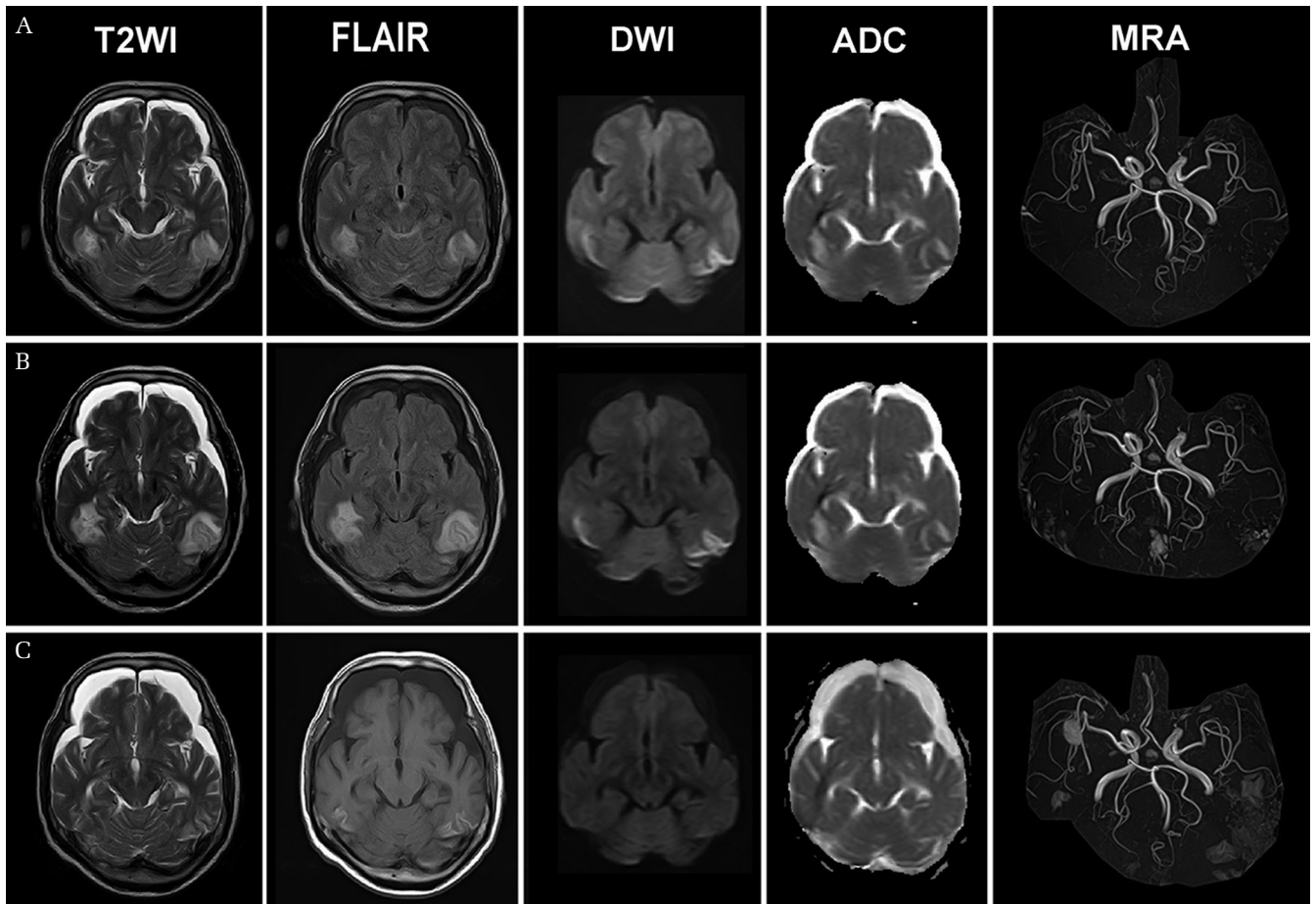
Fig. 2 (A) On admission. Brain MR imaging shows hyperintense on T2WI, FLAIR, DWI, and ADC images; (B) Twelve days after admission. Brain MR imaging shows increased signals of hyperintense regions on T2WI, FLAIR, DWI, and ADC images; (C) Twenty-four days after admission. Complete disappearance of the T2WI, FLAIR, DWI, and ADC hyperintense regions is consistent with the characteristic images of PRES.

sodium or glucose concentrations that is a risk factor of osmotic demyelination syndrome. Changes in signal intensty on DWI and ADC support that the lesion was vasogenic edema consistent with previous reports of PRES, but not cytotoxic edema caused by non-hemorrhagic infarcts, central pontine/extrapontine myelinolysis, and hypoxic or hypoglycemic encephalopathy.[4–6] Consequently, MR images in this case suggested PRES.

Many etiologies of PRES have been reported including hypertensive emergency, cytotoxic medications, sepsis, multiple organ dysfunction, triple-H therapy for vasospasm after SAH,[1] autoimmune diseases,[7] pregnancy-related vascular encephalopathy[7,8] and sympathomimetic drugs like phenylpropanolamine.[9] In addition, PRES has been reported both as an initial manifestation and as a complication of GBS.[7,10–19] According to these reports, in our case, PRES was considered to be associated with GBS.

The clinical diagnosis of GBS in this case was based on clinical symptoms including subacute tetraplegia, bulbar weakness, and respiratory failure with areflexia. In addition, CSF analysis showing albuminocytologic dissociation favored a diagnosis of GBS. Burwen et al.[20] developed the case definition for categorizing a patient as having definite, probable, or possible GBS, or as not a case by reviewing previously used definitions. According to the definition, our case was considered to be possible GBS. Differential diagnoses of subacute tetraplegia mimicking GBS including disorders such as periodic paralysis, poliomyelitis, myasthenia gravis, electrolyte disturbance, botulism and critical illness polyneuropathy (CIP), or critical illness myopathy (CIM) need to be considered.[21] Symptoms and lab data in this patient support none of them. Increased creatinine kinase was likely to be due to rhabdomyolysis caused by the falling accident of this patient. CIP is an acute axonal sensory-motor polyneuropathy and CIM is an

acute primary myopathy,[22] which are often difficult to be distinguished from GBS. Tetraplegia developed before intubation in this patient. While clinical symptoms such as tetraplegia or electromyogram are similar between CIP/CIM and GBS, bulbar palsy and albuminocytologic dissociation in CSF, both of which were clear in the patient, are more likely in GBS than in CIP/CIM.[23] Sepsis, acute respiratory distress syndrome or multiple organ failure are associated with CIP/CIM in intensive care unit,[23] none of which this patient had. Therefore, CIP/CIM was less likely in our patient.

The trigger of possible GBS in this case can be explained with several hypotheses: (i) infection, (ii) head trauma, and (iii) tetanus vaccination. Three days after admission, the patient had antibiotic-resistant pyrexia for 2 weeks. Most of the possible triggers causing GBS are gastrointestinal and respiratory infections.[24] The patient showed no respiratory or abdominal symptoms before and after the accident on a mountain. Blood and CSF cultures were negative, and a lung and abdomen CT scan revealed no findings of infection. Moreover, the patient had pyrexia even after WBC and CRP kept decreasing to almost normal range until 20 days after admission. According to the algorithm for the evaluation of fever in the traumatically brain injured patient,[25] the antibiotic-resistant pyrexia in this case was neurogenic fever due to head trauma. There have been several case reports of GBS after head trauma.[26–30] One retrospective study showed that 2% of GBS cases were triggered by trauma.[24] An association with the administration of a tetanus vaccination is reported.[31] However, the estimation of the risk of GBS after tetanus toxoid was 0.3 cases of GBS per million person-weeks, concluding that tetanus vaccination has no public health significance.[31] In this case, therefore, head trauma is the most reasonable cause of possible GBS.

The underlying mechanism of the possible association between PRES and GBS in this patient is still not clear. One of the possible explanations on the pathophysiology is transient hypertension.[2,11,32,33] Almost two-thirds of GBS patients have transient hypertension.[34] Rapidly developing hypertension can exceed the upper limit of cerebral blood flow autoregulation.[2] Blood pressure instability may cause capillary infiltration pressure, resulting in endothelial damage.[33] However, the mean arterial pressure of our patient was 100 mmHg, which was below the usually quoted upper limit of cerebral blood flow autoregulation (≥140–150 mmHg).[2] Another possible explanation is the disruption of the BBB and inflammation caused by head injury. Endothelial cells, pericytes and astrocytes maintain the integrity of BBB. Endothelial cells create tight junctions that prevent paracellular diffusion. Tomkins et al.[35] reported that the disruption of BBB was indicated in almost half of mild traumatic brain injury patients. Animal models suggest that molecular changes of the BBB can happen after traumatic brain injury. Rapid loss of pericytes was reported in a mice model.[36] In addition, the level of expression of BBB proteins such as caveolin-1 and claudin-5 fluctuated.[37] Disruption of BBB allows transmigration of immune cells from the systemic circulation into central nervous system (CNS).[38] Infiltrated neutrophils produce pro-inflammatory mediators, reactive oxygen species, and pro-apoptotic proteins.[39] For example, neutrophils can secrete vascular endothelial growth factor (VEGF) inside the CNS.[40] Increased VEGF promotes increased vascular permeability, leading to interstitial brain edema.[2,39,40] In addition to recruited inflammatory cells, resident cells in the CNS such as microglia have a role in development of inflammation. When exposed to myelin or recruited lymphocytes, microglia get activated, resulting in phagocytosis and production of various immunomodulatory cytokines and chemokines.[38,41] Activated microglia present antigen such as degenerated myelin to recruited T- and B-cells.[42] Peripheral circulation of those activated T- and B-cells through disrupted BBB might cause demyelinating diseases or axonal damage in the peripheral nervous system.[30] Based on the foregoing discussion, it may be assumed that the traumatic brain injury caused the disruption of BBB followed by inflammation inside the CNS, resulting in PRES and GBS.

Not only is this case rare, but also it is educational. The importance is that it highlights the neurologic signs/symptoms resembling GBS in head trauma patients showing PRES. GBS after head trauma is such a rarity that neurosurgeons might pay little attention to it as a possible complication of head trauma. Therefore, PRES in head trauma patients can be a helpful clinical feature as an indicator of GBS. If a patient after head trauma shows PRES, a careful management such as neurologic examination, blood tests including anti-gangliosides antibodies and evaluation of respiration might be necessary before severe respiratory failure happens.

Conclusion

Posterior reversible encephalopathy syndrome can be a useful clinical feature for raising a suspicion of GBS in head trauma patients, because GBS after head trauma is so rare that neurosurgeons might not consider it.

Acknowledgment

Conflicts of Interest Disclosure

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Address reprint requests to: Satoru Yonekura, MD, Tochigi Medical Center Shimotsuga, Ohira-machi Kawatsure 420-1, Tochigi, Tochigi 329-4498, Japan.
e-mail: yonechian@gmail.com