Pathogenesis, Surgical Treatment, and Cure for SUNCT Syndrome

Isao Kitahara[1], Ataru Fukuda[1], Yoshiki Imamura[2], Masako Ikawa[3], Tomoki Yokochi[4]

BACKGROUND: **Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) are characterized by attacks of moderate to severe stabbing pain, strictly unilateral, with periorbital or temporal distribution, associated with cranial autonomic symptoms, such as lacrimation and redness of the ipsilateral eye.**

METHODS: **To obtain mechanistic insights into the pathogenesis of SUNCT syndrome, more than 800 cases treated in our institution during the last 7 years were retrospectively reviewed. Two patients showed typical autonomic symptoms of SUNCT.**

RESULTS: **Magnetic resonance imaging suggested potential compression of the trigeminal nerve by the intracranial artery in these cases and complete remission was achieved by microvascular decompression.**

CONCLUSIONS: **Microvascular decompression provides an appropriate therapeutic choice if vascular compression of the trigeminal nerve is identified. From our 2 cases, we propose that, in some cases of SUNCT diagnosed previously, characteristic symptoms were induced by compression of the side surface of the first branch of the trigeminal nerve at the root exit zone by the intracranial artery.**

INTRODUCTION

Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is a rare but disabling primary headache disorder characterized by brief, severe, ipsilateral, orbitotemporal pain with autonomic features such as conjunctival injection, tearing, and rhinorrhea (7). The intense pain is typically localized at the distribution of the first division of the trigeminal nerve. Although a myriad of different pharmacological treatments have been tried, no single drug has achieved a definite response in these patients (10). Therefore, the development of efficient therapy for SUNCT is long overdue.

Recently, there has been compelling interest in surgical procedures as a possible therapeutic approach in the treatment of SUNCT (5, 8). In the absence of randomized clinical trials, it has been concluded that microvascular decompression is a therapeutic option in patients with medically refractory SUNCT in whom trigeminal nerve compression is demonstrated on magnetic resonance imaging (MRI) (13, 14). Some of literature even suggests a potential contribution of the superior cerebellar artery to SUNCT. However, details of pathogenic mechanism of SUNCT syndrome are largely unknown.

We performed microvascular decompression with solid results, demonstrating that arterial contact is one potential cause of SUNCT. In this article, we propose a pathogenic mechanism for SUNCT in detail. In addition, we discuss how cranial autonomic symptoms of SUNCT are induced and how the severe pain can be appropriately treated in surgery.

METHODS

Baseline Characteristics

Approximately 800 patients treated at the Department of Neurosurgery in our institution between 2007 and 2014, complaining of facial neuralgia including tic douloureux (trigeminal neuralgia), were retrospectively reviewed. Two hundred fifty-one patients underwent microvascular decompression (MVD) of the trigeminal nerve. The mean age at surgery was 63 years (range, 17–92 years)

Key words
- Microvascular decompression
- SUNA
- SUNCT
- Typical trigeminal neuralgia

Abbreviations and Acronyms
ICHD-3beta: The International Classification of Headache Disorders, 3rd edition (beta version)
MRI: Magnetic resonance imaging
MVD: Microvascular decompression
SUNA: Short-lasting unilateral neuralgiform headache attacks with cranial autonomic symptoms
SUNCT: Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing

From the [1]Department of Neurosurgery, Chiba Tokushukai Hospital, Funabashi; [2]Department of Oral Diagnostic Sciences, Nihon University School of Dentistry, Tokyo; [3]Department of Oral Surgery, Shizuoka-Shimizu Municipal Hospital, Shimizu; and [4]Department of Clinical Research, Chiba Tokushukai Hospital, Funabashi, Japan

To whom correspondence should be addressed: Isao Kitahara, M.D., Ph.D. [E-mail: isao.k@tokushukai.jp]

Citation: World Neurosurg. (2015) 84, 4:1080-1083.
http://dx.doi.org/10.1016/j.wneu.2015.05.024

*Journal homepage: **www.WORLDNEUROSURGERY.org***

*Available online: **www.sciencedirect.com***

with a female preponderance (male/female ratio, 2:5). Arterial compression was found in only 2 patients and they were concomitantly diagnosed with SUNCT according to the criteria in the International Classification of Headache Disorders, 3rd edition (beta version) (ICHD-3beta) (7).

Surgical Procedure

In the surgical treatment of SUNCT, a Jannetta procedure (1, 9) was essentially performed with a slight modification. Briefly, after craniotomy and dural opening, an operating microscope was brought in to identify the site of arterial compression. The culprit vessel was carefully dissected from the nerve to be freed from any adhesion. The vessel loop was mobilized away and was affixed to the cerebellar tentorium or petroclival dura mater by a small strip of Teflon felt with fibrin glue.

RESULTS

Case 1

In the spring of 2012, a 52-year-old man presented with a severe pain attack occurring over the right orbital area, accompanied by several autonomic symptoms, such as conjunctival injection, tearing, and rhinorrhea (Figure 1). These are typical clinical aspects of SUNCT syndrome. In November 2012, he was taken to our emergency room due to a bout of intense headache. The pain triggered by combing his hair was described as electric or lancinating (Visual Analog Scale score, 99), localized in the distribution of the first branch of the right trigeminal nerve. The severe attacks consisted of many stabs and did not resolve to normal, yielding a saw-tooth pattern (4) of pain lasting 6 minutes. There was no refractory period. Although carbamazepine had been tried previously with a slight response, it was ineffective on this occasion. In addition, the remission phase had disappeared before our treatment. Brain MRI suggested that a loop of the vertebral artery was compressing the trigeminal nerve from the lateral surface of the first branch (Figure 2A). According to ICHD-3beta (7), the patient was diagnosed with a subtype of trigeminal neuralgia and thus MVD was performed. At surgery, there was clear compression at the first branch side of the trigeminal root exit zone by the vertebral artery (Figure 2B). Microscopic demyelination was not observed. Just after the compression was resolved by surgery, the intense pain and all the accompanying signs and symptoms of SUNCT disappeared. There has been no recurrent attack so far (February 2015).

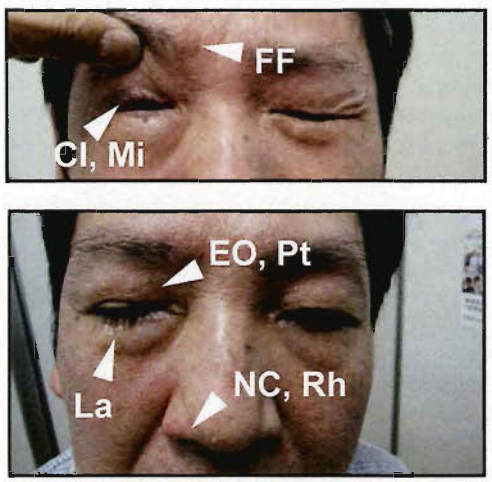

Figure 1. Autonomic symptoms or signs, ipsilateral to the pain, observed in case 1. Cl, conjunctival injection; EO, eyelid oedema; FF, forehead and facial flushing; La, lacrimation; Mi, miosis; NC, nasal congestion; Pt, ptosis; Rh, rhinorrhea.

Case 2

A 71-year-old man complained of headache attacks since January 2009 for 1 month. A severe headache lasting from a couple of seconds to minutes and spreading over the right orbit was accompanied by autonomic symptoms of SUNCT, such as conjunctival injection, tearing, and rhinorrhea. In June 2012, the patient presented with another shock-like pain in the distribution of the third branch of the trigeminal nerve. In August, the symptoms of SUNCT reappeared and lasted for almost 1 month after a remission phase. Because this patient experienced adverse effects with carbamazepine, zonisamide 400 mg/day and pregabalin 300 mg/day were administered. Although the attacks had decreased in frequency, the pain had not disappeared completely. In December, the attacks had worsened; paroxysms occurred in the area of distribution of the second branch, meaning that he experienced pain in the distribution of all branches. MRI suggested that compression of the trigeminal nerve was from both the sides of the first branch and the second and third branches (Figure 2C). Thus, we performed MVD, as trigeminal neuralgia was diagnosed although there was minor discrepancy with the ICHD-3beta description (7). At surgery, we found that the root exit zone was significantly compressed from the side of the first branch of the trigeminal nerve by the superior cerebellar artery and, in addition, from the side of the second and third branches by the anterior inferior cerebellar artery (Figure 2D). Demyelination was not observed microscopically. After the compression from both sides was resolved, the symptoms and severe pain immediately resolved. No recurrence has been observed during the last 2 years.

DISCUSSION

We have demonstrated that MVD was effective to treat SUNCT in 2 cases and yielded a complete response to resolve intense pain. The successful results of surgical treatment suggest that the symptoms of SUNCT were induced by compression of the trigeminal root exit zone from the side surface of the first branch by either the vertebral artery or the superior cerebellar artery.

Among 251 patients who underwent MVD to treat typical trigeminal neuralgia, 2 cases (1%) presented the symptoms of SUNCT. In both cases, arterial contact was identified at the root exit zone of the first branch of the trigeminal nerve. Therefore, it was assumed that SUNCT was at least partly due to the stimuli induced by physical interaction between the intracranial artery and the exiting trigeminal nerve root from the brainstem. Furthermore, we propose that arterial contact occurred at the side surface of the nerve fascicle, where the first branch of the trigeminal nerve

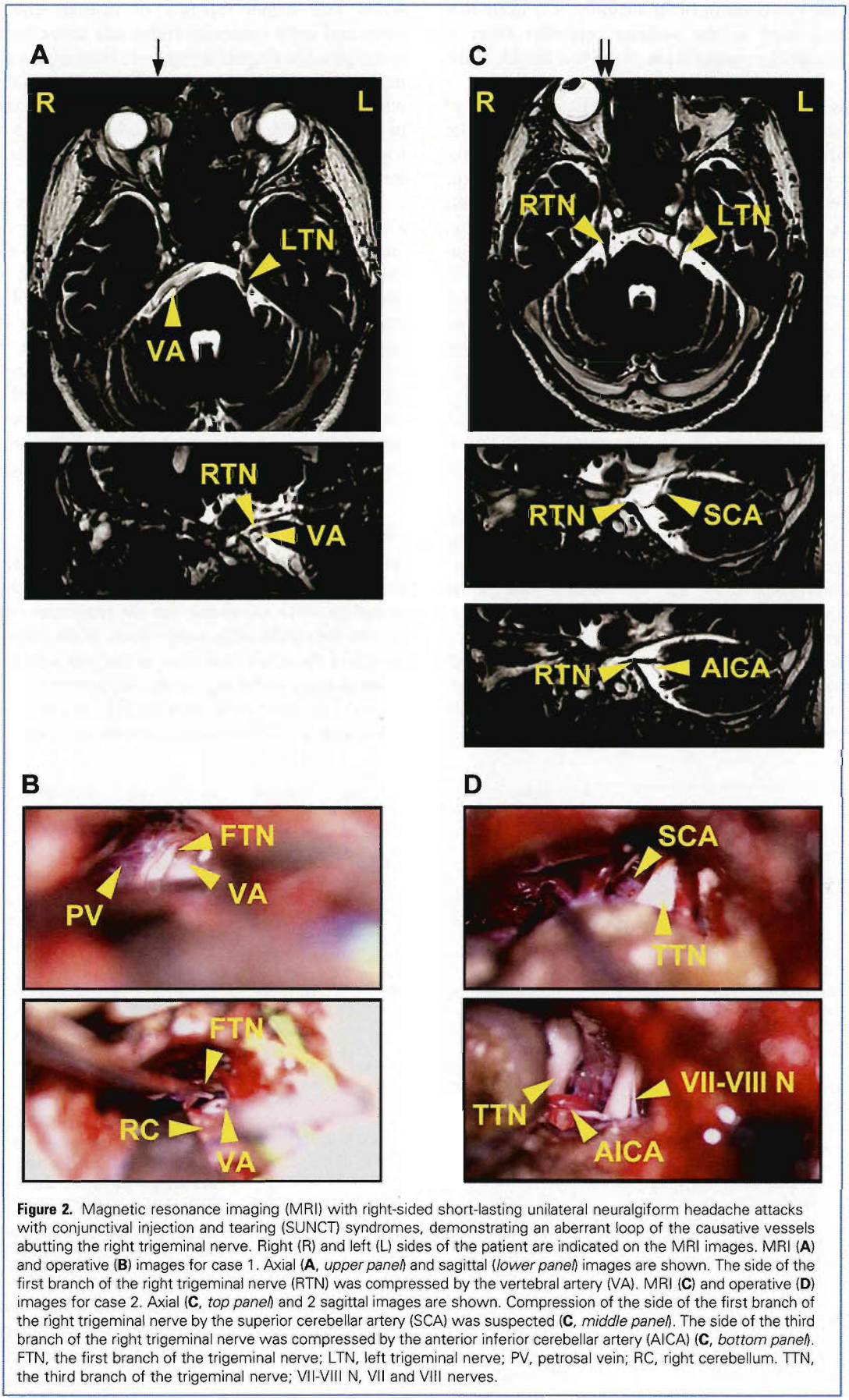

Figure 2. Magnetic resonance imaging (MRI) with right-sided short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) syndromes, demonstrating an aberrant loop of the causative vessels abutting the right trigeminal nerve. Right (R) and left (L) sides of the patient are indicated on the MRI images. MRI (**A**) and operative (**B**) images for case 1. Axial (**A**, *upper panel*) and sagittal (*lower panel*) images are shown. The side of the first branch of the right trigeminal nerve (RTN) was compressed by the vertebral artery (VA). MRI (**C**) and operative (**D**) images for case 2. Axial (**C**, *top panel*) and 2 sagittal images are shown. Compression of the side of the first branch of the right trigeminal nerve by the superior cerebellar artery (SCA) was suspected (**C**, *middle panel*). The side of the third branch of the right trigeminal nerve was compressed by the anterior inferior cerebellar artery (AICA) (**C**, *bottom panel*). FTN, the first branch of the trigeminal nerve; LTN, left trigeminal nerve; PV, petrosal vein; RC, right cerebellum. TTN, the third branch of the trigeminal nerve; VII-VIII N, VII and VIII nerves.

is located. From the viewpoint of brain anatomy, it is likely that either the vertebral artery or the superior cerebellar artery is responsible for the vascular compression of the first branch of the trigeminal nerve.

Our hypothesis explains several characteristic symptoms of SUNCT. First, vascular compression of the trigeminal nerve from the side surface of the first branch could account for cranial autonomic symptoms or signs in the distribution of the first branch, such as conjunctival injection and/or lacrimation, nasal congestion and/or rhinorrhea, eyelid oedema, forehead and facial sweating, forehead and facial flushing, sensation of fullness in the ear, and miosis and/or ptosis (7). Second, because the vertebral artery is thicker than the vicinal superior cerebellar artery and the anterior inferior cerebellar artery, and often has higher tortuosity as seen in dolichoectasia, it leads to intensive compression with a larger contact area on the surface of the trigeminal nerve. Therefore, the culprit vessel may contribute to prolonged and intensified attacks, resulting in the distinctive saw-tooth pattern of pain (4) and the absence of the refractory period usually observed in typical trigeminal neuralgia. Alternatively, the superior cerebellar artery could also put robust pressure on the trigeminal nerve. In this case, a tight bend of an arterial loop should be taken into account. Third, the pain associated with SUNCT/SUNA can be much more aggressive than typical trigeminal cephalalgias. Possibly, the compression from the first branch side is so intensive that carbamazepine could prove ineffective. In case 1, the pain was so severe as to result in suicidal ideation.

Although the literature suggests that several anticonvulsant drugs (10), such as lamotrigine, gabapentin, and topiramate, can be effective, no comparative study has been carried out, mainly because of the low prevalence rate of SUNCT/SUNA. Practically, it seems that higher intensity of vascular compression of the trigeminal nerve eventually makes this severe head pain refractory to any pharmacological treatments. Pioneering works with surgical treatment or deep brain stimulation have certainly achieved better results (2, 6, 8, 11-15). Definitive diagnosis and complete remission of SUNCT/SUNA are not easy to achieve because of the low prevalence rate and the technical difficulty of surgery (3, 5), in particular, for compression from the first branch side.

We assume that axial imaging on MRI does not often project a clear image of the arterial contact, because the culprit vessel interacts with the nerve from within the inner side of the brain. Therefore, when SUNCT or SUNA is suspected, it is undoubtedly advisable to compare axial, coronal, and sagittal planes in diagnostic imaging on MRI, focusing on the first branch of the trigeminal nerve, to identify arterial contact with the nerve. Intensive compression from the side of the first branch may be accompanied eventually by contact from the second or third branch side, as observed in case 2. Such widespread compression of the trigeminal nerve may yield variable intensity, sites, and duration of head pain, in contrast to the typical pain observed in regular trigeminal neuralgia.

CONCLUSIONS

We conclude that a dramatic response was achieved when SUNCT syndrome, with evidence of neurovascular conflict on MRI, was treated by MVD. We found that the symptoms of SUNCT in our 2 patients were induced by compression of the side surface of the first branch of the trigeminal nerve at the root exit zone by either the vertebral artery or the superior cerebellar artery. We assume that the surgical procedure could be applicable to patients previously diagnosed with SUNCT in order to resolve their aggressive head pain.

REFERENCES

1. Barker FG 2nd, Jannetta PJ, Bissonette DJ, Larkins MV, Jho HD: The long-term outcome of microvascular decompression for trigeminal neuralgia. N Engl J Med 334:1077-1083, 1996.

2. Bartsch T, Falk D, Knudsen K, Reese R, Raethjen J, Mehdorn HM, Volkmann J, Deuschl G: Deep brain stimulation of the posterior hypothalamic area in intractable short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT). Cephalalgia 31:1405-1408, 2011.

3. Black DF, Dodick DW: Two cases of medically and surgically intractable SUNCT: a reason for caution and an argument for a central mechanism. Cephalalgia 22:201-204, 2002.

4. Cohen AS, Matharu MS, Goadsby PJ: Short-lasting unilateral neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) or cranial autonomic features (SUNA)—a prospective clinical study of SUNCT and SUNA. Brain 129: 2746-2760, 2006.

5. Favoni V, Grimaldi D, Pierangeli G, Cortelli P, Cevoli S: SUNCT/SUNA and neurovascular compression: new cases and critical literature review. Cephalalgia 33:1337-1348, 2013.

6. Gardella L, Viruega A, Rojas H, Nagel J: A case of a patient with SUNCT syndrome treated with Jannetta procedure. Cephalalgia 21:996-999, 2001.

7. Headache Classification of the International Headache Society: The International Classification of Headache Disorders, 3rd edition (beta version). Cephalalgia 33:629-808, 2013.

8. Irimia P, Gonzalez-Redondo R, Dominguez PD, Diez-Valle R, Martinez-Vila E: Microvascular decompression may be effective for refractory SUNCT regardless of symptom duration. Cephalalgia 30:626-630, 2010.

9. Jannetta PJ: Arterial compression of the trigeminal nerve at the pons in patients with trigeminal neuralgia. J Neurosurg 26 (Suppl):159-162, 1967.

10. Lambru G, Matharu MS: SUNCT and SUNA: medical and surgical treatments. Neurol Sci 34 (Suppl 1):S75-81, 2013.

11. Leone M, Franzini A, D'Andrea G, Broggi G, Casucci G, Bussone G: Deep brain stimulation to relieve drug-resistant SUNCT. Ann Neurol 57: 924-927, 2005.

12. Lyons MK, Dodick DW, Evidente VG: Responsiveness of short-lasting unilateral neuralgiform headache with conjunctival injection and tearing to hypothalamic deep brain stimulation. J Neurosurg 110:279-281, 2009.

13. Sebastian S, Schweitzer D, Tan L, Broadley SA: Role of trigeminal microvascular decompression in the treatment of SUNCT and SUNA. Curr Pain Headache Rep 17:332-342, 2013.

14. Williams M, Bazina R, Tan L, Rice H, Broadley SA: Microvascular decompression of the trigeminal nerve in the treatment of SUNCT and SUNA. J Neurol Neurosurg Psychiatry 81:992-996, 2010.

15. Williams MH, Broadley SA: SUNCT and SUNA: clinical features and medical treatment. J Clin Neurosci 15:526-534, 2008.

Conflict of interest statement: The author declares that the article content was composed in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received 5 March 2015; accepted 18 May 2015

Citation: World Neurosurg. (2015) 84, 4:1080-1083. http://dx.doi.org/10.1016/j.wneu.2015.05.024

Journal homepage: ***www.WORLDNEUROSURGERY.org***

Available online: ***www.sciencedirect.com***