

# Hypertensive posterior reversible encephalopathy syndrome in Lesch–Nyhan disease: possible contribution of chronic hyperuricemia and renin activation – a case report

Akihisa Nitta

[a-nitta@dokkyomed.ac.jp](mailto:a-nitta@dokkyomed.ac.jp)

Dokkyo Medical University, Saitama Medical Center

Yuji Oto

Dokkyo Medical University, Saitama Medical Center

Satomi Koyama

Dokkyo Medical University, Saitama Medical Center

Tomozumi Takatani

Dokkyo Medical University, Saitama Medical Center

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## Case Report

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# Abstract

## Background

Posterior reversible encephalopathy syndrome (PRES) is characterized by seizures, altered consciousness, and vasogenic edema predominantly affecting the parieto-occipital regions. Although acute hypertension is a major precipitating factor, impaired cerebral autoregulation and endothelial dysfunction are also considered to contribute to its pathophysiology. Lesch–Nyhan disease (LND) is a rare X-linked disorder caused by hypoxanthine–guanine phosphoribosyltransferase deficiency and is associated with chronic hyperuricemia and severe neurological manifestations. Hypertension has rarely been described in association with LND.

## Case presentation

We report a 4-year-old boy with genetically confirmed LND who developed hypertensive PRES during status epilepticus. On admission, his blood pressure was markedly elevated (207/101 mmHg). Neurological symptoms improved promptly after antihypertensive therapy. Brain magnetic resonance imaging demonstrated bilateral occipital subcortical hyperintensities on T2-weighted and fluid-attenuated inversion recovery images. Echocardiography revealed left ventricular hypertrophy. Plasma renin activity was elevated prior to initiation of angiotensin-converting enzyme inhibitor therapy. No structural renal abnormalities were detected.

## Conclusions

This case suggests that chronic hyperuricemia-related vascular dysfunction, including cerebral vascular endothelial vulnerability, together with activation of the renin–angiotensin system, may increase susceptibility to the development of hypertensive PRES.

## Background

Posterior reversible encephalopathy syndrome (PRES) is a clinicoradiological entity characterized by seizures, headache, altered consciousness, and visual disturbances accompanied by reversible vasogenic edema predominantly in the posterior cerebral regions [1–3]. Although initially described as hypertensive encephalopathy, current understanding emphasizes failure of cerebral autoregulation and endothelial dysfunction triggered by acute hypertension, infection, or inflammation [2, 4].

In pediatric populations, hypertension is one of the most common precipitating factors of PRES, particularly in association with renal disorders and systemic conditions [5].

Lesch–Nyhan disease (LND) is an X-linked recessive metabolic disorder caused by deficiency of hypoxanthine–guanine phosphoribosyltransferase (HGPRT) [9, 10]. It is characterized by hyperuricemia,

dystonia, intellectual disability, and self-injurious behavior. Hypertension has rarely been reported in association with LND.

## Case presentation

A 4-year-old boy with genetically confirmed Lesch–Nyhan disease (LND) was transferred to our hospital because of prolonged seizures and impaired consciousness. Hyperuricemia had been detected during infancy (serum uric acid 16 mg/dL), and the diagnosis of LND was established at 8 months of age by genetic testing. He had been treated with allopurinol and rehabilitation therapy. His developmental milestones were delayed, and self-injurious behavior was present.

On the day of admission, he developed generalized clonic seizures followed by decreased consciousness. Upon arrival at the emergency department, his blood pressure was markedly elevated at 207/101 mmHg. Heart rate was 150 beats per minute. Because of respiratory failure, endotracheal intubation was performed and the patient was admitted to the intensive care unit.

Initial laboratory findings showed no significant electrolyte imbalance or evidence of infection. Serum creatinine was transiently elevated during hospitalization, and serum uric acid levels increased during the acute phase. Urinalysis showed no persistent proteinuria.

Continuous intravenous nicardipine infusion was initiated for blood pressure control, and midazolam was administered for seizure management. Blood pressure gradually decreased to the 120–140 mmHg range within 24 hours, accompanied by improvement in the level of consciousness.

Brain magnetic resonance imaging performed on hospital day 8 demonstrated bilateral hyperintense lesions predominantly involving the subcortical white matter of the occipital lobes on T2-weighted and fluid-attenuated inversion recovery sequences (Figure 1). These findings were consistent with PRES.

Abdominal magnetic resonance angiography showed no structural renal or vascular abnormalities. Plasma renin activity measured before initiation of angiotensin-converting enzyme inhibitor therapy was elevated (13 ng/mL/hr). Angiotensin-converting enzyme inhibitor therapy was introduced after stabilization of blood pressure.

Echocardiography revealed left ventricular hypertrophy. The patient recovered without neurological sequelae and was discharged on hospital day 15. At follow-up, blood pressure remained controlled under antihypertensive therapy.

## Discussion and conclusions

This case describes hypertensive posterior reversible encephalopathy syndrome (PRES) occurring in a child with Lesch–Nyhan disease (LND). The marked elevation in blood pressure at presentation and the rapid neurological improvement following antihypertensive treatment indicate that acute hypertension

was the immediate trigger. However, several findings suggest that this episode occurred on a background of chronic vascular vulnerability.

PRES is generally attributed to failure of cerebral autoregulation, leading to hyperperfusion and vasogenic edema in the posterior circulation [1–3]. Although abrupt elevation of blood pressure is a well-recognized precipitating factor, not all cases of PRES are explained solely by hypertension. Endothelial dysfunction is increasingly considered to play an important role, particularly in patients with systemic inflammatory or metabolic conditions [2,4]. In children, hypertension is among the most frequent triggers [5], yet the threshold at which autoregulation fails may vary depending on underlying vascular integrity.

In the present patient, prolonged seizures may have enhanced sympathetic activity and contributed to sudden blood pressure elevation. Nevertheless, the presence of left ventricular hypertrophy suggests that elevated blood pressure may have been present before this acute episode. In pediatric populations, left ventricular hypertrophy is regarded as evidence of sustained blood pressure load and target organ involvement, supporting the possibility of pre-existing hemodynamic stress.

Plasma renin activity was elevated before initiation of angiotensin-converting enzyme inhibitor therapy, suggesting activation of the renin–angiotensin system at presentation. Although no persistent proteinuria or structural renal abnormalities were identified, this finding implies functional alterations of the renal microvasculature rather than overt structural injury. Such renal microvascular dysfunction may contribute to renin–angiotensin system activation and subsequent blood pressure instability.

Chronic hyperuricemia has been linked to endothelial dysfunction and hypertension in both experimental and clinical studies [6–8]. Elevated uric acid levels have been shown to impair endothelial nitric oxide production, increase oxidative stress, and promote vascular stiffness. In addition to systemic vascular effects, chronic hyperuricemia may also influence cerebral vascular endothelial function, leading to increased vulnerability of cerebral microvasculature. This endothelial vulnerability may lower the threshold for cerebral autoregulatory failure and predispose patients to PRES under conditions of acute blood pressure elevation.

In LND, persistent hyperuricemia from early childhood could therefore contribute to subtle but chronic vascular alterations affecting both renal and cerebral microvasculature, even in the absence of overt renal structural abnormalities [9,10]. Furthermore, LND is associated with basal ganglia dysfunction and abnormalities in dopaminergic pathways. Although autonomic regulation in LND has not been systematically studied, central dysregulation of sympathetic tone cannot be excluded and may further lower the threshold for blood pressure instability during acute neurological stress.

Taken together, this episode may reflect an interaction between chronic hyperuricemia-related endothelial vulnerability, functional renal microvascular changes with renin–angiotensin system activation, and acute sympathetic stimulation during seizures (Figure 2). While causality cannot be established in a single case, this report highlights a potential mechanism underlying hypertensive PRES in patients with LND.

From a clinical perspective, regular blood pressure assessment and cardiovascular evaluation may be advisable in patients with LND, particularly during acute neurological events.

## Declarations

### Ethics approval and consent to participate

Ethics approval was waived because this is a retrospective case report.

This study is not a clinical trial; therefore trial registration is not applicable.

### Consent for publication

Written informed consent for publication of clinical details and images was obtained from the patient's guardian.

### Competing interests

The authors declare that they have no competing interests.

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### Authors' contributions

AN drafted the manuscript. YO, SK, and TT contributed to clinical management and critically revised the manuscript. All authors approved the final manuscript.

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## Figures

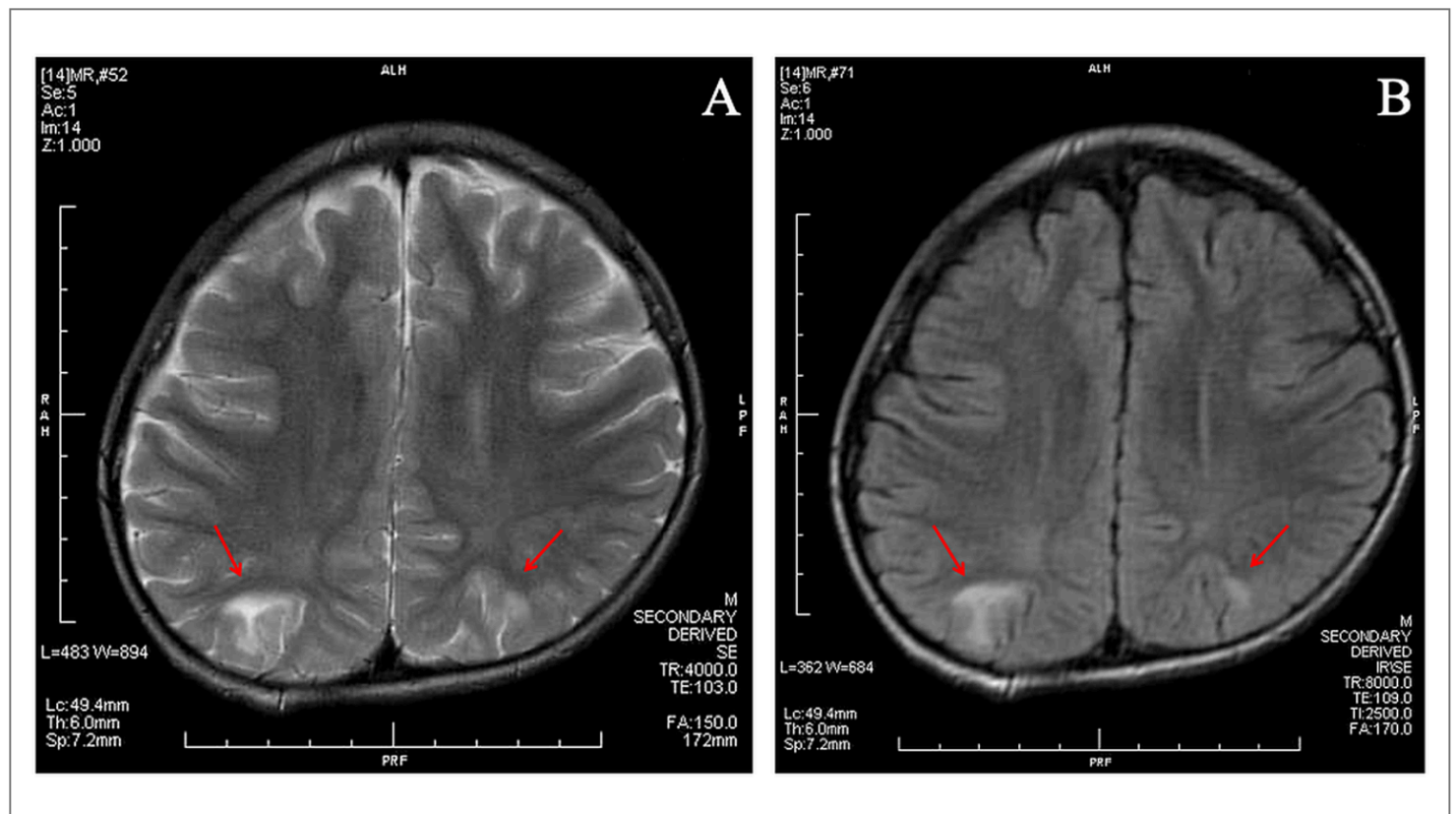


Figure 1

### Brain magnetic resonance imaging findings.

Axial T2-weighted (A) and fluid-attenuated inversion recovery (FLAIR) (B) images obtained on hospital

day 8 demonstrate bilateral hyperintense lesions predominantly involving the subcortical white matter of the occipital lobes (arrows). These findings are consistent with posterior reversible encephalopathy syndrome.

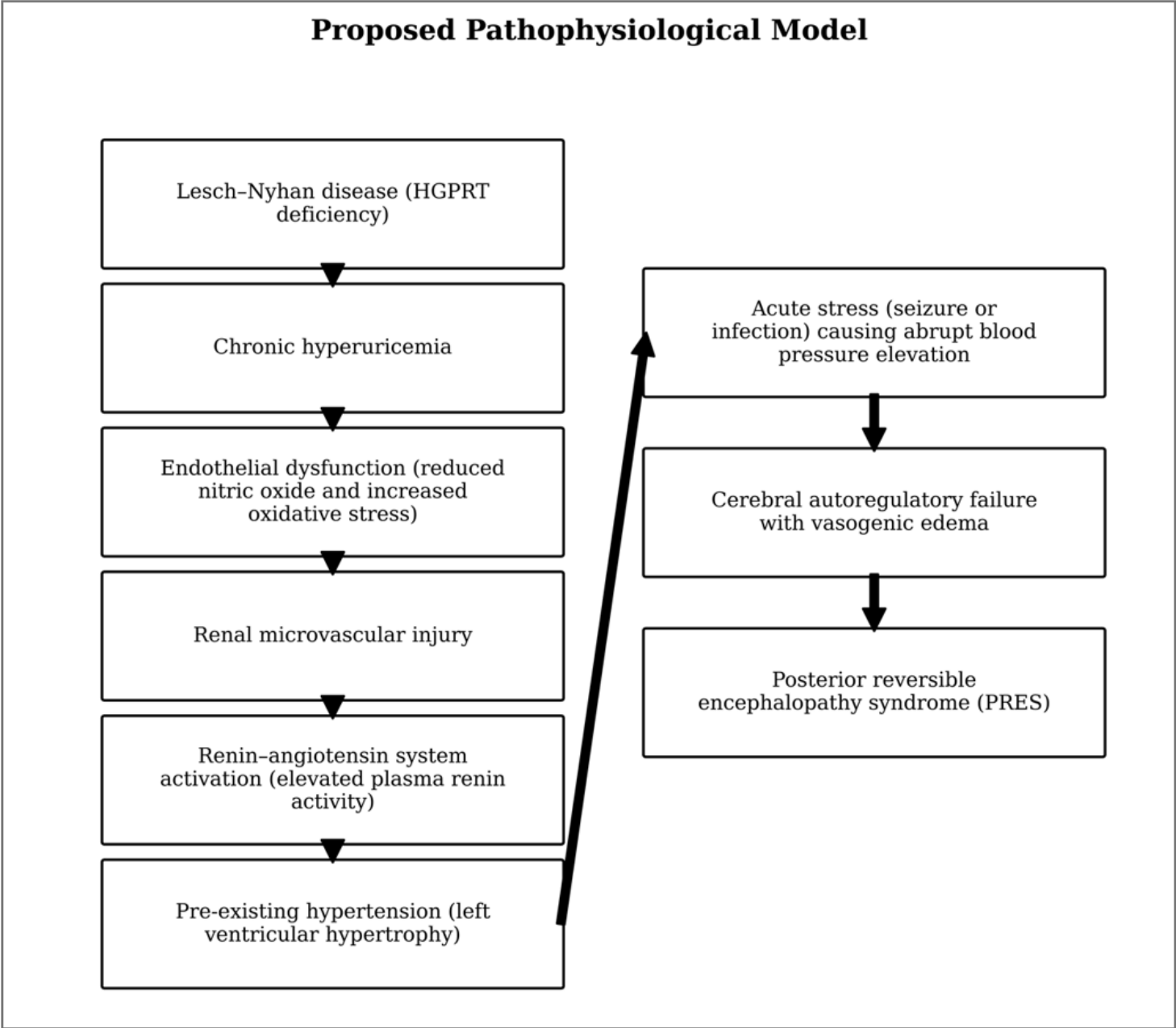


**Figure 2**

**Proposed pathophysiological model of hypertensive posterior reversible encephalopathy syndrome in Lesch–Nyhan disease.**

Chronic hyperuricemia associated with Lesch–Nyhan disease may contribute to endothelial dysfunction and activation of the renin–angiotensin system, leading to a predisposition to hypertension. Under acute stress conditions such as seizures, abrupt blood pressure elevation may exceed cerebral autoregulatory capacity and result in vasogenic edema characteristic of posterior reversible encephalopathy syndrome.