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A case of severe trigeminal neuralgia: recovery by means of stellate ganglion block with procaine. Discussion of possible mechanisms of action

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Abstract

Drug and invasive treatment options for trigeminal neuralgia (TN) are often fraught with problems. Knowledge of the involvement of the autonomic nervous system, especially the sympathetic portion, in the pain process has grown rapidly in recent years. Both nociceptive and neuropathic pain can be maintained by the sympathetic nervous system, known as 'sympathetically maintained pain' (SMP). This current case report describes a patient with refractory TN that was treated with a stellate ganglion block (SGB). After the first SGB, the patient experienced significant pain relief that became long-lasting after repeated application of the SGB. These findings suggest that this patient had a high level of SMP. In patients with a low percentage of SMP, SGB may be less or not successful. A literature search did not find any case reports or studies about patients with refractory idiopathic TN treated with sympathetic blocks using local anaesthetics. From our point of view, it might be useful to test by means of SGB the extent to which an individual has SMP present, and, if that is the case, to perform a short series of SGB, as done in this current patient. Studies are needed to provide further insights.

Keywords

Trigeminal neuralgia, autonomic nervous system, stellate ganglion block, neural therapy

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Introduction

Trigeminal neuralgia (TN) is a form of chronic facial pain in the sensitive supply area of the trigeminal nerve, the 5th cranial nerve.[1] The incidence of TN is 4–27/100 000 per year, with women affected more often

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than men.[2,3] The main age of onset is in the 5th decade of life.[2–5] Patients with TN characteristically suffer from unilateral, flashing pain in the area of any of the trigeminal branches V1, V2, or V3. Typical trigger factors are speaking, touching the face, shaving, and chewing. The pain attacks usually last only seconds to minutes at most; patients are usually pain-free during the intervals.[1,6]

The International Headache Society divides TN into the following subtypes:[1] (i) classical TN when pathological neurovascular contact between the superior cerebellar artery and the root of the trigeminal nerve is suspected; (ii) idiopathic TN when no morphological changes are detectable, with high-resolution magnetic resonance imaging and neurophysiological tests being inconspicuous; (iii) secondary TN when there is neuralgia in the setting of an underlying disease, e.g. multiple sclerosis or tumours.

First-line therapy in the treatment of TN consists of anticonvulsants.[4] Due to numerous drug interactions and central nervous system side-effects, long-term therapy with these drugs is often difficult and unsatisfactory.[5] Conventional analgesics such as nonsteroidal anti-inflammatory drugs, non-opioid analgesics and opioids, have not been shown to be effective and are not recommended for the treatment of TN.[7] If conservative methods fail, invasive interventions may be considered. These are divided into ablative and non-ablative procedures.[5] Microvascular decompression after Janetta, the only non-ablative procedure, is the preferred procedure for classical TN and provides the best outcome in terms of pain relief, complication rate and recurrence rate.[2] Several ablative procedures, such as gamma knife surgery and radiofrequency thermocoagulation, are competing with each other for treating idiopathic TN.[5,6,8,9]

All sympathetic efferent fibres for the head (and ipsilateral upper quarter of the body) pass through the stellate ganglion (SG) and part of it ascends further cranially via the cervical superior ganglion. This gives the possibility of an intervention at the SG with local anaesthetics (LA), which is wide-ranging (Figure 1) and includes a wide variety of indications as shown previously.[10–13]

Based on the difficulties in treating TN and the increasing knowledge of sympathetically maintained pain (SMP),[14] a patient with refractory TN was treated with a stellate ganglion block (SGB). This current case report describes the treatment course and discusses the role of the sympathetic nervous system and possible mechanisms of action.

Case report

In May 2016, an 82-year-old female patient of normal weight was referred to the Department of Complementary and Integrative Medicine, University of Bern, Bern, Switzerland for pain therapy. She was an otherwise healthy woman who had been suffering for more than 20 years from shooting, electrifying pain attacks in the right cheek and lower jaw region. The pain was triggered by chewing, talking, and touching the right side of the face and occurred between 20 and 40 times a day with a visual analogue scale (VAS) pain score of 9–10. The attacks also occurred approximately five times each night, considerably disturbing her sleep. The patient had been examined by neurologists who, after ruling out pathological neurovascular contact, diagnosed her with idiopathic TN II/III. The patient received 200 mg/day carbamazepine orally for 3 years, but this did not provide sufficient analgesic effects and was poorly tolerated by the patient due to the typical side-effects of fatigue and drowsiness. Other analgesic substances were equally ineffective. Acupuncture, too, failed to relieve the pain.

The patient was treated with a SGB according to the technique described in 2016.[11]

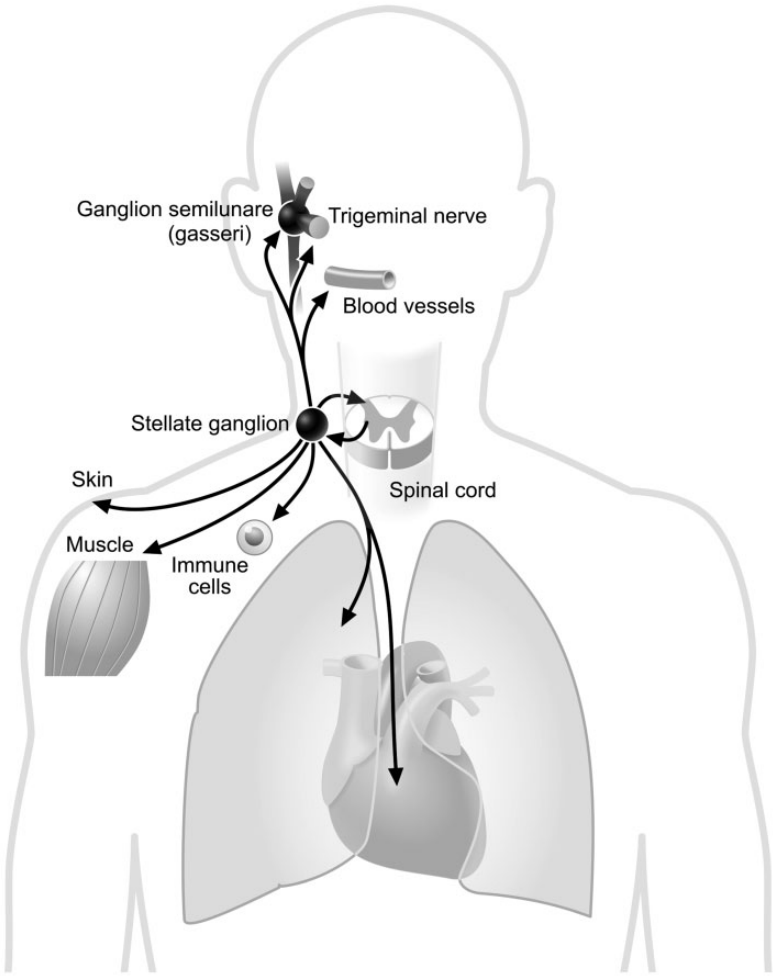

Figure 1. The stellate ganglion supplies various organs and organ systems. This simplified illustration shows the stellate ganglion and its efferents supplying all organ systems of the ipsilateral upper body quarter: somatic nerves via vasa nervorum (here: trigeminal nerve), blood vessels, the musculoskeletal system, internal organs and immune cells, via which the sympathetic nervous system can control inflammation and pain. For the sake of clarity, afferents in the sympathetic trunk, vagus nerve and nociceptors are not shown. They are nevertheless important, since they complete positive feedback loops that play an important role in the pain and inflammation processes. The short interruption of these feedback loops by injection of local anaesthetic to the stellate ganglion gives the system the chance to reorganize itself. Based on experience, stellate ganglion block is only successful in cases with a large proportion of sympathetically maintained pain.[11,13]

The temporary occurrence of Horner's syndrome is the most important sign of a successful blockade.[11] In our opinion,[15] contraindications of SGB are anticoagulation, severe cardiac decompensation, pathological bradycardia, severe conduction disorders such as second- or third-degree atrioventricular block, recurrent laryngeal or phrenic

nerve palsy on the opposite side, and massive pulmonary emphysema (risk of pneumothorax).

In the current patient, the SGB caused a complete cessation of pain attacks after only a few minutes, so that the patient was able to discontinue carbamazepine. After a few days, she again experienced a mild onset of pain when touching the skin in the morning (VAS 4), so the SGB was repeated once. After that, the patient was completely pain-free for 10 months. When pain attacks occurred again, but much milder ones (VAS 3), another SGB was performed (i.e. after 10 pain-free months) and again 3 months later. Since then, the patient has been completely pain-free (observation time 5 years). Apart from slight dizziness, which subsided a few minutes after the SGB was performed, no side-effects were observed in the current patient.

The reporting of this case conforms to CARE guidelines.[16] Signed informed consent to treatment and to publish was obtained from the patient. All patient details were de-identified.

Discussion

Our research group has used SGB primarily in the treatment of complex regional pain syndrome, post-zoster neuralgia, Raynaud's syndrome, traumatic brain injury, certain forms of headache, and as an adjuvant therapy in viral pneumonia.[13,15,17] The successful treatment of this current patient demonstrates that SGB can achieve rapid and long-lasting pain relief in certain TN patients that respond poorly to conventional therapy. The suggested hypothesis to explain this success is that the autonomic nervous system (ANS), particularly the sympathetic nervous system, may be significantly involved in the development and maintenance of TN symptomatology in some patients. The following is a review of the possible pathophysiological mechanisms that support the use of therapy for TN with a LA.

Pathophysiological considerations

Coupling processes. Under physiological conditions, the sympathetic nervous system has no influence on nociceptive afferent fibres. However, under pathological conditions (e.g. after a lesion), the efferent sympathetic system can short-circuit with nociceptive afferents,[14,18] which is called 'sympatho-afferent coupling'. It takes place at the following locations: (i) in the area of the extracellular matrix;[14,18,19] (ii) nociceptive nerve fibres can express catecholamine receptors after a lesion in their plasma membranes and thus can become susceptible to norepinephrine;[18,20–22] (iii) in the area of the spinal ganglia after spinal nerve lesions, so called 'sympathetic sprouting' can occur (although the analogy to the trigeminal ganglion has not been sufficiently clarified).[18,22–25] In summary, due to sympatho-afferent coupling processes, the efferent sympathetic nervous system can cause the activation of afferent nociceptive fibres, resulting in pain.[14,18,26]

Sensitization processes. Sensitization processes can lead to peripheral and central neuroplastic changes. These processes can also take place in sympathetic ganglia and can result in potentiation of the postsynaptic response to renewed consistent presynaptic stimulation.[27] Thus, the sympathetic nervous system can engrammatically store stimuli and responds to renewed physiological stimuli with an overshooting pathological response.[13,27–29] This is equated to a learning and memory process.[30] Any additional activation of the sympathetic nervous system (e.g. emotions or additional peripheral stimulation) can feed into the system and lead to increased pain,[15,31] involving positive feedback loops.[10,13,15,26]

Neuroimmunological interaction. Trigeminal neuralgia does not appear to be purely neuropathic pain. A previous study demonstrated that inflammation plays an important role in the aetiology and progression of TN.[32] Previous research has shown that the ANS and the immune system (and thus the inflammatory cascade) are inextricably coupled, with intense communication between autonomic nerve fibres and immune and inflammatory cells.[13,33,34] Further communication occurs between the periphery and the central nervous system (brain, brainstem and spinal cord).[35] In this process, sympathetic nerve fibres originating from the SG play an important role in the generation of pathological positive feedback loops leading to inflammation and pain.[13]

Sympathetically maintained pain in our patients. Coupling, sensitization processes and neuroimmunological interactions, together with the involvement of the sympathetic nervous system, cause so-called SMP.[18] Sympathetic blocks, in the current case the SGB, indicate, at least for the duration of action of the local anaesthetic, whether and to what extent pain is sympathetically maintained.[15,17,36] Interestingly, both neuropathic and nociceptive pain can be maintained by the sympathetic nervous system. SMP occurs to very different degrees in different patients.[18] Incidentally, SMP is also possible without clinically observable accompanying autonomic symptoms. How strongly a patient responds to a sympathetic blockade depends on how large the sympathetically maintained portion of the pain is. If only 20% of the pain is sympathetically maintained, only a 20% reduction in pain can be achieved for the duration of the sympathetic blockade. The sympathetically maintained percentage of the pain can change over the course of the pain disorder and varies from patient to patient.[18]

In view of the immediate improvement of neuralgia symptoms after application of the SGB in the current patient, it would be safe to assume that a large proportion of their pain was sympathetically maintained. In two other patients with refractory TN who were later referred to our clinic, the application of SGB resulted in less marked success in one case and no improvement in the other. It is assumed that the sympathetically maintained part of the pain in these latter patients was small.

Possible mechanisms of action

Much is still unknown but the long-term improvement after injection of procaine to the SG in the current patient suggests a desensitization and learning process that can be based on different mechanisms as follows. One important mechanism is the SGB-induced interruption of positive feedback loops maintained by the sympathetic nervous system,[13] allowing the pain processing system to reorganize itself after the short interruption.[10,13,15,28,31,37] Injection of procaine also generally inhibits peripheral sensitization of nociceptive neurons;[38] and the SGB has a regulating effect on the extracellular matrix. In this way, sympathetic afferent coupling is reduced and microcirculation in the matrix is improved,[15] which in turn counteracts peripheral sensitization. It can also be imagined that by regulating sympathetic innervation of the vasa nervorum by means of SGB, oxygenation of the trigeminal nerve and its ganglion can be improved.

Literature research

A literature search did not find any case reports or studies about patients with refractory idiopathic TN also treated with sympathetic blocks with LA. Two previous reports described the successful treatment of patients with secondary TN by means of SGB using mepivacaine and ropivacaine.[39,40] A similar case was published in

2013 that described a young man with atypical facial pain who was successfully treated with a SGB using 5 ml of bupivacaine 0.25% mixed with 8 mg of dexamethasone.[41] In that case, it was not clear which part of the success was due to the LA or to the steroid.[41]

In conclusion, this current case report described the successful treatment a patient with refractory TN by the repeated application of SGB using the LA procaine 1% and discussed the role of the sympathetic nervous system and possible mechanisms of action. The degree of pain reduction after SGB provides information about the proportion of SMP in each case of TN (at least for the duration of action of the LA). It is still unclear why this proportion varies between individuals (not only in TN). Only patients with a high proportion of SMP can benefit from an SGB. To identify these patients, performing an SGB with an LA (preferably procaine 1%) is recommended. As shown previously,[11] SGB performed *lege artis* is a low-risk and cost-effective treatment option for patients with TN and could be considered, in our opinion, in cases of drug ineffectiveness or intolerance as well as before performing invasive procedures with uncertain therapeutic value and potential complications. Studies are needed to provide further insights into SGB in TN. Further research on the ANS in pain, (auto)immune and inflammatory processes will provide further important pathophysiological insights and new therapeutic options.

Author contributions

C.A.L. performed the literature research, drafted a first summary and interpreted the mechanisms of action. L.F. treated the patient and participated in the interpretation of the findings. Both authors read and approved the final manuscript.

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