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*Case Report*

# Posterior reversible encephalopathy syndrome following paroxysmal nocturnal hemoglobinuria: a case report and literature review

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**Abstract:** Paroxysmal nocturnal hemoglobinuria (PNH) is a rare acquired disorder characterized by hemolytic anemia, marrow failure, and a high incidence of life-threatening venous thrombosis. It is subject to a considerable variety of complications like intestinal obstruction and visceral embolism. The current study firstly presents a 40-year-old male with a previous diagnosis of PNH who developed posterior reversible encephalopathy syndrome (PRES) during treatment with methylprednisolone. He was referred to our department with headache and two episodes of generalized tonic-clonic seizures. Laboratory examination revealed peripheral blood cytopenias and elevated count of reticulocyte. Brain magnetic resonance imaging (MRI) exhibited abnormal signal in the bilateral parieto-occipital lobes with symmetric distribution which confirmed the diagnosis of PRES. After receive treatment of dexamethasone, anti-hypertensive and neurotropic drugs, the patient made a complete clinical recovery; and the abnormal signals of MRI were almost completely absorbed. This case shows that PRES might be a rare complication of PNH. Furthermore, it points out the necessity of rapid diagnosis and treatment of PRES.

**Keywords:** Paroxysmal nocturnal hemoglobinuria, posterior reversible encephalopathy syndrome, seizures, methylprednisolone, magnetic resonance imaging

## Introduction

PNH is a rare acquired hematopoietic stem cell disorder which manifests with hemolytic anemia, thrombosis, bone marrow failure and peripheral blood cytopenias [1]. It is subject to a considerable variety of complications like intestinal obstruction and visceral embolism [2, 3]. Here we firstly describe a 40-year-old male with a previous diagnosis of PNH who developed posterior reversible encephalopathy syndrome (PRES) during treatment with methylprednisolone.

PRES was first described by Hinchey et al in 1996 [4]. Clinically it is marked by typical symptoms including headache, seizures, visual disturbances, altered mental status, nausea, vomiting, and focal neurological signs and accompanied by a typical computed tomography (CT) or MRI pattern [4]. The causes of PRES are varied and have been largely attributed to hypertension, eclampsia, malignancy, renal insufficiency, organ transplantation and the use of immune-suppressants [5, 6]. Although clinical manifestations of PRES are usually revisable and patients with PRES are mostly have a good prognosis, early diagnosis and treatment is essential as it may prevent progression to irreversible brain damage.

## Case report

A 40-year-old man presented to the emergency department after headache and two episodes of generalized tonic-clonic seizures at home. In his medical history, he had been diagnosed with paroxysmal nocturnal hemoglobinuria (PNH) for 8 years and slightly hypertension for 2 years. During the past 8 years, he has consecutively taken methylprednisolone orally (5 mg/d) to control the disease progression of PNH. A month ago, he was diagnosed as left lower limb deep venous thrombosis, as symptom progressing, he had to accept an amputation surgery consequently.

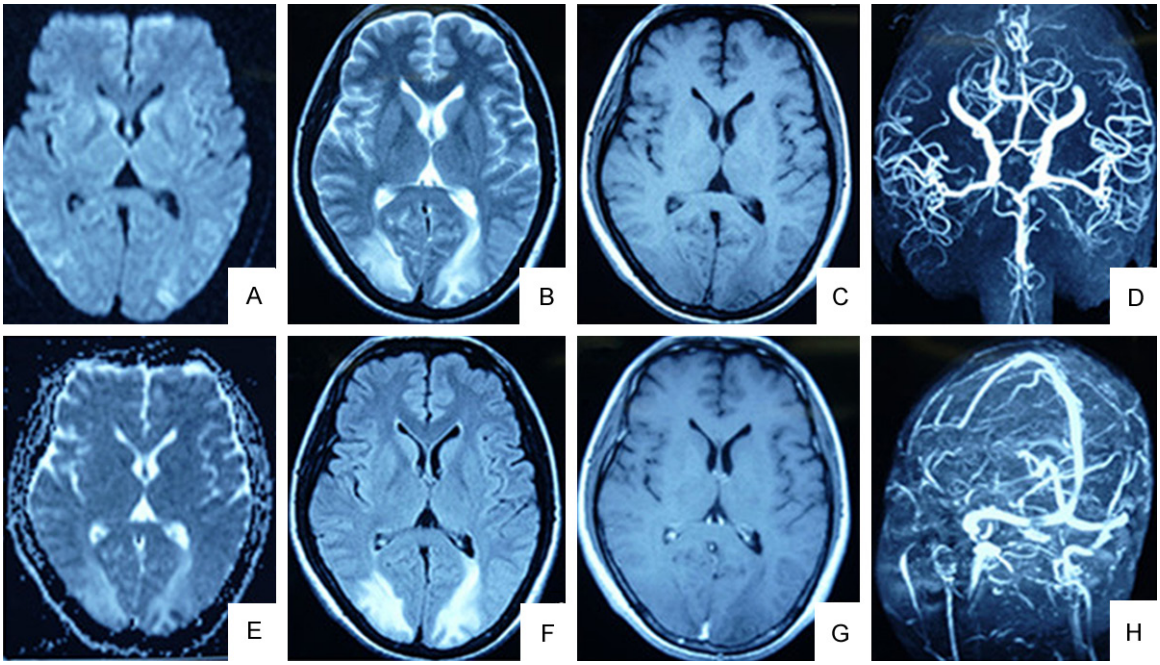


**Figure 1.** Brain MRI scanning of the patient after first hospitalization. Brain MRI of PRES demonstrates characteristic symmetric white matter changes involving parieto-occipital lobes. Cranial magnetic resonance tomography at the time of acute symptom DWI (A), T2-weighted sequence (B), ADC (E), FLAIR (F) shows bilateral parieto-occipital hyperintense signal in both cortex and white matter; T1-weighted sequence (C), enhanced sequence (G) shows equal signal, without a vascular pathology in the magnetic resonance angiography (D) and magnetic resonance venography (H).

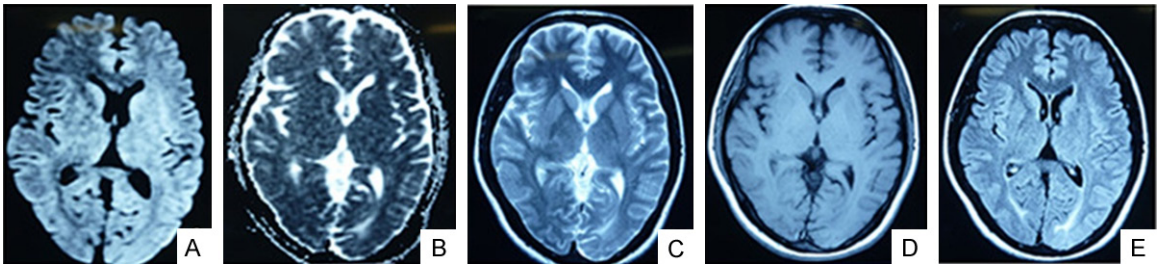


**Figure 2.** Brain MRI scanning of the patient after treatment. Seventeen days after the onset, the abnormal signal on every sequence of our MRI was significantly decreased in size.

Physical examination at the onset revealed blood pressure of 159/93 mmHg, heart rate of 69 beats/min; consciousness; equally big and round pupils with sensitive light reflex; no evidence of focal neurological deficit and meningeal signs were got by neurological examination. His laboratory examination showed hemoglobin of 77 g/L, a total white blood cells (WBC) count of $3.5\times10^9$/L, and platelet count of $83\times10^9$/L. The patient was negative for direct Coomb's test and corrected reticulocyte was 3%. His serum biochemistry results and serum immunity indicator levels were within normal limits except that complements were low (C3: 664 mg/L; C4: 216 mg/L). Serology for human immunodeficiency virus (HIV), syphilis, Epstein-Barr virus, cytomegalovirus, hepatitis A, B, C viruses, and tubercle bacillus were negative. Cerebral fluid (CSF) studies revealed clear and colorless fluid with normal opening pressure, cell counts, glucose and protein contents. Evaluations for infection, including virus, Tuberculosis, Cryptococcus, Gram's staining, India ink stain and cultures were unrevealing.

Brain MRI examination showed high signals on T2, fluid-attenuated inversion recovery (FLAIR) MRI, diffusion weight imaging (DWI) and appar-

ent diffusion coefficient (ADC), as well as equal signals on T1 and enhanced MRI in the bilateral parieto-occipital lobes with symmetric distribution (**Figure 1**). Following treatments were given: irbesartan to control blood pressure; dexamethasone to regulate immune function. The patient also received administration of the neurotropic drugs such as edaravone and ganglioside. After he presented in our hospital, no further seizure and other symptom occurred. A week later, the patient was discharged from the hospital with the advice to continue the antihypertensive drugs and methylprednisolone (50 mg begin and reduce 5 mg every week). Ten days after his discharge, re-examination with MRI showed that the abnormal signal decreased significantly in size compared with basis examination (**Figure 2**). The diagnosis of PRES was confirmed by imaging and clinical course.

## Discussion

With the widespread use of medical imaging in clinical practice, an increasing number of patients with PRES causing by diverse original diseases have been reported. Clinical features of PRES are typically characterized by acute to sub-acute disorder of headache, seizure, dizziness, altered consciousness, nausea, convulsions and transient visual disturbances [7-9]. Our patients presented with headache, seizures, slight hypertension which was similar to previous reports. This indicated despite PRES have various clinical features, not all symptoms appear in the whole process, and certain symptoms may occur repeatedly.

The underlying pathophysiological mechanisms still remain unclear [10]. There are two major hypotheses on the pathogenesis of PRES. The first hypothesis is the cytotoxic edema developing secondary to vasospasm, reactive to a sudden hypertensive attack, occurring especially in the areas of limited arterial blood supply. A more recently and widely accepted theory is that hypertension gives rise to the transient impairment in cerebral auto-regulation and this leads to cerebral vasodilatation, therefore, allows extravasation of fluid and causes vasogenic cerebral edema [11, 12]. There are several reports on causal factors of PRES in children or in adults, such as eclampsia [13], transplantation [11, 14], chemotherapies [11], infectious conditions, or autoimmune diseases [6]. To date, no reports demonstrate that PRES can be caused by PNH. PNH is one kind of autoimmune diseases characterized by hemolysis, diminished hematopoiesis, and thrombophilia [3]. Our patient was diagnosed with this disease 8 years ago. His symptom was well-regulated by a low dose glucocorticoid treatment before this hospitalization. Further research is needed to study the association between PNH and PRES.

Although reversible by definition, if the patient did not undergo early recognition and timely treatment, irreversible brain damages may occur. Our patient's MRI revealed increased signal in the bilateral parieto-occipital lobe on T2-weighted, FLAIR, DWI and ADC sequences. These findings were considered consistent with PRES [15], attributable to a manifestation of vasogenic and cytotoxic edema. Treatment of PRES includes better blood pressure control, withdrawal/decreased doses of the offending medications, and seizure management [16]. In our patient, the antiepileptic drugs were not used and we continue the glucocorticoid treatment. Following the treatment mentioned above, his neurological complaints improved. We thus conjecture that PRES should be a complication of PNH, as well as thrombosis. To our knowledge, our patient was the first patient to develop PRES associated with PNH.

In conclusion, PRES is a rare complication of different diseases or some special treatments; it also can be followed by PNH. The diagnosis of PRES is made by recognition of the clinical manifestation, Imaging feature, especially MRI. MRI is very helpful to rule out alternative causes and to confirm the diagnosis. In order to prevent progression to permanent neurological damage and death, the underlying cause should be addressed, and treatment should be initiated as soon as possible [17].

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## Disclosure of conflict of interest

None.

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