CASE REPORT

Herpes zoster ophthalmicus evolving into headache characterised as hemicrania continua

Sanjay Prakash, Ankit Dave, Hemant Joshi

Department of Neurology, Smt BK Shah Medical Institute and Research Centre, Vadodara, India

Correspondence to
Sanjay Prakash,
drprakashs@yahoo.co.in

Accepted 10 March 2018

SUMMARY

Postherpetic neuralgia (PHN) is the most common chronic complication of herpes zoster infection. However, a few patients may develop different types of pain after herpetic lesions. We are reporting two patients who developed postherpetic hemicrania continua (HC). Case 1: a 54-year-old woman had a 10-month history of continuous left-sided pain with superimposed exacerbations. The pain started with the onset of herpetic lesions in the ophthalmic division. The lesions subsided in a few weeks. However, the pain persisted and it responded exclusively to indomethacin. Case 2: a 61-year-old woman developed clinical features pertinent to PHN. However, later on, the pattern and associated clinical features changed. The patient fulfilled the criteria of HC and showed a complete response to indomethacin. We suggest that every patient with PHN should be asked for cranial autonomic features and a trial of indomethacin should be given in refractory herpes zoster neuropathy.

BACKGROUND

Herpes zoster ophthalmicus (HZO) is a type of shingles in which rashes develop in the ophthalmic division of the fifth cranial nerve. Postherpetic neuralgia (PHN) is a neuropathic pain that persists or develops after the dermatomal rash has healed. The character and the site of pain may overlap with headaches and facial pain disorders.^{1,2} Herein, we report two patients with HZO who developed hemicrania continua (HC)-like headache. Written informed consent was taken from both cases for the publication of this report. The study does not require approval by the Institute Ethics Committee as per the local regulations for case reports.

CASE PRESENTATION**Case 1**

A 54-year-old woman had a history of left-sided herpetic lesions in the ophthalmic division of the trigeminal nerve (HZO) about 10 months back. The skin lesion resolved completely within 4–5 weeks. The pain, however, persisted in the same areas. The pain was continuous with superimposed exacerbations. The continuous pain was described as dull and mild to moderate intensity. The exacerbations, a few minutes to a few hours' duration (2 min to 2 hours), 5–20 times in a day, were described as stabbing and burning in the character. The exacerbations were associated with cutaneous allodynia at the site of pain. The patient noted conjunctival

injection and tearing in the left eye in about 25% of exacerbations. Previous treatment with various drugs never produced complete improvement. At the time of presentation, at our outpatient clinic, she was taking carbamazepine (400 mg three times a day) and tramadol (50 mg two times a day). This had only minimal effect on her ongoing pain. Physical examinations and MRI of the brain did not give any extra information. Although the patient's history was highly suggestive of PHN, it also fulfilled the criteria of HC. Carbamazepine and tramadol were withdrawn and a trial of indomethacin was started. The patient felt complete improvement at a dose of 75 mg three times a day in 10 days duration.

Case 2

A 61-year-old woman had a history of herpes zoster infection on the left side about 3 years back. The lesions were restricted mainly to the ophthalmic division (V1) of the trigeminal nerve. The lesions were mainly on the left side of the forehead and the left upper eyelid. The patient was initially seen by an ophthalmologist and there was not any lesion within eye. The lesions subsided within 3–4 weeks. However, even after the resolution of the lesions, she had pain in the affected areas. The pain was paroxysmal in the earlier years and was described as severe, sharp and burning type. The usual duration of pain was 30 s to 2 min. The frequency of attacks was variable (5–25 attacks in a day). The attacks of pain were well controlled with the drugs (gabapentin and carbamazepine) in the first 10–12 months. However, the response to drugs gradually faded. She tried a number of drugs over 2 years with very little response. She also noted change in the pattern of headaches. The patient continued to have paroxysms of pain of a few seconds to a few minutes. However, several attacks were more prolonged (up to 12 hours). On questioning, the patient admitted to have continuous pain on the right side of the skull and face. Conjunctival injection and tearing in the left eye were noted in about 50% exacerbations, especially with the exacerbations of the longer duration. The patient had been restless and had shown pacing activity during exacerbations. The exacerbations were occasionally precipitated by chewing and eating foods. She never noted nausea, vomiting, phonophobia, photophobia or any type of aura with the exacerbations.

At the time of presentation, she had been receiving amitriptyline (25 mg daily), carbamazepine (300 mg two times a day) and gabapentin (300 mg three times a day). However, despite these

To cite: Prakash S, Dave A, Joshi H. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2018-224235

drugs, she had daily continuous headache with a few exacerbations. Physical and neurological examinations did not reveal any abnormality. Routine haematological and biochemical parameters were normal. MRI of the brain and orbit did not reveal any abnormality.

We started indomethacin at a dose of 25 mg three times a day and was gradually titrated up to 75 mg three times a day. She showed almost complete improvement in 2 weeks duration at this dose.

OUTCOME AND FOLLOW-UP

Case 1

The patient was followed up for the next 12 months. Skipping of the drug or reduction of the dose of indomethacin has always led to recurrence of the symptoms. It further confirmed the possibility of HC.

Case 2

One month later, indomethacin was withdrawn because of gastritis. The pain reappeared with the same frequency and the intensity. A few weeks later, indomethacin (25 mg two times a day) was restarted with gastric protection. The patient had about 60%–70% response with this dose and we could not increase the dose because of fear of gastrointestinal side effects. The patient was satisfied with this treatment in the next 9 months follow-up.

DISCUSSION

Headache or facial pain as a feature of PHN has been acknowledged in the International Classification of Headache Disorders third edition (ICHD-3 β). However, the details of pain (such as character, frequency and duration) are lacking in the diagnostic criteria.² In general, the pain in PHN may be stimulus-independent continuous pain, stimulus-independent intermittent pain and stimulus-evoked pain (allodynia). Spontaneous continuous pain is present all of the time with fluctuation in the intensity. Spontaneous intermittent pain is episodic and has a relatively short period when it occurs. The quality of the pain in the patients with PHN may be aching, throbbing, burning or shooting.^{1 3} The literature is silent regarding the presence of cranial autonomic features during PHN state.¹

The differential diagnosis in our patients largely include PHN and postherpetic HC. Both patients fulfilled the ICHD-3 β criteria for PHN. In parallel, both cases also fulfilled the ICHD-3 β criteria for HC.² However, the presence of cranial autonomic features and a complete response to indomethacin in both patients are in favour of HC.

Both patients had continuous pain with variable superimposed exacerbations. Variable exacerbations on the background pain is highly suggestive of HC.⁴ Case 1 reported continuous background pain with variable exacerbations (a few seconds to a few hours) since the beginning. However, case 2 have predictable pattern of paroxysm of pain (30 s to 2 min). Later on, the pattern changed and it was noted as continuous background headache with variable exacerbations (a few seconds to 12 hours). We speculate that case 1 developed HC since the beginning of the symptoms. However, case 2 initially had symptoms more likely of PHN and later it developed into postherpetic HC.

Ipsilateral cranial autonomic symptoms are specific of trigeminal autonomic cephalalgias (including HC). However, the prevalence of cranial autonomic features in HC is somewhat lower than other trigeminal autonomic cephalalgias (TACs). It varies from 17% to 90%.⁴ Both of our patients reported cranial autonomic features during exacerbations.

There was a temporal relation in the disappearance of pain and the administration of indomethacin in both patients. The reappearance of pain on skipping of the drug rules out the placebo response in both patients.⁵ There is no evidence to support the use of non-steroidal anti-inflammatory drugs in the treatment of PHN.¹ Therefore, the complete response to indomethacin in both patients suggests that these cases may not be a true representation of PHN and these cases may be the secondary HC. However, a possibility of coexistence of PHN with HC also exists.

To the best of our literature search, postherpetic HC cases have not been described in the literature. However, some inter-relations between short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) and herpes zoster have been reported in the recent past. Kürşad *et al* reported two patients of HZO mimicking SUNCT-like pain.⁶ Mathew *et al* reported two patients postherpetic SUNCT.⁷ In the first case, symptoms of SUNCT developed after 1 year of herpes zoster infection. In the second case, SUNCT-like symptoms developed just after 1 month of the herpes zoster lesions.

Characteristically, cranial autonomic feature is not a feature of PHN and other neuropathic pains. However, these may be noted in a few percentages of patients with trigeminal neuralgia (another neuropathic head pain).⁸ A few patients of Trigeminal Neuralgia (TN) have evolved into SUNCT (a neuralgiform head pain with marked autonomic features).⁸ Goadsby *et al* have suggested that some degree of cranial parasympathetic activation is a normal physiological response to nociceptive input in the first division of the trigeminal nerve.⁹ Herpes zoster is a disease of somatosensory cells. However, other neurons may be involved due to spread of inflammatory cells and molecules from nearby infected somatosensory cells.¹⁰

Trigeminal-autonomic reflex (TAR) (consisting of a brainstem connection between trigeminal nerve and facial parasympathetic outflow) is considered essential for the manifestations of HC and other trigeminal autonomic pain syndromes. Activation of the trigeminal nerve could trigger TAR.¹¹ A number of secondary HC had produced symptoms probably by activating trigeminal nerve.¹² Cornea is innervated by ophthalmic division of trigeminal nerve. Therefore, activation of cornea by any pathology may activate TAR. Leprosy, a predominantly sensory neuropathy, has been reported as a cause of secondary HC.^{4 12}

The pathophysiology of PHN is largely obscure.^{1 13} However, both peripheral and central pathophysiological mechanisms are involved for PHN pain. In the periphery, thinning and loss of axon and myelin sheath is the most important finding. Infiltration of chronic inflammatory cells is also reported in the dorsal root and nerve.¹⁴ It has been suggested that constant pain arises from a marked loss of nociceptive afferents, whereas paroxysmal pain is related to demyelination.¹² Allodynia is explained by central sensitisation. However, the areas of the central nervous system involved in PHN pain are still being determined. A connection

Learning points

- ▶ Hemicrania continua-like symptoms may occur after herpetic zoster infection of the V1 trigeminal nerve.
- ▶ It may be differentiated by the presence of variable superimposed exacerbations and presence of cranial autonomic features.
- ▶ Diagnosis is very important as it responds dramatically to indomethacin.

between the trigeminal nucleus caudalis and the posterior thalamus has been described in rats. Information from trigeminal territories reaches the hypothalamus through the trigemino-hypothalamic tract.¹⁵ Therefore, a possibility of activation of TAR exists in the patients with HZO and it may be the reason for the evolving of (or coexistence of) HC from HZO. Therefore, we suggest that every patient with HZO should be asked for cranial autonomic features and we recommend a trial of indomethacin in this subset of patients with HZO.

Contributors SP, AD and HJ were involved in the conception and design of the study. SP and AD were involved in the acquisition of data. SP was involved in the manuscript preparation. AD and HJ were involved in revising the draft for intellectual content. All authors approved the final version of this manuscript.

Funding The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2018. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- Johnson RW, Rice AS. Clinical practice. Postherpetic neuralgia. *N Engl J Med* 2014;371:1526–33.
- Headache Classification Committee of the International Headache Society (IHS). The international classification of headache disorders, 3rd edition (beta version). *Cephalalgia* 2013;33:629–808.
- Dworkin RH, Gnann JW, Oaklander AL, et al. Diagnosis and assessment of pain associated with herpes zoster and postherpetic neuralgia. *J Pain* 2008;9(1 Suppl 1):37–44.
- Prakash S, Patel P. Hemicrania continua: clinical review, diagnosis and management. *J Pain Res* 2017;10:1493–509.
- Sjaastad O, Antonaci F. A piroxicam derivative partly effective in chronic paroxysmal hemicrania and hemicrania continua. *Headache* 1995;35:549–50.
- Akpınar ÇK, Doğru H, Erdoğan S, et al. Herpes zoster ophthalmicus that mimics the SUNCT syndrome. *Noro Psikiyatr Ars* 2016;53:184–5.
- Mathew T, Srinivas M, Badachi S, et al. Post herpes zoster SUNCT like syndrome: Insights from two case reports. *Cephalalgia* 2018;38:0333102416677052.
- Benoliel R, Sharav Y. Trigeminal neuralgia with lacrimation or SUNCT syndrome? *Cephalalgia* 1998;18:85–90.
- Goadsby PJ, Matharu MS, Boes CJ. SUNCT syndrome or trigeminal neuralgia with lacrimation. *Cephalalgia* 2001;21:82–3.
- Oaklander AL. Mechanisms of pain and itch caused by herpes zoster (shingles). *J Pain* 2008;9(1 Suppl 1):10–18.
- Goadsby PJ, Lipton RB. A review of paroxysmal hemicranias, SUNCT syndrome and other short-lasting headaches with autonomic feature, including new cases. *Brain* 1997;120(Pt 1):193–209.
- Prakash S, Shah ND, Soni RK. Secondary hemicrania continua: Case reports and a literature review. *J Neurol Sci* 2009;280:29–34.
- Fields HL, Rowbotham M, Baron R. Postherpetic neuralgia: irritable nociceptors and deafferentation. *Neurobiol Dis* 1998;5:209–27.
- Nurmikko T. Clinical features and pathophysiologic mechanisms of postherpetic neuralgia. *Neurology* 1995;45(12 Suppl 8):S54–5.
- Malick A, Strassman RM, Burstein R. Trigemino-hypothalamic and reticulohypothalamic tract neurons in the upper cervical spinal cord and caudal medulla of the rat. *J Neurophysiol* 2000;84:2078–112.

Copyright 2018 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- ▶ Submit as many cases as you like
- ▶ Enjoy fast sympathetic peer review and rapid publication of accepted articles
- ▶ Access all the published articles
- ▶ Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow