

An uncommon coexistence of primary sexual, cough and exercise headaches: the first three cases from Greece

Bougea A, Constantinides V, Anagnostou E, Kararizou E

First Department of Neurology, Medical School, National and Kapodistrian University of Athens, Athens, Greece

Abstract

Background: The “other primary headaches” encompasses a group of uncommon but distinct headache disorders. The coexistence of their subforms such as primary sexual and exercise headache is not a new phenomenon, but in association with cough headache is rather uncommon.

Report of cases: We report three cases with a rare coexistence of primary cough, exercise and associated with sexual activity headache.

Indomethacin was effective in all patients. The leading pathophysiological explanation involves a rapid rise in intra-abdominal pressure exertional factors or an inappropriate reaction in the cerebral vasculature.

Conclusions: Further studies are needed to confirm a common pathogenic mechanism in these patients. The coexistence of these headaches needs to be taken into account in the final classification that is expected to be available in 2016.

Hippokratia 2015; 19 (4): 369-371.

Keywords: Other primary headaches, cough headache, exercise headache, headache associated with sexual activity, New International Headache Classification, ICHD-3 beta criteria

Corresponding author: Anastasia Bougea MD, PhD, 1st department of Neurology. National and Kapodistrian University, Medical school of Athens Aeginition Hospital, 72-74 Vasilissis Sofias Avenue, 11528 Athens, Greece, tel: +306930481046, e-mail: annita139@yahoo.gr

Introduction

Along the same lines as previous editions, the new International Classification of Headache Disorders (ICHD-3 beta) differentiates primary headaches such as migraine, tension-type headache (TTH), cluster headache and other trigeminal autonomic headaches from other primary headaches¹. Other primary headaches form a heterogeneous group of fairly rare headaches characterized by transient paroxysmal pain that are not linked to tissue injury¹. These include primary cough headache (PCH), primary exercise headache (PEH), and primary headache associated with sexual activity (PHASA)^{1,2}. PCH is currently defined as a bilateral headache lasting up to 30 minutes, triggered by coughing rather than prolonged physical activity, and not ascribed to any intracranial disorder^{1,2}. PEH is precipitated by exercise frequently comorbid with migraine². PHASA is a dull bilateral headache precipitated by sexual activity. It intensifies with sexual excitement and is not associated with any intracranial disorder^{1,2}. Indomethacin is recommended for the both the treatment of PCH and as an acute treatment for PEH. It is also recommended as short-term prophylaxis administered one hour before physical activity at a dosage of 25–30 mg, or as short-term prophylactic treatment in PHASA³.

To our knowledge, these are the first three patients who fulfilled these criteria with a rare coexistence of PCH, PEH and PHASA in the same time in each of them.

Case 1

A 59-year-old male patient was referred to the Neurological Clinic of the University of Athens because of recurrent headache episodes for the last five years. The pain was localized temporally with throbbing quality and triggered in the context of physical exercise. This pain was severe enough to interfere with his daily functioning. For the preceding year, he also described headaches of explosive quality lasting for five minutes. The headache occurred in association with coughing and Valsalva manoeuvre. Besides cough, the headache could be also provoked by just before or at the moment of orgasm. There was no comorbidity with migraine or nausea, vomiting, light or sound sensitivity.

On examination, the patient was alert and oriented. Tendon reflexes were brisk, and plantar responses were flexor bilaterally. Muscle tone and sensory examination were normal. Complete laboratory tests including blood biochemistry, hemoglobin electrophoresis, serology, thyroid hormones were within normal range. The opening cerebrospinal fluid (CSF) pressure was 17 cm H₂O without presence of white or red cells. Levels of protein and glucose concentrations were found to be 19 mg/dl, and 65 mg/dl respectively. Chest X-ray was normal. Brain CT and cranio-cervical Magnetic resonance imaging (MRI) with contrast medium, revealed no abnormalities. Moreover, magnetic resonance venography (MRV) revealed normal appearing cerebral vessels. Treatment with indo-

methacin 100 mg per os was effective and well tolerated. Patient did not receive angiotensin converting enzyme inhibitors.

Case 2

A 46-year-old male trainer without any relevant medical or headache history was referred to our Headache Clinic with a three-month-history of headaches. The headaches were of explosive onset, holocranial location, and exclusively triggered by sexual activity. Their duration was 5-30 min. The patient also described another type of headache with episodes starting one month after the initial presentation of the orgasm-related headache. This headache differed inasmuch as it was dull, bilateral, moderate in intensity, and manifested during physical exercise. This particular type of headache usually occurs just after exercise (such as weight-lifting, aerobics, or jogging) and lasts just five minutes. A week before his visit, he had experienced eight episodes of sudden short-lasting headaches triggered by coughing (Valsalva manoeuvre). Neurological examination was normal. A secondary cause was ruled out (normal chest X-ray, cranio-cervical MRI including brain vessels, normal CSF opening pressure 16 cm H₂O). Beta-blockers, such as propranolol (40–200 mg per os per day), were discontinued due to ineffectiveness. Administration of 75 mg of indomethacin per os one hour before sexual activity proved to be effective as a prophylactic measure. He did not receive any treatment with angiotensin converting enzyme inhibitors. No vomiting, or conjunctival injection were noted.

Case 3

A 41-year-old man presented complaining of a new onset headache during or immediately after exercise that had first presented four months earlier. The pain was precipitated by coughing and Valsalva manoeuvre. He also complained of experiencing thunderclap headaches over the past two months with the onset of severe pain at orgasm. The pain was localized in the occipital area. His neurological examination was unremarkable, as were routine blood and CSF tests. Cranio-cervical MRI and MR angiography with contrast medium were negative for vascular malformations. Chest X-ray was normal. Indomethacin in doses of 100 mg per day per os was effective. These headaches were not related with vomiting or rhinorrhea.

Discussion

We report these three cases, all of which presented with the rare coexistence of PEH, PCH and PHASA. However, the relationship between these three headaches remains unclear.

In two cases, Lance⁴ showed that physical exercise did not play an important role in patients with PHASA. In contrast, and in line with previous studies, 40% of Silbert's patients had both PEH and PHASA^{5,6}. In an analysis of 72 cases, Pascual et al⁷ did not find a relationship between PEH and PCH. In their recent prospective study of 98 patients with PEH, they again confirmed the total

disconnection of PCH from PEH and PHASA⁸. Nevertheless, their findings, which included pain characteristics, comorbidity (migraine), response to indomethacin and coexistence of PHASA and PEH, concur with Silbert's results⁵. All three diagnoses display male predominance⁹. Likewise, our three patients were male and they all responded to indomethacin. In Pascual's study, four patients had migraine and two patients with PEH had TTH. As a rule, based on ICHD 3beta, TTH is not aggravated by physical activity. Similar to PEH, PHASA may be a manifestation of a benign primary headache disorder such as migraine (19% to 47%), TTH, and (less commonly) PCH^{5,8-11}. Conversely, as already pointed out, these three headache conditions coexist without migraine or other primary headache.

The mechanisms involved in the pathogenesis of these headache types are not fully understood. PCH, PEH and PHASA have been reported to be Valsalva manoeuvre-induced, which could explain their pathogenesis in part. Pain is most likely related to a deficit in the mechanism of intracranial pressure control⁹⁻¹⁴. Precipitants such as coughing, laughing, nose-blowing, bending or straining can raise intra-abdominal and intrathoracic pressure, which transmits to epidural veins. This in turn causes spinal cord compression and increased pressure in the spinal canal. Indomethacin has been shown to be effective in inhibiting nitric oxide-induced dural vasodilation, as opposed to other COX inhibitors¹². Conversely, venous abnormalities such as stenosis of the jugular veins or transverse sinus were identified in 12 out of 19 patients presenting with PHASA^{2,9}. This highlights the need for appropriate neuroimaging to rule out any underlying pathology.

However, the probability of a fortuitous event due to this coexistence is extremely low in light of the common mechanism. The most likely pathophysiological explanation for all three categories seems to lie in the rapid increase in intra-abdominal pressure caused by exertion or an inappropriate reaction of the cerebral vasculature. This is also supported by the fact that all patients responded to indomethacin. The exact mechanism of vasoconstriction associated with blockage of the cyclooxygenase pathway remains unclear. However, we should mention that there are no data available from large clinical trials to support level A recommendations for indomethacin.

Conclusions

Although ICHD-3 beta criteria separate these three headache disorders, previous studies have shown that the criteria cannot be completely fulfilled. Due to the low prevalence of these diseases, controlled trials are lacking. Hence, classification of this rare group is based on case reports and small case series. We suggest that large-scaled studies are warranted for further revisions of ICHD-3 beta criteria. The coexistence of these headaches needs to be taken into account in a new classification; wherein a new group should be introduced classing PHASA, PCH and PEH as headaches associated with exertional factors.

Conflict of interest

Authors declare no conflict of interest.

Reference

1. Headache Classification Committee of the International Headache Society (IHS). The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia*. 2013; 33: 629-808.
2. Kararizou E, Bougea A, Giotopoulou D, Anagnostou E, Gkiata A, Gkiatas C, et al. An update of the less-known group of other primary headaches- a review. *Eur Neurol Rev*. 2014; 9: 71-77.
3. Evers S, Goadsby P, Jensen R, May A, Pascual J, Sixt G; EFNS task force. Treatment of miscellaneous idiopathic headache disorders (Group 4 of the IHS classification)--report of an EFNS task force. *Eur J Neurol*. 2011; 18: 803-812.
4. Lance JW. Solved and unsolved headache problems. *Headache*. 1991; 31: 439-445.
5. Silbert PL, Edis RH, Stewart-Wynne EG, Gubbay SS. Benign vascular sexual headache and exertional headache: interrelationships and long term prognosis. *J Neurol Neurosurg Psychiatry*. 1991; 54:417-421.
6. Edis RH, Silbert PL. Sequential benign sexual headache and exertional headache. *Lancet*. 1988; 1: 993.
7. Pascual J, Inglesias F, Oterino MD, Vázquez-Barquero A, Berciano J. Cough, exertional, and sexual headaches: an analysis of 72 benign and symptomatic cases. *Neurology*. 1996; 46: 1520-1524.
8. Pascual J, González-Mandly A, Martin R, Oterino A. Headaches precipitated by cough, prolonged exercise or sexual activity: a prospective etiological and clinical study. *J Headache Pain*. 2008; 9: 259-266.
9. Donnet A, Valade D, Houdart E, Lanteri-Minet M, Raffaelli C, Demarquay G, et al. Primary cough headache, primary exertional headache, and primary headache associated with sexual activity: a clinical and radiological study. *Neuroradiology*. 2013; 55: 297-305.
10. Tuğba T, Serap U, Esra O, Ozlem C, Ufuk E, Levent EI. Features of stabbing, cough, exertional and sexual headaches in a Turkish population of headache patients. *J Clin Neurosci*. 2008; 15: 774-777.
11. Frese A, Eikermann A, Frese K, Schwaag S, Husstedt IW, Evers S. Headache associated with sexual activity: demography, clinical features and comorbidity. *Neurology*. 2003; 61: 796-800.
12. Summ O, Andreou AP, Akerman S, Goadsby PJ. A potential nitrergic mechanism of action for indomethacin, but not of other COX inhibitors: relevance to indomethacin-sensitive headaches. *J Headache Pain*. 2010; 11: 477-483.
13. Cordenier A, De Hertogh W, De Keyser J, Versijpt J. Headache associated with cough: a review. *J Headache Pain*. 2013; 14: 42.
14. Wang SJ, Fuh JL. The "other" headaches: primary cough, exertion, sex, and primary stabbing headaches. *Curr Pain Headache Rep*. 2010; 14: 41-46.