Cough headache as a presenting feature of posterior reversible encephalopathy syndrome (PRES)

Author: Boby Varkey Maramattom[A]

ABSTRACT

A 23-year-old man with chronic renal failure on maintenance haemodialysis was referred to the neurology outpatient clinic with new onset cough headache. On evaluation, his blood pressure was 220/120 mmHg and outpatient fundus photography showed grade IV hypertensive retinopathy. Urgent magnetic resonance imaging showed features of posterior reversible encephalopathy syndrome (PRES). Emergent treatment of hypertension led to a rapid resolution of his cough headache. New onset cough headache may be a marker of PRES.

KEYWORDS: cough headache, PRES, posterior reversible encephalopathy syndrome

DOI: 10.7861/clinmed.2020-1080

Case presentation

A 23-year-old man on haemodialysis presented to us with a new onset headache of 10 days duration. He had undergone a live related-donor renal transplant 10 years previously for bilateral multi-cystic dysplastic native kidney disease. With triple immunosuppression (tacrolimus, mycophenolate mofetil and prednisolone), he maintained stable graft functions for 7 years. After this, he developed a progressive worsening of renal functions. In April 2019, a graft biopsy showed features of chronic antibody mediated rejection, and haemodialysis had been initiated 4 months earlier. His current headache appeared during bouts of coughing or sneezing. It was a generalised, severe, brief (<1 minute) holo-cranial headache that subsided spontaneously, and it occurred 2–3 times a day. He had a history of hypertension for the past 1 year and was taking metoprolol, hydralazine and prazosin. His medications included subcutaneous epoetin beta (RhEPO; a synthetic, recombinant of erythropoietin) 4,000 IU three times per week. His blood pressure was 220/120 mmHg. A neurology outpatient fundus photograph revealed grade IV hypertensive retinopathy without any other neurological findings. Serum creatinine levels were 663 µmol/L and electrolytes were normal.

Author: [A]lead consultant neurologist, Aster Medcity, Kochi, India

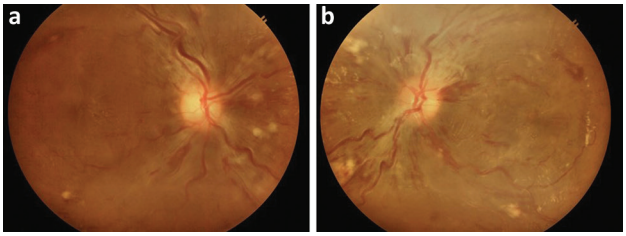

Fig 1. Fundus photographs showing optic disc oedema with cotton wool spots and scattered blotchy haemorrhages. a) Right eye. b) Left eye.

Diagnosis

A diagnosis of secondary cough headache was considered. The possibilities were a hypertensive urgency, posterior reversible encephalopathy syndrome (PRES) or a structural posterior fossa lesion.

Initial management and prognosis

He was admitted to the intensive care unit. Intravenous labetalol and nitroglycerin infusions were used to lower his blood pressure. He also required escalation of his oral antihypertensions with addition of clonidine 0.6 µg/day and nifedipine 20 mg three time a day. Magnetic resonance imaging (MRI) of the brain showed extensive fluid-attenuated inversion recovery (FLAIR) hyperintensities involving the temporo-occipital cortex and cerebellar white matter without diffusion restriction, MR angiography was normal and the MRI findings were compatible with PRES syndrome.

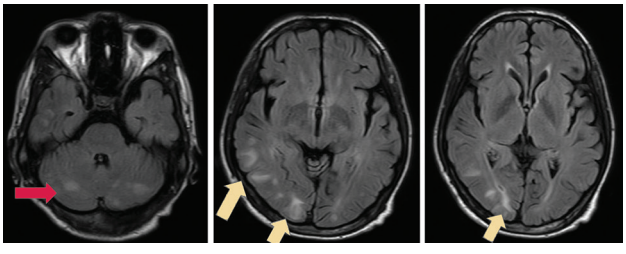

Fig 2. Axial fluid-attenuated inversion recovery magnetic resonance imaging of the brain showing scattered hyperintensities in the cerebellum (red arrow), and temporal cortices, occipital cortices and subcortical U-fibres (yellow arrows).

Box 1. Conditions associated with a secondary cough headache

- Chiari type I malformation.
- Posterior fossa lesion
  - meningioma.
- Obstructive hydrocephalus.
- Spontaneous intracranial hypotension.
- Subdural hematoma.
- Brain metastases.
- Acute sphenoid sinusitis.
- Meningitis.
- Cerebral aneurysms.
- Posterior reversible encephalopathy syndrome

Case progression and outcome

A diagnosis of cough headache secondary to PRES was considered. RhEPO was identified as a potential culprit and discontinued. Over the next 3 days, his blood pressure reduced to 160/100 mmHg and his cough headache disappeared. Levetiracetam was started pre-emptively for seizures. He was discharged uneventfully after 5 days.

Discussion

Cough headache is a well described, but rare headache.[1] Headaches are characteristically triggered by a rapid increase in intra-abdominal pressure which occurs with coughing, sneezing or straining. Two types of cough headache are described: primary and secondary (symptomatic) cough headache. Primary cough headache is defined by the International Headache Society (IHS) as a headache, precipitated by coughing or straining in the absence of any intracranial disorder and lasting up to 30 minutes.[2] Almost any other type of underlying headache (such as migraine or tension type headache) can be exacerbated by coughing, but are not included in the rubric of cough headache. Secondary (symptomatic) cough headache (SCH) comprises around 40% of cough headaches and is associated with a wide variety of aetiologies. Prominent among them are posterior fossa lesions and Chiari malformations, which account for nearly 80% of SCH (Box 1).[3]

PRES is a characterised by headache, seizures, altered mental status or cortical visual disorders (such as cortical blindness and hemianopsia). Headaches are reported in up to 50% of patients with PRES. Most often, headaches are diffuse and gradual in onset, or of the thunderclap variant (in which MR angiography changes of reversible cerebral vasoconstriction accompany PRES). Cough headache has not been described in PRES.

MRI shows white matter vasogenic oedema predominantly affecting the subcortical and cortical regions of the occipito-parietal lobes, however, oedema can involve the cerebellum, brainstem or even frontal regions in more severe cases.[4] These changes are well appreciated on T2 or T2-FLAIR MRI sequences. Severe PRES can lead to cerebral infarction or haemorrhage. Prompt recognition and treatment of the underlying condition can lead to good outcomes and reversibility of the MRI changes on follow-up. Most patients experience a good outcome within weeks, although up to 15% of patients can develop morbidity or mortality with severe PRES.

PRES is associated with hypertension only in 70–80% of cases. Although the exact pathophysiological mechanisms are unclear, hypertension and endothelial dysfunction are key components in many cases. Other triggers of PRES include eclampsia (5–15%), renal failure (~0.35–0.5%), autoimmune disorders (5–10%), sepsis (5–15%) and use of medications, of which, immunosuppressants, chemotherapeutic agents (20–60%) and RhEPO are well-known culprits.[5] Acute or chronic endothelial dysfunction, loss of cerebral autoregulation, endothelial cell inflammation and attack by antigen-antibody complexes or cytokines can all lead to PRES by impairing the blood–brain barrier and causing vasogenic oedema.[6] All these insults initiate a compensatory vasoconstrictive cerebral autoregulatory response which mitigates damage to some extent. However, the posterior circulation arteries of the brain lack a robust sympathetic innervation compared with the anterior circulation (the sympathetic nerves travel intracranially along the internal carotid artery into the cranial cavity). This partly explains the posterior predominance of PRES.

RhEPO which is commonly prescribed to patients with end-stage renal disease (ESRD) for treatment of an underlying normocytic anaemia, is well known to exacerbate hypertension in patients with ESRD as well as contribute to endothelial dysfunction. Fortunately, recurrences of PRES are rare, even when patients are re-exposed to the same insults.[7] PRES is an important differential diagnosis in patients with a new onset cough headache.

Key points

- Cough headache should prompt neuro-imaging to identify symptomatic causes.
- Cough headaches could indicate an evolving PRES.
- Treatment of accelerated hypertension may be sufficient to cure cough headaches in certain cases. ■

References

1 Tinel J. La Céphalée à l'effort. Syndrome de distension douloureuse des veines intracrâniennes. *Méd (Paris)* 1932;14:113–8.
2 Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia* 2004;14(Suppl 1):9–160.
3 Cordenier A, De Hertogh W, De Keyser J, Versijpt J. Headache associated with cough: a review. *J Headache Pain.* 2013;14:42.
4 McKinney AM, Short J, Truwit CL *et al.* Posterior reversible encephalopathy syndrome: incidence of atypical regions of involvement and imaging findings. *Am J Roentgenol* 2007;189:904–12.
5 Delanty N, Vaughan C, Frucht S, Stubgen P. Erythropoietin-associated hypertensive posterior leukoencephalopathy. *Neurology* 1997;49:686–9.
6 Gao B, Lyu C, Lerner A, McKinney AM. Controversy of posterior reversible encephalopathy syndrome: what have we learnt in the last 20 years? *J Neurol Neurosurg Psychiatry* 2018;89:14–20.
7 Roth C, Ferbert A. Posterior reversible encephalopathy syndrome: long-term follow-up. *J Neurol Neurosurg Psychiatry* 2010;81:773–7.

Address for correspondence: Dr Boby Varkey Maramattom, Department of Neurology, Aster Medcity, Kuttisahib Road, South Chittoor, Kochi, Kerala 682023, India.
Email: bobvarkey@gmail.com