Effects of Surgical Treatment for Classical Trigeminal Neuralgia with Concomitant Persistent Facial Pain

Noboru Noma[1], Isao Kitahara[2], Masako Iseki[3], Yung-Chu Hsu[4], Kosuke Watanabe[1], Takuya Naganawa[5], Yoshiki Imamura[1]

Abtract

Purpose: Classical trigeminal neuralgia with concomitant persistent facial pain responds poorly to conservative treatment. The authors describe the effects of microvascular decompression and radiofrequency thermocoagulation for patients with classical trigeminal neuralgia and concomitant persistent facial pain.

Case report: Case 1 was a 61-year-old man with dull, continuous, aching pain in the left maxillary and mandibular molar area. Case 2 was a 68-year-old woman with aching pain in the maxillary right molar. Case 3 was a 67-year-old woman with severe pain in the right upper lip and maxillary right second premolar. Case 4 was a 42-year-old man with orofacial pain of 14 months' duration. Cases 1 and 2 underwent radiofrequency thermocoagulation and reported good relief of symptoms. Cases 3 and 4 underwent microvascular decompression and attained excellent relief.

Conclusion: Microvascular decompression may be more effective than radiofrequency thermocoagulation for patients with classical trigeminal neuralgia with concomitant persistent facial pain.

Key words: classical trigeminal neuralgia, concomitant persistent facial pain, microvascular decompression, radiofrequency thermocoagulation

Acta Neurol Taiwan 2019;28:17-24

INTRODUCTION

Classical trigeminal neuralgia (CTN) is a facial pain disorder described in the International Classification of Headache Disorders (ICHD-3 version) as “unilateral pain characterized by brief electric shock sensations limited to one or more divisions of the trigeminal nerve”, and has

From the [1]Department of Oral Diagnostic Sciences, Nihon University school of Dentistry Tokyo, Japan; [2]Department of Neurosurgery, Chiba Tokushukai Hospital, Funabashi, Japan; [3]Department of Anesthesiology and Pain Medicine, Juntendo University School of Medicine, Tokyo, Japan; [4]Division of Neurology, Department of Internal Medicine, Ditmanson Medical Foundation Chia-Yi Christian Hospital, Chiayi, Taiwan; [5]Department of Oral and Maxillofacial Surgery, Tokyo Women’s Medical University, School of Medicine, Tokyo, Japan.

Received May 31, 2018.
Revised July 16, 2018. Accepted February 26, 2019.

Correspondence to: Noboru Noma, Department of Oral Diagnostic Sciences, Nihon University school of Dentistry Tokyo, Japan
E-mail: noma.noboru@nihon-u.ac.jp

a code of 13.1.1[1]. In 2018, the International Headache Society further classified CTN as "classical trigeminal neuralgia, purely paroxysmal (13.1.1.1)" and "classical trigeminal neuralgia with concomitant persistent facial pain (13.1.1.2)" [1-4]. Development of the subcategory "CTN with concomitant persistent facial pain" was based on strong evidence that up to 50% of patients with CTN describe paroxysmal attacks of short, sharp pain. CTN with concomitant persistent facial pain may respond poorly to conservative treatment[5]. When oral medication is ineffective in patients who have CTN with concomitant persistent facial pain, microvascular decompression (MVD) or radiofrequency thermocoagulation (RFT) should be considered[6,7]. Here, we report a case series including four such patients and compare the neurosurgical effects of MVD and RFT.

Baseline patient characteristics

Approximately 90 patients treated for orofacial neuralgia at the Orofacial Pain Clinic at Nihon University Dental Hospital between 2001 and 2016 were retrospectively reviewed. Only 7 patients were diagnosed to have classical trigeminal neuralgia with concomitant persistent facial pain according to the ICHD-3 criteria. Three of these 7 patients responded well to pharmacologic therapy and 4 underwent surgical treatment with MVD or RFT (Data sharing).

CASE REPORT

Case 1

A 61-year-old man presented with a chief complaint of dull, continuous, aching pain of 2 year's duration in the left maxillary and mandibular molar areas. Two years earlier, the patient had consulted an oral and maxillofacial surgeon who diagnosed possible trigeminal neuralgia (TN) and started him on treatment with carbamazepine. Approximately 18 months after that diagnosis, the quality of his pain was varying from a dull ache to TN-like pain; a white patch lesion was surgically removed at this time because the oral surgeon believed it might be the cause of the TN-like pain. Leukoplakia was diagnosed on the basis of pathologic findings. The pain persisted, so the patient was referred to a headache specialist who obtained computed tomography (CT) images; these images showed no evidence of intracranial pathology or abnormal resorption of mandibular bone (Figure 1).

The intensity of the background pain was usually mild (with a visual analog scale [VAS] score of 3.6), but the patient described occasional exacerbations of severe pain (VAS score 10). A neurologic examination revealed lancinating pain of 10–20 seconds' duration,

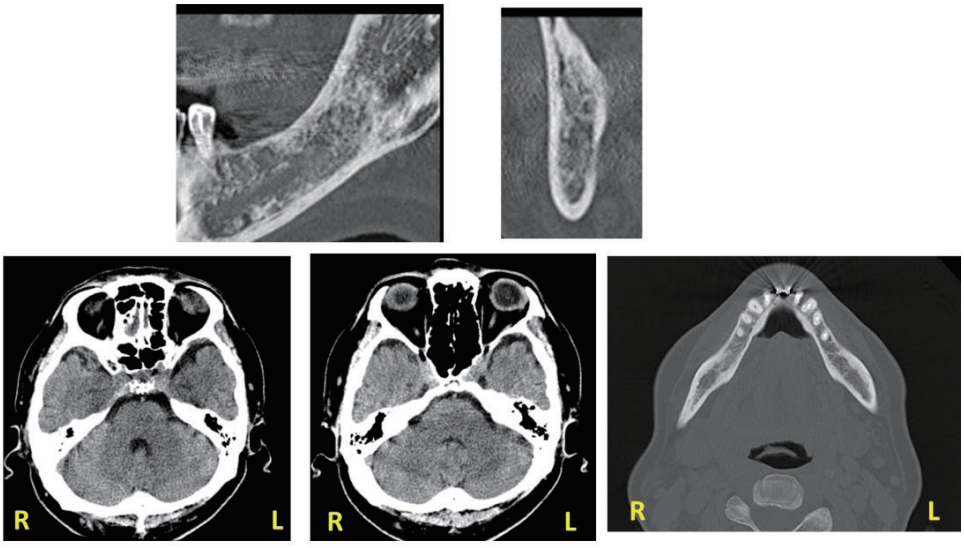


Figure 1. a, b, c: Computed tomography images showing no abnormal resorption of mandibular bone. c, d: CT showing no intracranial pathology. R: right, L: left

which was provoked by light touch to the left mandibular gingiva. Further neurologic assessment revealed no other abnormalities. The temporomandibular joint was within normal limits. Muscle palpation elicited mild tenderness in the left master muscle. Vertical and horizontal percussion was painless. Panoramic radiography and CT revealed no abnormal findings in the left mandibular bone. He had been taking carbamazepine, pregabalin, and gabapentin for 2 months, without relief of pain. He was referred to us for pain control because he had declined MVD. RFT was performed for the infraorbital and mental nerves in accordance with a diagnosis of CTN with concomitant persistent facial pain because of the characteristics of the pain. Although the pain was partially relieved, the patient continued to report continuous pain with intermittent mild pain.

Case 2

A 68-year-old woman was referred to us with a 2-year history of aching pain in the right maxillary molar region. Approximately 9 months earlier, she had consulted a dentist for treatment of aching pain in the same region. Although dentinal hypersensitivity was diagnosed and treatment for hypersensitivity was performed, the pain continued. Four months after the dental treatment, pulpectomy was performed for the right maxillary first molar, which was ultimately extracted. The quality of her pain varied from a dull ache to TN-like pain. On neurologic examination, the temporomandibular joint was within normal limits. Muscle palpation elicited mild tenderness in the left temporalis muscle. Vertical and horizontal percussion in the maxillary right molar region was painful, but not pain that was familiar to the patient. A light touch with a cotton swab to the maxillary right gingiva provoked sharp, lancinating pain that persisted for a few seconds. Her background pain was described as aching and usually mild (VAS score 3.0), but with occasional increases in intensity (VAS score 6.0). Further neurologic assessment revealed no other abnormalities. Magnetic resonance imaging (MRI) revealed neurovascular compression at the root entry zone (Figure 2). The background pain was well controlled with carbamazepine 200 mg per day, but the paroxysmal pain did not resolve. Moreover, the patient developed thrombocytopenia (less than half the normal platelet count) developed soon after starting carbamazepine. She

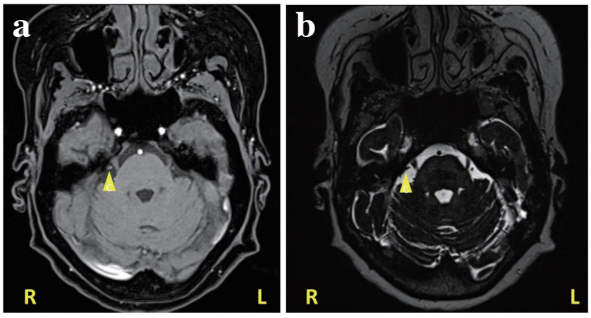


Figure 2. a, b: MRI scans showing compression of the right trigeminal nerve (RTN) by the superior cerebellar artery (SCA). R: right, L: left

opted for RFT rather than MVD, and was referred to our department. RFT of the infraorbital nerve was performed, after which her paroxysmal and background pain decreased but did not resolve.

Case 3

A 67-year-old woman presented with severe pain in the right upper lip and maxillary right second premolar. The pain has started around a maxillary right canine tooth 2 years earlier. At that time she consulted her dentist, and was referred to a headache specialist who diagnosed trigeminal neuralgia with concomitant persistent facial pain. MRI performed at that time did not indicate any intracranial pathology but revealed that the right superior cerebellar artery abutted the root entry zone of the left trigeminal nerve (Figure 3). The patient was started on carbamazepine but later developed dizziness and sleepiness. Her constant and paroxysmal pain were both localized in the distribution of the right maxillary branch of the trigeminal nerve. The paroxysmal pain was

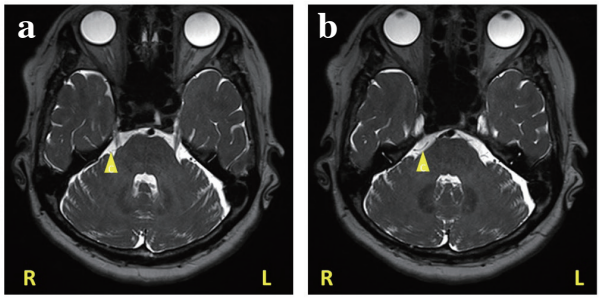


Figure 3. a, b: MRI scans showing an aberrant loop of the SCA abutting the RTN. R: right, L: left

provoked by eating, face-washing, and toothbrushing. Her VAS score was 2.2 for the constant pain and 7.7 for the paroxysmal pain. Further neurologic assessment revealed no other abnormalities. Pregabalin was prescribed for her TN (neuropathic pain), but the pain remained poorly controlled. Her pain continued to vary in quality from a dull ache to electric shock-like pain, so she opted for MVD. The procedure was performed a month later under general anesthesia and resulted in complete resolution of pain.

Case 4

A 42-year-old man with a chief complaint of orofacial pain of 14 months' duration was seen at our pain clinic. He then consulted an otorhinolaryngologist, who prescribed an antihistamine for treatment of possible maxillary sinusitis. The patient then presented for treatment at Nihon University Hospital, where the temporomandibular joint was found to be within normal limits. Muscle palpation elicited no tenderness in the temporalis muscle. However, a neurologic examination revealed severe pain, persisting for a few seconds, that was provoked by touch to the maxillary right anterior teeth and the hard palate around those teeth. Further neurologic assessment revealed no other abnormalities. An MRI revealed neurovascular conflict (Figure 4). A clinical diagnosis of TN was made, and the patient was started on oral carbamazepine 200 mg twice daily, which did not result in pain relief. The carbamazepine dosage was increased to 400 mg twice daily, which resulted in some relief of symptoms. After 7 months of treatment with carbamazepine, the patient was referred for neurologic assessment because of side effects, including vomiting, vertigo, and electric shock-like pain.

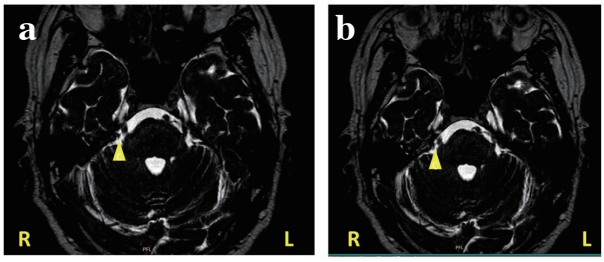


Figure 4. a, b: MRI scan showing neurovascular compression at the root entry zone, the right trigeminal nerve (RTN), and the superior cerebellar artery (SCA). R: right, L: left

MVD was performed at Chiba Tokushukai Hospital under general anesthesia and resulted in complete resolution of facial pain immediately after surgery.

DISCUSSION

The term "pre-trigeminal neuralgia (PTN)" was coined by Fromm[2] to describe persistent facial pain preceding paroxysmal pain in TN. PTN-related pain is located in the teeth, alveolar bone, and/or sinus regions. PTN has been characterized as a dull ache, sharp, shooting, and lancinating pain, but the reports contain variable descriptions. Pain may be continuous or episodic, lasting minutes to several hours, and may persist for days to years before appearance of typical TN symptoms. In the ICHD-3, the terms "typical TN symptom with background pain including PTN," "atypical trigeminal neuralgia," and "trigeminal neuralgia type 2" were changed to "CTN with concomitant persistent facial pain" [1,8,9].

The authors propose an algorithm for diagnosis of CTN with concomitant persistent facial pain (Table 1). First, when evaluating a patient with orofacial pain, it is essential to perform a focused history and physical examination. The POUNDing mnemonic is both easy to remember and effective for ruling in or ruling out a diagnosis of CTN with concomitant persistent facial pain. Regarding the physical examination, if the patient presents to a dental practitioner with a chief complaint of pain in the maxillary premolars, molars, or cheeks, possible dental conditions should be ruled out with appropriate testing, such as percussion, gingival tenderness, and sensitivity to air. Patients may complain of dental pain with those tests, but the dentist needs to confirm if this is familiar pain or headache. The dentist should also test for myofascial pain. The palpation pressure for myalgia is 1 kg for 2 s. However, according to the Diagnostic Criteria for Temporomandibular Disorders, to differentiate the three types of myalgia, the duration of the 1 kg of palpation pressure should be increased to 5 s to allow more time to elicit spreading or referred pain, if present. To diagnose acute rhinosinusitis, the forward bend test should be performed with topical anesthesia to the middle or superior turbinates. If the pain does not subside, the dentist should consider other orofacial pain disorders such as the trigeminal autonomic cephalalgias[1]. In case of dentist

confirmed trigger maneuvers, resulting in diagnosing CTN with concomitant persistent facial pain if paroxysmal pain is the main complaint, but it may be accompanied by continuous pain. If advanced MRI shows neurovascular compression with morphologic changes in the trigeminal nerve root, then MVD may be effective.

In the present case series, the background pain continued for 9 to 23 (mean 13.5) months before the onset of typical symptoms of TN (Table 2). Tumors in the cerebellopontine angle, such as vestibular schwannomas (acoustic neuromas) or meningiomas, may manifest as typical TN with background pain[10,11]. The presence of typical clinical symptoms of TN, together with persistent facial pain and normal CT and MRI findings, excluded a diagnosis of symptomatic TN, and CTN with concomitant persistent facial pain was diagnosed by a neurosurgeon or anesthesiologist in all the four patients in the present series.

Carbamazepine remains the medical treatment of choice for CTN with concomitant persistent facial pain. Alternative agents include gabapentin, pregabalin, topiramate, and some of the older anticonvulsants[12-15]. Most patients with a diagnosis of CTN with concomitant persistent facial pain are treated with carbamazepine before undergoing MVD[15,16]. A previous study found that carbamazepine was ineffective in 96% of patients with atypical TN who later underwent MVD[6]. Moreover, a commentary in the ICHD-3 states that CTN with concomitant persistent facial pain responds poorly to conservative treatment, such as medication[1]. However, Maarbjerg et al. maintained that the response to carbamazepine was very high for both the paroxysmal and persistent pain components[5]. In the present series, the response of case 2 to carbamazepine was excellent, but the patient was forced to discontinue carbamazepine because of thrombocytopenia. The pain decreased but did not resolve after carbamazepine in cases 1, 3, and 4[4].

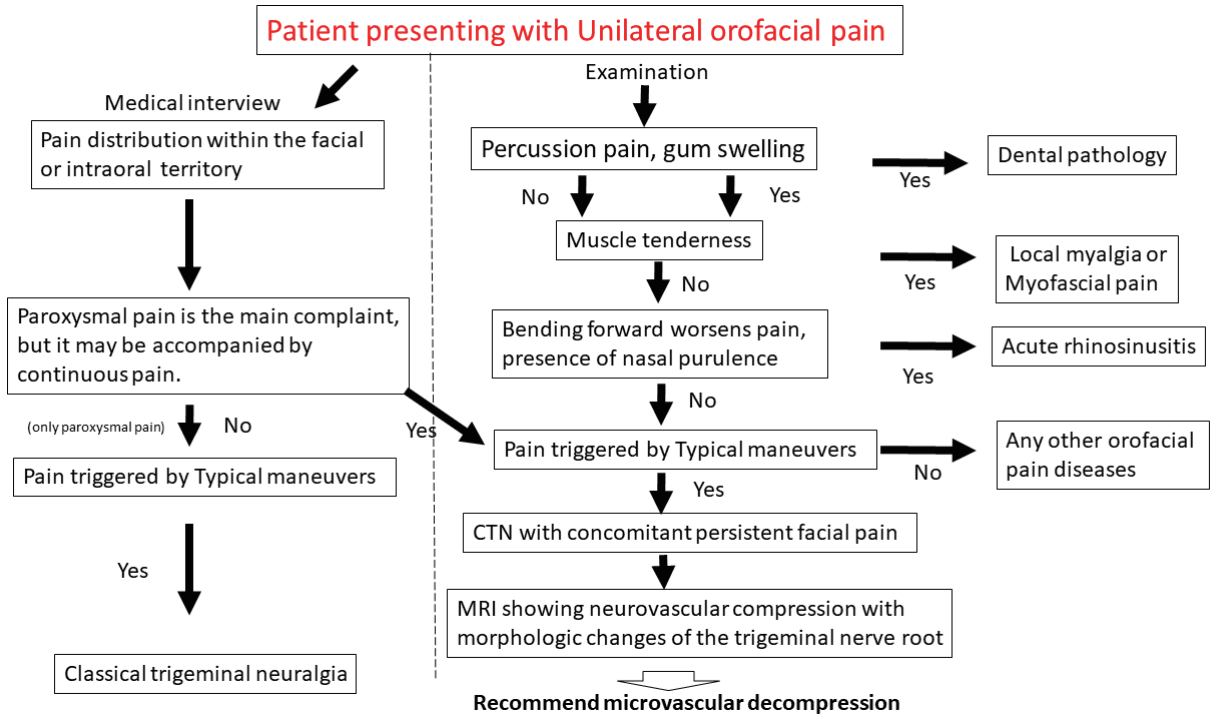
Other options should be considered if oral medication is ineffective or patients have side effects, such as ataxia or cognitive impairment[15]. MVD is a first-line neurosurgical approach for classical TN with neurovascular conflict[17,18]. There is evidence suggesting that concomitant background facial pain is a clinical predictor of a worse response to surgical treatment[5]. MVD and rhizotomy are less

Table 2: Pain characteristics and treatment.

RFT: radiofrequency thermocoagulation, MVD: microvascular decompression, SCA: superior cerebellar artery, CBZ: carbamazepine, Gaba: gabapentin, PGB: pregabalin, V2: second division of trigeminal nerve, V3: third division of trigeminal nerve. M: male, F: female

	Patient 1	Patient 2	Patient 3	Patient 4
Onset age(years)	61	68	67	42
Gender(M, F)	M	F	F	M
Duration of illness(months)	15	9	23	7
Attack duration (seconds)	10-20	2-3	2-3	60-120
Location	V2+V3left	V2right	V2right	V2right
Quality	dull, aching	aching pain	electric-like pain	electric-like pain
Severe pain intensity(VAS)	100	60	77	100
Accompanying symptoms	NO	NO	NO	tearing
Response Cbz(side effect)	+−	+(thrombocytopenia)	+−(dizziness)	+−(vomiting, vertigo)
Response Gaba/PGB	Gaba/PGB +−		PGB −	
MRI(neurovascular conflict)		Positive	Positive	Positive
Offending vessel		SCA	SCA	SCA
Surgical treatment	RFT	RFT	MVD	MVD
Clinical effect	good	good	excellent	excellent

Table 1: Diagnosis and treatment of classical trigeminal neuralgia with concomitant persistent facial pain



successful in such cases.

Martin et al. suggested that the long-term results of MVD depend on the patient phenotype[19]. In patients identified to have neurovascular conflict (classical TN), the response rate may be as high as 90%[20]. However, the long-term response rates in patients with concomitant persistent facial pain may be as low as 40%[16]. In a study of the immediate postoperative pain relief (for up to 5 years) achieved by MVD, Tyler-Kabara et al. reported the long-term results were excellent in only 35% of cases and good in an additional 16%, for overall significant pain relief in only 51%[16].

In the present series, MRI revealed neurovascular conflict with the superior cerebellar artery in cases 3 and 4, which was confirmed intraoperatively; postoperative pain relief was excellent at 47 months and 6 months after MVD, respectively (Table 2). The postoperative outcomes in our patients were comparable with those reported by Tyler-Kabara et al[16].

For patients with TN who decline MVD, like cases 1 and 2 in our series, RFT should be considered as second-line surgical treatment. However, only one study investigated RFT for atypical TN. Shibin et al. suggested that RFT is an effective treatment for typical TN in cases with neurovascular contact on preoperative MRI[21]. In cases 1 and 2, RFT was performed and background pain decreased but did not resolve. The authors could not confirm neurovascular contact in case 1 because CT was used, but neurovascular contact was observed on an MRI scan in case 2.

The etiology of persistent pain is unclear, but a defective pain modulation system or central sensitization are putative causes[3]. CTN patients with persistent pain experience no experimental provocation of conditioned pain modulation, which indicates a deficiency in diffuse noxious inhibitory controls. An electrophysiological study found facilitation of central trigeminal processing, presumably at a supraspinal level, which was indicative of central sensitization in TN with concomitant persistent pain. Central facilitation of trigeminal nociceptive processing is sometimes detected in patients with TN with concomitant chronic facial pain, indicating overactivation of central sensory transmission[22].

Carbamazepine works through various pathways

and affects central and peripheral nerve endings[14]. It reduces central sensitization caused by tissue damage at multiple levels of the nervous system. However, MVD and RFT affect peripheral nerve endings but not central sensitization; yet, in cases 3 and 4, the pain completely disappeared after surgery. Disease duration and neurovascular conflict might be important in inducing facial pain and triggering central sensitization[23,24]. Therefore, decompressing the offending vessel, thereby terminating demyelination, may be necessary.

The main limitation of this research in that there were only 4 patients in our case series, so the study sample was small. Further studies with in larger samples could provide more definitive results following MVD or RFT in patients with CTN with concomitant persistent facial pain.

CONCLUSION

Background facial pain precedes typical TN. Therefore, it may be difficult to diagnose CTN with concomitant persistent facial pain before the appearance of typical TN symptoms. When oral medication is ineffective or causes intolerable side effects, MVD or RFT should be considered. MVD may be effective when neurovascular contact at the root entry zone is observed on preoperative MRI scans in patients who have CTN with concomitant persistent facial pain.

ACKNOWLEDGMENTS

This study was supported in part by research grants from Sato funds and a grant from the Nihon University School of Dentistry, Dental Research Center.

Data Sharing Statement

All data used for this manuscript is included in the published article.

REFERENCE

1. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018;38:1-211.
2. Fromm GH, Graff-Radford SB, Terrence CF, Sweet WH. Pre-trigeminal neuralgia. Neurology 1990; 40(10):1493-1495.
3. Hu WH, Zhang K, Zhang JG. Atypical trigeminal neuralgia: a consequence of central sensitization? Med Hypotheses 2010; 75(1): 65-66.
4. Melzack R, Terrence C, Fromm G, Amsel R. Trigeminal neuralgia and atypical facial pain: use of the McGill Pain Questionnaire for discrimination and diagnosis. Pain 1986; 27:297-302.
5. Maarbjerg S, A. Gozalov, J. Olesen, Bendtsen L. Concomitant persistent pain in classical trigeminal neuralgia--evidence for different subtypes. Headache 2014; 54(7): 1173-1183.
6. Hamasaki T, Yano S, Nakamura K, Yamada K. Pregabalin as a salvage preoperative treatment for refractory trigeminal neuralgia. J Clin Neurosci 2018; 47:240-244.
7. Heinskou TB, Rochat P, Maarbjerg S, Wolfram F, Brennum J, Olesen J, Bendtsen L. Prognostic factors for outcome of microvascular decompression in trigeminal neuralgia: A prospective systematic study using independent assessors. Cephalalgia. 2018 Jan 1:333102418783294.
8. Nurmikko TJ, Eldridge PR. Trigeminal neuralgia--pathophysiology, diagnosis and current treatment. Br J Anaesth 2001;87(1):117-132.
9. Burchiel KJ. A new classification for facial pain. Neurosurgery 2003;53(5):1164-1167.
10. Niwant P, Motwani M, Naik S. Atypical Trigeminal Neuralgia Secondary to Meningioma. Case Rep Dent 2015:462569.
11. Noma N, Hayashi M, Kitahara I, Young A, Yamamoto M, Watanabe K, Imamura Y. Painful Trigeminal Neuropathy Attributed to a Space-occupying Lesion Presenting as a Toothache: A Report of 4 Cases. J Endod 2017; 43(7):1201-1206.
12. Solaro C, Messmer Uccelli M, Uccelli A, Leandri M, Mancardi GL. Low-dose gabapentin combined with either lamotrigine or carbamazepine can be useful therapies for trigeminal neuralgia in multiple sclerosis. Eur Neurol 2000; 44(1):45-48
13. Pérez C, Navarro A, Saldaña MT, Martínez S, Rejas J. Patient-reported outcomes in subjects with painful trigeminal neuralgia receiving pregabalin: evidence from medical practice in primary care settings.

Cephalalgia 2009;29(7):781-90.
14. Benoliel R, Zini A, Khan J, Almoznino G, Sharav Y, Haviv Y. Trigeminal neuralgia (part II): Factors affecting early pharmacotherapeutic outcome. Cephalalgia 2016;36 (8) :747-759.
15. Cruccu G, Finnerup NB, Jensen TS, Scholz J, Sindou M, Svensson P, Treede RD, Zakrzewska JM, Nurmikko T. Trigeminal neuralgia: New classification and diagnostic grading for practice and research. Neurology 2016; 87:220-228.
16. Tyler-Kabara EC, Kassam AB, Horowitz MH, Urgo L, Hadjipanayis C, Levy EI, Chang YF. Predictors of outcome in surgically managed patients with typical and atypical trigeminal neuralgia: comparison of results following microvascular decompression. J Neurosurg 2002;96 (3):527-531.
17. Maarbjerg S, Di Stefano G, Bendtsen L, Cruccu G. Trigeminal neuralgia - diagnosis and treatment. Cephalalgia 2017; 37 (7):648-657.
18. Cruccu G, Gronseth G, Alksne J, Argoff C, Brainin M, Burchiel K, Nurmikko T, Zakrzewska JM. American Academy of Neurology Society; European Federation of Neurological Society. AAN-EFNS guidelines on trigeminal neuralgia management. Eur J Neurol 2008;15(10):1013-1028.
19. Jakobs M, Unterberg A, Treede RD, Schuh-Hofer S, Ahmadi R. Subcutaneous trigeminal nerve field stimulation for refractory trigeminal pain: a cohort analysis. Acta Neurochir (Wien) 2016;158 (9): 1767-1774.
20. Sandel T, Eide PK. Long-term results of microvascular decompression for trigeminal neuralgia and hemifacial spasms according to preoperative symptomatology. Acta Neurochir (Wien) 2013;155 (9):1681-1692.
21. Du S, Ma X, Li X, Yuan H. Ophthalmic branch radiofrequency thermocoagulation for atypical trigeminal neuralgia:a case report. Springerplus 2015(4):813.
22. Obermann M, Yoon MS, Ese D, Maschke M, Kaube H, Diener HC, Katsarava Z. Impaired trigeminal nociceptive processing in patients with trigeminal neuralgia. Neurology 2007;28 (69):835-841.
23. Maarbjerg S, Wolfram F, Gozalov A, Olesen J, Bendtsen L. Association between neurovascular contact and clinical characteristics in classical trigeminal neuralgia: A prospective clinical study using 3.0 Tesla MRI. Cephalalgia 2015;35 (12): 1077-1084.
24. Maarbjerg S, Wolfram F, Gozalov A, Olesen J, Bendtsen L. Significance of neurovascular contact in classical trigeminal neuralgia. Brain 2015;138(2): 311-319.