References

- 1 Yusuf S, Teo KK, Pogue J, et al; for the ONTARGET investigators: Telmisartan, ramipril, or both in patients at high risk for vascular events. *N Engl J Med* 2008;358:1547–1559.
- 2 Graves SW, Moore TJ, Seely EW: Increased platelet angiotensin II receptor number in pregnancy-induced hypertension. *Hypertension* 1992;20:627–632.
- 3 Serebruany VL, Malinin AI, Lowry DR, Sane DC, Webb RL, Gottlieb SO, Hennekens CH: Platelet inhibition by valsartan and valeryl 4-hydroxy valsartan: a possible missing link to explain benefits of angiotensin II receptor blockers in patients after acute vascular events. *J Cardiovasc Pharmacol* 2004;43:677–684.
- 4 Serebruany VL, Pokov A, Malinin AI, J-F Tanguay, Bhatt DL, Sane DC, Hennekens CH: Valsartan inhibits platelet activity at different doses in mild to moderate hypertensives: Valsartan Inhibits Platelets (VIP) Trial. *Am Heart J* 2006;151:92–99.
- 5 Diener HC, Sacco R, Yusuf S; Steering Committee; PROFESS Study Group: Rationale, design and baseline data of a randomized, double-blind, controlled trial comparing two antithrombotic regimens (a fixed-dose combination of extended-release dipyridamole plus ASA with clopidogrel) and telmisartan versus placebo in patients with strokes: the Prevention Regimen for Effectively Avoiding Second Strokes Trial (PROFESS). *Cerebrovasc Dis* 2007;23:368–380.

Dr. Viktor L. Serebruany
HeartDrug™
Research Laboratories
Johns Hopkins University
Osler Medical Building, 7600 Osler Drive, Suite 307
Towson, MD 21204 (USA)
Tel. +1 410 847 9490, Fax +1 443 583 0205, E-Mail heartdrug@aol.com

Cerebrovasc Dis 2008;26:564–566

DOI: [10.1159/000164556](https://doi.org/10.1159/000164556)

Atypical Cases of Posterior Reversible Encephalopathy Syndrome

Clinical and MRI Features

Satyakam Bhagavati^a, Jai Choi^b

^aDepartment of Neurology and ^bNeuroradiology Division,
Department of Radiology, SUNY Downstate Medical Center,
Brooklyn, N.Y., USA

Posterior reversible encephalopathy syndrome (PRES) describes a neurological syndrome with multiple described causes and is characterized by headache, altered mental status, seizures or loss of vision [1]. The typical imaging findings are hyperintensities on magnetic resonance (MR) FLAIR images in the parieto-occipital, posterior frontal cortical and subcortical white matter. The brain stem, basal ganglia and cerebellum are less commonly involved. The pathogenetic mechanism of this entity is poorly understood. One hypothesis states that surges of hyperperfusion in hypertensive patients, primarily in the vertebrobasilar circulation, due to impaired autoregulation lead to extravasation of fluid and vasogenic edema [2]. Alternatively, it has been proposed

that vasoconstriction and hypo-perfusion cause ischemia and edema [3, 4].

We describe here 2 atypical cases of PRES which may shed some light on possible cerebrovascular pathogenetic mechanisms. One patient with a history of pre-eclampsia presented with uncommon MR imaging (MRI) findings of a pontine lesion and multifocal constrictions of the basilar, posterior cerebral and carotid arteries and their branches, suggestive of vasospasm. The other one, in an acute alcoholic stupor, had a potentially new cause of PRES. We emphasize the vasoconstrictive response which may underlie the pathogenesis of PRES in patients with diverse etiologies.

Case 1

A 21-year-old woman presented 10 days postpartum after induction of vaginal delivery for severe pre-eclampsia at 39 weeks of gestational age. She complained of severe, generalized headaches for 1 day and transient episodes of blurred vision and a feeling of numbness of the right side of her face which lasted about 5 min. On examination the blood pressure was 160/120 mm Hg. The only neurological abnormality noted was bilateral hyperreflexia in both the upper and lower extremities. A cranial T₂-weighted MRI scan revealed an abnormal, hyperintense signal in the pons (fig. 1a). No other cerebral lesions were noted. MR angiography showed focal constriction of the mid basilar artery (fig. 1b) and the cavernous portion of the right internal carotid artery (fig. 1c). Multifocal stenoses (beads-on-string appearance) of branches of the anterior and posterior cerebral arteries were also noted (fig. 1b, c). The blood pressure was controlled with antihypertensive medication. Extensive workup for vasculitis (including antinuclear antibodies, anti-DNA antibodies, rheumatoid factor) was negative. The patient showed rapid improvement in her symptoms over 3–4 days. A repeat MRI and MR angiography scan after 4 weeks was normal with complete resolution of the pontine lesion and all vascular abnormalities.

Case 2

A 57-year-old patient with a history of chronic alcohol abuse, who had been found by his wife to be walking unsteadily and in a confused state, suddenly collapsed and did not respond to commands. A history of consumption of large amounts of whisky for the past 2 days was provided by the wife. He was rushed to the emergency room. On examination the blood pressure was 131/88 mm Hg and the daily blood pressure readings over the following 2 weeks remained normal. He was minimally responsive to painful stimuli and did not react to verbal commands. The blood alcohol level was very high (358 mg/dl). Toxic screen did not reveal any other drugs. Cranial MRI FLAIR images done at the time of admission revealed bilateral cortical and subcortical, parieto-occipital and posterior frontal hyperintense lesions (fig. 1d). MR angiography did not show any abnormalities. A repeat cranial MRI scan after 2 weeks was normal with resolution of all lesions (fig. 1e) and complete clinical improvement.

Discussion

PRES can occur due to many causes including acute severe hypertension, pre-eclampsia and eclampsia, renal disease, immunosuppressive and cytotoxic drugs (such as cyclosporine and tacrolimus), collagen vascular disorders like systemic lupus erythematosus and hematological disorders such as thrombotic thrombocytopenic purpura and hemolytic-uremic syndrome [1]. Re-

Fig. 1. Case 1: **a** Pre-eclamptic patient 10 days after delivery. Axial T₂-weighted MRI shows high-signal lesion in the pons (arrow). **b** MR angiogram reveals mid basilar narrowing (arrow) and multiple other areas of focal constriction in both posterior cerebral arteries (arrowheads), suggestive of vasospasm. Note string-of-bead appearance of both posterior cerebral arteries. **c** MR angiogram shows focal constriction of the cavernous portion of the right carotid artery (arrow) and anterior cerebral artery branch (arrowhead). Repeat MRI and MR angiogram after 1 month were completely normal (not shown). Case 2: A 57-year-old man in alcoholic stupor. **d** Axial MRI FLAIR image of bilateral parieto-occipital cortical and subcortical hyperintense lesions (arrows). **e** Repeat MRI scan after 2 weeks shows complete resolution of all abnormalities.

cently, PRES has also been mentioned in association with severe infection, sepsis or shock [5].

We describe here (case 2) a potentially new cause for PRES: acute, severe, alcoholic intoxication. Our patient was admitted in an acute alcoholic coma, secondary to binge drinking, with very high blood alcohol levels and had typical MRI findings of PRES which resolved with complete clinical improvement in 2 weeks. He was normotensive at all times and we excluded all other possible causes of PRES by careful clinical evaluation and blood tests. We considered Wernicke's encephalopathy unlikely because of the absence of the typical clinical features of ophthalmoplegia and nystagmus and lack of the typical findings on MRI scans of in-

creased signal in mammillary bodies, medial thalamus or periaqueductal gray matter. In the only other report [6] of a link between alcohol intake and PRES, in a recent extensive review of 76 cases of PRES, alcoholic withdrawal was suggested as a potentially new cause in 1 patient. Unlike ours, this patient had evidence of restricted diffusion on MRI scanning. We are not aware of any previous report of PRES in a patient in alcoholic stupor or coma.

Case 1 had PRES secondary to pre-eclampsia, with evidence of a hyperintense pontine lesion. In addition, MR angiography revealed multifocal vasoconstriction in the major cerebral vessels (basilar, posterior cerebral, carotid and anterior cerebral arteries and their branches) suggestive of vasospasm. All abnormalities

had resolved on repeat evaluation after 1 month. The presence of the pontine hyperintense lesion associated with basilar artery vasoconstriction and other areas of focal vascular stenoses in our patient raised the possibility of an acute ischemic insult secondary to vasculitis. However, the absence of clinical or serological features of vasculitis and the rapid clinical and MRI resolution were supportive of a diagnosis of PRES.

Two previous studies reported single cases of pre-eclamptic pregnant women at 34 and 42 weeks of gestation who presented with confusion or stupor [3, 4] and were shown to have diffuse vasospasm of the posterior, middle and anterior cerebral arteries on angiography. Cranial CT scan showed brain stem and thalamic low-density ischemic lesions in 1 patient [3]. The subjects improved and these findings resolved in 1 month. Furthermore, an extensive recent study [7] of catheter and MR angiography in 47 PRES patients showed that 86% had diffuse or focal cerebral vasoconstriction most commonly affecting second- or third-order branches or vessel pruning in the anterior, middle or posterior cerebral artery territories.

The radiological confirmation of the presence of vasoconstriction suggests that the primary abnormality in PRES may be hypoperfusion and ischemia with secondary edema. It is likely that endothelial injury may underlie the vasoconstriction seen in PRES. It is known that PRES secondary to diverse causes including eclampsia, hypertension, autoimmune diseases, sepsis or cyclosporine is associated with systemic inflammation, endothelial activation and injury and significant release of cytokines [7, 8]. Cytokines such as tumor necrosis factor- α and interleukin-1 are known to promote endothelin-1 production, a potent vasoconstrictor [8]. Moreover, endothelial injury may lead to increased white blood cell and platelet adherence resulting in decreased flow.

We speculate that, in a similar manner, acute, severe, alcoholic intoxication may have caused cerebrovascular ischemia and PRES in our patient. High alcohol concentrations have been unequivocally shown to be associated with dose-related vasoconstriction and to impair the dilatation of cerebral vessels [9, 10]. Although the mechanism of this vasoconstriction is not fully understood, it is hypothesized that high ethanol levels may directly stimulate the synthesis/release of the vasoconstrictor, endothelin-1, and also impair the synthesis and release of nitric oxide, a potent vasodilator [9, 10]. The vasoconstrictive effects of high ethanol levels are transitory and dose dependent, which may explain the fact that cerebrovascular changes were not detected in our patient on MR angiography.

Although more cases need to be studied, acute, severe alcoholic intoxication is a potentially new cause of PRES. Secondly, it is important for prompt and accurate diagnosis to recognize that patients with PRES (as in our pre-eclamptic subject) may have multiple areas of focal vasoconstriction of cerebral blood vessels, which are usually fully reversible. In conclusion, the patients we describe here support the hypothesis that a wide and diverse array of etiologic factors may cause PRES by altering vascular reactivity, inducing cerebral vasoconstriction and secondary edema.

References

- Hinchey J, Chaves C, Appignani B, et al: A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996;334:494–500.
- Johansson B: The blood-brain barrier and cerebral blood flow in acute hypertension. *Acta Med Scand Suppl* 1983;678:107–112.

- Trommer BL, Homer D, Mikhael MA: Cerebral vasospasm and eclampsia. *Stroke* 1988;19:326–329.
- Ito T, Sakai K, Inagawa S, et al: MR angiography of cerebral vasospasm in preeclampsia. *Am J Neuroradiol* 1995;16:1344–1346.
- Bartynski WS, Boardman JF, Zeigler ZR, et al: Posterior reversible encephalopathy syndrome in infection, sepsis, and shock. *Am J Neuroradiol* 2006;27:2179–2190.
- McKinney AM, Short J, Truwit CL, et al: Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. *AJR Am J Roentgenol* 2007;189:904–912.
- Bartynski WS, Boardman JF: Catheter angiography, MR angiography, and MR perfusion in posterior reversible encephalopathy syndrome. *Am J Neuroradiol* 2008;29:447–455.
- Friedman SA, Schiff E, Emeis JJ, et al: Biochemical corroboration of endothelial involvement in severe preeclampsia. *Am J Obstet Gynecol* 1995;172:202–203.
- Mayhan WG, Didion SP: Acute effects of ethanol on responses of cerebral arterioles. *Stroke* 1995;26:2097–2102.
- Gordon EL, Nguyen TS, Ngai CA, et al: Differential effects of alcohol on cerebral arterioles: ethanol alone causes vasoconstriction. *J Cereb Blood Flow Metab* 1995;15:532–538.

Dr. S. Bhagavati

Department of Neurology, SUNY Downstate Medical Center
450 Clarkson Avenue
Brooklyn, NY 11203 (USA)
Tel. +1 718 270 2841, Fax +1 718 270 3840
E-Mail Sbhagavati@downstate.edu

Cerebrovasc Dis 2008;26:566–568

DOI: [10.1159/000164557](https://doi.org/10.1159/000164557)

Traveler's Stroke: It Is Not Just Flying That Does It

O. Ayo-Martín^{a,b}, J. García-García^a, D. Sopenana^a, T. Segura^{a,b}

^aDepartment of Neurology, Complejo Hospitalario Universitario de Albacete, Albacete, and ^bDepartment of Medical Sciences, Faculty of Medicine, Universidad Castilla-La Mancha, Albacete, Spain

Introduction

The term *economy class syndrome* refers to venous thromboembolism associated with air travel [1]. This term was chosen to emphasize that a cramped seating condition is an important risk factor in this syndrome, although *traveler's thrombosis* has recently been chosen as a more appropriate term [2].

Stroke may occur after long flights, and the expression *economy class stroke syndrome* (ECSS) was first used in 2002 [3]. All patients fit the following characteristics [3–6]:

- stroke onset after a long-haul flight, in the first 10 min after standing up;
- patent foramen ovale (PFO) present;
- no evidence of stroke being caused by other circumstances.