

Constant Face Pain in Typical Trigeminal Neuralgia and Response to Gamma Knife Radiosurgery

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Key Words

Trigeminal neuralgia · Constant face pain · Gamma Knife radiosurgery · Typical trigeminal neuralgia · Face pain

Abstract

Background/Aims: Constant pain, especially if prominent, is sometimes considered incompatible with a diagnosis of typical idiopathic trigeminal neuralgia. This study aims to clarify the frequency of patient-reported constant pain in patients with medically intractable, typical, idiopathic trigeminal neuralgia as diagnosed with standard clinical parameters and confirmed by the response to a modified McGill questionnaire, a ‘hold-still’ test that eliminated triggers and the response to Gamma Knife radiosurgery. **Method:** Forty consecutive patients with typical trigeminal neuralgia were given questionnaires prior to Gamma Knife radiosurgery. Those with constant pain were further tested by being advised to hold completely still for up to 3 min. Final pain relief was evaluated after Gamma Knife radiosurgery. **Results:** Twenty of forty patients indicated on a questionnaire that they had constant face pain. Pain decreased on the ‘hold-still’ test on all 12 patients who were tested. Following Gamma Knife radiosurgery, there was no significant difference in pain relief in those without or with constant pain. **Conclusion:** Patients with typical idiopathic trigeminal neuralgia frequently report that 50% or more of their pain is constant. This constant

pain is markedly decreased if the patient holds completely still for a few minutes and does not affect the outcome of Gamma Knife radiosurgery. Copyright © 2013 S. Karger AG, Basel

Introduction

Patients with medically intractable typical trigeminal neuralgia (tic douloureux) respond very well to neurosurgical intervention with either Gamma Knife radiosurgery [2, 9, 13, 22], needle rhizotomy (radiofrequency, glycerol or balloon microcompression) [7, 12, 20] or microvascular decompression [1]. Those with atypical trigeminal neuralgia may respond but less frequently [2, 10, 13, 21, 22], and those with atypical facial pain (now called ‘persistent idiopathic face pain’) are unlikely to respond [17]. Clear criteria for diagnosis of typical trigeminal neuralgia are therefore important for the selection of patients for treatment and comparisons of therapeutic results in different studies.

Constant facial pain occurs occasionally in patients with typical trigeminal neuralgia [8, 14], often in atypical trigeminal neuralgia [23] and is characteristic of atypical facial pain [24]. A different classification has been proposed that is based on information obtained from the patient’s medical history: in patients with face pain of spon-

Table 1. Clinical characteristics of patients at time of index Gamma Knife radiosurgery

Characteristic	Constant pain	No constant pain	p
Total patients, n	20	20	
Right side, n	13 (65%)	14 (70%)	1.0
Female, n	12 (60%)	11 (55%)	1.0
Distribution of pain, n			
V3 only	5 (25%)	7 (35%)	
V2 only	6 (30%)	5 (25%)	
V2 and 3	8 (40%)	4 (20%)	
V1 and 2	1 (5%)	4 (20%)	0.313 ¹
Hypoalgesia, n	4 (20%)	3 (15%)	1.0
Triggered pain, n ²	20 (100%)	20 (100%)	1.0
Carbamazepine or oxcarbazepine help, n	17 (85%)	17 (85%)	1.0
Prior surgery (any), n	12 (60%)	6 (30%)	0.111 ³
At least one GKRS, n	10 (50%)	5 (25%)	0.191
At least one RFE, n	2 (10%)	3 (15%)	1.0
Mean age, years	75.9	74.4	0.676
Duration of symptoms, months			
Mean	107.2	127.2	0.57
Range	5–468	4–420	
Visual analogue scale ⁴	7.0	3.5	0.003
Pain index ⁴	3.8	2.6	0.30
Vessel at nerve on MRI, n ⁵	14 (70%)	15 (88%)	0.246
Maximum dose at GKRS, Gy			
Mean	65.8	72.5	0.1
Range	50–80	40–80	

Age, duration of symptoms, visual analogue scale and pain index: mean test, independent samples t test for equality of means, 2-sided. Equal variance not assumed. GKRS = Gamma Knife radiosurgery.

Side, gender, prior surgery, hypoalgesia, vessel at nerve on MRI: cross tabs, 2-sided Fisher's exact test.

¹ Pearson's 2-sided χ^2 .

² Triggered by light touch such as in talking, eating, washing or brushing the teeth.

³ Pearson's 2-sided χ^2 is 0.057.

⁴ Measured by the patient at office visit when it was decided to do the Gamma Knife radiosurgery.

⁵ MRI on 37 patients, 20 with and 17 without constant pain (the other 3 had CT).

taneous onset, TN1 is diagnosed when >50% of the pain is shock-like and TN2 when >50% of the pain is constant [4, 6]. It has been suggested that TN1 is similar to typical trigeminal neuralgia and TN2 to atypical trigeminal neuralgia [4, 6].

The present study evaluates patient-reported constant facial pain in patients diagnosed as having typical trigeminal neuralgia by traditional criteria. The results of a

modified McGill Pain Questionnaire, a 'hold-still' test that temporarily eliminates triggers and the response to Gamma Knife radiosurgery help confirm the initial diagnosis of typical trigeminal neuralgia.

By having independent data about the patient's assessment of constant pain and the standard criteria of diagnosing typical trigeminal neuralgia, the present report compares the TN1 and TN2 classification system with the more traditional diagnoses of trigeminal neuralgia and atypical trigeminal neuralgia and evaluates the relevance of the concept of patient-reported constant pain to the diagnosis of typical trigeminal neuralgia.

Materials and Method

This study was approved by the Human Investigation Review Board of Columbia University. Forty consecutive patients with medically intractable typical trigeminal neuralgia of spontaneous onset were evaluated prior to Gamma Knife radiosurgery. No patient had multiple sclerosis or a brain tumor. Patients gave a detailed history and were examined by a clinician experienced in the diagnosis and treatment of trigeminal neuralgia.

Those who had constant pain at the time of the examination were further tested by being advised to hold completely still, not to talk, hum, move the tongue, face or head and give their pain severity on a scale of 0–10 every minute before and after holding still. The test was terminated if pain reduction was at least 70% or 3 min were reached.

A clinical diagnosis of typical trigeminal neuralgia was made in the presence of paroxysmal, triggered, trigeminally distributed, unilateral pain and fit criteria established in the Classification of Chronic Pain by the International Association for the Study of Pain (IASP) [14] and the Headache Classification Subcommittee of the International Headache Society (IHS) [8] with the exception that patients with hypoalgesia from a previous neurosurgical procedure were not excluded. The diagnosis was not based on the responses to questionnaires, which were also filled out by the patients on the same day prior to the examination.

Gamma Knife radiosurgery was done using the Elekta Gamma Knife unit (model B; Elekta Instruments, Inc., Atlanta, Ga., USA). Three-dimensional volumetric axial T1-weighted magnetic resonance images (0.8-mm-thick slices) were obtained through the area of the trigeminal nerve at its exit from the brainstem after injection of contrast (three dimensional gradient echo acquisition in steady state, 20-degree flip angle, 30 ms TR, 7 s TE, 256 × 256 matrix, one excitation, 28 frames, and 24-cm field of view). T2 sequences using Fast Imaging Employing Steady State Acquisition (FIESTA) images were also obtained. One 4-mm isocenter was located at the cisternal trigeminal nerve a few millimeters from the brainstem. Usually, the 20–40% isodose line came to the outer surface of the brainstem contour. A first Gamma Knife radiosurgery was done with 75–80 Gy maximum; those who had previously been treated with Gamma Knife radiosurgery were now treated with a maximum dose of 40 (in 1 patient) to 70 Gy (table 1). After the Gamma Knife radiosurgery, a final follow-up

Table 2. Results of Constant Pain Questionnaire (20 patients)

	Mean	Median	Range	Patients with available data, n
What percentage of awake time do you have constant pain?	91.5	100	70–100	17
What percentage of your total face pain is constant pain?	70.1	70	25–100 ¹	13

¹ ≥50% in 12 patients.

was obtained with a standardized questionnaire [2] either by mail or telephone interview.

Before the Gamma Knife radiosurgery, the following questionnaires asked the patient to respond based on his or her current (day of examination) pain: the short modified McGill Pain Questionnaire asked the patient to give a score of none (0), mild (1), moderate (2) or severe (3) for each 19 types of pain (table 4). A pain index was established by asking the patient to check the word most appropriate to his or her pain: no pain (0), mild (1), discomforting (2), distressing (3), horrible (4), or excruciating (5). Visual analogue pain scores were determined by asking the patient to mark the pain severity on a 10-cm line. The Constant Face Pain Questionnaire asked the patient the following questions: ‘Do you have constant pain?’ If the answer was yes, then ‘What percentage of your awake time do you have constant face pain? And what percentage of your total face pain is the constant pain?’.

Statistical Analysis

The statistical software program SPSS (SPSS, Inc., Chicago, Ill., USA) was used for the analysis. To compare groups for significant differences by using data in categories, cross-tabulations were performed with the 2-tailed Fisher exact test. The difference between means of numerical data was determined using the t test for equality of means. Differences in Kaplan-Meier plots were determined using the log rank (Mantel-Cox) test for significance. A probability value <0.05 was considered statistically significant.

Results

Clinical characteristics of the 40 patients are described in table 1. Twenty of forty patients (50%) indicated on the questionnaire that they had constant face pain and another 3 did so at the time of the physical examination (15–30 min after they filled out the questionnaire). Constant pain was at least 70% of their waking time in all 17 patients who answered this question, and it was at least 50% of their total pain in 12 of 13 who responded to this question (table 2); this would be consistent with a diagnosis of TN2. Those with constant pain were more likely to have a higher visual analogue pain score for severity of pain ($p = 0.003$) (table 1).

Table 3. Final pain relief

	Constant pain		
	no	yes	total
Patients (follow-up data available), n	20	17	37
Final pain relief, n			
No pain no meds	6 (30%)	6 (35.3%)	12 (32.4%)
≥90% relief + meds	4 (20%)	5 (29.4%)	9 (24.3%)
75–89% relief	0	1 (5.9%)	1 (2.7%)
50–74% relief	5 (25%)	1 (5.9%)	6 (16.2%)
No relief	3 (15%)	1 (5.9%)	4 (10.8%)
Reoperation	2 (10%)	3 (17.6%)	5 (13.5%)
Follow-up, months			
Mean	20.0	17.3	
Range	5.7–31.1	4.9–28.9	

No significant difference in final pain relief between those with or without constant pain: Pearson χ^2 , $p = 0.445$. Percent of final pain relief was provided by the patient.

There was reduction in pain on the ‘hold-still’ test on all 13 patients who were tested and the reduction was ≥67% in 12 of 13 patients. The reduction was usually marked and very quick as testing was done for 1 min in 11 patients and 2 and 3 min in 1 patient each.

There was no significant difference between patients with or without constant pain as to side, gender, hypoalgesia, prior surgery, response to carbamazepine (Tegretol) or oxcarbazepine (Trileptal), duration of symptoms, presence of pain triggered by light touch (present in all patients), presence of blood vessel contact with the cisternal trigeminal nerve as seen on high-resolution MRI (table 1) or pain relief following Gamma Knife radiosurgery (table 3; fig. 1, 2). At the final follow-up at a mean of 20 months for those without constant pain and 17 months

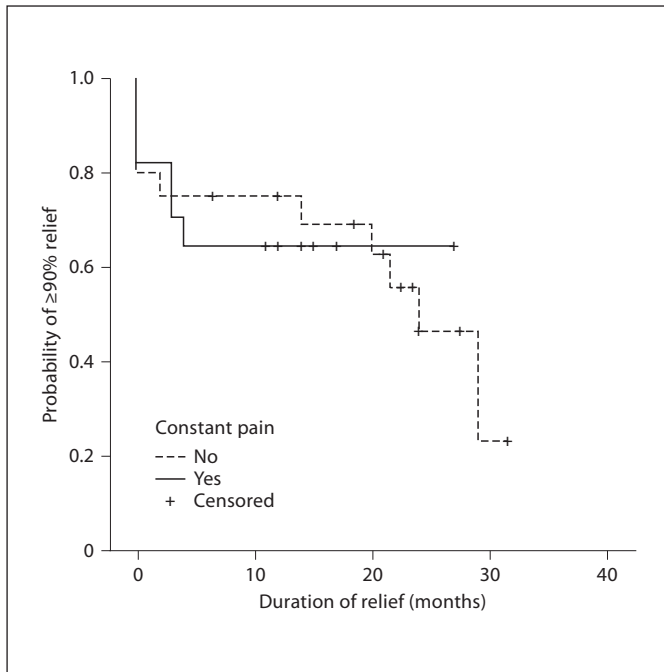


Fig. 1. Kaplan-Meier plots showing the probability of attaining and maintaining $\geq 90\%$ pain relief. There was no difference in pain relief in those with constant pain (17 patients) versus those without constant pain (20 patients): $p = 0.968$.

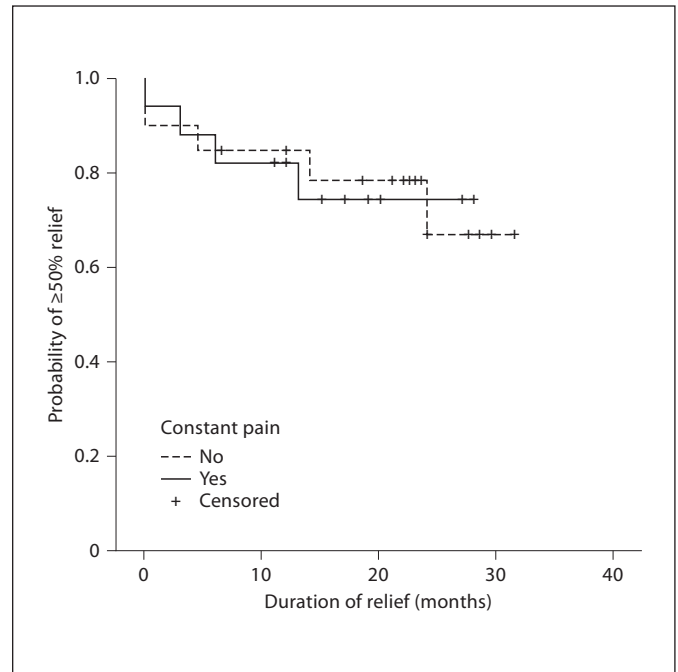


Fig. 2. Kaplan-Meier plots showing the probability of attaining and maintaining $\geq 50\%$ pain relief. There was no difference in pain relief in those with constant pain (17 patients) versus those without constant pain (20 patients): $p = 0.961$.

for those with constant pain, there were, respectively, 10 of 20 patients (50%) and 11 of 17 (64.7%) who had 90% or greater pain relief and 15 (75%) and 13 (76.5%) who had 50% or greater pain relief ($p = 0.445$).

Of the 3 patients in each group who could not give a definite history of pain responsive to carbamazepine or oxcarbazepine, 5 were not sure about the response as they had usually stopped the medicine many years ago following some adverse effect and 1 stopped it after only 2 pills because of an adverse effect.

Quality of pain as determined on the modified short McGill Pain Questionnaire is tabulated in table 4. Shooting, stabbing and sharp were the more frequent pain descriptors in both patients with constant as well as not constant pain. The only suggestion of a difference in quality of pain between the groups was 'crawling', which was present in 6 patients with constant pain and 1 without constant pain (Fisher's exact test, $p = 0.091$; Pearson's χ^2 , $p = 0.037$). Four of the 6 patients with constant pain and the one patient without constant pain had had prior Gamma Knife radiosurgery.

Discussion

As seen in the present study, many patients with typical trigeminal neuralgia will indicate that they have constant face pain (50% of patients based on a questionnaire and another 6.5% during a direct interview), and they usually describe this constant pain as being 50% or more of their pain (table 2). Many patients who are classified under the TN1/TN2 system as TN2 really have typical trigeminal neuralgia.

Similarly, some patients classified as TN2 may not have trigeminal neuralgia at all but rather persistent idiopathic facial pain [3]. These patients never had pain that was paroxysmal, triggered by light touch or responsive to carbamazepine.

Some with TN2 will have atypical trigeminal neuralgia if in addition to having more than 50% of their pain as nontriggered constant pain they have a component of paroxysmal, triggered, trigeminally distributed, carbamazepine- or oxcarbazepine-responsive pain.

Another characteristic feature of typical trigeminal neuralgia is that it responds to carbamazepine or oxcarbazepine. Such was the case in the present study in 85%

of patients with constant pain as well as 85% without constant pain (table 1). Occasionally, in patients with typical trigeminal neuralgia, this history cannot be clearly elicited. This often occurs when a patient took one or two pills and then stopped them because of an adverse response or did have initial pain relief but cannot remember this.

Although pains that were shooting, stabbing and sharp are characteristic of typical trigeminal neuralgia and were noted by most of the present study patients, and similarly by those with constant as well as nonconstant pain, many of these patients used numerous other descriptors for their pain, including throbbing, burning and aching whether or not they had constant pain (table 4).

Although it has been suggested that a dull background pain may persist in some long-standing cases of classical trigeminal neuralgia [14] and may even predominate [5], the patients in the present study with constant pain did not have a longer duration of symptoms than those without constant pain (table 1).

Prior denervation may cause a constant dysesthetic pain that must be distinguished from the paroxysmal, triggered pain of trigeminal neuralgia. There was no difference in the incidence of clinically detectable hypoalgesia in those with constant versus no constant pain (table 1). Among those who never had a prior neurosurgical procedure, there still were a significant number of patients with constant pain (8 of 21 patients).

It is not reliable to use a patient's self-reporting on a questionnaire as the exclusive method for determining constant pain. Although many patients wrote on a questionnaire that 50% or more of their face pain was constant, they usually confirmed when directly questioned that the constant face pain was not really there all the time. Because these patients were having severe trigeminal neuralgia pain much of the time, they perceived their pain as being constant.

The 'hold-still' test can often help to distinguish between different kinds of constant pain. Those who have a marked decrease in their pain when they hold completely still really have a triggered pain that subsides when all triggers are eliminated. A marked reduction in pain after the patient holds still is consistent with typical trigeminal neuralgia even if the patient says that the constant pain constitutes 50% or more of his or her pain. Patients with persistent idiopathic facial pain usually find that when they hold still, the pain either does not improve at all, or often gets worse, and they do not have paroxysmal, triggered pain at all. Patients who have constant pain that does not get better at all when they hold still but also have

Table 4. Short modified McGill Pain Questionnaire in 38 patients

Type of pain	Constant			Not constant		
	n	%	total score ¹	n	%	total score ¹
Throbbing	10	53	25	6	32	15
Shooting	14	74	39	15	79	37
Stabbing	14	74	38	14	74	35
Sharp	17	89	46	14	74	37
Gnawing	3	16	8	5	26	13
Hot/burning	6	32	16	4	21	12
Tingling	9	47	22	7	37	14
Aching	11	58	25	11	58	27
Tender	9	47	23	7	37	20
Tiring	9	47	24	5	26	13
Frightening	9	47	25	7	37	19
Vicious	10	53	27	10	53	26
Miserable	12	63	30	13	68	34
Unbearable	15	79	43	11	58	26
Nagging	8	42	18	9	47	20
Itching	4	21	10	2	11	2
Crawling ²	6	32	16	1	5	1
Tightness	5	26	12	3	16	7
Numbing	5	26	11	3	16	5
Mean total score ³			23.7			19.2
<hr/>						
Throb, burn, ache						
One (of the above)	6	32		6	32	
Two (of the above)	6	32		6	32	
Three (of the above)	3	16		1	5	
Mean total score ⁴			3.47			2.84
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Shoot, stab, sharp						
One (of the above)	3	16		3	16	
Two (of the above)	3	16		3	16	
Three (of the above)	12	63		11	58	
Mean total score ⁴			6.47			5.74

¹ Each item was given a score of 0 (no pain), 1 (mild pain), 2 (moderate pain) and 3 (severe pain).

² The only suggestion of a significant difference was for the number of patients with crawling pain (constant vs. not constant pain): Fisher's exact test, $p = 0.091$; Pearson's χ^2 , $p = 0.037$.

³ Maximum total score was 57 (3 multiplied by 19).

⁴ Maximum possible was 9 (3 multiplied by 3). Nineteen patients with no constant pain and 19 patients with constant pain filled out the McGill Questionnaire.

a superimposed paroxysmal, triggered carbamazepine-responsive pain usually have atypical trigeminal neuralgia.

All the patients in the present study, including those with a history of constant pain, met well-established criteria for typical trigeminal neuralgia [8, 14]. As further confirmation that all of these patients represent one main

classification of typical trigeminal neuralgia, the two subgroups of patients were very similar as to many features that are characteristic of typical trigeminal neuralgia (tables 1, 3, 4).

The fact that there was no difference in pain relief following Gamma Knife radiosurgery in patients with or without constant pain in the present study supports the suggestion that all the patients had the same kind of trigeminal neuralgia (table 3; fig. 1, 2). Additional evidence for a lack of a worse outcome in those with constant pain in the present study is provided by the fact that those with constant pain were more likely to be treated with a lower dose because they had a prior Gamma Knife radiosurgery (table 1) and such a lower dose is more likely to be associated with either the same or a decreased chance for pain relief [9].

Further confirmation for the suggestion that both groups (with and without constant pain) had typical trigeminal neuralgia (and not atypical trigeminal neuralgia) is that the response of each group to Gamma Knife radiosurgery at 20 months (Kaplan-Meier data, fig. 1, 2) $\geq 50\%$ in 75–79% and $\geq 90\%$ in 63–65% closely approximates the response of patients with typical trigeminal neuralgia to Gamma Knife radiosurgery as established in three large published series $\geq 50\%$ in 65, 68 and 73% [2, 13, 22] and $\geq 90\%$ in 50 and 60% [2, 13] and those responses were significantly better than in patients who had atypical trigeminal neuralgia: $\geq 50\%$ in 33 and 45% [2, 22] and $\geq 90\%$ in 18% [2].

One apparent paradox in the literature is that while many papers show that patients with trigeminal neuralgia and constant pain [2, 10, 21] or those with TN2 [15] are less likely to achieve and maintain pain relief than are those without constant pain, there are some studies that show a similar response to neurosurgical intervention in

patients with or without constant pain [16, 18]. When a study shows that patients with trigeminal neuralgia without constant pain do as well following neurosurgical intervention as those with constant pain, as does the present study, it is because it is dealing with the kind of constant pain that is often seen in patients with typical trigeminal neuralgia. This constant pain is markedly decreased when the patient holds completely still; may have been present in a person who has or used to have typical trigeminal neuralgia before he or she had the constant pain, and is markedly relieved by carbamazepine or oxcarbazepine. There are different kinds of constant facial pain. And it is this difference that distinguishes typical trigeminal neuralgia from atypical trigeminal neuralgia or persistent idiopathic facial pain rather than an exclusive determination of the percentage of time that the patient claims that constant pain is present.

The many subtleties involved in the diagnosis of typical trigeminal neuralgia make it imperative for an experienced clinician to obtain a careful history. It is not sufficient just to let the patient fill out questionnaires.

Conclusion

Patients with typical idiopathic trigeminal neuralgia frequently report that 50% or more of their pain is constant. This constant pain is markedly decreased if the patient holds completely still for a few minutes and does not affect the outcome following Gamma Knife radiosurgery.

Disclosure Statement

There are no conflicts of interest.

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