Introduction

Chronic paroxysmal hemicrania (CPH) is a rare, often still poorly recognized, headache syndrome, which is typically responsive to indomethacin. Other treatments have been reported to be potentially effective, although the rarity of the condition itself can result in diagnostic uncertainty in case of lack of response or intolerance to indomethacin.

Case reports

Case 1

This 68-year-old woman was referred to the department with a 3-month history of headaches. She described them as daily, affecting the right eye and fronto-orbital region, occurring mainly during the night when they would wake her up, being extremely intense, pulsating, lasting between 5 and 10 minutes only. The frequency of the episodes varied between 2 and 5 daily. Associated tearing, conjunctival injection and rhinorrhea were reported ipsilaterally. She had a history of insulin-dependent diabetes, hypertension and hypercholesterolemia for which she was on an angiotensin converting enzyme inhibitor and a statin. She denied any history of headaches or facial pains. The patient prior to her referral was started on carbamazepine at the dose of 400 mg daily which resulted in an almost immediate marked reduction in the frequency of the episodes to one every 3–4 days only. Within a fortnight of treatment initiation however, she developed a severe skin rash and the drug had to be discontinued. The painful attacks then recurred with the initial frequency, Gabapentin was then started, at a dose of 600 mg daily, which was maintained for four weeks, with however no favorable effect on frequency, intensity or duration of symptoms. This drug was then withdrawn and replaced by verapamil, at a dose of 120 mg daily, a diagnosis of cluster headache being suspected at that stage. The episodes, within weeks then lessened in frequency, and were described as occurring with however identical intensity and duration, twice weekly on average.
She was at that stage seen in the neurology outpatients unit. Neurological examination showed unimpaired cranial nerve functions, no pyramidal tract signs or cerebellar abnormalities and normal fundi. A precautionary magnetic resonance (MRI) brain scan was normal. Since the attacks were compatible with CPH, indomethacin was suggested at an initial dose of 25 mg twice daily and instructions were provided to gradually increase up to 50 mg three times daily if necessary. This was attempted to further reduce the frequency of the episodes, but resulted in severe nausea, vomiting, light-headedness and gastric pain, experienced at the low initial dose. No change of frequency of the attacks occurred. Indomethacin was then completely withdrawn, and an increase in the dose of verapamil was advised. This resulted in marked improvement, and the patient reported only 2 monthly episodes on a dose of 180 mg daily.

Case 2

This 30-year-old woman was referred to the Neurology Unit for a 9-month history of headaches. They were described as of sudden onset, exclusively right-sided, mainly temporal, extremely intense, stabbing and pulsating, lasting between 2 and 5 minutes, occurring up to 6 times daily. There were no definite accompanying autonomic features. The pains were reported as radiating occasionally posteriorly in the parieto-occipital regions. There was no trigger zone or triggering facial movements, residual pains in between attacks, or allodynia. She had been on a 3-month trial with amitriptyline (25 mg daily) without effect. She had a history of asthma, and gastroesophageal reflux for which she used a proton pump inhibitor. Neurological examination was entirely normal, and an unenhanced computed tomography (CT) brain scan showed no abnormalities.

A diagnosis of CPH was made and she was started on indomethacin (25 mg twice daily) but experienced severe drowsiness, which led to treatment discontinuation within 48 hours. During that time, the episodic headaches persisted. A trial with rizatRIPTAN was then attempted, with no effect. Upon review, she was advised to try ketoprofen (50 mg daily), which resulted in total disappearance of her symptoms within days. She interrupted the treatment for 1 week due to gastrointestinal symptoms, which she attributed to food poisoning, following which the paroxysmal pains recurred at a similar frequency as previously. She then restarted the ketoprofen at the same dose, and had been free of any further episodes on follow-up, 4 months later.

Discussion

Chronic paroxysmal hemicrania (CPH) is a rare disorder, initially described in 1974 [1] and classified among the “indomethacin-responsive headache syndromes”. It affects mainly young women, and causes multiple attacks of severe, short-lasting, unilateral pains, maximally felt in the periorbital and temporal regions. The attacks last between 2 and 45 minutes, are accompanied by ipsilateral autonomic features such as lacrimation, ptosis or rhinorrhea, and recur 1–40 times daily [2]. Occasionally, the autonomic features can be absent in otherwise typical cases [3, 4] as for case 2. Response to indomethacin is rapid, complete and often permanent, and has been part of the International Headache Society’s criteria for diagnosis [5], although this has been subject to controversy, this responsiveness being thought to be a strong indicator rather than definite evidence of a positive diagnosis [2].

Although indomethacin is the obvious first-line drug to be used, side effects can be frequent. The dose required might also be higher than usual in some patients who could then become intolerant to the drug. The most convincing alternative preventive agent reported in the literature has been verapamil [6, 7]. Response appears dose-related as for case 1. Although previously described as ineffective for CPH [7], carbamazepine was however initially useful for this patient. Other non-steroidal anti-inflammatory drugs such as naproxen and diclofenac have been reported to be effective [7]. Similarly ketoprofen, although not previously used for CPH to my knowledge, was effective for case 2.

The rarity of CPH can unfortunately result in misdiagnosis and patients missing out on appropriate treatment. These two cases illustrate furthermore that lack of improvement on indomethacin, in fact related to intolerance, as well as probably also true unresponsiveness to the drug, could in practice result in an initial correct diagnosis of CPH being questioned, this in turn resulting in inappropriate treatment. Trial with verapamil or with other non-steroidal anti-inflammatory agents such as ketoprofen or naproxen, would appear in such cases justified and carbamazepine could also be a potentially useful option in some patients.

References

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