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GUILLAIN-BARRÉ SYNDROME COMPLICATED BY POSTERIOR REVERSIBLE ENCEPHALOPATHY SYNDROME AND REVERSIBLE CEREBRAL VASOCONSTRICTION SYNDROME

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ABSTRACT

Introduction: Guillain-Barré syndrome is an immune-mediated inflammatory polyneuritis characterised by rapidly progressive flaccid paralysis. Guillain-Barré syndrome may present with posterior reversible encephalopathy syndrome or reversible cerebral vasoconstriction syndrome in rare cases.

Case description: A woman in her 60s with a history of follicular lymphoma presented with a one-week history of difficulty walking and thunderclap headaches. The patient was diagnosed with Guillain-Barré syndrome based on neurological examination, cerebrospinal fluid analysis and nerve conduction findings. Further diagnosis of posterior reversible encephalopathy and reversible cerebral vasoconstriction syndromes was based on imaging findings and headache history. The patient was treated with intravenous immunoglobulin and amlodipine, and symptoms improved.

Discussion: We reviewed the literature on Guillain-Barré syndrome associated with posterior reversible encephalopathy and/or reversible cerebral vasoconstriction syndrome. The underlying pathophysiology may involve dysautonomia resulting in unstable blood pressure, and hyponatraemia causing endothelial dysfunction. The SNOOP mnemonic highlights the 'red flags'. This SNOOP mnemonic suggests the possibility of secondary headaches that require imaging studies. In this case, the patient exhibited three SNOOP symptoms: S (history of malignancy: follicular lymphoma), O (sudden-onset headache) and O (over 50 years old).

Conclusion: This case highlights the importance of considering coexisting central neurological disorders in patients with Guillain-Barré syndrome.

KEYWORDS

Guillain-Barré syndrome, posterior reversible encephalopathy syndrome, reversible cerebral vasoconstriction syndrome, hyponatraemia

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LEARNING POINTS

- Guillain-Barré syndrome (GBS) alone rarely causes headaches; therefore, when GBS patients complain of severe headaches, especially when the headache is associated with 'red flags', other complications and differential diagnosis should be considered.
- Posterior reversible encephalopathy syndrome (PRES) and reversible cerebral vasoconstriction syndrome (RCVS) can be triggered by GBS.
- Hyponatraemia, age over 50 years and female gender may be risk factors for developing PRES and RCVS in GBS patients.

INTRODUCTION

Guillain-Barré syndrome (GBS) is an immune-mediated inflammatory polyneuritis, a disease clinically characterised by rapidly progressive flaccid paralysis and various sensory disturbances[1]. Although rare, GBS is an independent risk factor for posterior reversible encephalopathy syndrome (PRES)[2-5]. Reversible cerebral vasoconstriction syndrome (RCVS) has also been reported in patients with GBS[6]. PRES is a neurological disorder characterised by visual disturbances, headaches, vomiting, seizures and disorientation. There are no specific diagnostic criteria; the diagnosis is confirmed based on characteristic clinical symptoms and imaging findings on computed tomography (CT) or magnetic resonance imaging (MRI).

Patients with RCVS usually present with recurrent thunderclap headaches along with other symptoms, including seizures and focal neuropathy that usually follow the onset of headaches. The diagnosis of RCVS is also clinicoradiological, based on a combination of clinical features such as thunderclap headaches and vasogenic oedema on head CT/MRI, cerebral arterial vasoconstriction findings on magnetic resonance angiography (MRA) and absence of aneurysmal subarachnoid haemorrhage. Conversely, head imaging is not required to diagnose GBS.

We report a case that suggests this relationship may not simply be coincidental but may instead be causal and/or belong to a continuum between GBS as immune-mediated inflammatory polyneuritis and the central neurologic syndromes PRES and RCVS.

CASE PRESENTATION

A woman in her 60s was referred to the neurology clinic with a one-week history of difficulty walking, which started following an episode of fever. The patient reported recent thunderclap headaches, which began one week previously. The onset of the headache was sudden, holocranial, with a 10 out of 10 intensity. The patient had been taking non-steroidal anti-inflammatory drugs daily and had a history of follicular lymphoma for 2 years preceding the day of the admission. The patient had been treated with chemotherapy for 5 months and was in remission at the time. The patient had no history of hypertension, migraine or immunosuppressive medication use for at least a year. Brain metastasis was considered at an outside hospital and a head CT was performed, which showed no acute intracranial infarction or haemorrhage; however, hypoattenuation in the bilateral occipital lobes was observed *(Fig. 1)*. The patient was transferred to our hospital for further evaluation and treatment.

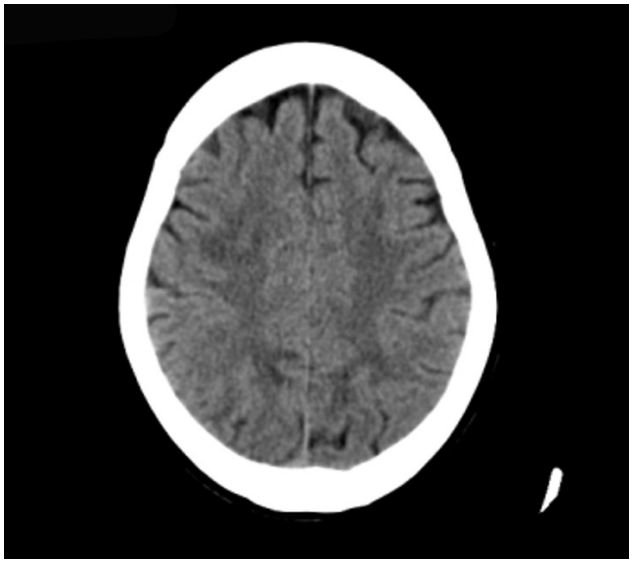

Figure 1. Computed tomography examination showing symmetric bilateral hypodensities predominantly in the occipital lobes and part of the frontal lobes.

Her vital signs on arrival were as follows: heart rate 95 beats/min (regular rhythm), blood pressure 168/93 mmHg, respiratory rate 17/min, oxygen saturation 95% (breathing ambient air) and body temperature 36.5 °C. No papilloedema was observed. Neurologic examination revealed muscle weakness in the extremities (Medical Research Council grade 4/5 in the upper extremities and 3/5 in the lower extremities) and loss of tendon reflexes in bilateral upper and lower extremities. The tactile sensation was reduced in the right L5 region; the remaining neurological parameters were within normal limits. Nuchal rigidity, and Kernig's and Brudzinski's signs were all absent. Laboratory tests revealed a white blood cell (WBC) count of 5.4×10^3/µl (reference range: 4.0×10^3–9.0×10^3/µl) and hyponatraemia (121 mmol/l; reference range 135–145 mmol/l). The C-reactive protein level and erythrocyte sedimentation rate were normal (0.07 mg/dl; reference range: 0.00–0.14 mg/dl and 10 mm/h; reference range: 1–20 mm/h, respectively). The results of other complete blood count and comprehensive metabolic panels were also unremarkable. Cerebrospinal fluid (CSF) examination showed a WBC count of 1/µl (reference range: 0–3/µl) and protein level of 536.8 g/l (reference range: 15–40 g/l), indicating albuminocytologic dissociation. The CSF

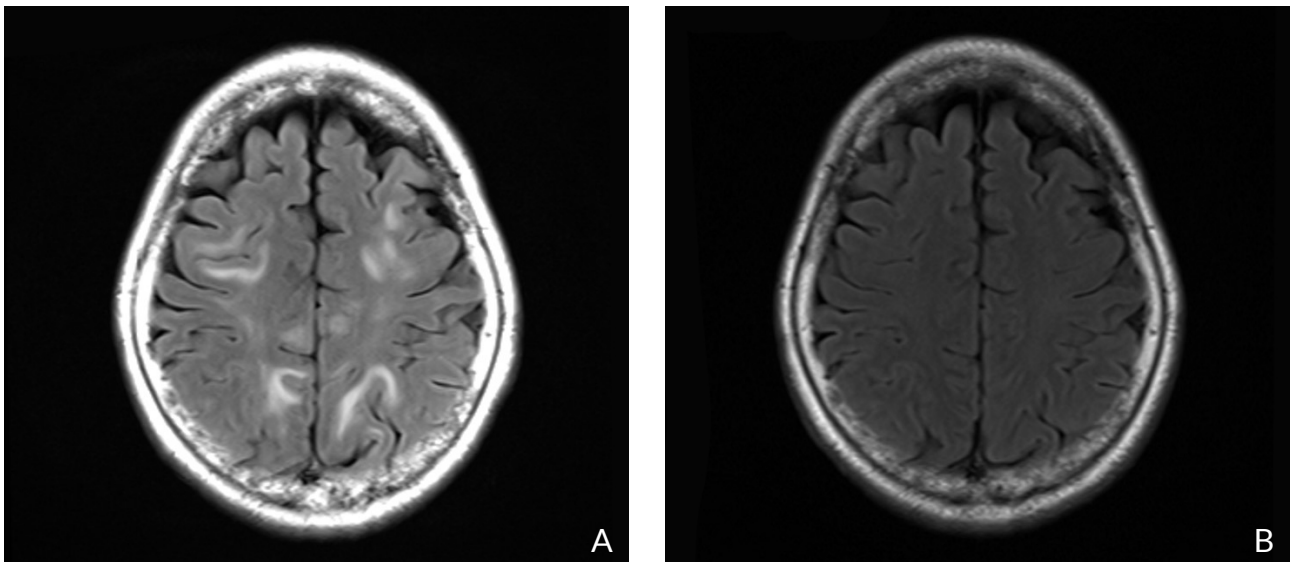

Figure 2. (A): Magnetic resonance imaging showing symmetric bilateral cortical and subcortical hyperintensities on T2-fluid-attenuated inversion recovery images predominantly in the occipital lobes, parietal lobes, and part of the frontal lobes. (B): After 3 months, magnetic resonance imaging showing the disappearance of the area of hyperintensities on T2-fluid-attenuated inversion recovery images.

opening pressure, glucose level, Gram staining and culture were unremarkable.

Brain MRI T2-fluid-attenuated inversion recovery images showed hyperintensity in the parieto-occipital region more predominantly than in the bilateral occipital regions *(Fig. 2A)*. MRA demonstrated poor delineation of the cortical branches of the bilateral middle cerebral arteries *(Fig. 2B)*. The nerve conduction study (NCS) conducted 4 days after admission showed decreased amplitude in the motor nerves, whereas the motor conduction velocity was largely retained, along with prolonged distal motor latency. The conduction velocity of sensory nerves was relatively preserved, whereas the amplitude was depressed. Those results indicated predominant acute motor sensory axonal neuropathy with traces of distal motor demyelination. Both anti-GM1 immunoglobulin G (IgG) and anti-GQ1b IgG antibodies were negative. Based on the neurological examination findings, CSF analysis revealing albuminocytologic dissociation and NCS findings, a diagnosis of GBS was confirmed. The patient was also diagnosed with PRES and RCVS based on headache history and MRI findings.

Intravenous immunoglobulin (0.4 g/kg) was administered for 5 days. Hypertension was controlled with amlodipine (5 mg). Her headaches and blood pressure stabilised in 9 days, and amlodipine was discontinued. The patient was transferred to another hospital for rehabilitation. After 1 month, the neurological status improved and the patient was discharged.

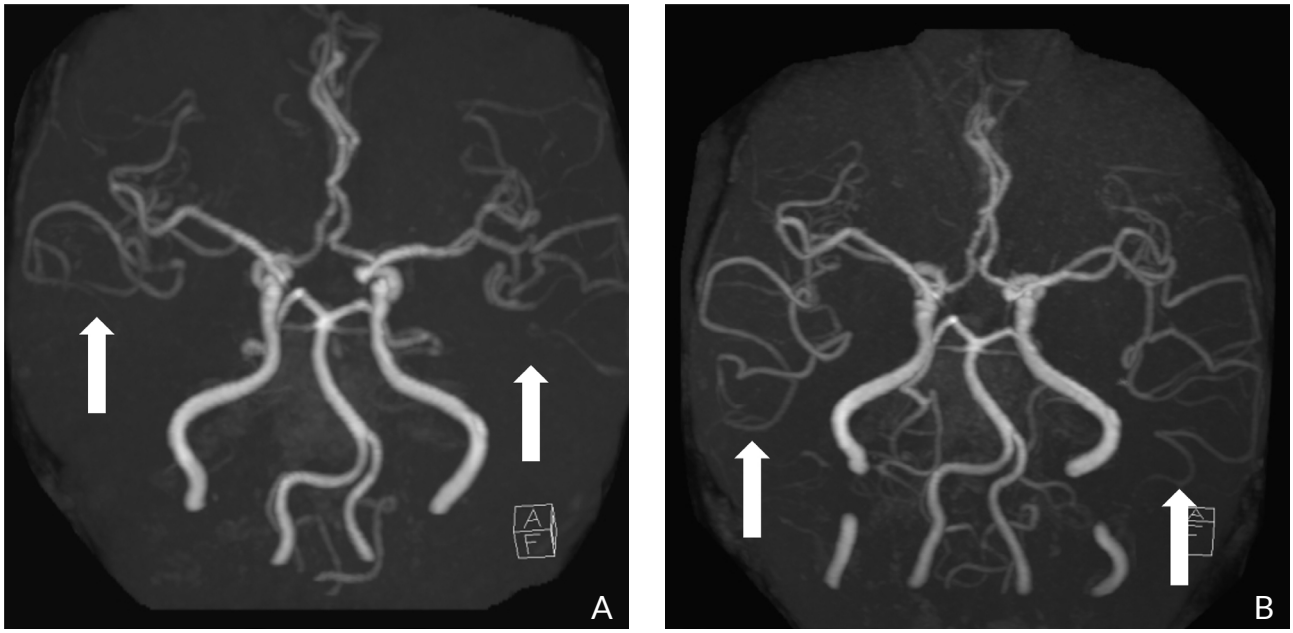

Figure 3. (A): Magnetic resonance angiography demonstrates poor delineation of the cortical branches of the bilateral middle cerebral arteries. (B): Magnetic resonance angiography showing an increase in the cortical branches of the bilateral middle cerebral arteries, whose brightness was further increased.

Three months after the initial imaging, brain MRI showed improvement in the frontal and occipital lobes *(Fig. 3)*.

DISCUSSION

We present a case of GBS complicated by PRES and RCVS. RCVS and PRES share precipitating factors, clinical and radiological features, and are frequently associated with each other, implying similar pathophysiology related to reversible dysregulation of the cerebral vasculature, endothelial dysfunction and disruption of the blood–brain barrier[7]. A hypothetical pathophysiology of GBS complicated by PRES has been reported, suggesting that endothelial dysfunction of any cause can affect the regulation of cerebral arterial tone and trigger vasoconstriction with subsequent hypoperfusion, disruption of the blood–brain barrier and vasogenic oedema[8]. Approximately 30 cases of GBS complicated by PRES have been reported to date, and the possible triggers include hypertension and hyponatraemia, which were also observed in our case[1,5,9]. Dysautonomia due to GBS, resulting in unstable blood pressure, can lead to cerebral oedema, causing endothelial dysfunction that may be responsible for the development of PRES[1]. A previous report of PRES in a normotensive patient with hyponatraemia suggested that a rapid change in sodium level can disrupt cerebral autoregulation, resulting in PRES[5,9]. The incidence of hyponatraemia in patients with GBS has been reported in 21.5%–48% of patients with GBS[10]. In our literature search of patients with listed sodium values, all three cases of overlapping GBS and PRES exhibited hyponatraemia. In the present GBS case, hyponatraemia may also be one of the triggers of PRES. Further investigation involving a larger cohort is required to confirm this hypothesis.

PRES and RCVS are usually reversible with early diagnosis and prompt treatment, which ensures a favourable prognosis. The development of haemorrhagic or ischaemic brain lesions, in some cases, often results in a poor prognosis. Therefore, early diagnosis and treatment are important[11].

GBS is generally a peripheral nerve disorder; therefore, imaging of the central nervous system, such as head CT and MRI of the brain, are unnecessary. The present case was diagnosed as GBS based on clinical, CSF and NCS findings. Because headache is an uncommon symptom of GBS[3], further imaging tests were required in this case, which revealed vasogenic oedema predominantly in the occipital lobe. Cerebral vascular imaging showed vasoconstriction of the cortical branches of the bilateral middle cerebral arteries, leading to the diagnosis of PRES and RCVS. PRES and RCVS cause headaches, visual symptoms, seizures and confusion. However, each syndrome displays characteristic imaging findings. In PRES, head CT and MR imaging are usually symmetrical and show reversible vasogenic oedema in the subcortical region, while in RCVS, cerebral vascular imaging shows partial vasoconstriction–vasodilation characteristics.

The SNOOP mnemonic highlights red flags, which suggest the possibility of secondary headaches that require imaging studies and can be expanded as follows[12]:

S: Systemic symptoms (fever, weight loss), secondary risks (history of immunocompromised state, history of malignancy)

N: Neurologic symptoms/signs (altered consciousness, focal deficits)

O: Onset (sudden-onset headache)

O: Older (new headache in patients over the age of 50 years)

P: Progressive, positional, papilloedema

The patient fulfilled at least three of the SNOOP red flags (history of malignancy, sudden onset of headache, new headache in a person older than 50 years of age), which warranted imaging tests that confirmed the diagnosis.

CONCLUSION

We present a case that may aid associating GBS and PRES/RCVS as belonging to the continuum of a syndrome due to underlying dysautonomia resulting in unstable blood pressure with or without hyponatraemia, causing endothelial dysfunction and thereby disrupting cerebral autoregulation. The workup of GBS, when associated with a headache syndrome, can be facilitated by cerebral imaging. Clinicians should carefully enquire about any history of headaches and consider imaging tests when the patient fulfils any of the red flags.

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