CASE REPORT

An unusual cause of altered mental status: the importance of monitoring a patient's blood pressure

Jacob Mathew Jr,¹ Matthew Koo,² Irina R Crook,¹ Jay Jahanmir¹

¹Department of Medicine, Tripler Army Medical Center, Honolulu, Hawaii, USA
²University of Hawaii John A. Burns School of Medicine, Honolulu, Hawaii, USA

Correspondence to
 Dr Jacob Mathew Jr, jacob.j.mathew.mil@mail.mil

Accepted 3 May 2014

SUMMARY

A 73-year-old man presented to the emergency room for acute onset altered mental status. The initial work-up yielded no definitive cause. An MRI demonstrated lesions in the bilateral posterior occipital lobes (not noted on an earlier MRI obtained from an outside institution) that were suggestive of posterior reversible encephalopathy syndrome (PRES). He had a history of Parkinson's disease complicated by autonomic instability (wide blood pressure fluctuations) that was medically controlled in the outpatient setting. During the early course of his hospitalisation, he again displayed wide blood pressure fluctuations. After his blood pressure stabilised, his mental status eventually improved to baseline. A repeat MRI obtained demonstrated near-complete resolution of the previously noted lesions and confirmed the diagnosis of PRES.

BACKGROUND

Altered mental status is a common condition, with a large differential diagnosis, that physicians face on a daily basis. Posterior reversible encephalopathy syndrome (PRES; also known as reversible posterior leucoencephalopathy syndrome (RPLS)) is often not placed high on the differential diagnosis. But in patients who present acutely with elevated blood pressure (BP)—and have any underlying condition that can predispose to autonomic instability (eg, Parkinson's disease or diabetes mellitus)—PRES should be more strongly considered. MRI can be helpful in obtaining the diagnosis; in cases of PRES, bilateral lesions of the posterior occipital lobes are typically present. Timely control of the patient's BP may allow for reversal of the disease manifestations (figures 1 and 2).

CASE PRESENTATION

A 73-year-old man presented to the Tripler Army Medical Center (TAMC), with his ex-wife, because of worsening mental status.

Approximately 1 month prior to his arrival in Hawaii, he was seen by his neurologist in Oregon for a follow-up visit regarding his Parkinson's dementia. At the time, it appeared well controlled and no medication changes were made. He was deemed stable for travel. Two weeks later, he travelled to Hawaii to visit one of his daughters and he remained in his normal state of health. Approximately 1 month into his trip, and 10 days prior to his presentation to the hospital, his ex-wife noticed that he was becoming more agitated and aggressive with family members. Furthermore, he refrained from following directions and was unable

to accurately state his location. Relatives unsuccessfully attempted to redirect him on multiple occasions and his condition continued to worsen. He was then brought to TAMC for further care.

In addition to Parkinson's disease, his medical history was also significant for coronary artery disease and chronic obstructive pulmonary disease. His Parkinson's was treated with entacapone 200 mg four times a day, carbidopa/levodopa 25 mg/100 mg five times a day and amantadine 100 mg every morning, and were self-administered by the patient prior to his presenting illness. Owing to the recent change in his mental status, family members were forced to provide him with his medications. He had no significant surgical history, allergies or family history of memory disorders. The patient was a resident of Oregon, where he lived with one of his daughters. Reportedly, he was a life-long non-smoker, did not drink alcohol and never used illicit drugs. Aside from travelling to Hawaii, he had no other travel history in the 2 years prior to admission.

On examination, the patient appeared dishevelled. His initial BP was 135/75 mm Hg; the remainder of his vital signs was stable. He was alert, but oriented only to person. His neurological examination was significant for shuffling gait, bilateral cogwheel rigidity of the upper extremities and a resting tremor. Owing to the patient's non-compliance, an adequate cranial nerve examination was unable to be performed. The remainder of the examination was unremarkable. Routine laboratory tests showed a white cell count within normal limits, hyponatraemia (130 mmol/L) without other electrolyte abnormalities and a normal urinalysis. The urine drug screen was negative. A chest X-ray showed no acute airway disease. A non-contrast CT scan of the head was unremarkable for haemorrhage and ischaemia; ventricles were normal in size.

INVESTIGATIONS

MRI—Owing to the patient's tremors and inability to remain stable, an MRI under sedation was obtained. The scan showed small foci of signal abnormalities in the cortical and subcortical bilateral occipital lobes consistent with hypertensive encephalopathy. A repeat MRI was obtained when the patient's BP was strictly controlled; it showed near-complete resolution of the bilateral occipital lobe opacities. Thus, the diagnosis of PRES was confirmed.

Lumbar puncture—This was a technically difficult procedure because of the patient's persistent tremor and bradykinesia. Owing to suboptimal

CrossMark

To cite: Mathew J, Koo M, Crook IR, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2013-203181

Figure 1 MRI without gadolinium revealing hypodensities present in cortical and subcortical occipital lobes bilaterally in the parieto-occipital regions.

positioning, only minimal amounts of cerebrospinal fluid (CSF) were obtained. Analysis of the clear CSF showed an elevated protein (584 mg/dL), normal glucose (42 mg/dL), leucocytes (368/ μ L) with prominent lymphocytosis (87%) and normal opening pressure of 20 mm Hg. Given these results, viral central nervous system (CNS) infections (ie, herpes simplex virus (HSV) and West Nile virus (WNV)) were considered. Although the suspicion for HSV encephalitis was low, following an infectious diseases consultation, he was empirically treated with acyclovir because the medication is often well tolerated and if true HSV encephalitis remains untreated, multiple areas of the nervous system can be destroyed quite rapidly.¹ But ultimately, HSV PCR of the CSF, serum WNV IgM and IgG and routine CSF cultures for bacteria and fungus were all negative.

Figure 2 MRI without gadolinium showing resolution of hypodensities originally present in the parieto-occipital regions.

EEG—Multiple EEGs performed showed generalised slowing, consistent with a diffuse cerebral disturbance (metabolic encephalopathy, dementia, etc). No seizure or periodic lateralised epileptiform discharge activity was noted.

DIFFERENTIAL DIAGNOSIS

Occurring in 30% of elderly hospitalised patients, the differential diagnosis of acute onset altered mental status (delirium) is quite broad.² Since the patient had Parkinson's disease, he was at increased risk for delirium superimposed onto dementia (delirium is seen in nearly 50% of those with baseline dementia).³ The most common aetiologies that should be evaluated include infection, electrolyte abnormality, medication/drug toxicity and metabolic disturbance. Less common aetiologies include external lines/devices, constipation, seizures, stroke and paraneoplastic syndrome.

TREATMENT

Given the multiple medications he required as an outpatient, we began treatment by simplifying his medication regimen to rule out the possibility that medication side effects were the culprit. Under the guidance of the TAMC neurology service, carbidopa/levodopa was reduced in frequency to three times a day.

When he did not improve with this simplification, we focused on an infectious cause for his acute mental decline. His urinalysis was within normal limits, a chest film showed no evidence of infiltrates and the initial complete blood count (CBC) showed no leucocytosis. Blood and viral cultures were negative. While the patient's only invasive device, a single peripheral intravenous, showed no evidence of infection, it was replaced multiple times throughout his hospitalisation for precaution. While MRI of the head was desired on presentation, it could not be obtained due to the patient's constant limb movements and his inability to follow commands. Eventually, the patient was sedated to allow MRI to be performed. Results showed bilateral enhancing foci of the posterior occiputs that were new compared with MRI obtained the year prior to admission from Oregon. This new finding raised our suspicion for PRES. Since PRES can be related to fluctuations in BP,⁴ we closely monitored his BP with a combination of lisinopril and metoprolol; and, as needed, metoprolol for breakthrough hypertension. To confirm PRES, the patient would have to have stable BP with an improvement in his mental status. As a result, we employed the above therapy and continued to investigate other causes of his mental status change.

A lumbar puncture was then performed; CSF analysis revealed elevated protein and leucocyte count in the setting of a normal glucose and opening pressure. The findings were consistent with those expected in the setting of viral meningitis. He was empirically placed on acyclovir for 3 days to cover HSV infection of the CNS while laboratory studies returned (see Investigations).

Serum WNV IgG and IgM, viral cultures and HSV PCR were negative. An EEG was obtained to rule out underlying seizure and showed non-specific slowing. Viral cultures from CSF returned negative.

With the return of multiple negative laboratory results, our suspicion for an infectious aetiology waned. We then focused on atypical causes of altered mental status. A heavy metal screen and a panel of paraneoplastic antibodies (to include ANNA-1,2,3, AGNA-1, PCA-1,2,Tr, CRMP5-IgG) were negative. Since severe constipation has been shown to cause altered mental status,⁵ his bowel movements were closely monitored; they remained regular throughout his hospitalisation. Other causes of encephalopathy were also ruled out such as NPH (ruled out due to normal sized ventricles), vitamin deficiency (no history of alcohol abuse to suggest thiamine deficiency,

however, the patient was treated prophylactically and the thiamine level was normal, along with vitamin B₁₂/folate) and endocrinopathies (anti-TPO antibody was negative to rule out Hashimoto's, NH₃ normal to suggest no hepatic impairment and AM cortisol was also normal).

As the hospitalisation continued, analysis of the patient's vitals showed that on nearly a daily basis, his systolic BP increased up to 40 mm Hg above baseline and returned to baseline levels without intervention within hours. Therefore, given the multiple negative laboratory results and procedures as noted above, we ultimately felt that PRES was the underlying cause of the patient's presentation.

OUTCOME AND FOLLOW-UP

After approximately 1 week of stable BPs, the patient's mental status improved. He remained unable to recall any of the events leading up to his hospitalisation, but he was able to joke about past memories and hold pleasant conversations with the hospital staff. When he returned to his functional baseline (per family), a repeat MRI was obtained, and it demonstrated a near-complete resolution of the occipital lesions and provided radiographic confirmation of the diagnosis of PRES. After his stay at our hospital facility, the patient returned to Oregon to stay with his daughter.

DISCUSSION

PRES, or RPLS, is a relatively rare condition in which patients may present with altered mental status, headache, seizures and cortical blindness.⁶ It shares many features with reversible cerebral vasoconstriction syndrome, which is similarly characterised by the onset of thunderclap headaches, thought to be due to diffuse segmental constriction of the cerebral arteries.⁶ These headaches are associated with elevations in BP, as in PRES, and clinically manifest with confusion, seizures and visual changes.⁶ MRI shows transient hyperintensities on T2 and fluid-attenuated inversion recovery imaging of the parieto-occipital lobes of the cortex and subcortical and deep white matter that are thought to be secondary to cerebral oedema caused by the severe BP elevations and certain medications that compromise the normal function of the blood-brain barrier.⁴ Its reversibility can be predicted by initial MRI findings of isolated areas of increased signal on proton density and T2-weighted images; if imaging is obtained with gadolinium, gyriform enhancement can be seen.^{7,8} A high diffusion-weighted imaging (DWI) signal may correlate with progression from vasogenic oedema to cytotoxic oedema, a sign of irreversible pathology.⁹

The majority of the case reports describing PRES are related to hypertensive encephalopathy in patients presenting with either pre-eclampsia or extreme elevations in BP.¹⁰ Other reports are related to specific medications, such as ciclosporin, that are known to predispose patients to the condition.¹¹ There are no current reports of the condition occurring in patients with autonomic instability, which can cause fluctuations in BP as high as those with hypertensive urgency.

The treatment of PRES involves managing its triggering factor. In cases of hypertensive emergencies, transfer to an intensive care unit may be required to continuously monitor the patient's neurological, cardiac and haemodynamic status. Currently, the recommendation is to reduce the mean arterial pressure (MAP) no more than 20–25% over 2 h¹²; if the MAP is reduced too rapidly, cerebral perfusion may decrease, thereby doing more damage. The use of an easily titratable (short half-life, intravenous) antihypertensive agent such as clevidipine may prove beneficial.¹²

In cases of pre-eclampsia, treatment follows the current recommendations to control pregnancy-related hypertension

(prompt delivery via either induction or caesarean section; and supportive measures to include intravenous fluids, thromboprophylaxis, BP control and seizure prophylaxis (magnesium sulfate)).¹⁰ While hydralazine is the most commonly used antihypertensive in the setting of pre-eclampsia, calcium channel blockers (dihydropyridines, in particular) have also proven effective.¹⁰ ACE inhibitors and angiotensin receptor blockers should be avoided in pregnancy.¹⁰

In cases of seizure or status epilepticus, management requires anticonvulsants (like intravenous lorazepam), airway protection and possibly mechanical ventilation. Arterial blood gases should be obtained to guide management of acid-base status and the airway. Status epilepticus refractory to first-line therapy (benzodiazepines, phenytoin, valproate and phenobarbital) may require continuous intravenous pentobarbital. Therapy should continue until there is clinical and EEG evidences of the absence of further seizure activity.

Rarely, PRES may lead to obstructive hydrocephalus requiring surgical drainage methods (external ventricular drain or ventriculoperitoneal shunt). Typically, improvement to baseline is demonstrated within 3 days of successful surgical intervention—provided the underlying cause is properly managed as well.

The condition is important to recognise early, since timely control of the patient's BP may allow the reversal of symptoms. Pavlakis *et al*¹³ demonstrate reversal of lesions suggestive of PRES on repeat MRI after the patient's BP was controlled. Our patient's initial presentation was atypical, and the initial diagnostic work-up did not reveal an answer to his altered mental status. In these patients, MRI can be critical to clinching an accurate diagnosis.

Learning points

- ▶ Altered mental status has a large differential diagnosis. However, in patients who have an elevated, or widely fluctuating, blood pressure, posterior reversible encephalopathy syndrome (PRES) should be considered.
- ▶ Acute fluctuations of blood pressure and medications that disrupt the blood-brain barrier can predispose an individual to PRES. In patients with suspected PRES and autonomic instability, vital signs (particularly haemodynamic markers) should be closely monitored and controlled.
- ▶ MRI obtained early can expedite the diagnosis, save further investigation and guide proper management. MRI findings of PRES are unique and comprise of signal intensities of the parieto-occipital lobes on diffusion-weighted imaging.

Acknowledgements The authors would like to acknowledge all the nursing staff involved in the patient's care.

Competing interests None.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

REFERENCES

- 1 Banatvala JE. Herpes simplex encephalitis. *Lancet Infect Dis* 2011;11:80–1.
- 2 Dyer CB. Postoperative delirium. A review of 80 primary data-collection studies. *Arch Intern Med* 1995;155:461.
- 3 Francis J. Delirium in older adults. *J Am Geriatr Soc* 1992;40:829–38.
- 4 Hinchey J, Chaves C, Appignani B, *et al*. A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996;334:494–500.
- 5 Morley John E. Constipation and irritable bowel syndrome in the elderly. *Clin Geriatr Med* 2007;23:823–32.

- 6 Ducros A. Reversible cerebral vasoconstriction syndrome. *Lancet Neurol* 2012;11:906–17.
- 7 Lamy C, Oppenheim C, Méder JF, *et al.* Neuroimaging in posterior reversible encephalopathy syndrome. *J Neuroimaging* 2004;14:89.
- 8 Schwartz RB, Jones KM, Kalina P, *et al.* Hypertensive encephalopathy: findings on CT, MR imaging, and SPECT imaging in 14 cases. *AJR Am J Roentgenol* 1992;159:379.
- 9 Covarrubias DJ, Luetmer PH, Campeau NG. Posterior reversible encephalopathy syndrome: prognostic utility of quantitative diffusion-weighted MR images. *AJNR Am J Neuroradiol* 2002;23:1038.
- 10 Koch S, Rabinstein A, Falcone S, *et al.* Diffusion-weighted imaging shows cytotoxic and vasogenic edema in eclampsia. *AJNR Am J Neuroradiol* 2001;22:1068.
- 11 Lanzino G, Cloft H, Hemstreet MK, *et al.* Reversible posterior leukoencephalopathy following organ transplantation description of two cases. *Clin Neurol Neurosurg* 1997;99:222–26.
- 12 Pedraza R, Marik PE, Varon J. Posterior reversible encephalopathy syndrome: a review. *Crit Care Shock* 2009;12:135–43.
- 13 Pavlakis SG, Frank Y, Chusid R. Hypertensive encephalopathy, reversible occipitoparietal encephalopathy, or reversible posterior leukoencephalopathy: three names for an old syndrome. *J Child Neurol* 1999;14:277–81.

Copyright 2014 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow