TRIGEMINAL NEURALGIA: A CASE STUDY AND LITERATURE REVIEW

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CASE INFORMATION

Case: 73 years old Thai female from Ayuthaya
Chief complaint: Left facial pain 5 years PTA
Present Illness: 5 years prior to hospitalization the patient started feeling sharp shooting pain on the left side of her face. The pain was on and off persisting for the entire day. Patient reported a pain score of 6/10 and the pain disrupts her quality of life.

Pain was most prominent at the left half of the nasolabial fold and left zygoma. The pain around the area left to the nose and gum was exacerbated by activities such as chewing food and brushing teeth. And pain was also triggered when mentioned areas were touched. However the patient does not experience facial pain when she is asleep.

There was no pain on the right half of her face. She denies facial palsy , weakness, hearing deficits. Facial tactile, proprioceptive and nociceptive sensation are all intact. Patient can masticate food normally without any weakness. She has normal vision, with intact sensation around her eyelids, forehead and conjunctiva. Patient reports she can walk with good balance and has no vertigo. There is no change in the patient's voice quality and how she talks. The patient has an intact sense of smell, taste, no decrease in appetite and no sudden weight loss.

There was no history of fever, facial trauma and no clear papules or other skin lesions at her face. She mentions that she has dental caries but already treated with the dentist.

Patient was known to be allergic to carbamazepine (causing generalized rash) so she was treated with pregabalin. When the medication failed to improve her facial pain. Patient had also tried treatment with facial acupuncture for many times but the pain is refractory.

Past History:

- Underlying diseases: Dyslipidemia , Impaired fasting glucose, Transient ischemic attack(9/62 Rt hemiparesis, MRI, MRA found no radial diffusivity, FAZEKAS WM1)

Family History: Denies family history of family members of the same symptoms, neurological conditions, metabolic disease or malignancy

Social History:

- History of surgery: Hemorrhoidectomy 20 years ago, Polpectomy 10 years

- History of trauma: none
- History of cigarette smoking: none
- History of alcohol drinking: none
- History of steroidal drug or herbal use: none

Drug Allergies:

- Sulfa drugs
- Positive HLA-B*1502: Carbamazepine

Physical examination:

- **V/S :** BP 142/62 mmHg, PR 68 bpm, RR 18/min, BT 36C, O2 sat 99%
- **Body weight**: 70 kg, Height: 165 cm, BMI: 25.2 kg/m2
- **General Appearance** : Alert, good consciousness, well-cooperative
- **HEENT** : No pale conjunctiva, anicteric sclera, no palpable cervical lymph nodes
- **Cardiovascular System**: No active precordium, no heave, no thrill, normal S1S2 heart sounds, no murmur, capillary refill < 2 seconds, full and regular pulse all extremities
- **Respiratory System**: Clear and equal breath sound both lungs, no adventitious sounds
- **Gastrointestinal System**: no distension, soft, no guarding, not tender, normoactive bowel sounds
- **Skin**: no mass, no rash, no deformities
- **Neurological examination**:
  - Consciousness: alert, good consciousness, well cooperative, oriented to time, place and person, E4V5M6
  - Cranial Nerves:

- CN I: not tested
- CN II, III : Pupil 4 mm RTL right eye, sluggishly RTL left eye, RAPD negative, VF intact, VA 20/200 both eyes (pinhole was not available), fundoscopy: cannot see optic disc and cup due to voluntary eye movements, horizontal diplopia
- CN III, IV, VI : Full EOM, no ptosis, saccadic pursuit
- CN V : equal sensation of V1, V2, V3, intact masseter muscle both sides
- CN VII : Symmetrical facial movements, orbicularis oculi and orbicularis oris muscle is intact
- CN VIII : Equal hearing both ears by finger rubs, Weber and Rinne tests

were not tested
- CN IX, X : Decreased gag reflex, uvula at midline
- CN XI: Intact trapezius muscle both sides
- CN XII : No tongue deviation

- Motor grade V all extremities, normal muscle tone
- Sensory: Pain, temperature, light touch sensation intact all extremities
- Proprioception: normal sense of distal joints

- Reflexes:

- DTR 2+ all extremities
- Babinski's sign: plantarflexion both sides

- Cortical lobe signs:

- Dominant: no alexia, no acalculia, no finger agnosia, no left-right confusion, no aphasia
-Non Dominant: no neglect, no apraxia, normal stereognosis

- Cerebellar signs

- Finger to nose test: No dysmetria
- Heel to shin test: Normal
- Nystagmus : Negative
- No ataxic gait
- No dysdiadochokinesia
- No wide-based gait, tandem gait normal
- Overshoot test: Negative
- Rebound phenomenon: Normal
- No slurred speech

Pertinent Findings: Lancinating pain along V2-V3
Problem List: Lancinating pain along V2-V3

Approach and Differential Diagnosis

From the patient's symptoms of sharp shooting pain on the left side of her face as well as the history of touching her face or doing activities such as chewing food or brushing her teeth causing exacerbation of pain. All of these signs and symptoms helps us differentiate these possible diseases which includes:

Trigeminal neuralgia is the first disease in the list of all the differential diagnoses because the pain that the patient experiences localizes towards the side of her face. Furthermore, the pain is a sharp shooting pain which correlates with the trigeminal nerve (cranial nerve V). The typical characteristics that makes trigeminal neuralgia the first differential diagnosis is the fact that he has unilateral facial pain that gets aggravated by touching, chewing food or brushing her teeth.

Furthermore, another one of the possible differential diagnoses is postherpetic Neuralgia. The reason this disease is thought of is because post herpetic neuralgia can present with pain that is described as burning or squeezing pain which can be similar with symptoms that the patient explains. However, the reason that makes us sure that it is not this disease is through physical examination because in this patient, there are no group of vesicles on erythematous base seen anywhere on her face or body thus makes us think less about post herpetic neuralgia in this patient.

Another possible differential diagnosis is dental pain due to dental caries. However, the reason it is less likely this cause is due to the fact that dental pain is usually intraoral pain that is dull or throbbing pain which is different from this patient because she mentions that her pain is sharp shooting pain. However the similarities between dental pain and the patient's symptom is that while chewing or brushing her teeth, she experiences pain which these actions are intraoral actions which means she could be compressing the teeth which causes the pain. However, as already mentioned, the characteristic of pain in this patient is different to the longstanding pain experienced in dental pain. Furthermore, another factor that helps suggest that it does not seem like dental pain is the fact that she has a history of dental caries that was already treated by the dentist thus this history helps support that the patient's clinical characteristics does not seem to be caused by dental pain.

Management:

Neuroimaging investigations included an MRI brain to differentiate etiology of trigeminal neuralgia in this patient. Etiology of trigeminal neuralgia could be categorized as classic and secondary type. Where classic trigeminal neuralgia is related to neuromuscular compression due to vascular structures. Whereas, secondary trigeminal neuralgia is defined as neuromuscular compression secondary to an underlying condition such as cerebellopontine angle tumor, multiple sclerosis or arteriovenous malformations. In this patient, MRI brain findings revealed the left **AICA loop contacting transitional zones of left CNV without definite displacement,** as shown in Fig. 1. Other associated findings include normal bilateral IACs and facial nerves without mass or abnormal enhancement. Bilateral cochlear and semicircular canals are also normal. Moreover, the rest of normal signal intensity of brain parenchyma shows on all pulse sequences without focal lesion. These findings suggest that the patient has 'classic' trigeminal neuralgia due to vascular compression of the left CNV alone which explains the positive clinical findings found in this patient.

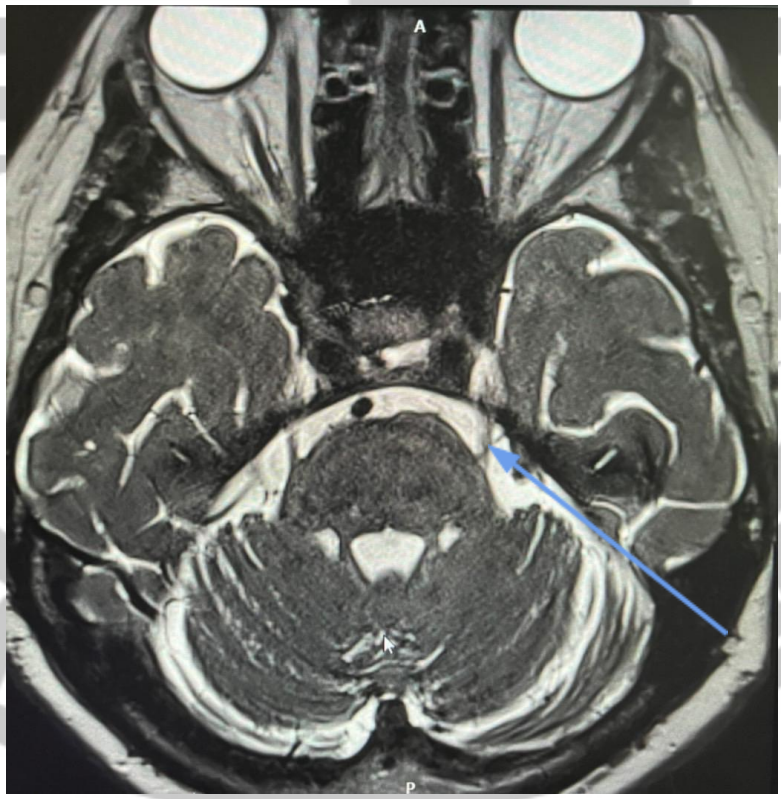

Figure 1. MRI brain T2 image in axial view
Blue arrow shows the suspected lesion in MRI

- **Definite Treatment:**
  - Left suboccipital craniotomy (SOC) with microvascular transposition (MVD)
- **Supportive Treatment**:
  - The patient underwent operation on 08/06/2565
- **Postoperative:**
  - Patient is alert (E4V5M6)
  - Patient claims of having tinnitus in left ear and dizziness in sitting position
  - There is still persistent left facial pain, pain score of 6/10 (same severity as preoperative)
  - Plan for set OR (10/06/2565) for Left Craniotomy with Microvascular Transposition (MVT) due to suspected failure of vascular transposition with Teflon-felt soaked Tisseel.
  - After reoperation patients report that her facial pain has been resolved.

TRIGEMINAL NEURALGIA INFORMATION

INTRODUCTION

Trigeminal neuralgia is a condition that causes recurrent and brief episodes of unilateral facial pain at the distributive areas of the trigeminal nerve (also known cranial nerve V). The pain characterizes as electric shock-like pain, and can occur at any or all divisions of the trigeminal nerve. Trigeminal neuralgia symptoms are often triggered by inoculation of the trigeminal nerve [1].

EPIDEMIOLOGY

Trigeminal neuralgia is a rare neurological condition, with an overall prevalence of less than 0.1% and an annual incidence of four to thirteen per 100,000 people [2,3]. This condition affects females more than males and occurs more in the older adult population [4].

ANATOMY

Before understanding the cause of trigeminal neuralgia, we must know the anatomy and functions of the trigeminal nerve. The trigeminal nerve functions as a sensory supply to the face as well as sensory and motor supply to the mastication muscles. It originates at mid lateral surface of pons, while the sensory ganglion is located in the floor of middle cranial fossa.The three major divisions of the trigeminal nerve are ophthalmic nerve (V1), maxillary nerve (V2), and mandibular nerve (V3) [1].

ETIOLOGY AND PATHOPHYSIOLOGY

The main cause of trigeminal neuralgia is compression of the trigeminal nerve root, although a small proportion is caused by brainstem lesion [5]. A detailed explanation of different etiologies are discussed below:

1. Compression of the trigeminal nerve root
   Compression of the trigeminal nerve root remains the most common cause of trigeminal neuralgia. The trigeminal nerve compression is related to demyelination of the trigeminal nerve, which is believed to create an electrical conduction of a nerve impulse at fibers mediating light touch and painful sensation ("ephaptic transmission") upon light tactile stimulation of the trigeminal nerves. Vascular compression by veins or arteries are thought to account for most of the cases [6]. Other causes of compression include tumors, aneurysms, and arteriovenous malformation.

2. Multiple Sclerosis and brainstem lesion
   Multiple sclerosis, tumors located at the cerebellopontine angle, or other brainstem lesions could also cause demyelination of the trigeminal nerve [7]. The demyelination of the nerve results in the same manner of clinical manifestation as described for compressive etiologies.

Trigeminal neuralgia is divided into 3 subtypes according to The International Classification of Headache Disorders, Third Edition (ICHD-3) [1]: classic, secondary, and idiopathic trigeminal neuralgia.

- **Classic Trigeminal Neuralgia** (75% of cases): This subtype develops due to compression of the trigeminal nerve with morphological changes in the trigeminal nerve root. The most common trigger zones for classic trigeminal neuralgia are located in the V2 and V3 divisions of the trigeminal nerve [1], predominantly in the perioral and nasal region [26].
- **Secondary Trigeminal Neuralgia** (15% of cases): This subtype is caused by an underlying disease such as multiple sclerosis, brainstem lesion, or arteriovenous malformation.
- **Idiopathic Trigeminal Neuralgia** (10% of cases) : This subtype develops without evidence of abnormalities in the imaging studies or electrophysiological tests.

CLINICAL FEATURES [1,7-9]

★ ***Pain characteristics described as:***

- Intense, sharp, superficial, or stabbing pain strictly within the distribution of the trigeminal nerve
- Occurs suddenly and is maximal at onset
- Lasts briefly (several seconds)
- Recur from 0 to more than 50 times per day
- Typically unilateral

★ ***Autonomic symptoms may be presented as:***

- Lacrimation
- Conjunctival injection
- Rhinorrhea

★ ***Pain precipitated by manipulation at the "trigger zones" such as:***

- Light touch along the distribution of trigeminal nerve (innocuous stimuli)
- Chewing
- Talking
- Brushing teeth
- Cold air
- Smiling
- Grimacing

DIAGNOSIS

Diagnostic Criteria of Trigeminal Neuralgia

The International Classification of Headache Disorders, Third Edition (ICHD-3) [1]

Criteria A	• **HAVE** recurrent paroxysms of unilateral facial pain in the distribution of one or more divisions of the trigeminal nerve • **HAVE** criteria B and C. • **NO** radiation beyond the distribution of trigeminal nerve
Criteria B	Pain has **ALL** of the following characteristics: • Lasting from a fraction of a second to two minutes • Severe intensity • Electric shock-like, shooting, stabbing, or sharp in quality
Criteria C	Precipitated by **innocuous stimuli** within the affected trigeminal distribution
Criteria D	**NOT** better accounted for by another ICHD-3 diagnosis

Headache Classification Committee of the International HeadacheSociety (IHS) The International Classification of Headache Disorders,3rd edition. Cephalalgia 2018;38:1.

INVESTIGATION

Trigeminal neuralgia is **diagnosed based on the clinical symptoms**. Once trigeminal neuralgia is diagnosed, secondary trigeminal neuralgia should be identified as the main treatment of secondary trigeminal neuralgia is controlling the patient's causative underlying disease [12].

MRI Brain with thin cuts through the trigeminal ganglion

Detects neurovascular compression and/or structural brain lesions due to high resolution for visualization of the trigeminal nerve and adjacent lesions [10,11]. CT scan is an option if MRI is not available.

DIFFERENTIAL DIAGNOSES

Differential diagnosis for clinical presentations similar to trigeminal neuralgia are described below:

Differential Diagnoses

Trigeminal Neuropathy

Trigeminal neuropathy is presented as facial pain in the distribution of the trigeminal nerve caused by other conditions that result in neural damage. These conditions include herpes zoster and postherpetic neuralgia.

Unlike trigeminal neuralgia, trigeminal neuropathy is characterized by continuous pain described as burning, squeezing, or pins and needles sensation. Trigeminal neuropathy can be distinguished with trigeminal neuralgia via history taking. For example, herpes zoster and postherpetic neuropathy should be suspected with patients with a history of herpes zoster infection (presented as a painful grouped vesicular erythematous rash).

Dental Pain

Dental pain can also present as facial pain, and may be confused with trigeminal neuralgia since trigeminal neuralgia pain can be aggravated by brushing teeth and chewing.

However, unlike sharp electric shock-like pain presented in trigeminal neuralgia, dental pain tends to be continuous intraoral pain that is dull or throbbing.

Traumatic Trigeminal Nerve Injury

Post-traumatic trigeminal neuropathy can also be presented as facial pain along the distribution of the trigeminal nerve due to neural damage.

Regardless, patients with this condition should be presented with a clear trauma history to the areas of trigeminal nerve before patterns of neuropathy occurred. In addition, the pain characteristic of post-traumatic neuropathy is continuous pain, unlike brief sharp-shooting pain that is presented in trigeminal neuralgia.

TREATMENT

❖ Medical Treatment

First line therapy is **carbamazepine or oxcarbazepine** for pain control.

- **Carbamazepine** is the best studied and an effective treatment for classic trigeminal neuralgia [5,12-14]. The usual starting dose of carbamazepine is 100 to 200 mg twice daily. Side effects can be a problem but are generally manageable. One severe complication common in south East Asian population is Steven Johnson syndrome where HLA-B*15:02 allele in genetically at risk population testing is suggested before initiating treatment.
- **Oxcarbazepine** is an effective drug that some experts prefer over carbamazepine, due to better tolerability and decreased risk of drug interactions [15]. The starting dose is a total of 600 mg per day given in two divided doses.

Alternative medication for nonresponders are gabapentin and lamotrigine [18-20]. Otherwise, surgical referral is recommended.

When can the patient wean off the medication?

There should be a sustained pain-free interval of at least six to eight weeks on medication before slow dose tapering can be done. The patients should be advised that pain recurrence is high, and restart of medication may be required after weaning.

❖ Surgical Treatment

It is worth noting that surgical treatment should be recommended to patients whose symptoms are not improved by medical treatments. Patients should be candidates who are able to tolerate surgical procedures.

Classic Trigeminal Neuralgia Surgical Treatment

Microvascular decompression is suggested in patients with confirmatory imaging of neurovascular compression of the trigeminal nerve. However, this procedure requires craniotomy (surgical removal of a part of bone from the skull to expose the brain) [21-24]. Therefore, patients who are not able to tolerate this procedure have the alternative options such as gamma knife stereotactic radiosurgery and percutaneous ganglion lesioning.

However, it is important to note some disadvantages of the alternative options to the surgical treatment. Gamma knife surgery was found to have a delayed pain relief up to one month with otherwise no important differences compared to the surgical treatment. On the other hand, the percutaneous techniques were found to achieve only initial pain relief, as the pain-free rates declined to 68 percent and 50 percent of patients in one and five years, respectively [12]. The percutaneous techniques also come with increased complications such as perioperative aseptic meningitis in 0.2%, postoperative dysesthesia described as burning and aching feeling in 12%, and long-term sequelae such as trigeminal distribution sensory loss in nearly 50% of all cases [12].

Secondary Trigeminal Neuralgia Surgical Treatment

Some case series have suggested that surgical interventions including microvascular decompression, gamma-knife radiosurgery, and percutaneous ganglion lesioning provided short-term improvement among patients with trigeminal neuralgia secondary to multiple sclerosis [24-25].

Idiopathic Trigeminal Neuralgia Surgical Treatment

There is still limited data on surgical intervention for idiopathic trigeminal neuralgia. However, microvascular decompression surgery may be helpful in allowing surgeons to identify and remove compression that was not visualized in the imaging studies.

REFERENCES

1. Headache Classification Committee of the International Headache Society (IHS) The International Classification of Headache Disorders, 3rd edition. Cephalalgia 2018; 38:1.
2. MacDonald BK, Cockerell OC, Sander JW, Shorvon SD. The incidence and lifetime prevalence of neurological disorders in a prospective community-based study in the UK. Brain 2000; 123 (Pt 4):665.
3. van Hecke O, Austin SK, Khan RA, et al. Neuropathic pain in the general population: a systematic review of epidemiological studies. Pain 2014; 155:654.
4. Katusic S, Beard CM, Bergstralh E, Kurland LT. Incidence and clinical features of trigeminal neuralgia, Rochester, Minnesota, 1945-1984. Ann Neurol 1990; 27:89.
5. Cruccu G, Di Stefano G, Truini A. Trigeminal Neuralgia. N Engl J Med 2020; 383:754.
6. Love S, Hilton DA, Coakham HB. Central demyelination of the Vth nerve root in trigeminal neuralgia associated with vascular compression. Brain Pathol 1998; 8:1.
7. Cheng TM, Cascino TL, Onofrio BM. Comprehensive study of diagnosis and treatment of trigeminal neuralgia secondary to tumors. Neurology 1993; 43:2298.
8. Maarbjerg S, Gozalov A, Olesen J, Bendtsen L. Concomitant persistent pain in classical trigeminal neuralgia--evidence for different subtypes. Headache 2014; 54:1173.
9. Sjaastad O, Pareja JA, Zukerman E, et al. Trigeminal neuralgia. Clinical manifestations of first division involvement. Headache 1997; 37:346.
10. Borges A, Casselman J. Imaging the trigeminal nerve. Eur J Radiol 2010; 74:323.
11. Blitz AM, Northcutt B, Shin J, et al. Contrast-Enhanced CISS Imaging for Evaluation of Neurovascular Compression in Trigeminal Neuralgia: Improved Correlation with Symptoms and Prediction of Surgical Outcomes. AJNR Am J Neuroradiol 2018; 39:1724.
12. Gronseth G, Cruccu G, Alksne J, 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.
13. Campbell FG, Graham JG, Zilkha KJ. Clinical trial of carbamazepine (tegretol) in trigeminal neuralgia. J Neurol Neurosurg Psychiatry 1966; 29:265.

14. Killian JM, Fromm GH. Carbamazepine in the treatment of neuralgia. Use of side effects. Arch Neurol 1968; 19:129.
15. Di Stefano G, La Cesa S, Truini A, Cruccu G. Natural history and outcome of 200 outpatients with classical trigeminal neuralgia treated with carbamazepine or oxcarbazepine in a tertiary centre for neuropathic pain. J Headache Pain 2014; 15:34.
16. Cruccu G. Trigeminal Neuralgia. Continuum (Minneap Minn) 2017; 23:396.
17. Nurmikko TJ, Eldridge PR. Trigeminal neuralgia--pathophysiology, diagnosis and current treatment. Br J Anaesth 2001; 87:117.
18. Yuan M, Zhou HY, Xiao ZL, et al. Efficacy and Safety of Gabapentin vs. Carbamazepine in the Treatment of Trigeminal Neuralgia: A Meta-Analysis. Pain Pract 2016; 16:1083.
19. Zakrzewska JM, Chaudhry Z, Nurmikko TJ, et al. Lamotrigine (lamictal) in refractory trigeminal neuralgia: results from a double-blind placebo controlled crossover trial. Pain 1997; 73:223.
20. Lunardi G, Leandri M, Albano C, et al. Clinical effectiveness of lamotrigine and plasma levels in essential and symptomatic trigeminal neuralgia. Neurology 1997; 48:1714.
21. Broggi G, Ferroli P, Franzini A, et al. Role of microvascular decompression in trigeminal neuralgia and multiple sclerosis. Lancet 1999; 354:1878.
22. Zakrzewska JM, Akram H. Neurosurgical interventions for the treatment of classical trigeminal neuralgia. Cochrane Database Syst Rev 2011; :CD007312.
23. Jannetta PJ. Microsurgical management of trigeminal neuralgia. Arch Neurol 1985; 42:800.
24. Broggi G, Ferroli P, Franzini A, et al. Microvascular decompression for trigeminal neuralgia: comments on a series of 250 cases, including 10 patients with multiple sclerosis. J Neurol Neurosurg Psychiatry 2000; 68:59.
25. Sheehan J, Pan HC, Stroila M, Steiner L. Gamma knife surgery for trigeminal neuralgia: outcomes and prognostic factors. J Neurosurg 2005; 102:434.
26. Stefano, G. & Maarbjerg, Stine & Nurmikko, Turo & Truini, Andrea & Cruccu, Giorgio. (2017). Triggering trigeminal neuralgia. Cephalalgia : an international journal of headache. 38. 333102417721677. 10.1177/0333102417721677.