

Congenital epidermoid cyst presenting as isolated painful trigeminal neuropathy: indications for neuroimaging in the diagnostic process.

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Abstract

This article reports a case of a cerebellopontine angle epidermoid cyst presenting as isolated painful trigeminal neuropathy. The indolent nature of these uncommon benign tumours leads to frequent delays in their presentation and diagnosis, with patients often initially undergoing dental procedures, as illustrated here. This case highlights the difficulties in identifying trigeminal neuralgia (TN), particularly in its early phases, and supports current recommendations for routine neuroimaging in suspected cases of painful trigeminal neuropathy (which, unlike classical TN, is caused by another disorder other than neurovascular compression), particularly in younger patients with atypical features, even in the absence of additional neurological symptoms or signs. Additionally, it offers a unique patient perspective of living with TN, with a detailed description of the nature of the pain and its impact by one of the authors.

Key words

Trigeminal neuralgia; trigeminal neuropathy; epidermoid cyst; cerebellopontine angle; facial pain; trigeminal nerve

Introduction

Trigeminal neuralgia (TN) is the archetypal craniofacial pain syndrome characterised by episodes of intense pain along the distribution of one or more branches of the trigeminal nerve, usually affecting its second or third divisions. It is a relatively rare disorder, with a prevalence of between 3 in 1000 to 10000 individuals and a predilection for women.¹ Most patients are diagnosed between 37 to 67 years of age¹. The International Classification of Headache Disorders (ICHD) defines classical TN by more specific diagnostic criteria, including (a) severe paroxysms of unilateral, electric shock-like, stabbing or sharp pain lasting up to two minutes, (b) absence of radiation beyond the trigeminal distribution, (c) precipitation by innocuous stimuli (e.g. talking, washing the face, shaving, tooth-brushing) to the affected side of the face, (d) absence of any neurological deficit, and (e) at least three episodes fulfilling criteria (a) and (b).² A subform of classical TN includes, in addition, persistent facial pain of a less severe intensity in the affected area.²

The classical form of TN is caused by vascular compression of the trigeminal nerve root, usually by the superior cerebellar artery, leading to local demyelination.^{1,3,4} Treatment includes medical management using neuropathic pain medications (e.g. gabapentin) or antiepileptics (e.g. carbamazepine, oxcarbazepine, lamotrigine), surgery (microvascular decompression, percutaneous nerve ablation) or stereotactic radiosurgery, all with varying degrees of success.^{4,5}

When TN is caused by another disorder apart from neurovascular compression, such as demyelination (e.g. multiple sclerosis) or cerebellopontine angle mass lesions, this is termed painful trigeminal neuropathy² and can account for up to 15%

of cases.⁶ A routine MRI is now recommended to exclude these as part of the diagnostic process.^{2,3} Apart from symptoms not fulfilling classical TN criteria, younger age, abnormal trigeminal reflexes (e.g. the corneal reflex), sensory deficits, and other cranial neuropathies (e.g. hearing loss, dizziness, vertigo, tinnitus, visual changes) are all indicative of the possibility of trigeminal neuropathy rather than classical TN.^{6,7} However, the evolution of pain in emerging trigeminal neuropathy may not always be typically neuropathic, leading to significant delays in diagnosis, as illustrated here by a case of TN initially presenting atypically in a young adult patient who was subsequently found to have a cerebellopontine epidermoid cyst requiring neurosurgery.

Case report

A 32-year-old Chinese male presented to the maxillofacial surgery department with a six-month history of intermittent, unpredictable right jaw pain, which had increased in frequency from two episodes three months apart to occurring daily. Initially, the pain was described as a dull aching sensation which was difficult to localise and arose from deep within the oromucosal surface of the right mandibular angle, but over the ensuing six months this evolved into more intense episodes with occasional sharp lancinating pains down towards the midline of the lower lip and up towards the external auditory meatus. The pain was not consistently relieved by non-opioid analgesics or non-steroidal anti-inflammatory medications, and the patient had resorted to applying topical local anaesthetic gel (containing lidocaine hydrochloride 0.66%), with some temporary relief of symptoms.

Dental X-rays revealed a mesio-angularly impacted wisdom tooth in the lower right jaw and suggested distocervical caries or resorption of the adjacent molar with a close relationship to the inferior alveolar nerve canal. A cone beam CT scan confirmed these findings and a coronectomy was performed on the wisdom tooth.

Unfortunately, 48 hours after the coronectomy, the pain returned and intensified further, with episodes lasting up to 30 minutes and becoming biphasic in nature, changing from electric shock-like to throbbing in character midway through the episodes, as well as extending superiorly to the right temporal region. The episodes were preceded by an “aura” of right cheek and lower lip paraesthesiae including sensations of crawling and pins-and-needles. The patient remained completely pain-free and asymptomatic between episodes, with symptoms never occurring at night. Due to persistent pain, the lower right second molar tooth was also removed.

Despite this, the paroxysms of pain persisted, triggered inconsistently by chewing, tooth brushing, and yawning. In between episodes, his neurological examination otherwise remained completely normal, and sensation to light touch, pain and two-point discrimination throughout all trigeminal dermatomes was never affected. A trial of gabapentin was started with rapid escalation from 100 mg to 300 mg three times daily, with a reduction in intensity and duration of the episodes, but with the side effect of increasing lethargy which was not well tolerated by the patient. Whilst carbamazepine is usually considered for the treatment of TN, due to the increased risk of Stevens-Johnson syndrome in association with the HLA-B*15:02 allele in patients of southern Chinese origin,⁸ lamotrigine was added instead at a dose of 25 mg then 50 mg twice daily initially leading to nearly complete relief of symptoms. A

plan for subsequent reduction of the gabapentin dose was made but this was never successfully achieved as the severe paroxysms of pain returned. An MRI was subsequently performed due to the persistent symptoms, revealing a large epidermoid cyst in the cerebellopontine angle, distorting the trigeminal nerve (Figure 1a-c). A near total resection was achieved by using an endoscopic retromastoid approach. Histology confirmed necrotic fragments containing keratin lined by stratified squamous epithelium, in keeping with an epidermoid cyst. The postoperative course was complicated only by a methicillin-resistant *Staphylococcus aureus* (MRSA) wound infection requiring further debridement and a six-week course of intravenous teicoplanin.

Following near-total resection, the patient noted immediate relief of his symptoms. He made a gradual recovery and was weaned entirely off his medications. 2 years after the initial procedure he remains symptom-free with no neurological deficit, and his MRI demonstrates only a small volume of residual tumour exhibiting restricted diffusion that has remained stable over this period (Figure 1b). He continues to undergo annual MRI surveillance to monitor for tumour regrowth.

Patient perspective, Hoong-Wei Gan

“Time is a great diagnostician”, a senior colleague once told me, and in my case, this certainly rang true. The evolution of my pain took months before it became distinctly neuropathic – I still remember the day I experienced my first textbook electric shock-like paroxysm in its full excruciating knock-the-wind-out-of-you moment, after multiple episodes of what was no more than a vague, dull jaw ache. At its peak, so many daily activities we take for granted

became a conscious, laborious effort: from chewing (I eventually developed an ache in my contralateral jaw due to constantly using that side to eat), to giving up using my electric toothbrush (the vibrations would trigger episodes and I had to use a soft handheld toothbrush instead), to kissing my wife. All of these could trigger episodes which at their worst would leave me rolling around on the floor in tears. The unpredictability also meant that holding conversations with patients became difficult – they probably wondered why their doctor had to keep running to the toilet mid-conversation to hide my grimaces of agony. One then realises how much of our communication with patients depends on non-verbal facial expressions which rely on a full range of movement to be able to display emotions from happiness to empathy. Strangely enough my symptoms were never triggered by cutaneous stimuli (unlike classical TN), and I was still able to shave. I found eventually that I could “control” the propagation of an episode by grinding my teeth or holding myself slack-jawed, lending new meaning to the term *tic douloureux*.

Doctors are trained to take a pain history even before their first clinical encounter as medical students, but being on the other side of the fence, and having to actually put into words the agony I was going through each day made me appreciate what a monumental task we have in teasing out a patient’s “pain story”. Like most patients nowadays, I spent hours scouring the internet in poor attempts at self-diagnosis, but the more difficult task initially was finding the right adjectives to type into the search engine! The episodic nature of my pain made it even more difficult, as I spent a fair few consultations finding it frustrating that people could not see how terrible my

affliction was when I was pain-free at that very moment, and I even found myself willing a paroxysm to occur in front of my doctors' eyes so they could see what I was talking about. Dr. Chong's line diagrams certainly helped me visualise the pattern of my pain much more clearly than any words could (Figure 2) and I will certainly be taking that lesson back to my own clinical practice!

Discussion

In this case, isolated painful trigeminal neuropathy was a presenting feature of a congenital epidermoid cyst, which are uncommon benign, slow-growing congenital lesions accounting for 0.2-1.8% of all primary intracranial tumours.⁹ They are most commonly found in the cerebellopontine angle (33-50%) and are the third most common mass in this region after acoustic neuromas and meningiomas.^{9,10,11} Other less common sites are the sellar and parasellar regions (10-33%), cerebral hemispheres (up to 25%), fourth ventricle (17%), cerebellum, pineal gland, or extradural sites such as the skull and spine.^{9,10,11,12} They are usually located off-midline and arise as a result of abnormal inclusion of ectodermal epithelial cells during neural tube closure. This results in cysts lined with stratified squamous epithelium typically containing keratin, haemorrhagic debris, granulation tissue, and cholesterol crystals, but no dermal appendages such as hair or sebaceous glands (in contrast to dermoid cysts which also present in the midline).^{9,11,13}

Despite being congenital lesions, cerebellopontine angle (CPA) epidermoid cysts typically present between 30-40 years of age, most commonly with headaches (6-57%), hemifacial weakness (53%), asymmetric sensorineural hearing loss (12-50%),

or vertigo and/ or a loss of sense of balance (28-43%).^{14,15,16} Neurological examination usually reveals cranial neuropathy, most typically involving eighth (28-59%), seventh (6-43%) and fifth (26-37%) cranial nerves (the latter usually involving the motor component of the mandibular division), cerebellar signs including vertigo (43-47%) or other features due to raised intracranial pressure (e.g. papilloedema) or local tumour extension (e.g. diplopia, hemiparesis and lower cranial neuropathies).^{14,15}

Whilst TN may be present in 12-26% of cases,^{14,15,16} isolated TN (i.e. with no other neurological features) as a presenting feature appears to be relatively uncommon, with <50 cases previously reported in the literature.^{17,18,19,20,21,22,23,24} Conversely, in a cohort of 134 patients diagnosed with TN undergoing further radiological investigation, 10% were found to have CPA tumours, of which 71% were epidermoid cysts.²⁵ Similarly, in cohorts of patients undergoing surgery for TN, 1-6% were found to have causative lesions, of which 41-64% were CPA epidermoid cysts.^{19,26} The ICHD classification makes it clear that where a non-neurovascular cause for TN is found, this is termed painful trigeminal neuropathy rather than classical TN.² In this case, the patient's younger age of onset, lack of consistent triggering stimuli, and prolonged episodes lasting more than two minutes all point towards the possibility of this former diagnosis and were indications for further neuroimaging, as is currently recommended by the International Headache Society.²

Presentation can be markedly delayed, with cases only being diagnosed up to 23 years from symptom onset.¹⁹ Like the patient illustrated above, multiple initial consultations with dental and maxillofacial teams is not uncommon, and pain may

not always be classically neuropathic initially.^{17,21,22,23} Up to two-thirds of patients receive various invasive dental treatments as part of the diagnostic process which may be unjustified in retrospect.²⁷ Given the patient's initial pattern of pain, it is difficult to postulate whether the impacted wisdom tooth contributed in any way toward the symptoms, or was a triggering event leading to further compression of an already distorted trigeminal nerve due to the underlying cyst. Additionally, whilst it might have been difficult to make a decision for neuroimaging based on the patient's initial symptoms, the change in the nature of his pain post-coronectomy may have justified an earlier MRI, thereby avoiding the second dental extraction.

Neuroradiologically, epidermoid cysts usually appear as non-enhancing lesions which are isointense with cerebrospinal fluid on both T₁- and T₂-weighted MR imaging.^{9,13} Differentiating them from arachnoid cysts requires diffusion-weighted imaging (DWI; epidermoid cysts typically show clear restricted diffusion) and fluid attenuation inverse recovery sequences (FLAIR; epidermoid cysts typically show incomplete suppression). Calcification can be present in up to 25% of cases,⁹ and both intracystic haemorrhage and increased cyst protein content can result in atypical appearances with changes in signal intensity.^{11,28} Management is predominantly neurosurgical, with incomplete resection being advocated for cases where the tumour capsule is adherent to surrounding neurovascular structures or the brainstem.^{14,15,20} Post-operative complications include aseptic meningitis, persistent pain, and new or worsening neurological deficits, many of which are transient.^{14,15,16,23} Recurrence occurs in 6-29% of patients, occurring at an average of 4.5-9 years post-operatively.^{14,15,16} Some patients remain symptom-free for as many as 15 years post-diagnosis.^{15,20,28} There is as yet no consensus as to the

optimum frequency of MRI surveillance, and the patient continues to receive annual scans as part of his follow-up. However, given the benign nature of the tumour, it is very unlikely that intervention will be required in the absence of clinical symptomatology.

Conclusions

Congenital epidermoid cysts and other cerebellopontine angle space-occupying lesions are rare causes of TN, and must be included in the differential diagnosis, particularly in cases that do not fulfill ICHD criteria. Whilst the ICHD classification terms such cases as painful trigeminal neuropathy, this diagnosis is only possible retrospectively once a secondary cause is found. This patient's atypical age of presentation, the inconsistency of triggering factors, and the presence of an "aura" prior to each episode all suggest that his symptoms were due to painful trigeminal neuropathy and not classical TN, highlighting the need for consideration of neuroimaging early on in the diagnostic process.

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Conflicts of interest

No conflicts declared.

Figure legends

Figure 1 T₂-weighted axial MR images with gadolinium contrast of the patient's epidermoid cyst (arrowheads). (a) Before surgery; a 3.4 x 2.2 x 3.2 cm mass is visible in the right cerebellopontine cistern (arrowheads) which demonstrates restricted diffusion (increased signal intensity on diffusion-weighted imaging, (b)) and is partially suppressed on coronal FLAIR sequences (c), causing mass effect on the pons and right superior cerebellar hemisphere. The trigeminal nerve is just visible on the right and its path is much more tortuous compared to the left (arrows, (a)). Other sections not demonstrated here show full encasement of the abducens nerve with slight displacement of the facial and audiovestibular nerves. (d) 16 months post-surgery; only a tiny amount of residual cyst is visible in the right cerebellopontine angle cistern (arrowheads) with continued mild distortion of the pons, but the trigeminal nerve is in a much more normal position (arrow).

Figure 2 Line diagrams illustrating different patterns of pain. (a) Episodic pain with a gradual onset of each episode and complete resolution in between episodes. (b) Constant pain with no change in severity. (c) Pulsating pain with no resolution. (d) Episodic pain with a gradual onset of each episode and repeated pulses or periods of waxing and waning before complete resolution.

Figure 1

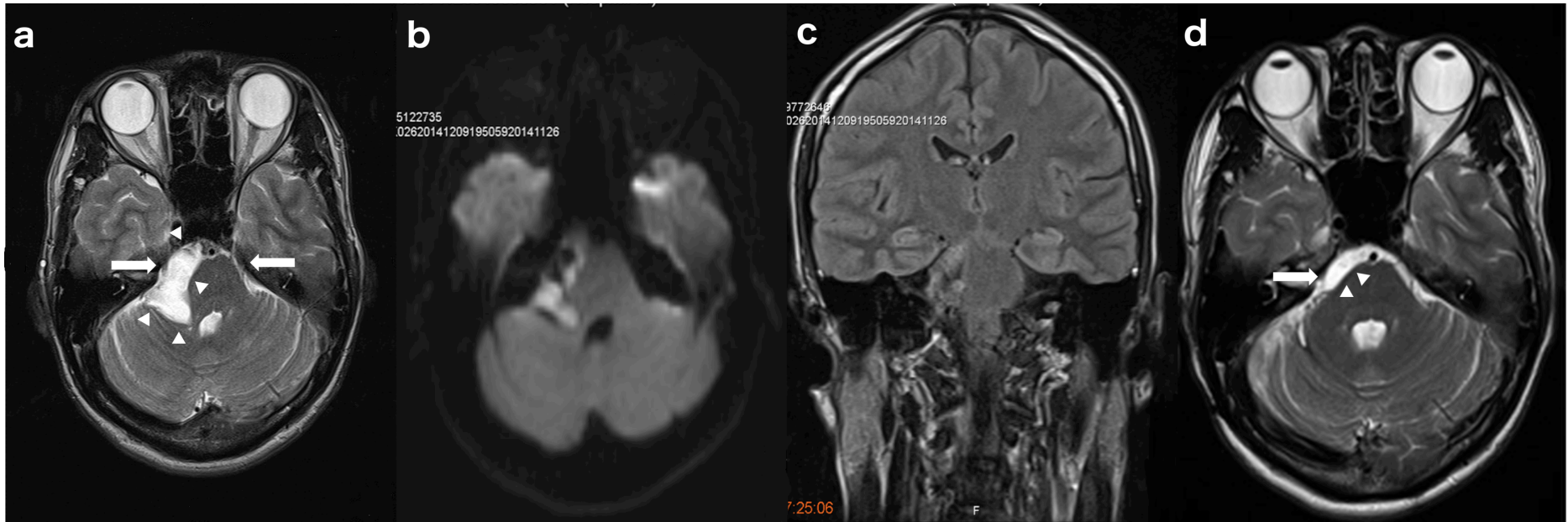
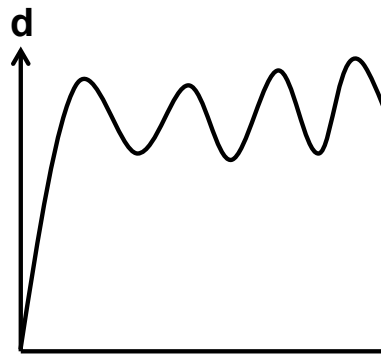
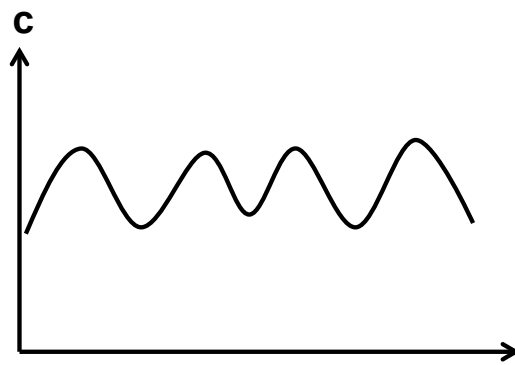
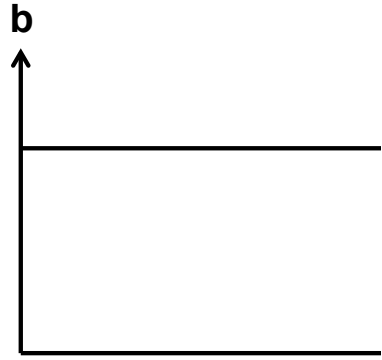
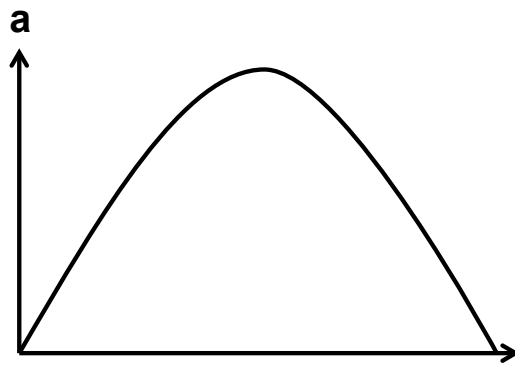


Figure 2



References

1. De Toledo IP, Conti Reus J, Fernandes M, Porporatti AL, Peres MA, Takaschima A, et al. Prevalence of trigeminal neuralgia: A systematic review. *J Am Dent Assoc* 2016;147:570-576 e572.
2. Headache Classification Committee of the International Headache S. The International Classification of Headache Disorders, 3rd edition (beta version). *Cephalalgia* 2013;33:629-808.
3. Cruccu G, Finnerup NB, Jensen TS, Scholz J, Sindou M, Svensson P, et al. Trigeminal neuralgia: New classification and diagnostic grading for practice and research. *Neurology* 2016;87:220-228.
4. Patel SK, Liu JK. Overview and History of Trigeminal Neuralgia. *Neurosurg Clin N Am* 2016;27:265-276.
5. Zakrzewska JM, Linskey ME. Trigeminal neuralgia. *BMJ* 2015;350:h1238.
6. Gronseth G, Cruccu G, Alksne J, Argoff C, Brainin M, Burchiel K, et al. Practice parameter: the diagnostic evaluation and treatment of trigeminal neuralgia (an evidence-based review): report of the Quality Standards Subcommittee of the American Academy of Neurology and the European Federation of Neurological Societies. *Neurology* 2008;71:1183-1190.
7. Krafft RM. Trigeminal neuralgia. *Am Fam Physician* 2008;77:1291-1296.
8. Amstutz U, Shear NH, Rieder MJ, Hwang S, Fung V, Nakamura H, et al. Recommendations for HLA-B*15:02 and HLA-A*31:01 genetic testing to reduce the risk of carbamazepine-induced hypersensitivity reactions. *Epilepsia* 2014;55:496-506.

9. Osborn AG, Preece MT. Intracranial cysts: radiologic-pathologic correlation and imaging approach. *Radiology* 2006;239:650-664.
10. Chowdhury FH, Haque MR, Sarker MH. Intracranial epidermoid tumor; microneurosurgical management: An experience of 23 cases. *Asian J Neurosurg* 2013;8:21-28.
11. Ren X, Lin S, Wang Z, Luo L, Jiang Z, Sui D, et al. Clinical, radiological, and pathological features of 24 atypical intracranial epidermoid cysts. *J Neurosurg* 2012;116:611-621.
12. Hassani FD, Bouchaouch A, El Fatemi N, Gana R, El Abbadi N, Maaqili MR. Pineal epidermoid cyst: case report and review of the literature. *Pan Afr Med J* 2014;18:259.
13. Schroeder JW, Vezina LG. Pediatric sellar and suprasellar lesions. *Pediatr Radiol* 2011;41:287-298.
14. Czernicki T, Kunert P, Nowak A, Wojciechowski J, Marchel A. Epidermoid cysts of the cerebellopontine angle: Clinical features and treatment outcomes. *Neurol Neurochir Pol* 2016;50:75-82.
15. deSouza CE, deSouza R, da Costa S, Sperling N, Yoon TH, Abdelhamid MM, et al. Cerebellopontine angle epidermoid cysts: a report on 30 cases. *J Neurol Neurosurg Psychiatry* 1989;52:986-990.
16. Yawn RJ, Patel NS, Driscoll CL, Link MJ, Haynes DS, Wanna GB, et al. Primary Epidermoid Tumors of the Cerebellopontine Angle: A Review of 47 Cases. *Otol Neurotol* 2016;37:951-955.
17. Hung LC, Wu CS, Lin CC, Fang WK, Hsu YC. Epidermoid cyst presenting as isolated trigeminal neuralgia - two case reports. *Acta Neurol Taiwan* 2013;22:133-137.

18. Rodgers SD, Marascalchi BJ, Strom RG, Huang PP. Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing syndrome secondary to an epidermoid tumor in the cerebellopontine angle. *Neurosurg Focus* 2013;34:E1.
19. Shulev Y, Trashin A, Gordienko K. Secondary trigeminal neuralgia in cerebellopontine angle tumors. *Skull Base* 2011;21:287-294.
20. Son DW, Choi CH, Cha SH. Epidermoid tumors in the cerebellopontine angle presenting with trigeminal neuralgia. *J Korean Neurosurg Soc* 2010;47:271-277.
21. Guttal KS, Naikmasur VG, Joshi SK, Bathi RJ. Trigeminal neuralgia secondary to epidermoid cyst at the cerebellopontine angle: case report and brief overview. *Odontology* 2009;97:54-56.
22. Klieb HB, Freeman BV. Trigeminal neuralgia caused by intracranial epidermoid tumour: report of a case. *J Can Dent Assoc* 2008;74:63-65.
23. Meng L, Yuguang L, Feng L, Wandong S, Shugan Z, Chengyuan W. Cerebellopontine angle epidermoids presenting with trigeminal neuralgia. *J Clin Neurosci* 2005;12:784-786.
24. Mohanty A, Venkatrama SK, Rao BR, Chandramouli BA, Jayakumar PN, Das BS. Experience with cerebellopontine angle epidermoids. *Neurosurgery* 1997;40:24-29.
25. Khan Afridi EA, Khan SA, Qureshi WU, Bhatti SN, Muhammad G, Mahmood S, et al. Frequency of cerebellopontine angle tumours in patients with trigeminal neuralgia. *J Ayub Med Coll Abbottabad* 2014;26:331-333.
26. Liu MX, Zhong J, Dou NN, Xia L, Li B, Li ST. Management of symptomatic hemifacial spasm or trigeminal neuralgia. *Neurosurg Rev* 2016;39:411-418.

27. von Eckardstein KL, Keil M, Rohde V. Unnecessary dental procedures as a consequence of trigeminal neuralgia. *Neurosurg Rev* 2015;38:355-360.
28. Chen CY, Wong JS, Hsieh SC, Chu JS, Chan WP. Intracranial epidermoid cyst with hemorrhage: MR imaging findings. *AJNR Am J Neuroradiol* 2006;27:427-429.