Please use this PDF proof to check the layout of your article. If you would like any changes to be made to the layout, you can leave instructions in the online proofing interface. First, return to the online proofing interface by clicking the Edit button at the top of the page, then insert a Comment in the relevant location. Making your changes directly in the online proofing interface is the quickest, easiest way to correct and submit your proof.

Please note that changes made to the article in the online proofing interface will be added to the article before publication, but are not reflected in this PDF proof.

AUTHOR QUERIES

DATE 1/22/2026
JOB NAME PAINREPORTS

ARTICLE PAINREPORTS-D-25-0230

QUERIES FOR AUTHORS Zwergal et al

THIS QUERY FORM MUST BE RETURNED WITH ALL PROOFS FOR CORRECTIONS

AU1) Please provide telephone number in the correspondence section.
AU2) Please note that as per style, the abstract sub headings should be “Introduction, Objectives, Methods, Results, and Conclusion.” Please check and change if necessary.
AU3) Please note that keywords have been taken from the provided pdf. Please check and correct if necessary.
AU4) Please define or spell out “ICHD” in text.
AU5) Please confirm the conflict of interest statement.
AU6) Please note that references “11 and 17” are not cited in the text. Please cite it in the text or delete from the reference list.

General Section
Case Report

OPEN

PAIN REPORTS

A rare case of secondary paroxysmal hemicrania caused by a T1 nerve root schwannoma

Rachel-Maria Zwergal[a,*], Filipp Filippopulos[a,b], Andreas Straube[a], Max Wuehr[b], Andreas Zwergal[a,b]

Abstract

Objective: Paroxysmal hemicrania (PH) is a rare headache disorder of severe intensity which is classified within the group of trigeminal autonomic cephalalgias and is renowned for its prompt response to indomethacin. Since its first description in 1974, only few cases of secondary PH have been published and even fewer with distinct lesions and a clear pathophysiological association.

Methods: We here present a unique case of long-standing secondary PH, which resolved permanently after resection of a schwannoma of the T1 nerve root, which carries sympathetic projections to the periorbital region.

Results: The current case stresses the importance of sympathetic/parasympathetic dysregulation in the pathophysiological origination of PH, which is far beyond purely central mechanisms. It is the first case ever published, which shows a quite remote peripheral pathology causing a trigeminal autonomic headache disorder.

Conclusion: This case has important implications on a better understanding of the pathophysiology and future diagnostic workup of PH, which should ideally include imaging not only of the brain but also of the spine down to the thoracic level.

Keywords: Paroxysmal hemicrania, Headache, Sympathetic system, Trigeminal autonomic cephalalgias

1. Introduction

Paroxysmal hemicrania (PH) is a rare headache disorder of severe intensity which is classified within the group of trigeminal autonomic cephalalgias (TAC) and is renowned for its prompt response to indomethacin. This distinguishes PH along with the related hemicrania continua from other TAC like cluster headache or short-lasting unilateral headache. Epidemiological data indicate a first onset typically around the fourth decade of life and shows a slight female predominance. Much has been speculated about its pathophysiology, and there is currently intense discussion as to whether central, peripheral, or neurovascular mechanisms are primarily responsible.[2] Secondary symptomatic cases may help to improve our understanding of disease development and pathophysiology. But since its first description in 1974 by Sjaastad and Dale,[20] only few cases of secondary PH have been published and even fewer with distinct lesions and a clear pathophysiological association.

2. Methods

We here present a unique case of long-standing secondary PH, which resolved permanently after resection of a schwannoma of the T1 nerve root, which carries sympathetic projections to the periorbital region.

3. Results

The male patient, a neuropediatrician, first sought medical advice in 2013 at age 64 years with ongoing bouts of headache since 2011. The symptoms initially occurred in clusters of active episodes and had striking peculiar features: The pain was of excruciating intensity (8–10 on a 10-point rating scale), strictly bound to the left periorbital and temporal region and accompanied by tearing and miosis of the left eye. Duration of attacks was exactly 10 minutes, followed by an interictal phase of exactly 90 minutes until the next attack appeared. During the active episodes, this pattern continued for 2 to 10 weeks, meaning he had a severe headache attack every 90 minutes all day and night.

Sponsorships or competing interests that may be relevant to content are disclosed at the end of this article.

[a] *Department of Neurology, LMU University Hospital, LMU Munich, Munich, Germany,* [b] *German Center for Vertigo and Balance Disorders (DSGZ), LMU University Hospital, Munich, Germany*

**Corresponding author. Address: Department of Neurology, LMU University Hospital, LMU Munich, Marchioninistr. 15, 81377 Munich, Germany. E-mail address: Rachel-Maria.Zwergal@med.uni-muenchen.de (R.-M. Zwergal).*

PR9 11 (2026) e1404

http://dx.doi.org/10.1097/PR9.0000000000001404

In the beginning he noticed a circannual accumulation with more active episodes during spring and fall. An active episode began with constant painless tearing of the left eye for 2 days and then the headache attacks set in. The headache showed a dramatic response to indomethacin, stopping the pattern of bouts abruptly and preventing new headache attacks on a dosage of 50 mg daily. Initial diagnostic workup showed no focal-neurological deficits. An MRI of the brain and cervical spine depicted lesions, which could explain the new onset of headaches. The patient was AU4 diagnosed with primary episodic PH based on ICHD criteria.[16] He was advised to take indomethacin daily. The patient was able to stop the medication after the active phase had ended, delaying the intake of the drug every 24 hours. If no headache appeared, the episode had stopped but reoccurred reliably after a few weeks. Over the next years, attacks appeared regularly with increasing frequency and were documented in detail in a digital headache diary along with blood pressure and heart rate by the patient (**Fig. 1A**). During attacks, these recordings indicated F1 reproducibly a significant relative decrease of the heart rate and a slight significant increase of systolic blood pressure (**Fig. 1B**). Since 2020, the patient was treated for elevated blood pressure with lercanidipine (5–10 mg/d), candesartan (4–16 mg/d), and metoprolol (47.5 mg/d). Otherwise, there was no indication of cardiac disorders.

In 2022, the frequency of active headache episodes further increased, and the patient had a new onset of bilateral back pain and some tingling of the legs. A contrast-enhanced T1-weighted MRI of the cervical and thoracic spine depicted an extramedullary tumor with a dimension of 2 × 1 cm at T1 level, which locally compressed the spinal cord and affected the nerve roots T1 (**Fig. 2A**). There were no clinical signs of a myelopathy, ie, no F2 paresis, proprioceptive, gait, or bladder dysfunction.

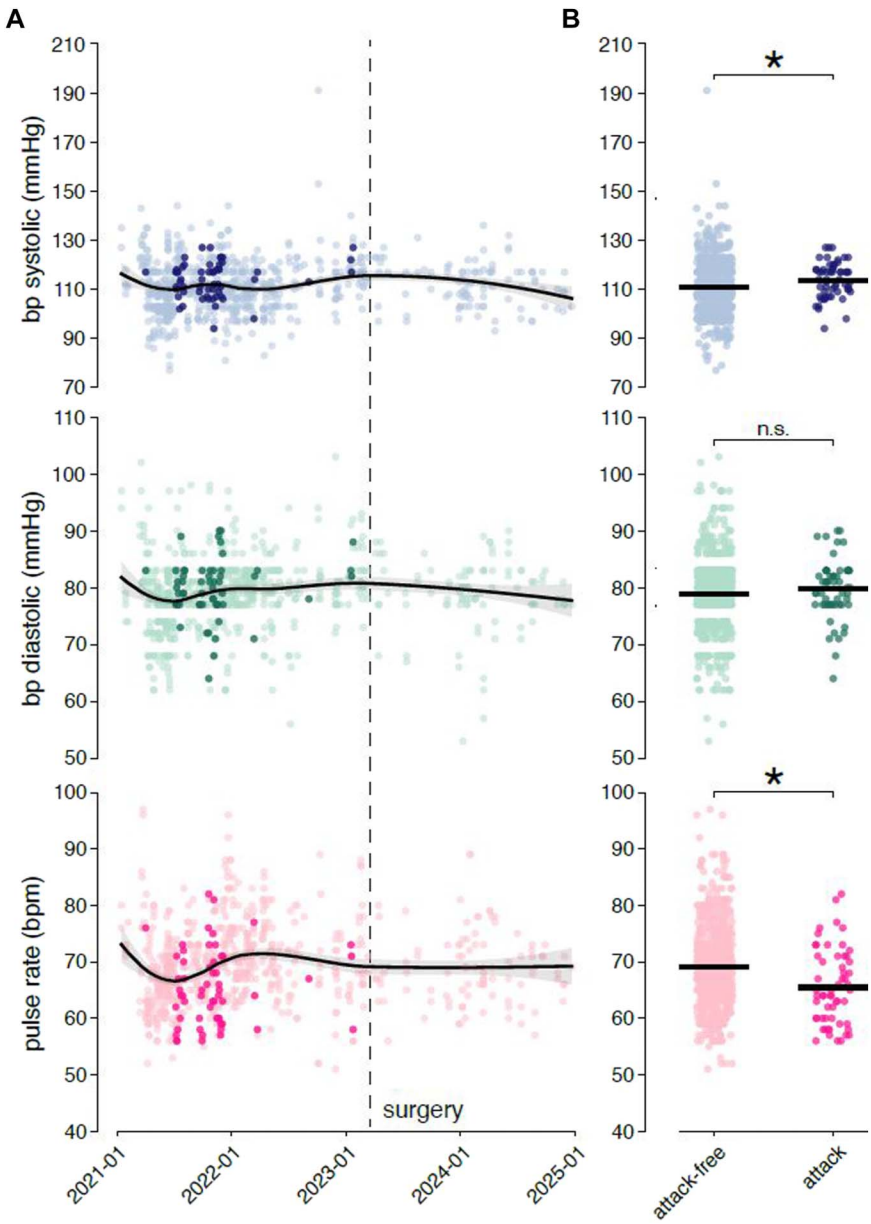

Figure 1. Fluctuations of vital signs in relation to PH symptom trajectory. (A) Long-term tracking of vital signs by a health care app before and after surgical removal of the T1 nerve root schwannoma. (B) Statistical comparison of systolic and diastolic blood pressure and heart rate in the attack-free interval (pale colors) and attacks (bright colors). *$P < 0.05$ (paired t test). bp, blood pressure; PH, paroxysmal hemicrania.

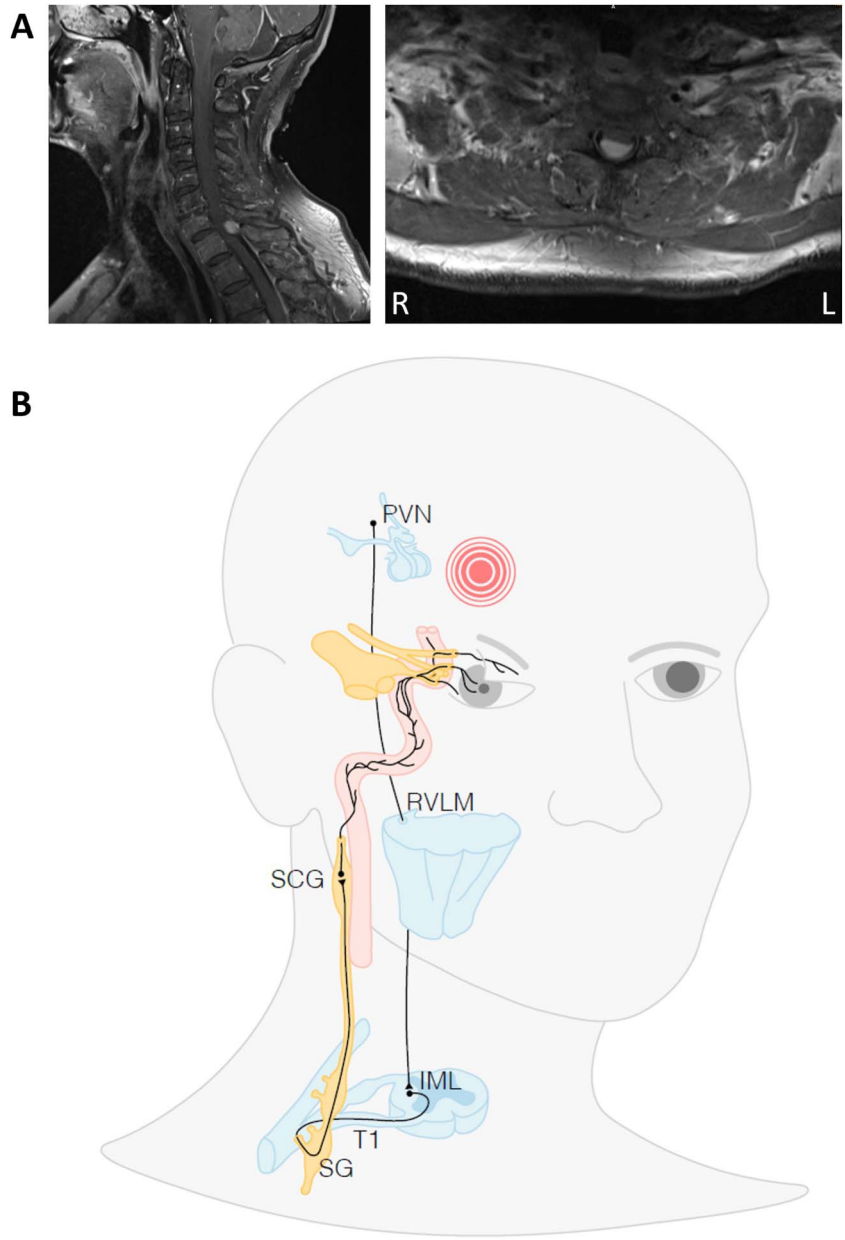

Figure 2. Magnetic resonance imaging of T1 schwannoma and schematic overview of sympathetic pathways potentially involved in PH. (A) Axial and transversal T1-weighted MRI sections (turbo-spin-echo sequence with application of contrast agent) depicting a contrast-enhancing tumor with a dimension of 2 × 1 cm at T1 level. (B) Schematic drawing of the central and peripheral sympathetic networks projecting to the periorbital region, potentially involved in the pathophysiology of secondary paroxysmal hemicrania. IML, intermediolateral nucleus; L, left; PVN, paraventricular nucleus; R, right; RVLM, rostral ventrolateral medulla; SG, stellate ganglion; SCG, superior cervical ganglion; T1, nerve root T1.

Surgical removal of the tumor was performed in March 2023 to treat the enduring back pain and prevent further spinal cord compression in case of tumor progression. Intraoperative inspection showed an attachment of the tumor to the nerve roots T1. The tumor could be removed with a partial preservation of the nerve root. Pathological analysis confirmed the diagnosis of a schwannoma grade 1. Interestingly, the patient perceived a sudden complete cessation of his headache from the day of the surgery. He was able to stop the indomethacin treatment completely. On a 24-month follow-up, no further headache attacks appeared. A reevaluation of the patient case led to the diagnosis of a secondary PH provoked by the schwannoma of the nerve root T1.

4. Discussion

How could a tumor at this level cause the picture of PH, and what could we possibly learn from this case for the general pathophysiology of PH?

It is well known that the nerve root T1 carries sympathetic fibers, which travel with the sympathetic trunk to the stellate ganglion and superior cervical ganglion. From there, the tertiary fibers reach the forehead and periorbital region, where they branch with fibers from the trigeminal nerve. Further fibers travel to the heart to contribute to its sympathetic innervation and rise along the external carotid artery to reach meningeal vessels.[25] An affection of the T1 nerve root by tumor growth or compression, therefore, could well impair the sympathetic system. The clinical signs in our case with tearing and miosis of the left eye speak for

a transient imbalance of the parasympathetic and sympathetic input during symptomatic phases. This view is reinforced by a well-documented decrease of heart rate within the attacks. This decrease in sympathetic tone matched the initial descriptions by Sjaastad et al.[21] who discussed a sympathetic deficit as a decisive pathophysiological feature of PH, as the autonomic symptoms during the attack and interictal findings pointed to a transient functional sympathetic deficit or sympathetic/parasympathetic imbalance. In line, Drummond[8] suggested a sympathetic deficit and parasympathetic overactivation during active episodes in chronic PH. This hypothesis was also confirmed in other TAC. A reduction of sympathetic tone would cause a relative parasympathetic predominance and therefore an ipsilateral vasodilation of the meningeal vessels, which could contribute to the manifestation of hemicrania through an activation of trigeminal nociceptive fibers, as proposed also for the pathophysiology of TAC.[6] This theory is facilitated by one case report, where the onset of secondary PH was associated with the intake of vasodilative drugs.[23] The proposed action of indomethacin in our case could be through its comparably potent vasoconstrictive potential in combination with its anti-inflammatory action.[1] The gradual increase of the attack frequency over a decade fits with the suspected slow growth of a benign schwannoma. The instantaneous and long-term enduring cessation of headaches after its removal strongly suggests a causal relation. In the literature, very few cases of secondary PH exist, of which only 3 cases completely fulfilled the ICHD-3 criteria and provided adequate MR imaging.[12,19,24] There are 12 more lesional cases, which do not fully cover the ICHD-3 criteria mostly because indomethacin was not applied ("probable PH")[3–5,7,9,10,13–15,18,22,26] (Supplementary Table 1, http://links.lww.com/PR9/A382).

Until now, it was presumed that all these lesions with a PH phenotype cannot be aligned to a certain cerebral region or network, making it difficult to establish a clear pathophysiological relation to the headache.[2] However, most of the reported lesions affect central or peripheral sympathetic networks, including the pituitary-hypothalamic region (ie, the paraventricular nucleus), the brainstem (ie, the nucleus of the solitary tract, caudal, and rostral ventrolateral medulla), and the sympathetic trunk. The current case—being the first with a distinct focal lesion at the crossroad of central and peripheral sympathetic networks at T1 level—shows clearly that a rather remote sympathetic lesion can lead to a dysfunction of autonomic networks through the mechanisms described above.

The slight circannual rhythmicity described by the patient could be explained by the well-known circannual oscillation of the autonomic system in higher mammals and humans,[6] which may contribute to a vulnerability because of physiological seasonal changes, making it more susceptible to damage from tumor associated pressure or other affections.

Some specifics of the current case may impact its generalizability to other cases of PH: Lercanidipine, candesartan, and metoprolol may have affected heart rate and blood pressure data because they inhibit the sympathetic effects on cardiovascular regulation. However, the relative decrease in heart rate during attacks cannot be explained sufficiently by drug effects only. It cannot be excluded that the tumor removal caused some indirect effects on pain dynamics including placebo effects. The patient did not expect an effect of the surgery on PH based on pretreatment consultation though.

Overall, the current case reinforces previous hypotheses on the contribution of the autonomic nerve system to the pathophysiology of PH (**Fig. 2B**). To our knowledge, it is the first to show that a pathology at T1 level can cause a trigeminal autonomic headache disorder. Consequently, diagnosis of exclusion in PH should ideally include imaging of the brain, the spinal cord to the thoracic level, and the mediastinal and neck region, especially if the demographic features of the patients do not align with the "typical" epidemiology of primary PH such as female preponderance and mid age.

Disclosures

The authors have no conflict of interest to declare. AU5

Acknowledgements

The authors thank Katie Göttlinger for copyediting of the manuscript.

Supplemental digital content

Supplemental digital content associated with this article can be found online at http://links.lww.com/PR9/A382.

Article history:
Received 22 July 2025
Received in revised form 19 November 2025
Accepted 25 November 2025

References

[1] Antonaci F, Pareja JA, Caminero AB, Sjaastad O. Chronic paroxysmal hemicrania and hemicrania continua: lack of efficacy of sumatriptan. Headache 1998;38:197–200. AU6
[2] Bahra A. Paroxysmal hemicrania and hemicrania continua: review on pathophysiology, clinical features and treatment. Cephalalgia 2023;43:3331024231214239.
[3] Beams JL, Rozen TD. Paroxysmal hemicrania as the clinical presentation of giant cell arteritis. Clin Pract 2011;1:e111.
[4] Boes CJ, Dodick DW. Refining the clinical spectrum of chronic paroxysmal hemicrania: a review of 74 patients. Headache 2002;42:699–708.
[5] Bonazzi A, Giagnorio F, Salpietro V. Lesione del simpatico cervicale e cefalea oculotemporale: descrizione di due casi [in Italian]. Confinia Cephalalgica 1993;2:39–41.
[6] Buijs RM, van Eden CG, Goncharuk VD, Kalsbeek A. The biological clock tunes the organs of the body: timing by hormones and the autonomic nervous system. J Endocrinol 2003;177:17–26.
[7] Delreux V, Kevers L, Callewaert A. Paroxysmal hemicrania preceding Pancoast's syndrome. Rev Neurol 1998;145:151–2.
[8] Drummond PD. Thermographic and pupillary asymmetry in chronic paroxysmal hemicrania. A case study. Cephalalgia 1985;5:133–6.
[9] Favier I, van Vliet JA, Roon KI, Witteveen RJ, Verschuuren JJ, Ferrari MD, Haan J. Trigeminal autonomic cephalgias due to structural lesions: a review of 31 cases. Arch Neurol 2007;64:25–31.
[10] Gatzonis S, Mitsikostas DD, Ilias A, Zournas CH, Papageorgiou C. Two more secondary headaches mimicking chronic paroxysmal hemicrania. Is this the exception or the rule? Headache 1996;36:511–3.
[11] Giani L, Proietti Cecchini A, Leone M. Cluster headache and TACs: state of the art. Neurol Sci 2020;41:367–75.
[12] Grangeon L, Moscatelli L, Zanin A, Rouille A, Maltete D, Guegan-Massardier E. Indomethacin-responsive paroxysmal hemicrania in an elderly man: an unusual presentation of pituitary apoplexy. Headache 2017;57:1624–6.
[13] Greve E, Mai J. Cluster headache-like headaches: a symptomatic feature?: a report of three patients with intracranial pathologic findings. Cephalalgia 1988;8:79–82.
[14] Medina JL. Organic headaches mimicking chronic paroxysmal hemicrania. Headache 1992;32:73–4.
[15] Mehta DG, Swanson JW. Cerebral sinus venous thrombosis mimicking probable paroxysmal hemicrania: a case report. Headache 2020;60:992–3.

[16] Olesen J. Headache classification committee of the international headache society (IHS) the international classification of headache disorders. Cephalalgia 2018;38:1–211.
[17] Paliwal VK, Uniyal R. Paroxysmal hemicrania: an update. Neurol India 2021;69(suppl 1):S135–43.
[18] Pauri F, Tilia G, Cisternino MD, Pierelli F. Tuber cinereum hamartomas mimicking chronic paroxysmal hemicrania. Ital J Neurol Sci 1993;14:132.
[19] Sarov M, Valade D, Jublanc C, Ducros A. Chronic paroxysmal hemicrania in a patient with a macroprolactinoma. Cephalalgia 2006;26:738–41.
[20] Sjaastad O, Dale I. Evidence for a new (?) treatable headache entity. Headache 1974;14:105–8.
[21] Sjaastad O, Aasly J, Fredriksen T, Wysocka Bakowska MMW. Chronic paroxysmal hemicrania. X. On the autonomic involvement. Cephalalgia 1986;6:113–24.
[22] Sjaastad O, Stovner LJ, Stolt-Nielsen A, Antonaci F, Fredriksen TA. CPH and hemicrania continua: requirements of high indomethacin dosages-an ominous sign? Headache 1995;35:363–7.
[23] Taga A, Russo M, Genovese A, Manzoni GC, Torelli P. Paroxysmal hemicrania-like headache secondary to phosphodiesterase inhibitors administration: a case report. Headache 2017;57:663–4.
[24] Vijayan N. Symptomatic chronic paroxysmal hemicrania. Cephalalgia 1992;12:111–3.
[25] Wehrwein EA, Orer HS, Barman SM. Overview of the anatomy, physiology, and pharmacology of the autonomic nervous system. Compr Physiol 2016;6:1239–78.
[26] Zhuang C, Beeman B. Carotid body tumor as a potential cause of paroxysmal hemicrania. J Vasc Surg Cases Innov Tech 2020;6:495–7.