Clinical Reasoning:

A 62-year-old migraineur with a new kind of headache attacks

Manuel Bertschi, MD
Matthias Sturzenegger,
MD
Christian W. Hess, MD

Correspondence & reprint
requests to Dr. Bertschi:
manuel.bertschi@insel.ch

SECTION 1

A 62-year-old man presented with novel headache attacks with acute onset 4 weeks previously strictly confined to the right side. The attacks occurred almost daily, often after midnight, lasting 1 to 3 hours, occasionally longer. The pain was localized around and behind the right eye. The pain intensity was excruciating and the pain quality pulsatile. Ipsilateral lacrimation, conjunctival injection, and prominence of the temporal artery accompanied these attacks. During the attacks, the patient reported a sense of restlessness. Alcohol consumption and physical activity provoked attacks. No recent major trauma was identified.

In his personal history, the patient had had tension-type headache and mainly left-sided migraine-like headache attacks for many years. The latter were of a hammering quality, irradiating from the occipital to the frontal region, and accompanied by nausea, photophobia, and phonophobia. In comparison, the new onset current attacks clearly differed from the previous attacks in terms of location, pain quality, intensity, frequency, duration, and attendant symptoms. Ancillary diagnoses included arterial hypertension, treated with amlodipine, and α -1 antitrypsin deficiency.

Family history revealed a twin brother, who died of aneurysmal subarachnoid hemorrhage 6 years previously. Several relatives had migraine.

On clinical examination, reduced width of the palpebral fissure on the right side compared to the left (ptosis), right miosis, and anhidrosis of the forehead (figure 1, A and B) were noticed.

Figure 1 Complete right Horner triad

(A) Right eye “ptosis” (or, more correct, reduced width of the palpebral fissure on the right side compared to the left) and miosis. (B) Right forehead anhidrosis, visualized using pon-cieu dye.

These findings persisted during the pain-free interval.

Questions for consideration:

1. How would you classify these new onset headache attacks?
2. Are there any atypical features or red flags pointing to a secondary headache?

GO TO SECTION 2

From the Department of Neurology, Inselspital, Bern University Hospital, and University of Bern, Switzerland.

Disclosure: Author disclosures are provided at the end of the article.

SECTION 2

At first glance, the patient's complaints and clinical findings match the criteria of the International Classification of Headache Disorders (International Headache Society [IHS]) for cluster headache.¹ The patient has more than 5 attacks of very severe, unilateral, retro-orbital pain, usually lasting no longer than 3 hours. As requested furthermore, accompanying ipsilateral autonomic features were present and the frequency of attacks was between 1 every other day and 8 per day. However, the IHS criteria wisely require that the history and neurologic examination do not suggest the presence of a symptomatic headache.

In the present case, several red flags raise suspicion of a secondary headache, i.e., a symptomatic cluster-like headache. First, age at onset of cluster headache

usually lies between 20 and 40 years.¹ In a patient presenting with a novel headache beyond age 40, always consider an underlying disease. Second, 2 features of the depicted Horner syndrome are atypical features of autonomic symptoms in primary cluster headache: persistency of Horner syndrome during pain-free interval, and ipsilateral facial anhidrosis.^{1–3} During primary cluster headache attacks, the typical finding is increased sweating of the ipsilateral forehead.⁴ Third, the history of a twin brother with aneurysmal subarachnoid hemorrhage also deserves consideration.

Questions for consideration:

1. What is the most likely etiology of the supposed secondary headache in this case?
2. What would be the appropriate diagnostic tests?

GO TO SECTION 3

Figure 2 MRI

Axial T1-weighted scan with fat suppression technique at the level of the foramen occipitale. There is a semilunar shaped intramural hematoma (hyperintense signal in A and B, arrowheads) of the right distal cervical internal carotid artery, without narrowing of the vessel lumen (black flow void signal in B, arrows) but with widening of the external vessel diameter (shown in A: 15.0 mm right, 9.5 mm left) as compared to the healthy left side.

SECTION 3

Persistency of oculosympathetic palsy during pain-free interval with ipsilateral facial anhidrosis points to carotid artery dissection. Cerebral MRI with magnetic resonance angiography is the appropriate diagnostic test. In our patient, it revealed right internal carotid artery dissection (ICAD) of the distal cervical segment just before entering the skull base (figure 2, A and B). The additionally performed neurosonography did not show any relevant stenosis of the carotid artery. According to the International Classification of Headache Disorders, this case has to be classified as headache, attributed to arterial dissection, mimicking cluster headache.¹

Question for consideration:

1. How would you treat this patient?

GO TO SECTION 4

SECTION 4

As there was no relevant stenosis of the carotid artery, treatment of the ICAD consisted of low-dose acetylsalicylic acid. The headache attacks responded well to nasal zolmitriptan. Oxygen proved to be less effective. In order to reduce intensity and frequency of attacks, verapamil at a tentative target dose of 240 mg was introduced, replacing the former antihypertensive treatment with amlodipine.

DISCUSSION In a patient with a new headache type, distinct from prior headaches, as well as in a patient with headache and any neurologic deficit (e.g., Horner syndrome), imaging should always be done. As outlined above, in the present case additional red flags such as age at onset of cluster headache and atypical autonomic features raise suspicion of a secondary headache. Regarding altered facial sweating in ICAD, there are some controversial issues: Horner syndrome and oculosympathetic palsy are frequently used interchangeably without paying attention to facial anhidrosis, which in the clinical setting often is not examined in detail, and according to the original description is mandatory for diagnosing Horner syndrome (triad). The pathways of sympathetic innervation of the forehead sweat glands have been a matter of debate due to inconsistent findings as to whether these fibers travel with the internal or the external carotid artery. Recent studies suggest that the medial part of the forehead sweat glands is supplied by sympathetic fibers from the internal carotid plexus and the lateral part from those originating from the external carotid artery plexus.⁵ However, the extent of frontal internal carotid plexus supply may be individually variable. In our experience, forehead anhidrosis in ICAD is frequent, although not mandatory. In contrast, the sweating pattern within cluster headache attacks is usually that of ipsilateral hyperhidrosis.⁴ Anhidrosis, if present, suggests ICAD. Further reported warning signs suggesting symptomatic cluster headache include atypical pain quality or localization, attacks of longer duration than 3 hours, lack of pain-free interval, absence of diurnal periodicity, presence of tinnitus, or other neurologic deficits.^{2,6} However, even clinically typical cluster headache without warning signs can be secondary, and therefore, in case of any doubt, MRI should be performed.⁷

Ipsilateral headache is the most common symptom of ICAD, usually limited to the frontotemporal region and sometimes accompanied by anterolateral neck pain. A painful Horner syndrome is present in about one-third of patients with ICAD. However, headache in ICAD, which may indeed have periorbital localization, usually is of continuous time

course. The pain lasts from hours to years, with a median duration of 3–5 days.⁸ To our knowledge, there are no data indicating how often headache in ICAD has an intermittent presentation and how often cluster headache is secondary, i.e., due to an underlying disease. However, in view of a number of case reports, it does not seem to be rare for ICAD to present as cluster headache. A wide range of structural lesions may cause secondary cluster-like headache, including vascular lesions, tumors, and infectious and demyelinating disease.² The mechanisms by which ICAD causes cluster-like headache are not known, but probably in the presence of a Horner syndrome they have a sympathetic origin. Figure 2 nicely demonstrates that in the case of a subadventitial location of mural hemorrhage there is only minor or no stenosis of the vessel lumen, and therefore dissection may be missed by sonography, especially when located in the high-cervical retro-mandibular region. Subadventitial hemorrhage, however, may cause considerable expansion of the outer vessel diameter, stretching the pericarotid sympathetic nerve fiber network and thus leading to Horner syndrome.

The role of α -1 antitrypsin deficiency in spontaneous carotid artery dissection remains controversial. Whereas previous reports suggested that alpha-1 antitrypsin deficiency might be a risk factor for spontaneous carotid artery dissection, this could not be confirmed.⁹

In order to prevent cerebral ischemia in carotid artery dissection, antithrombotic agents are used. To date, there is no evidence in favor of either antiplatelet drugs or oral anticoagulation. Based on pathophysiologic considerations and clinical observation, anticoagulation is favored in patients with high-grade stenosis or occlusion of the dissected artery, multiple ischemic events in the same territory, or with free floating thrombus. In turn, in patients with large cerebral infarction, intracranial dissection, or absence of cerebral artery stenosis, antiplatelet agents seem preferable.¹⁰ A full review of this issue is beyond the scope of this case.

Concerning pain treatment in symptomatic cluster headache, only data from case reports are available. Headache attacks have been attenuated with nasal sumatriptan, nonsteroidal anti-inflammatory drugs, oxygen, and acetaminophen with codeine. Hence a good response to analgetics or even triptans does not rule out secondary cluster headache. Successful prophylactic therapy was reported using verapamil or steroids also in symptomatic cluster headache.⁶ Thus, the response to standard acute and prophylactic treatments does not allow any conclu-

sions as to whether the “cluster headache” is idiopathic or secondary.

AUTHOR CONTRIBUTIONS

Dr. Bertschi: drafting/revising the manuscript. Prof. Sturzenegger: drafting/revising the manuscript, analysis or interpretation of data, acquisition of data. Prof. Hess: drafting/revising the manuscript.

DISCLOSURE

Dr. Bertschi and Prof. Sturzenegger report no disclosures. Prof. Hess has served on a scientific advisory board for Pfizer Inc and serves on the editorial boards of *Swiss Archives of Neurology & Psychiatry* and *Klinische Neurophysiologie*.

REFERENCES

1. Headache Classification Subcommittee of the International Headache Society. The International Classification of Headache Disorders: 2nd edition. *Cephalalgia* 2004; 24(suppl 1):9–160.
2. Mainardi F, Trucco M, Maggioni F, Palestini C, Dainese F, Zanchin G. Cluster-like headache: a comprehensive reappraisal. *Cephalalgia* 2010;30:399–412.
3. Frigerio S, Bühler R, Hess CW, Sturzenegger M. Symptomatic cluster headache in internal carotid artery dissection: consider anhidrosis. *Headache* 2003;43:896–900.
4. Sjaastad O, Saunte C, Russell D, Hestnes A, Mårvik R. Cluster headache: the sweating pattern during spontaneous attacks. *Cephalalgia* 1981;1:233–244.
5. Salvesen R. Innervation of sweat glands in the forehead: a study in patients with Horner’s syndrome. *J Neurol Sci* 2001;183:39–42.
6. Tobin J, Flitman S. Cluster-like headaches with internal carotid artery dissection responsive to verapamil. *Headache* 2008;48:461–466.
7. Wilbrink LA, Ferrari MD, Kruit MC, Haan J. Neuroimaging in trigeminal autonomic cephalalgias: when, how, and of what? *Curr Opin Neurol* 2009;22:247–253.
8. Bioussé V, D’Anglejan-Chatillon J, Massiou H, Bousser MG. Head pain in non-traumatic carotid artery dissection: a series of 65 patients. *Cephalalgia* 1994;14:33–36.
9. Debette S, Leys D. Cervical-artery dissections: predisposing factors, diagnosis, and outcome. *Lancet Neurol* 2009; 8:668–678.
10. Engelter ST, Brandt T, Debette S, et al. Antiplatelets versus anticoagulation in cervical artery dissection. *Stroke* 2007;38:2605–2611.

Neurology[®]

Clinical Reasoning: A 62-year-old migraineur with a new kind of headache attacks

Manuel Bertschi, Matthias Sturzenegger and Christian W. Hess

Neurology 2012;78:e48-e52

DOI 10.1212/WNL.0b013e318247ca7b

This information is current as of February 20, 2012

Updated Information & Services	including high resolution figures, can be found at: http://n.neurology.org/content/78/8/e48.full
References	This article cites 10 articles, 1 of which you can access for free at: http://n.neurology.org/content/78/8/e48.full#ref-list-1
Subspecialty Collections	This article, along with others on similar topics, appears in the following collection(s): Carotid artery dissection http://n.neurology.org/cgi/collection/carotid_artery_dissection Cluster headache http://n.neurology.org/cgi/collection/cluster_headache Secondary headache disorders http://n.neurology.org/cgi/collection/secondary_headache_disorders
Permissions & Licensing	Information about reproducing this article in parts (figures, tables) or in its entirety can be found online at: http://www.neurology.org/about/about_the_journal#permissions
Reprints	Information about ordering reprints can be found online: http://n.neurology.org/subscribers/advertise

Neurology® is the official journal of the American Academy of Neurology. Published continuously since 1951, it is now a weekly with 48 issues per year. Copyright Copyright © 2012 by AAN Enterprises, Inc.. All rights reserved. Print ISSN: 0028-3878. Online ISSN: 1526-632X.