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Letter to the Editor

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When Should Nitroglycerine Be Avoided in Hypertensive Encephalopathy?

To the Editor:

Intravenous nitroglycerin is a well-recognized treatment of acute hypertension and hypertensive encephalopathy.¹ We are reporting a patient presented with posterior reversible encephalopathy syndrome (PRES) secondary to hypertensive crisis who deteriorated when his blood pressure was treated with intravenous nitroglycerin. We, therefore, suggest that nitroglycerine should be discontinued in all patients with hypertensive encephalopathy with worsening neurological status or in the presence of typical radiological findings.

A 63-year-old man with a history of hypertension and diabetes mellitus presented with a severe headache, associated with nausea and vomiting. He had a history of alcohol abuse complicated by liver cirrhosis but denies drinking for many years. His medications include insulin glargine, atenolol 50 mg, gabapentin, zolpidem, and tamsulosin. His blood pressure was 222/110 mm Hg, and his pulse rate was 68 bpm. Neurological examination revealed mild disorientation but no papilledema or focal neurological deficit. Abnormal laboratory studies on admission included blood glucose 382 mg/dL, alanine transaminase 55 U/L, and aspartate aminotransferase 43 U/L. Toxicology screen was positive for benzodiazepines. Urinalysis revealed proteinuria and glycosuria. A brain computed tomography scan showed hypodensities in the white matter of posterior parietal lobes bilaterally (Figure 1A and 1B). He was started on intravenous labetalol but then became bradycardic, so an intravenous nitroglycerin drip was initiated. His medications stopped temporarily because of the nausea and vomiting, and insulin drip was initiated for proper glycemic control. The next day, the blood pressure was 180/100 mm Hg, the heart rate was 90 bpm, and blood sugar was 206 mg/dL, but the conscious level deteriorated, and he started to report visual loss. A follow-up computed tomography scan of the head showed worsening of the initial findings (Figure 2A and 2B). Brain MRI showed abnormal signal on the fluid-attenuated inversion recovery and T2-weighted images involving the occipital lobes with extension to parietal and frontal lobes bilaterally (Figure 3A and 3B). Diffusion-weighted images showed no areas of restriction, excluding infarction, and confirming the diagnosis of PRES. Intravenous nitroglycerin was stopped. We decided to restart the intravenous labetalol drip because his heart rate was 90 bpm. After 12 hours of labetalol infusion, his blood pressure was 145/80 mm Hg, and his conscious level gradually improved. He was fully conscious and coherent the following day. We assumed that the clinical and radiological deterioration was secondary to the intravenous nitroglycerine, because, in spite of gradual lowering of the blood pressure, his neurological deficit became markedly worse. Also, the patient improved when nitroglycerine was replaced.

The term "hypertensive encephalopathy" was first used in 1928 to indicate the concept of transient neurological dysfunction precipitated by malignant hypertension.² Symptoms typically start 12 to 48 hours after a sudden and sustained increase in blood pressure and include severe headache, vomiting, confu-

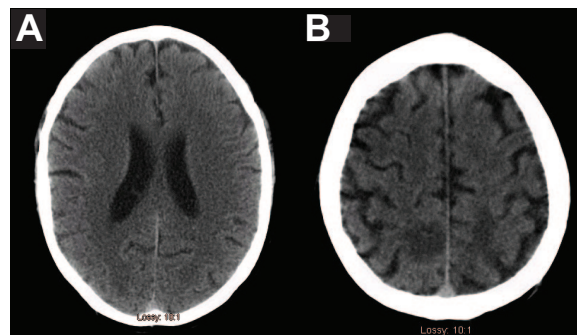


Figure 1. CT scan of the head without contrast before nitroglycerine.

sion, seizures, visual changes, and, in untreated cases stupor, and coma.³ Treatment consists of acute blood pressure control using intravenous medications, including nitroglycerine, and patients who are promptly treated usually recover without deficit.¹

PRES was first reported in 1996 in a series of acutely ill patients admitted for reversible neurological symptoms with abnormal and also reversible brain imaging,⁴ and, despite 15 years of increasing attention, the pathophysiology is still not entirely understood. The most popular hypothesis is that PRES is related to a cerebral hyperperfusion state, with breakdown of the blood-brain barrier, and extravasation of fluid, which is potentially containing blood or macromolecules, resulting in cortical and subcortical edema.⁵⁻⁷ However, some patients have demonstrable vasoconstriction on radiological imaging^{8,9} and perfusion deficits in radionuclide studies^{10,11} that may be explained by disordered cerebral autoregulation, leading to reactive focal vasoconstriction.¹²⁻¹⁴ Finally, compression of the microcirculation from the mass effect of vasogenic edema may play a role.

The most common presenting symptoms include severe headache, confusion, visual symptoms, and seizures. Common triggers include acute hypertension and the administration of cyclosporine and tacrolimus. Less commonly reported triggers are cocaine and methamphetamine abuse, cancer chemotherapy, systemic lupus erythematosus, chronic renal failure, and hemolytic uremic syndrome. Chronic hypertension alters the structure of cerebral blood vessels through atherosclerosis, lipohyalinosis, hypertrophy, remodeling, stiffening, alterations in resting cerebral blood flow, and endothelial dysfunction. It also disrupts vasoregulatory mechanisms that assure an adequate blood supply to the brain.¹⁵ Apart from hypertrophy and remodeling, these vascular changes are injurious and may make the brain tissue more susceptible to PRES.

The regions of the brain most commonly involved in imaging studies are the parieto-occipital and temporal lobes. It is not entirely known why PRES favors the posterior circulation, but this may arise from a relative lack of sympathetic innervation at the level of the arterioles supplied by the vertebrobasilar system compared with the anterior circulation.^{7,16-18} Clinical recovery usually occurs within 1 to 53 days, with 25% of patients

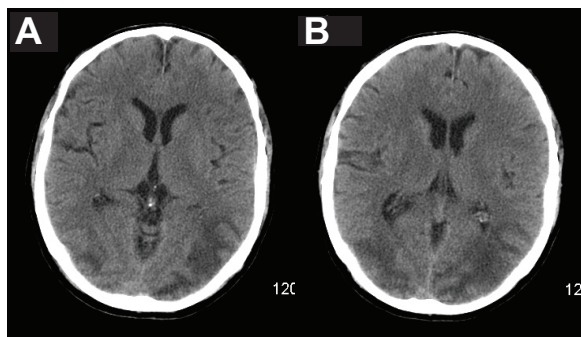


Figure 2. CT scan of the head without contrast after nitroglycerine.

recovering within 1 day. Recurrence is infrequent, although triggering factors for PRES have repeatedly been experienced by some patients.¹⁹

Perspectives

Our patient presented with hypertensive encephalopathy and a computed tomography scan of the head that suggested PRES. His neurological deficit became markedly worse, both clinically and radiographically, when we treated him with intravenous nitroglycerin, but then improved when this medication was replaced. Nitroglycerin dilates cerebral arteries and alters both the global and regional cerebral blood flow, which may augment the autoregulation failure. This adverse effect of nitroglycerine in PRES has been reported previously in the form of 2 case reports.^{20,21} However, nitroglycerin remains an established treatment for hypertensive encephalopathy. Furthermore, the distinction between hypertensive encephalopathy and hypertensive PRES may be artificial and would appear to rest primarily on the presence or absence of radiographic findings, which may be subtle and could be missed on the computed tomography scan. In other words, the diagnosis of PRES may not be immediately obvious in a patient presenting with hypertensive encephalopathy, particularly if brain imaging is not immediately available. We would, therefore, recommend using nitroglycerin with caution. Also, we recommend immediate discontinuation of intravenous nitroglycerine in the presence of worsening neurological status or typical radiological findings. Alternate parenteral blood pressure-lowering agents include labetalol, enalapril, and nicardipine.

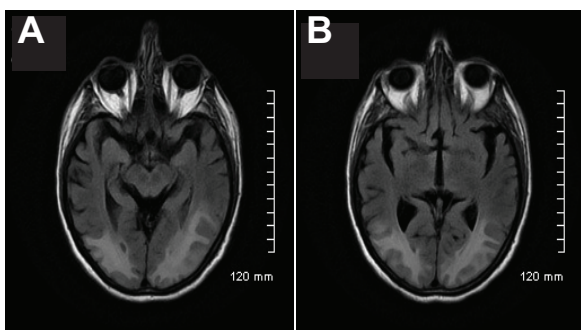


Figure 3. MRI FLAIR images of the brain after nitroglycerine.

Disclosures

None.

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