Retrospective Analysis

Retrospective Analysis of Clinical Feature in Trigeminal Neuralgia

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Background: Trigeminal neuralgia (TN) is usually established using characteristic clinical features such as sudden, severe, and unilateral facial pain. Studies about diverse clinical features and epidemiologic data of TN have been reported previously; however, most of the previous studies have evaluated in and focused on Caucasian and Western populations.

Objectives: The purpose of this study was to evaluate diverse clinical features, currently applied types of treatment, and brain imaging studies in patients with TN in a Korean population.

Study Design: Retrospective analysis.

Setting: An interventional pain management practice in South Korea.

Methods: Patients with a primary diagnosis of TN were identified using Clinical Data Warehouse v 2.5 (CDW, Planit Healthcare, Seoul, Korea) using the key words "trigeminal neuralgia and G50.0 (International classification of disease 10 code)."

Results: TN occurred predominantly between the fifth and seventh decades of life, with female predominance. The V3 division and unilateral right-side involvement were the most common affected region. An electric shock like sensation and the intraoral side (teeth and gingiva) were the most common pain description and location, respectively. Normal brain imaging studies and vascular compression on the trigeminal nerve were observed in 92 (64.7%) and 36 (25%) patients, respectively. The superior cerebellar artery was the most common offending vessel (19;13.3%). Monotherapy with carbamazepine alone was the most common (91;37.7%), whereas radiofrequency thermoablation was the most common invasive treatment.

Limitations: The results of this study were based on data on TN patients from a single center. The generalizability of the findings to the Korean population is thus limited.

Conclusion: There is little difference between Korean and other Asian patients with TN in their demographic and clinical characteristics.

Key words: Brain imaging, clinical feature, electric shock-like sensation, intraoral side, trigeminal neuralgia, vascular compression

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The diagnosis of trigeminal neuralgia (TN) is usually established using characteristic clinical features such as sudden, severe, and unilateral facial pain. According to the beta version of the 3rd edition of the International Classification of Headache Disorders (ICHD-3 beta), TN is defined by recurrent, unilateral, and brief electric shock-like pain with an abrupt onset and termination. The pain is located in one or more of the trigeminal nerve divisions and is triggered by innocuous sensations (1). Among cranial neuralgias, TN is reported to be the most common and excruciating disease. Such severe and disabling pain can significantly impair the quality of life, which may result in psychological distress and even suicide (2). Vascular compression near the dorsal root entry zone of the trigeminal nerve has been known to be an

important cause of TN; however, idiopathic conditions or intracranial lesions like multiple sclerosis, cysts, and tumors can also cause TN (3,4). Although the incidence of secondary TN due to intracranial tumor compression of the trigeminal nerve is less than 10%, magnetic resonance imaging (MRI) evaluation of the brain is necessary to exclude specific lesions in the posterior cranial fossa.

Since most patients with TN are diagnosed by clinically characterized features, elaborate studies on such features are important to minimize the misdiagnosis. In the pain clinic, we encounter patients with TN who have been misdiagnosed with other types of facial neuralgia, which result in improper treatments. On the other hand, patients with other types of facial pain have been misdiagnosed with TN. An accurate diagnosis is a crucial step since clinical treatments differ among diverse forms of facial pain or neuralgia (3,4).

TN demonstrates a good response to oral medication; thus, pharmacotherapy should be considered as the first line of treatment. Carbamazepine and oxcarbazepine are the drugs of choice for the long-term treatment of TN. Other commonly applied anti-epileptics are gabapentin, pregabalin, phenytoin sodium, and lamotrigine (3,5).

Studies about the diverse clinical features and epidemiologic data of TN have been reported previously; however, most previous studies have evaluated and focused on Caucasian and Western countries (3). Although there were several studies on the clinical features of TN in Asian populations, the included number of patients was small, or detailed information about clinical features was lacking (5-7).

The purpose of this study was to evaluate diverse clinical features, currently applied types of treatment, and brain imaging studies in patients with TN in a Korean population.

Methods

Patients

This retrospective study was approved by our institutional review board (2022-08-023), which waived the need for an informed patient consent. From January 2017 to January 2022, the electronic records of 351 consecutive patients with a primary diagnosis of TN were initially reviewed and evaluated for suitability for inclusion in this study. Only patients diagnosed with TN based on the diagnostic criteria of ICHD-3 (8) and followed up regularly for at least 6 months were included in this study. Medical records with one or 2 missing data points were included for analysis. However, 110 incomplete medical records with more than 3 missing data points or those of facial neuralgia other than TN were excluded. Therefore, data from 241 consecutive patients were included in the final analysis.

Records of patients with a primary diagnosis of TN were retrieved using Clinical Data Warehouse v 2.5 (CDW, Planit Healthcare, Seoul, Korea) using the key words "trigeminal neuralgia and G50.0 (International classification of disease 10 code)."

Data Analysis

Data on the distribution of age and gender, region of trigeminal nerve involvement, pain characteristics, primary location of pain, distribution of triggering factors, combined medical disease, initial therapeutic regimen, and type of invasive treatment were obtained subsequent to careful evaluation of medical records. In evaluating brain imaging studies, only the conclusive reports which were confirmed by a radiologic specialist were used. The results of the brain imaging studies were classified as normal, vascular compression, or brain tumor. The specific type of brain tumor and the offending vessel were elucidated.

Statistics

Values are presented as the number of patients (%). The chi-squared test or Fisher's exact test was used to test the significance of comparisons between the groups. The level of significance was set at $P < 0.05$. All analyses were performed using SPSS v 22.0 (IBM Corporation, Armonk, NY).

Results

The medical records of 241 patients were analyzed finally after excluding incomplete records with more than 3 missing data.

Demographic Characteristics

TN occurred predominantly between the fifth and seventh decades of life, with the patient age ranging between 22 and 94 years (Fig. 1). The mean age of TN diagnosis was 58.7 ± 10 years. TN presented more frequently in female patients (70.1%).

Clinical Features

Unilateral right-side involvement was the most common affected region (131;54.3%), whereas bilateral involvement was rare (9;3.7%). V3 was the most

common trigeminal nerve division (88;36.4%) involved, followed by V2 (84;34.8%) and V2 + V3 (50;20.7%). The V1 was the least affected division of the trigeminal nerve (8;3.3%, Table 1).

The most common description of pain was an electric shock-like sensation (158;65.5%), followed by dull nature pain (34;14.1%, Table 2). The most common primary locations of pain were intraoral, involving teeth and gingiva (69;28.5%), followed by the temporal area, chin, and lips (Table 3). Most patients presented more than one triggering activity. The various causative factors of pain reported were chewing, speaking, washing the face, touching, brushing the teeth, opening the mouth, swallowing, and shaving. Among various triggering activities, intraoral activities such as chewing (101;41.9%) and brushing teeth (72;29.8%) were the most commonly reported (Table 4).

MRI Findings

Among patients who were included in this study, 142 patients (58.9%) underwent evaluation by brain MRI. Normal MRI findings were observed in 92 (64.7%) patients. Thirty-six patients (25%) showed vascular compression on the trigeminal nerve, and the most common compressing vessel was the superior cerebellar artery (19;13.3%). Brain tumors were noted in 15 patients (10.5%, Table 5).

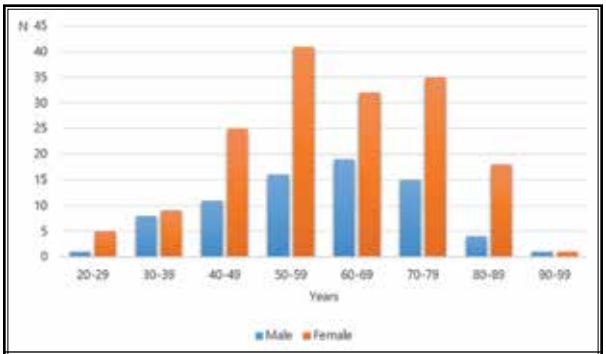

Fig 1. *Distribution of age and gender in patients of trigeminal neuralgia.*

Table 1. *Distribution of trigeminal nerve involvement in patients of trigeminal neuralgia.*

Division	Bilateral	Right	Left	Total n (%)	*P* value
V1	0	3	5	8 (3.3)	
V2	3	53	26	84 (34.8)	
V3	5	46	37	88 (36.4)	
V1 + V2	0	8	3	11 (4.5)	
V2 + V3	1	20	29	50 (20.7)	
V1 + V2 + V3	0	1	1	2 (0.8)	
Total	9	131	101	241 (100)	0.165

V1, ophthalmic division of trigeminal nerve; V2, maxillary division of trigeminal nerve; V3, mandibular division of trigeminal nerve

Table 2. *Pain characteristics in patients with trigeminal neuralgia in relation to gender.*

Pain Characteristics	Men	Women	Total N (%)	*P* value
Electric shock-like	47	111	158 (65.5%)	
Dull nature	14	20	34 (14.1%)	
Numbness	1	0	1 (0.4 %)	
Burning Stinging	0 0	1 2	1 (0.4 %) 2 (0.8%)	
Stretching	1	0	1 (0.4 %)	
Aching	2	0	2 (0.8%)	
Unknown Total	10 77	32 169	42 (17.4%) 241 (100%)	 0.054

Table 3. *Primary location of pain in patients with trigeminal neuralgia.*

Location of pain	N (%)
Teeth & gingiva Temporal area Chin	69 (28.5%) 32 (13.2%) 27 (11.2%)
Lip	25 (10.3%)
Nose	11 (4.5%)
Eye	17 (7.0%)
Forehead	17 (7.0%)
Cheek	25 (10.3%)
Ear	7 (2.9%)

Table 4. *Distribution of pain-triggering factors in trigeminal neuralgia.*

Triggering factor	n (%)
Chewing	101 (41.9%)
Speaking	14 (5.8%)
Washing face	33 (13.6%)
Touch	20 (8.2%)
Brush teeth	72 (29.8%)
Open mouth	9 (3.7%)
Swallowing	8 (3.3%)
Shaving	2 (0.8%)
None	1 (0.4%)

Combined Medical Illness

Hypertension (58,24.0%) and diabetes mellitus (32,13.2%) were the most commonly found combined medical illness (Table 6).

Treatment

As an initial medical treatment for TN, carbamazepine alone or in combination with other medication was prescribed most commonly (128;53.1%). Among various types of prescription of carbamazepine, monotherapy with carbamazepine alone was the most common (91;37.7%, Table 7). Forty-three (17.8%) patients underwent invasive treatments, including microvascular compression, gamma knife, alcohol neurolysis, and radiofrequency thermoablation. Of these, radiofrequency thermoablation was the most common (Table 8).

Discussion

Most of the findings in this study are similar to those in previous reports. The peak age of incidence between the fifth and seventh decades of life and female predominance were in agreement with previous studies (1,3,4,6,7,9).

In the present study, the right side of TN was found more frequently than the left side. Anatomical variation and asymmetry can be observed on the right and left sides of the foramen ovale or foramen rotundum (10). When asymmetry in size or shape was found in the foramen rotundum, the left side was observed as larger than the right side. The previous report suggested that due to this difference in size of the foramen rotundum, the smaller foramen could lead to a secondary compression of the maxillary nerve in the cases of TN caused by vascular compression (10,11). This phenomenon is possibly the most important causative factor of the higher incidence of right-sided TN.

Bilateral TN was observed in 9 patients (3.7%) in this study, and this incidence was lower than the incidence of the Singaporean study, which reported 6.8% (6). The V3 division was the most commonly affected branch, followed by V2. In contrast, studies that were performed in Western countries demonstrated a slightly higher incidence of V2 division (12,13). Single involvement of trigeminal nerve division was more

Table 5. *Cause of trigeminal neuralgia according to findings of magnetic resonance imaging.*

Finding of magnetic resonance imaging	n (%)
Normal	92 (64.7%)
Vascular compression	
Superior cerebellar artery	19 (13.3%)
Inferior cerebellar artery	3 (2.1%)
Other vessels	14 (9.8%)
Brain tumor location	
Cerebellopontine angle	10 (7.0%)
Petrous ridge	3 (2.1%)
Other	2 (1.4%)
Total	142 (100%)

Other tumor includes a basal ganglia cystic tumor and cavernous sinus tumor.

Table 6. *Combined medical disease in trigeminal neuralgia.*

Medical disease	n (%)
No medical disease	135 (63%)
With medical disease	
Diabetes mellitus	32 (13.2%)
Hypertension	58 (24.0%)
Heart disease	18 (7.4%)
Liver disease	6 (2.4%)
Cerebrovascular disease	16 (6.6%)
Pulmonary disease	4 (1.6%)
Other	7 (2.9%)

Table 7. *Initial therapeutic regimen in trigeminal neuralgia.*

Therapeutic regimen	n (%)
Carbamazepine alone	91 (37.7%)
Carbamazepine + anticonvulsant or antidepressant	46 (19.1%)
Oxycarbamazepine	5 (2.0%)
Gabapentine alone Pregabaline alone Other medication	6 (2.4%) 4 (1.6%) 86 (35.6%)
none Unknown Total	3 (1.2%) 15 (6.2%) 241 (100%)

Other medication includes single use or combination of acetaminophen, nonsteroidal anti-inflammatory drug, benzodiazepine, antidepressant or anticonvulsant.

Table 8. *Distribution of patients who received invasive treatment.*

Type of treatment	n (%)
Microvascular decompression	2 (0.8%)
Gamma knife	2 (0.8%)
Radiofrequency thermoablation	37 (15.3%)
Alcohol neurolysis	2 (0.8%)
No invasive treatment Total	199 (82.5%) 241 (100%)

common than that of 2 or 3 divisions. This finding was in agreement with those of previous studies (5,6).

Since the diagnosis of TN is mainly based on clinical symptomology, understanding the description of pain which patients explain is important. The predominant feature of pain characteristics in this study was an electric shock-like sensation in the face. The interpretations of "electric shock-like sensation" include an intense, brief, and sharp pain. These characteristics of pain are a mandatory component and an important feature of the diagnosis of TN (3). However, concomitant dull nature pain was also present in this study. A previous study demonstrated that concomitant persistent pain was reported by 78 (49%) patients among TN (14). This is an important consideration to avoid excluding a case as TN since patients can present with dull, persistent pain concomitantly with an electric shock-like pain; that is, both conflicting natures of pain can occur in TN. Although we did not evaluate pain according to the cause of TN (i.e., classical, idiopathic, or secondary TN), the pain nature or symptomatology of TN is remarkably the same across all known causes of TN (3). A detailed description of pain symptomology and a careful clinical assessment are important to the diagnostic process and to obtain a conclusive diagnosis of TN.

In the pain clinic, we can encounter TN patients who were inaccurately diagnosed with a dental problem. In a previous report, 25 patients (47.1%) underwent an unnecessary tooth extraction before they were diagnosed with TN. The upper premolar (V2) was the most common tooth extracted (15). These findings are confirmed by the results of the present study, which reported that the most common primary location of pain was the intraoral rather than the extraoral side. Furthermore, the study by Jainkittivong et al (9) reported that the most common sites of pain were a previous tooth extraction site and existing teeth. If patients complain of a sudden and severe toothache, such symptoms could misleadingly indicate an odontogenic problem. In many cases, such symptomatic teeth have been extracted unnecessarily with no improvement of pain (9,15). Since the initiation of pain in TN primarily happens in the oral cavity, many patients with TN were initially seen by a dentist. To avoid misdiagnosis, which might lead to unnecessary tooth extraction, a dentist also should know the nature and clinical characteristics of TN.

Evaluating the presence of triggering or provoking factors is important, and the presence of evoked pain is one of the mandatory components, according to the diagnostic criteria of ICHD-3 (8). The type of triggering factor was various, and the majority of the patients in this study reported that their pain was stimulated by intraoral activity such as chewing and brushing their teeth. Consequently, patients with TN might be limited in dental hygiene activity and even intraoral food intake, which decreases the quality of life. Although this study could not observe, the previous report suggested atypical triggers such as cold weather and certain types of food (16).

Neuroimaging studies, especially MRI, are important for the classification of TN into either primary or secondary TN, which is typically caused by multiple sclerosis or a brain tumor in the posterior cranial fossa. A combination of 3-dimensional (3D), T2-weighted, 3D time of flight, and MR angiography, along with 3D T1-weighted gadolinium imaging, has proven to be reliable in visualizing vascular compression and the degree of root compression (3,17).

Neurovascular conflict is frequently observed in typical TN and refers to the compression of the trigeminal cistern by arteries and, rarely, veins. The superior cerebellar artery is the most common invading vessel, followed by the inferior and anterior cerebellar arteries (17,18). The present study also reported the superior cerebellar artery as the most common invading vessel of the trigeminal cistern. However, neurovascular contact is frequently observed in asymptomatic patients and the nonpainful side in symptomatic TN patients (3,17,18). Therefore, neurovascular contact on brain imaging study alone is not enough for the diagnosis of TN if an appropriate symptomatic feature is lacking.

The initial treatment of TN is usually pharmacological monotherapy with carbamazepine. However, combined therapy with different types of anticonvulsants or antidepressants can be used if the effect of monotherapy is lacking (3,19). Carbamazepine and oxcarbazepine are recommended as first-line medications; however, their comparative efficacy in patients with TN is not sufficient. Thus, both medications might be changed or combined with gabapentin, pregabalin, topiramate, or baclofen. Carbamazepine is the only medication approved by the Food and Drug Administration of the United States for the resolution of TN, with 70% effectiveness in controlling pain (3,19).

Patients with TN who do not show any responsiveness or tolerance to pharmacologic treatment or those who are intolerable due to the occurrence of side effects are potential candidates for more invasive treatment. In this study, radiofrequency thermoablation was

performed most commonly. A recent study involving 156 patients with TN showed that percutaneous radiofrequency thermocoagulation of the trigeminal ganglion was a safe and effective procedure. However, the effectiveness of the treatment reportedly decreased over time (20).

Limitations

This study includes several limitations. First, this study involved a small study population and data obtained from a single center. Therefore, the generalizability to the Korean population of the clinical features reported in this study is limited. Further study involving large datasets obtained from multiple centers is needed. Second, this study is limited by its retrospective design and includes medical records with one or 2 missing data points.

Conclusion

In conclusion, this study showed that few differences exist between Korean and other Asian TN patients in their demographic and clinical characteristics.

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