

Pain Relief in Short-Lasting Unilateral Neuralgiform Headache with Conjunctival Injection and Tearing Syndrome with Intravenous Ketamine: A Case Report

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Abstract

Purpose: Short-lasting unilateral neuralgiform headache with conjunctival injection and tearing (SUNCT) is a rare form of primary headache, classified as trigeminal autonomic cephalalgia. Since the underlying mechanism of the pathogenesis has not yet been determined, a standardized therapeutic strategy for SUNCT is unavailable. We present a case of SUNCT syndrome with successful pain relief by intravenous administration of ketamine, an N-methyl-D-aspartate receptor (NMDAR) antagonist.

Case report: A 56-year-old male patient reported severe throbbing and shooting pain in forehead, temporal and periorbital region. We confirmed conjunctival injection, lacrimation, blepharoptosis, and miosis as symptoms related to autonomic activity, and made a diagnosis of SUNCT based on ICHD-3 beta. Numerous treatments were attempted, including pregabalin, gabapentine, non-steroidal antiinflammatory drugs, acetaminophen, steroids, antidepressants, triptans, nerve blocks, and intravenous lidocaine with unsatisfactory results. Intravenous administration of ketamine (0.4 mg/kg) for one hour, was found to relieve the severe pain.

Conclusion: Intravenous ketamine can effectively treat SUNCT syndrome. This case demonstrated that involvement of NMDAR could be one of the mechanisms of SUNCT syndrome pathogenesis and establish a therapeutic strategy for this pain syndrome.

Keywords: SUNCT; Ketamine; NMDA receptor, Trigeminal neuralgia; neuropathic pain.

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INTRODUCTION

Short-lasting, unilateral, neuralgiform headache attacks with conjunctival injection and tearing (SUNCT) is

a syndrome characterized by short-lived, strictly unilateral, orbital, moderate-to-severe pain attacks, accompanied by rapidly developing conjunctival injection and lacrimation⁽¹⁾. The attacks occur several times during daytime hours

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and last for few minutes. The attacks are often very severe and adversely affect the patients' quality of life. Little is known about the mechanisms underlying the SUNCT syndrome. Although there have been some reports for the treatment of this syndrome, a satisfactory therapeutic strategy has yet to be established. Therefore, it is necessary to accumulate sufficient knowledge about the syndrome and establish a satisfactory treatment protocol.

We report the case of a 56-year-old male patient with SUNCT syndrome, wherein the syndrome-associated pain was relieved by administering ketamine. This case report helps determine the mechanism and establish a therapeutic strategy for this pain syndrome.

CASE REPORT

A 56-year-old male patient experienced shooting pain in the upper right orbit in September X-1 year. The patient consulted a neurosurgeon, and carbamazepine (300 mg/day) was prescribed for a diagnosis of trigeminal neuralgia. Although carbamazepine relieved the pain for 6 months, the pain recurred in the upper right orbit and oral cavity, associated with mastication or tooth brushing. Therefore, the patient visited our hospital in February X (year).

A similar diagnosis of trigeminal neuralgia (1 and 2 branches) was made because the magnetic resonance imaging (MRI) showed trigeminal nerve root compression by the superior cerebellar artery at the right cerebellopontine angle, and carbamazepine relieved the pain. We recommended an increased dosage of

carbamazepine (400 or 600 mg/day); however, the patient reported dizziness, which adversely affected his work as a driver. Although we recommended nerve block, gamma knife, and neurovascular decompression, the patient declined and stopped visiting our hospital.

In X+5 (year), the patient re-visited our hospital to receive nerve block because the frequency of the pain attacks and extent of the pain had increased after his work shift changed from day to night. The short attacks previously lasting few seconds, now occurred 100-200 times/day and lasted few hours. The patient felt severe throbbing and shooting pain in the forehead, temporal, and periorbital regions, and reported similar pain in the right upper first molar region. We confirmed conjunctival injection, lacrimation, blepharoptosis, and miosis as symptoms related to autonomic activity (Figures 1, 2). These autonomic symptoms were not detected during the first visit to our hospital in X (year). The brush sweeping evoked shaking and burning pain, and pinprick test elicited stronger pain than in the healthy side not only in the forehead region, but also in the temporal and parietal regions. There were no abnormal results in the blood or biochemical examinations. We made a diagnosis of SUNCT based on ICHD-3 beta.

We prescribed triptans, including sumatriptan, rizatriptan, eletriptan, and zolmitriptan. Although the patient consumed each drug for one week, there was no improvement in the pain attacks. Additionally, we administered sumatriptan subcutaneously, but this was ineffective and resulted in nausea. We then administered other drugs, including non-steroidal anti-inflammatory

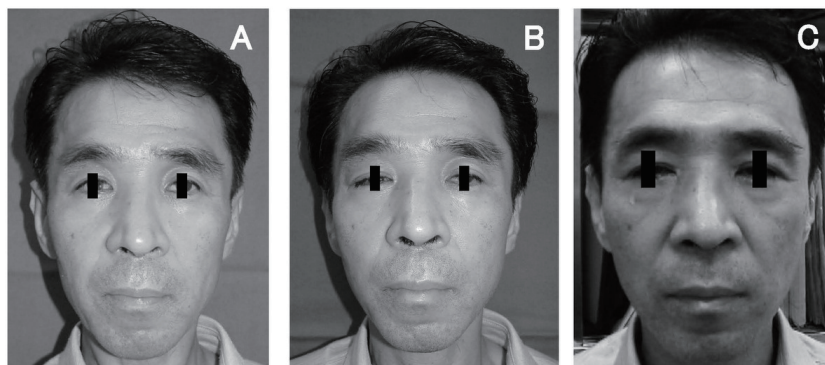


Fig. 1. A: Face at normal time; B and C: Face during attack time (B: Blepharoptosis; C: Lacrimation)

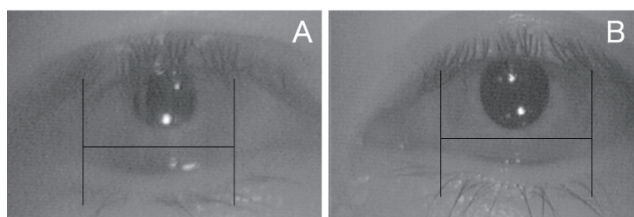


Fig. 2. A: Right side of the eye (Miosis and blepharoptosis are observed); B: Left side of the eye

drugs, acetaminophen, steroids, pregabalin, gabapentine, and antidepressants, but they too were ineffective. Only carbamazepine improved the attacks, so we prescribed carbamazepine (>300 mg/day). However, the patient declined our recommendation because carbamazepine caused dizziness, which adversely affected his work.

We performed supraorbital and auriculotemporal nerve block with 1% carbocaine during the attacks as a test block. These nerve blocks relieved the shooting pain, but burning pain remained. Furthermore, we performed trigger point injection and stellate ganglion block with 1% carbocaine, but these nerve blocks were ineffective.

Previous studies have shown that intravenous lidocaine administration relieved the attacks of SUNCT⁽²⁾ and trigeminal neuralgia. Therefore, this patient was administered lidocaine (2 mg/kg) intravenously for 30 minutes, after which the attacks were relieved moderately. However, the effect of lidocaine lasted only for an hour, and the pain reappeared.

The patient requested greater and longer pain relief. As the pain characteristics of this case resembled neuropathic pain, we administered ketamine (0.4 mg/kg) intravenously for one hour^(3,4). He did not experience any of the side-effects associated with ketamine, such as dizziness, light headedness, tiredness, sedation, headaches or hallucinations. The intravenous administration of ketamine relieved the pain attacks of SUNCT sufficiently, and provided longer pain relief that lasted for 24 hours. Intravenous ketamine was administered daily for a week, and then continued twice a week for one month and once a week for a month. Three months after commencement of intravenous ketamine, the pain attacks of SUNCT disappeared without intravenous ketamine administration. The administration of carbamazepine (200 mg/day) has been continued and the attacks are now well controlled.

DISCUSSION

This case was first diagnosed as trigeminal neuralgia and then as SUNCT five years later. Previous studies have reported a transformation from trigeminal neuralgia having a long process to SUNCT⁽⁵⁾. Thus, SUNCT may be a subtype of trigeminal neuralgia. However, the established treatment for trigeminal neuralgia, nerve block with local anesthetics, and administration of carbamazepine did not relieve the pain in our case of SUNCT. Therefore, the mechanisms of pain expression of SUNCT may differ from trigeminal neuralgia⁽⁶⁾.

Trigeminal neuralgia is caused by compression of the trigeminal nerve root by the superior or anterior inferior cerebellar artery at the cerebellopontine angle. This compression injures the nerve's protective myelin sheath leading to demyelination, which can cause spontaneous impulses from the injured nerve trunk. These impulses are conducted to afferent and efferent sides. Therefore, the trigeminal ganglion shows hyperactivity, and the nociceptive nerves are repeatedly excited. The patient was not given sufficient carbamazepine to control the attacks completely to avoid the side effect of dizziness. The patient had suffered severe pain for four years. Long-term, poorly controlled trigeminal neuralgia probably caused the onset of SUNCT. The noxious stimuli caused by trigeminal neuralgia can cause peripheral and central nerve sensitization, which may in turn have led to SUNCT syndrome development in this case.

Intravenous administration of lidocaine, sodium channel blocker partially relieved the attacks. It is known that sodium channels are involved in the pathogenesis of neuropathic pain, and that intravenous administration of lidocaine relieves neuropathic pain⁽⁷⁾. The patient showed symptoms of neuropathic pain, including allodynia and hyperalgesia in the painful regions⁽⁸⁾. These observations suggested that one of the probable pathogenic mechanisms of SUNCT could involve neuropathic pain. In our case, administration of ketamine, which is often used for the treatment of neuropathic pain⁽⁹⁾, relieved the attacks completely. Ketamine is predominately a non-competitive NMDAR antagonist but also has interactions on multiple receptor systems (e.g. opioid receptors, sigma receptor, muscarinic acetylcholine receptor, gamma-aminobutyric

acid receptors, α -amino-3-hydroxy-5-methyl-4-isoxazole propionic acid receptor), and inhibition of Na⁺ and K⁺ ion channels, activation of descending inhibitory pathways within the central nervous system⁽¹⁰⁾. In neuropathic pain, however, its main mechanism of action is a blockade of sensitized NMDAR⁽¹¹⁾. Thus, we can make hypothesis that NMDA receptors involvement can be one of the underlying mechanisms of SUNCT. However, further studies are required to clarify the mechanisms of SUNCT syndrome.

CONCLUSION

In this case, intravenous ketamine relieved the SUNCT pain, thus suggesting that the pathogenesis of this disease probably involves NMDAR. Intravenous ketamine could be the treatment strategy for SUNCT.

Disclosure of conflict of interest

The authors have no financial support or conflicts of interest to disclose.

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