

Ivan Garza
David F. Black

Persistent primary thunderclap headache responsive to gabapentin

Received: 21 August 2006

Accepted in revised form: 26 September 2006

Published online: 10 December 2006

I. Garza (✉) • D.F. Black
Department of Neurology,
Mayo Clinic,
200 First Street SW,
Rochester, MN 55905, USA
e-mail: garzaurdiales.ivan@mayo.edu
Tel.: +1-507-284-1588
Fax: +1-507-284-4795

Abstract We report the case of a woman with an apparent primary thunderclap headache which occurred frequently until she achieved a therapeutic dosage of gabapentin. Primary thunderclap headache is a rare type of headache that warrants significant testing to rule out more ominous possibilities. Whether gabapentin may help other primary thunderclap headache sufferers or not remains unclear. Further research is needed.

Keywords Thunderclap headache • Subarachnoid haemorrhage • Gabapentin

Introduction

Thunderclap headache (TCH) refers to an excruciating headache of instantaneous onset. Multiple life-threatening conditions may present this way. In the absence of these, however, TCH may occur as a benign idiopathic headache disorder, currently termed “primary thunderclap headache” (PTCH). The International Classification of Headache Disorders 2nd Edition diagnostic criteria for PTCH consist of a severe head pain of sudden onset, reaching maximum intensity in <1 min lasting from 1 h to 10 days; does not recur regularly over subsequent weeks or months; and is not attributed to another disorder [1]. Somewhat in contradistinction to these criteria, in up to one third of

patients, PTCH may persist beyond 10 days or recur over subsequent months to years, heavily impacting quality of life [2]. Evidence for effective symptomatic treatment in this setting is limited.

Case

A 49-year-old woman without prior headache history presented to the emergency department with a severe headache. At onset, upon clearing her throat, she felt a “snap” inside her head followed immediately by a sudden, extremely severe, bilateral temporal-parietal throbbing headache. Her pain reached a severe intensity

(10/10) within 5 s, and remained present for 3 h. She continuously paced and screamed. Three hours after onset, the severity came down to 8/10, and continued for 12 more hours after which the pain had a sudden offset. Nausea, vomiting, autonomic features, focal neurologic deficits and hypersensitivity to light, sound or smells were absent. General and neurologic exams were normal. Brain computed tomography (CT), chest X-ray, complete blood count, blood chemistry and lumbar puncture were all normal. Cerebrospinal fluid (CSF) revealed glucose 62 mg/dl, protein 27 mg/dl, 2 white blood cells, 128 red blood cells in first tube (14 in second) and no xanthochromia. Routine CSF cultures were normal. Hydromorphone and metoclopramide failed to provide relief.

Nine days before headache onset, she had a presumed viral upper respiratory infection while travelling through France. After the initial attack (day 1) she developed others, nearly everyday for 11 days. Attacks were stereotypic with “thunderclap” onset. Frequency was 1–3 a day, lasting 4–17 h each. An orthostatic component or time pattern were absent. Events occurred spontaneously, or were triggered by sitting or clearing her throat. On day 6, brain magnetic resonance image (MRI) and magnetic resonance angiography (MRA) were normal. On day 9, a neck MRI/MRA ruled out a dissection and rizatriptan failed to give analgesia.

On day 9, for unclear reasons, her local doctor started gabapentin 300 mg and increased it by 300 mg a day to a goal of 600 mg three times a day (reached by day 14). Her last prolonged TCH occurred on day 12. She then experienced a “crawling and soreness” sensation in her left parietal region half of the day, and a brief daily headache, 60 s each. These resolved without additional treatment other than the daily gabapentin and were identical to the original headaches except for the duration. On day 38 (our evaluation) her symptoms had not changed since day 12. Since day 44, her “crawling and soreness” had disappeared, and she was only experiencing one 60-s event every 3 days. She was still on gabapentin 1800 mg/day secondary to concerns for recurrence of the prolonged attacks as they had been so torturous.

Discussion

TCH refers to an excruciating headache of instantaneous onset – as sudden and as unexpected as a “clap of thunder” [3]. This term was first utilised to describe this type of headache as a presentation of an unruptured cerebral aneurysm, but a number of secondary causes are well known to present with TCH including subarachnoid

haemorrhage, cerebral venous sinus thrombosis (CVST), pituitary apoplexy, spontaneous intracranial hypotension (SIH), hypertensive encephalopathy, obstructive hydrocephalus, carotid artery dissection and retroclival haematomas [2, 4]. Although an association between the Erve virus and TCH has been suggested, a causative link has not been proven [5].

In the absence of secondary causes, TCH may occur as a benign idiopathic headache disorder, currently termed “PTCH” [1]. Because of the profound morbidity of most of the secondary causes of TCH, the diagnosis of PTCH is one of exclusion. A brain CT is obligatory to rule out a subarachnoid haemorrhage and, when negative, a CSF analysis including xanthochromia is required [2]. When initial CT and CSF examinations are normal, clinical judgement guides further investigations [2].

The absent xanthochromia and clearing of our patient’s CSF suggests a traumatic puncture as the cause of increased red blood cells. At the time of our evaluation, her prior tests had ruled out most, but not all, of the sinister conditions that can cause TCH. Hyperelastic joints and skin, pachymeningeal gadolinium enhancement, and “brain sag” on MRI, all of which could suggest SIH, were absent [6]. A brain magnetic resonance venogram (MRV) showed no evidence of CVST.

Migraine attacks occasionally have an abrupt onset (“crash migraine”), mimicking PTCH [7]. Although the distinction between these can be difficult, in the absence of nausea, vomiting, photophobia and phonophobia, migraine is an inadequate explanation [1].

Little is known about the symptomatic treatment of PTCH. Oral and intravenous nimodipine may be effective [8]. A long-term follow-up of patients with recurrent PTCH showed that individuals had substantial impairment in their working capacity and social functioning [9]. Our patient’s response to gabapentin was dramatic and impressive during a time when headaches were still worsening, suggesting medication effect more than the natural history of a resolving entity. The exact mechanism of action through which gabapentin decreases pain in headache is not known but multiple mechanisms might be involved. Gabapentin enhances GABA-mediated inhibition, inhibits GABA metabolism and modulates L-type calcium channels by binding to its $\alpha 2\delta$ subunit [10]. A limitation of our report is that, unfortunately, we could not have our patient stop gabapentin and evaluate her symptoms. However, in the presence of known significant disability and in the absence of effective treatment options associated with PTCH, gabapentin may be a reasonable and successful treatment for persistent PTCH. Further investigation is clearly needed.

Intriguing is the fact that our patient developed her headaches shortly after a presumed viral upper respiratory

infection upon returning from western France, where the natural focus of the Erve virus is thought to be located [5].

One can only speculate at this juncture about the potential association of her headache with the Erve or another virus.

References

1. International Headache Society Classification Committee (2004) International classification of headache disorders, 2nd edition. Cephalalgia 24[Suppl 1]:24–25,51–52
2. Dodick DW (2002) Thunderclap headache. Headache 42:309–315
3. Day JW, Raskin NH (1986) Thunderclap headache: symptom of unruptured cerebral aneurysm. Lancet 2:1247–1248
4. Lance JW, Goadsby PJ (2005) Other primary headaches and distinction from those with structural cause. Mechanism and management of headache. Elsevier Butterworth Heinemann, Philadelphia, PA, pp 264–265
5. Treib J, Dobler G, Haass A et al (1998) Thunderclap headache caused by Erve virus? Neurology 50:509–511
6. Mokri B, Maher CO, Sencakova D (2002) Spontaneous CSF leaks: underlying disorder of connective tissue. Neurology 58:814–816
7. Evans RW, Mathew NT (2005) First or worst headaches. Handbook of headache. Lippincott Williams and Wilkins, Philadelphia, PA, pp 47,181–183
8. Lu SR, Liao YC, Fuh JL et al (2004) Nimodipine for treatment of primary thunderclap headache. Neurology 62:1414–1416
9. Linn FHH, Rinkel GHE, Algra A, van Gijn J (1999) Follow-up of idiopathic thunderclap headache in general practice. J Neurol 246:946–948
10. Cutrer FM (2001) Antiepileptic drugs: how they work in headache. Headache 41[Suppl 1]:S3–S10