Reminder of important clinical lesson

Cortical blindness and posterior reversible encephalopathy syndrome in an older patient

Sabrina Ait,¹ Thomas Gilbert,¹ Francois Cotton,^{2,3} Marc Bonnefoy¹¹Service de Médecine Gériatrique, Centre Hospitalier Lyon-Sud, Pierre-Bénite, France;²Service de Radiologie, Université Lyon 1, Laboratoire d'Anatomie de Rockefeller, Lyon et Hospices civils de Lyon, Centre Hospitalier Lyon Sud, Pierre Bénite, France;³CNRS UMR 5220, Université de Lyon, Université Lyon 1, CREATIS-LRMN, Villeurbanne, France**Correspondence to** Dr Thomas Gilbert, thomasgilbertmiguet@yahoo.fr**Summary**

Posterior reversible encephalopathy syndrome (PRES) is a clinical and radiological entity. It associates, to varying extents, neurological symptoms such as headaches, confusion, seizures and visual alterations from haemianopsia to cortical blindness. The diagnosis relies on brain MRI, showing signs of subcortical and cortical oedema in the posterior regions of the brain, with hypersignals in T2/fluid attenuated inversion recovery (FLAIR) or diffusion sequences. With early diagnosis and control of the causal factors, the symptoms and radiological signs can be – as the name implies – totally regressive. PRES can be caused by various heterogeneous factors, such as hypertension, side effect of drug therapies, eclampsia, sepsis or autoimmune diseases. The authors report here the case of an 86-year-old woman, presenting totally regressive cortical blindness and seizures, with compatible imaging.

BACKGROUND

Posterior reversible encephalopathy syndrome (PRES) is a cause of regressive cortical blindness or epilepsy, by way of reaction to sudden blood pressure elevations, overcoming the brain vasculature's auto regulatory capacities.¹ PRES has mostly been described as a side effect of antineoplastic chemotherapies or other drugs. It has been reported to affect mainly children and young adults.^{2–3} Older patients can also be affected,^{4–6} but PRES probably remains an uncommon entity among the geriatric population. To our knowledge, no case affecting a patient above 85 years old had been described so far.

CASE PRESENTATION

An 86-year-old woman was brought to hospital after having lain on the ground for a long time following a fall. She had a history of hypertension, poorly controlled type 2 diabetes (recent haemoglobin A1C value of 13.6%), Alzheimer's disease and depression. She was being treated with donepezil, citalopram, alprazolam and metformine, but received no treatment for hypertension on admission.

On admission, she had no haemodynamic failure. Her blood pressure was of 142/58 mm Hg. She presented symptoms of disorientation, disturbance of consciousness and acute bilateral blindness. An episode of absence associated with rhythmic eye lid blinking, lip smacking and tonic-clonic movements limited to the right arm had been observed before her admission.

Clinical examination revealed normal pupillary reflexes, but there was no eye blinking in response to stimulus – suggesting a bilateral cortical blindness. Apart from the visual deficit, there were no other neurological focalised signs. Initial standard blood tests showed hyperglycaemia up to 21.5 mmol/l, acetonuria and compensated acidosis with the need for continuous intravenous insulin supply. Complete blood count, ionogram and renal function were normal.

INVESTIGATIONS

On fundoscopic examination, no retinal or intravitreal haemorrhage was found. The electroencephalographic (EEG) evaluation revealed discharges in the left temporo-occipital region with contro-lateral diffusions. On T2/fluid attenuated inversion recovery (FLAIR) MRI examination, a subtle bilateral cortical hypersignal was found in the posterior regions of the parietal and occipital lobes (figure 1). The diffusion sequences also revealed hyperintensity, testifying to the recent nature of the lesions (figure 2). Furthermore, the apparent diffusion coefficient

Figure 1 On T2/fluid attenuated inversion recovery weighted MRI, a bilateral occipital cortices hypersignal is depicted. Ventricle enlargements can be considered as normal for age, due to leukoaraiosis.

Figure 2 Diffusion weighted images also reveal a discrete hypersignal of occipital cortices.

(ADC) was increased, indicative of non-cytotoxic oedema. Unfortunately, this MRI-scan was not performed on admission, but only 8 days later, as the symptoms were progressively resolving, probably through diminution of brain oedema.

DIFFERENTIAL DIAGNOSIS

Injected CT-scan was not indicative of recent ischaemia. MRI examination was also in favour of non-cytotoxic oedema. There was no sign for an intracranial tumorous process or abscess. Infectious brainstem encephalitis appears unlikely given the absence of fever or signs of infection, and the spontaneous improvement of the neurological deficits. The involvement in the confusion of the hyperglycaemia found on admission could also be discussed.

TREATMENT

An antiepileptic treatment associating clobazam and lev-etiracetam was initiated. During the patient's hospitalisation, the blood pressure has been stable, with no need for specific measures. Mean peak systolic blood was 130 mm Hg (minimum-maximum 100–159 mm Hg) and mean peak diastolic blood pressure was 70 mm Hg (minimum-maximum 46–98 mm Hg).

OUTCOME AND FOLLOW-UP

The evolution of the condition was progressively positive, towards complete recuperation of eyesight and improvement in the symptoms of confusion within 10 days. The control EEG (performed after a week) showed distinct improvement, with only rare residual sporadic spikes in the left temporal occipital region.

The combination of clinical and radiological signs was evocative of PRES, most likely caused by increased blood pressure given the history of untreated hypertension. No control imaging could be performed. We learnt that the patient died 2 months later after suffering a massive haemorrhagic stroke.

DISCUSSION

PRES was initially named as 'reversible posterior leukoencephalopathy syndrome', first described in 1996 by Hinchey *et al* as the combination of neurological and radiological signs.¹ It associates headaches, confusion, awareness and arousal disorders (or even coma), visual alterations such as scotoma, haemianopsia or cortical blindness and partial or secondarily generalised seizures.

The entity seems more frequent among children and younger adults. Two recent cohorts studies of 19 and 113 patients have placed the mean age at 19 and 48 years, respectively.^{2 3} A few cases of patients over 60 have been described,^{4–6} but to our knowledge, no patient over 85 had been reported to be affected so far.

Diagnosis confirmation relies on brain MRI, using T2/FLAIR and diffusion-weighted sequences. An extensive symmetric bilateral hyperintensity in T2 and FLAIR weighted images is generally observed, affecting the sub-cortical and cortical posterior (most frequently occipital) regions of the brain. Diffusion sequences can help to differentiate between cytotoxic and vasogenic oedema, by detecting a decrease or an increase in diffusion, respectively. ADC maps can be elaborated from diffusion-weighted sequences, and provide a quantitative measurement of the diffusion of water molecules. ADC maps show a decreased signal in case of cytotoxic oedema, whereas high ADC values are consistent with highly mobile water in areas of vasogenic oedema.⁷

Several physiopathological mechanisms have been described, including notably a deficit in the auto-regulatory capacity of the brain vasculature due to sudden elevations in systemic blood pressure. Dysfunction of the endothelial cells of the blood-brain barrier could be the cause of vasogenic oedema, particularly affecting the sub-cortical white matter of the occipital, parietal and temporal lobes. Sympathetic innervation, which is thought to have a protective role against this phenomenon, is indeed less developed in these regions of the brain. This distribution of autonomous innervation within the brain vasculature could, therefore, explain the topography of the lesions observed in PRES. A vasospasm can be created secondarily, leading to tissular ischemia and irreversible cytotoxic oedema.^{8–10} At this time, ADC values will decrease in the lesion, as can be observed in stroke.¹¹

Predisposing factors for PRES are numerous. The most frequently encountered cause is a brutal elevation of blood pressure that can sometimes exceed 250/130 mm Hg. Signs of cerebral dysfunction appear within 12 to 48 h from this elevation. Nevertheless, a sudden elevation of blood pressure, even if moderate, can be enough to trigger the phenomenon, and delay diagnosis.^{12 13} This can be suspected in the present case. No hypertension has been noted during the patient's hospitalisation, but we still think that a sudden rise in blood pressure could have initiated the phenomenon. Furthermore, the fact that the patient suffered a massive haemorrhagic stroke 2 month later also tends to corroborate the hypothesis of paroxysmic blood pressure elevations. The dosage of urinary catecholamine metabolites could have been interesting.

The other disorders usually associated with PRES are eclampsia, renal failure, thrombocytopenic purpura, systemic diseases (such as vasculites or connective tissue diseases),

auto-immunity, viral infections, sepsis or ionic imbalance. Iatrogenic causes have also been described, including immunosuppressive therapy particularly with cyclosporine and tacrolimus,¹⁴ high doses of corticosteroids, blood transfusions and antineoplastic drugs.^{15–17} To our knowledge, none of the medications currently taken by our patient has been associated with the generation of regressive brain vasogenic oedema.

Treatment of PRES requires blood pressure stabilisation and/or interruption of causal drugs.

Regression of the neurological symptoms can then be obtained within an average of 1 to 2 weeks.¹⁸ Antiepileptic drugs can be discontinued after about 3 months, as seizures do not usually progress to chronic epilepsy.¹⁹ When unrecognised and untreated, PRES can progress to brain ischaemia, infarction and death.²⁰

Learning points

- ▶ Although the neurological deficits due to PRES are potentially reversible, a risk of severe ischaemic or haemorrhagic cerebral complications will tend to persist.
- ▶ Early diagnosis and control of causal factors are, thus, essential for preventing the occurrence of irreversible sequelae.
- ▶ In this respect, PRES could well be an underestimated cause of neurological deficiencies among the older.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Hinchey J**, Chaves C, Appignani B, *et al*. A reversible posterior leukoencephalopathy syndrome. *N Engl J Med* 1996;**334**:494–500.
2. **Ni J**, Zhou LX, Hao HL, *et al*. The clinical and radiological spectrum of posterior reversible encephalopathy syndrome: a retrospective series of 24 patients. *J Neuroimaging* 2011;**21**:219–24.
3. **Fugate JE**, Claassen DO, Cloft HJ, *et al*. Posterior reversible encephalopathy syndrome: associated clinical and radiologic findings. *Mayo Clin Proc* 2010;**85**:427–32.
4. **Giraldo EA**, Fugate JE, Rabinstein AA, *et al*. Posterior reversible encephalopathy syndrome associated with hemodynamic augmentation in aneurysmal subarachnoid hemorrhage. *Neurocrit Care* 2011;**14**:427–32.
5. **Padhy BM**, Shanmugam SP, Gupta YK, *et al*. Reversible posterior leukoencephalopathy syndrome in an elderly male on sunitinib therapy. *Br J Clin Pharmacol* 2011;**71**:777–9.
6. **Ueda K**, Hoshi T, Yorozu S, *et al*. [Patient with posterior reversible encephalopathy syndrome with prolonged disturbance of consciousness and convulsion after cerebral aneurysm surgery]. *Masui* 2011;**60**:236–40.
7. **Doelken M**, Lanz S, Rennert J, *et al*. Differentiation of cytotoxic and vasogenic edema in a patient with reversible posterior leukoencephalopathy syndrome using diffusion-weighted MRI. *Diagn Interv Radiol* 2007;**13**:125–8.
8. **Mohebbi A**, Megarbane B, Chabriet H. Posterior-reversible encephalopathy syndrome. *Réanimation* 2007;**16**:490–7.
9. **Renard D**, Labauge P, Vandenberghe R. Reversible posterior leukoencephalopathy syndrome. *Translational Neuroscience* 2010;**1**:115–23.
10. **Kahana A**, Rowley HA, Weinstein JM. Cortical blindness: clinical and radiologic findings in reversible posterior leukoencephalopathy syndrome: case report and review of the literature. *Ophthalmology* 2005;**112**:e7–e11.
11. **Le Bihan D**, Breton E, Lallemand D, *et al*. MR imaging of intravoxel incoherent motions: application to diffusion and perfusion in neurologic disorders. *Radiology* 1986;**161**:401–7.
12. **Bonnaud I**, Cottier JP. [Reversible posterior leukoencephalopathy syndrome]. *Rev Neurol (Paris)* 2004;**160**:360–2.
13. **Mueller-Mang C**, Mang T, Pirker A, *et al*. Posterior reversible encephalopathy syndrome: do predisposing risk factors make a difference in MRI appearance? *Neuroradiology* 2009;**51**:373–83.
14. **Patejdl R**, Borchert k, Pagumbkea H, *et al*. Posterior reversible encephalopathy syndrome (PRES): an unusual primary manifestation of a diffuse large B-cell lymphoma. *Clin Neurol Neurosurg* 2011;**113**:819–21.
15. **Farheen M**, Shah K, Daryl P, *et al*. Reversible posterior leukoencephalopathy syndrome and anti-neoplastic agents: a review. *Oncol Rev* 2007;**1**:152–61.
16. **Baehring JM**, Fulbright RK. Delayed leukoencephalopathy with stroke-like presentation in chemotherapy recipients. *J Neurol Neurosurg Psychiatry* 2008;**79**:535–9.
17. **Lewis M**, Maddison P. Intravenous immunoglobulin causing reversible posterior leukoencephalopathy syndrome?. *J Mar Neurol Neurosurg Psychiatry* 2000;**69**:704.
18. **Roth C**, Ferbert A. Posterior reversible encephalopathy syndrome: long-term followup. *J Neurol Neurosurg Psychiatry* 2010;**81**:773–7.
19. **Roth C**, Ferbert A. The posterior reversible encephalopathy syndrome: what's certain, what's new? *Pract Neurol* 2011;**11**:136–44.
20. **Burnetta MM**, Hessb CP, Robertsc JP, *et al*. Presentation of reversible posterior leukoencephalopathy syndrome in patients on calcineurin inhibitors. *Clin Neurol Neurosurg* 2010;**112**:886–91.

This pdf has been created automatically from the final edited text and images.

Copyright 2012 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.

Please cite this article as follows (you will need to access the article online to obtain the date of publication).

Ait S, Gilbert T, Cotton F, Bonnefoy M. Cortical blindness and posterior reversible encephalopathy syndrome in an older patient.

BMJ Case Reports 2012;10.1136/bcr.09.2011.4782, Published XXX

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

Keep up to date with all published cases by signing up for an alert (all we need is your email address) <http://casereports.bmj.com/cgi/alerts/etoc>