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Case Report

Successful Treatment of Digital Ulcers in a Scleroderma Patient with Continuous Bilateral Thoracic Sympathetic Block

Kyung Ream Han, MD, PhD, Chan Kim, MD, PhD, and Eun Jung Park, MD

From: Pain Clinic, Department of Anesthesiology and Pain Medicine, Ajou University Hospital, Suwon, Korea

Dr. Han is Associate Professor, Pain Clinic, Department of Anesthesia and Pain Medicine, Ajou University Hospital, Suwon, Korea.
Dr. Kim is Director and Professor, Pain Clinic, Department of Anesthesia and Pain Medicine, Ajou University Hospital, Suwon, Korea.
Dr. Park is Fellow, Pain Clinic, Department of Anesthesia and Pain Medicine, Ajou University Hospital, Suwon, Korea.

Address correspondence:
Chan Kim, MD
Department of Anesthesia and Pain Medicine
Ajou University Hospital
San 5 Won-Cheon Dong Pal-Dal Gu,
Suwon, Korea 442-721
E-mail: painhan@hanmir.com

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Background: Raynaud's phenomenon (RP) associated with connective tissue disease (secondary RP) may be difficult to manage with conservative therapy. A combination of sympathetically mediated vasospasm and vaso-occlusion has been implicated as the etiology of digital ischemic phenomenon. Thoracic sympathetic outflow blocking has been performed with various techniques. However, there have been some limitations in all treatment options.

Objective: We report on a patient with medically refractory digital ulceration and gangrene caused by scleroderma who was successfully treated with a continuous infusion of mepivacaine into the thoracic sympathetic ganglions as a means to improve finger circulation.

Case Report: We are reporting on a 32-year-old female patient suffering from a medically intractable gangrenous ulcer in the right third finger and the left second and third fingers, accompanied by aching pain (VAS, visual analogue scale, 5 – 6/10) and numbness in both forearms. She underwent continuous infusion of mepivacaine through the thoracic sympathetic catheter placed in T2 vertebral segment for 13 days on the right and for 11 days on the left and cervical epidural infusion of mepivcaine with fentanyl for 10 days after the medical treatment failed. Her finger temperature increased 2°C – 5°C during the thoracic sympathetic block with continuous infusion of mepivacine. Her finger wounds healed completely with 13 days of the continuous thoracic sympathetic block without any complications.

Conclusions: Continuous infusion of mepivacaine into the thoracic sympathetic ganglionic space led to the healing of the medically refractory gangrenous ulcer of the fingers in the patient with scleroderma.

Key words: Scleroderma, Raynaud's phenomenon, thoracic sympathetic catheter

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Systemic sclerosis (scleroderma) is a connective tissue disease characterized by fibrosis of the skin and internal organs due to increased synthesis and deposition of extracellular matrix (1). Raynaud's phenomenon (RP) is the earliest and most common clinical manifestation of scleroderma, occurring in 90 to 98% of patients (2).

A combination of sympatheticallymediated vasospasm and vaso-occlusive disease has been implicated as the etiology of digital ischemic phenomenon (3,4), and treatment of RP is directed towards relieving vasospasm and restoring nutrient blood flow. Therefore, cervicothoracic or peripheral sympatholysis and digital artery reconstruction have been performed for medically refractory RP with scleroderma even though all procedures have some limitations.

Thoracoscopic symapthectomy has recently been shown to have an initial improvement, although al-

most always relapses 6 months after the treatment (5,6). Surgery of the hand, including digital sympathectomy and arterial reconstruction, for scleroderma might have favorable outcomes (7-12). However, it would be a limited treatment option because of a recurrent ulcer after some period of post-operation (10), delayed wound healing (10,11), and development of complex regional pain syndrome (12).

A decision for the treatment of RP should be based on the severity of symptoms, beginning with the least invasive treatment first followed by further treatments. Another alternative of less invasive treatment for blocking the sympathetic outflow would be a sympathetic or peripheral nerve block with local anesthetics (13-15). These therapies are based on the premise that excessive sympathetic activity may be involved in the pathogenesis of RP.

We describe a patient with medically refractory digital ulceration and gangrene caused by scleroderma who was successfully treated with a continuous infusion of mepivacaine into the cervical epidural space and thoracic sympathetic ganglions as a means to alleviate pain and to improve circulation.

Case Report

A 32-year-old female patient suffering from a medically intractable gangrenous ulcer in both third fingers, accompanied by aching pain (VAS, visual analogue scale, 5 – 6/10) and numbness in both forearms, was admitted in our rheumatology department. She had had a 1-year history of bilateral RP and cold intolerance secondary to scleroderma, and experienced worsening symptoms over the past 6 months, for which she daily took 90 mg nifedipine. In spite of the treatment with nifedipine, the ischemic symptoms progressed to ulcers and gangrene in her fingertips, and her right third fingertip was partially amputated a month prior at another hospital, although remained unhealed.

Physical examination on her admission to our rheumatology department revealed that the dorsal portion of her right third fingertip was partially removed including the nail bed, and the remaining soft tissue of fingertip had a gangrenous dirty wound. Her left second and third fingers had gangrenous ulcers in a very small portion of their tips and a reddish skin color below the digital interphalangeal joints (Fig. 1).

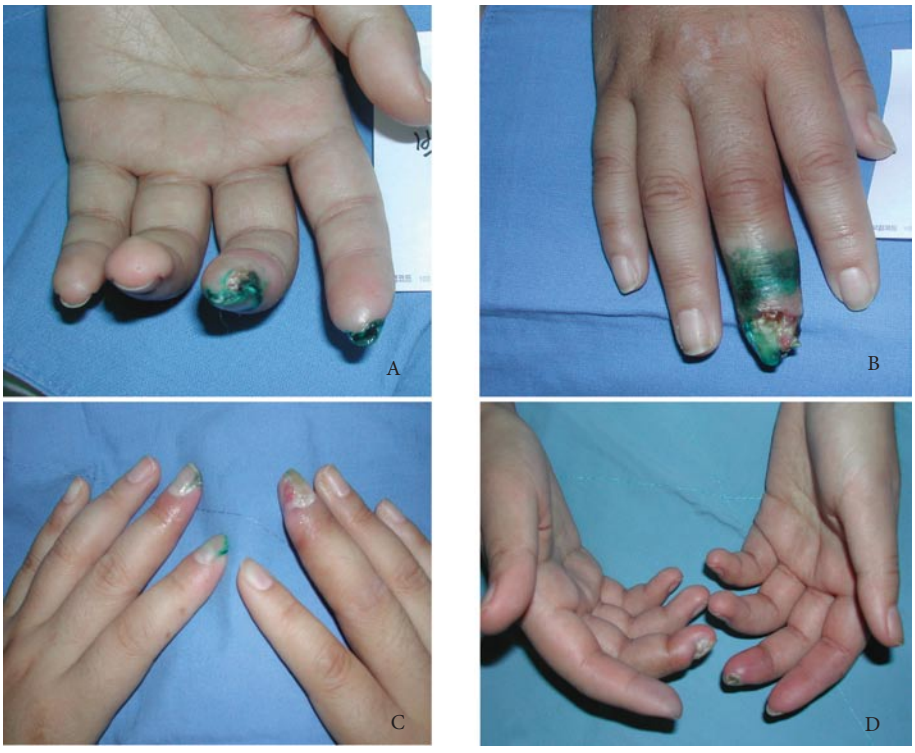

Fig. 1 *(A) and (B) show the fingers at the pre-treatment state. (C) and (D) demonstrate healing of the fingers after the 13 days of mepivacaine infusion for the thoracic sympathetic block.*

Her serum analysis showed positive anti-centromere antibodies (>300 u/ml) and high ANA (antinuclear antibody) titers (1:2560, discrete speckled). Other auto-antibodies were negative. CBC (complete blood count), ESR (erythrocyte sedimentation rate), CRP (C-reactive protein), RF (rheumatoid factor) and LFT (liver function test) were all within normal limits. A skin biopsy was performed in her inguinal area showing dark brown coloration, and the result showed a thickening of dermal collagen fibers. Angiography revealed a segmental occlusion and narrowing of multiple digital arteries in both hands (Fig. 2). She was diagnosed with limited systemic sclerosis, and was treated with medications, including daily nifedipine (90 mg p.o.), cilazapril (2.5 mg p.o.), losartan K (50 mg p.o.), and limaprost (30μg p.o.) as well as intravenous alprostadil (10ug i.v.), for one week at our in-patient clinic. However, there was no improvement of symptoms. She was referred to our pain clinic for the treatment of pain and unaltered wound status of her fingers on the seventh day.

On the first visit to our pain clinic department, she complained that she had suffered more from the worsening of the finger wound than from finger pain. Her finger pain score had a VAS 5 – 6/10 even with non-steroidal anti-inflammatory drug therapy at a resting state, nevertheless she could not perform normal household chores during the past 2 months.

Mepivacaine (0.32%) mixed with fentanyl (400 μg/day) was infused at 5 ml/hr through the cervical epidural catheter (Arrow International, Inc., PA, USA) as a treatment for pain relief and improvement of circulation. Skin temperature on her second fingers was monitored every morning at constant room temperature (21 – 22°C) with a finger temperature probe (GE Marquette DASH 3000, GE Medical Systems Company, Milwaukee, WI, USA). Her finger pain decreased to VAS 1 – 2/10, whereas her finger temperature 1 day after the infusion did not change from the pre-treatment value (28.3°C – 28.9°C) on both sides. Therefore, we concluded that our cervical epidural infusion could not increase the finger circulation.

Therefore, to improve finger circulation, both thoracic sympathetic catheters were installed at the T2 level under the fluoroscopic guidance 1 day after the cervical epidural infusion. The patient was placed in the swimmer's position, which is a prone position with a 15-cm high pillow underneath the patient's anterior chest hanging down the upper extremities. An epidural needle was used to place the thoracic sympathetic catheter, and the insertion point of the needle was 3.5 – 4 cm lateral to the spinous process in the T2 and T3 intercostal space. The thoracic sympathetic catheter was installed according to the modified technique of Ohseto's method (16,17). The Tuohy needle was inserted between the second and third ribs targeting the lateral edge of the T2 vertebral body on the AP view. Once the needle was touched to the lateral edge of the T2 vertebral body, the needle was advanced hugging the lateral vertebral body to the posterior one third of the vertebral body on the oblique view with alternatly checking the depth of needle on the lateral view. Once the proper needle position was obtained and the stylet was removed, the catheter was inserted though the needle gently (Fig 2). One gram of cefazoline dissolved in normal saline was given intravenously 2 times a day for the whole period of catheterization.

Thoracic sympathetic infusion on either side started with mepivacaine (0.32%) at 4 mL/hr and initial bolus injection of 4 ml of 1% mepivacaine on each side. One hour after the infusion of mepivacaine through the thoracic sympathetic catheter, the patient felt dizziness and her blood pressure decreased to 80/60 mmHg (from a normal of 110/70 mmHg). Nasal O2 was administered and the infusion rate was reduced to 4 mL/hr and 3 mL/hr for cervical and each side of the thoracic sympathetic catheters, respectively. She felt comfortable after the infusion rate was adjusted. The temperature of the second fingertip of the right and left hands increased from 28.9°C and 28.5°C at baseline mean temperature to 33.5°C and 32.2°C, respectively, during the day of sympathetic infusion. The cervical epidural catheter used for the pain control was removed on the tenth day of infusion. One day after the removal of the epidural catheter, her finger pain was not aggravated and the temperature still remained high. There was no need to reinsert a cervical epidural catheter. Thoracic sympathetic catheters were continued until the thirteenth day of infusion. The right thoracic sympathetic catheter was maintained for 13 days and the left catheter was removed and reinserted on the seventh day of infusion, due to a slow increase in temperature and wound healing of the left finger. The second left thoracic sympathetic catheter was maintained successfully for more than 4 additional days. On the thirteenth day of infusion therapy (twentieth hospital day), her wound was completely healed. She was discharged with daily maintenance medication of 90 mg nifedipine and 30μg of limaprost. She had no recurrence of ischemic symptoms on her fingers for

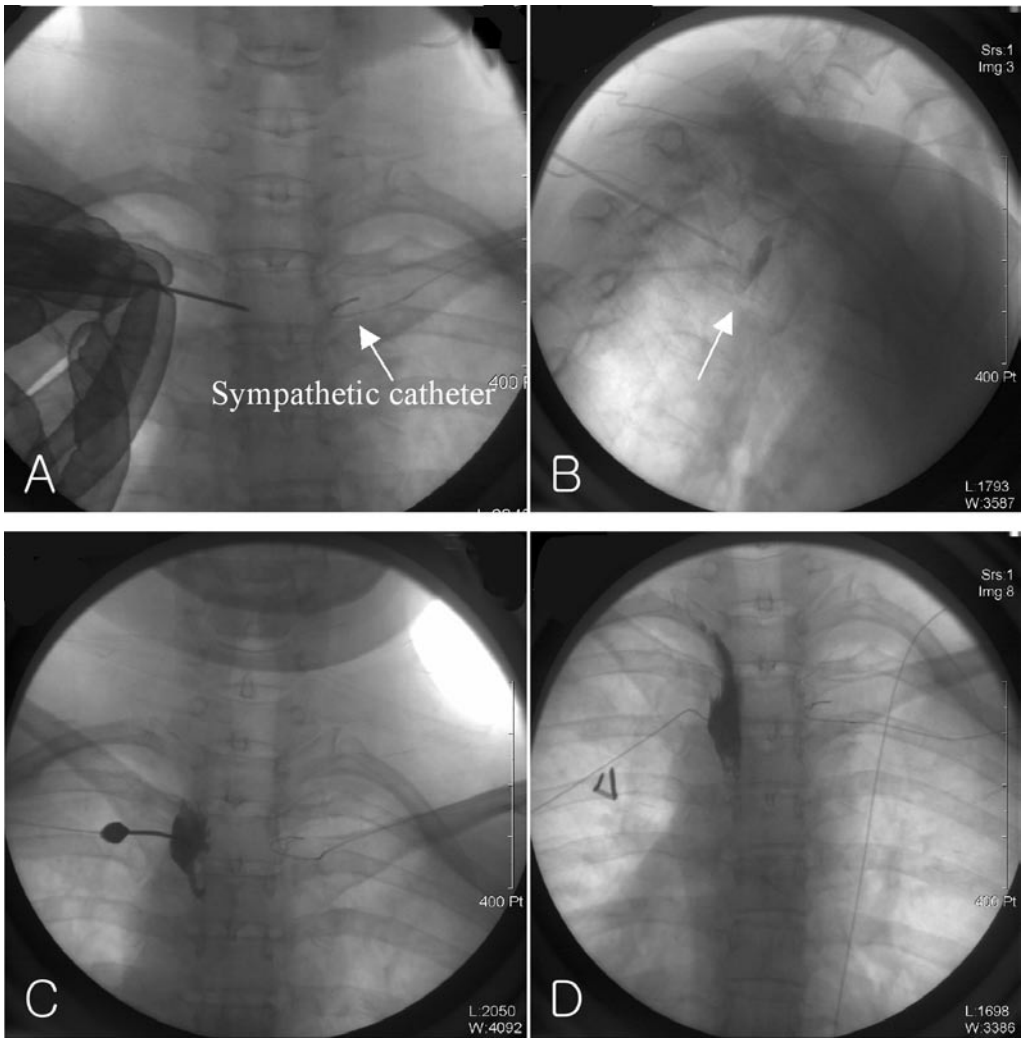

Fig. 2 *(A) A Tuohy needle is inserted in the posterior side of the vertebral body to measure the depth of the vertebral body on the AP view at the first step of the procedure. A Tuohy needle should be walked off and redirected and then advanced until contact with posterolateral side of the left T2 vertebral body below the pedicle on AP view. (B) Lateral view shows contrast media (0.5 ml) covering the lateral side of T2 vertebral body around the catheter tip (white arrow) outside of the Tuohy needle. The Tuohy needle tip is in the one fourth of the T2 vertebral body because of slight withdrawal. The catheter shows a loop shape at the midpoint of the vertebral body. (C) A spreading pattern of contrast media (2 ml) through the catheter in the posterolateral space of the left T2 vertebra on the AP view. (D) Both sympathetic catheters are placed at the T2 vertebral level.*

the 19-month follow-up period. A total of 14 days infusion with a low concentration of mepivacaine (0.32 %) through thoracic sympathetic catheters (total 13 days infusion) provided improved circulation and excellent wound healing of both fingertips.

Discussion

The treatment goal of RP in patients with scleroderma is to restore the insufficient arterial circulation of the hands caused by a combination of sympathetically mediated vasospasm or vascular occlusion (3,4). Cervicothoracic sympatholysis could be a rational option to overcome this condition. In the present case, a thoracic sympathetic ganglion block with continuous infusion of local anesthetics was performed to improve circulation to the finger. Although the continuous cervical epidural infusion was chosen for pain relief and improving circulation as the first treatment in our patient, it seems quite unlikely that the treatment improved digital perfusion based on the lack of change in finger temperature.

Stellate ganglion block has been reported to yield therapeutic benefits in some cases (18), however, it is often unsuccessful (13). Moreover, it often requires a large volume (20 mL) to block all sympathetic innervations in the upper limb (19), and may spread to unwanted places, resulting in side effects. Continuous infusion of brachial plexus block has usually been used as a postoperative or preoperative pain control and vasodilation for a few days in the microvascular surgery of ischemic hands (15,20). A major difficulty in using the continuous peripheral nerve block is to place the catheter close enough to the nerve sheath (15). Keeping the catheter for a given period of time is another difficulty in ambulatory patients, especially when dealing with both sides, as in the present case. A larger volume of local anesthetics than those needed for T2 thoracic sympathetic ganglions would be needed for blocking the brachial plexus.

Considering the disadvantages mentioned above in our present case, the second thoracic sympathetic ganglions were the target sites for infusion of local anesthetics instead of the peripheral nerve. The second thoracic ganglion could be the optimum target for sympatholysis of the blood vessels of upper limbs, since anatomically the sympathetic nerve supply to the upper limbs begins with preganglionic cell bodies located in the spinal segment T-2 to T-8, and terminates and synapses with postganglionic neurons mainly in the second thoracic ganglion (21).

The primary reason we used continuous infusion of local anesthetics into sympathetic ganglions instead of neuroablative sympathectomy in our patient was due to the fact that recurrence may occur at a high rate after thoracoscopic or chemically neurolytic sympathetomy (5,6,22,23). Most patients with RP show initial improvement (6), however, all relapse 6 months after the thoracoscopic sympathectomy (5). The high initial relief of symptoms and frequent recurrence from neurodestructive sympathectomy might be caused by denervation supersensitivity or nerve regeneration (24).

One of the concerns of our combined infusion technique through a cervical epidural space and thoracic sympathetic ganglions was systemic toxicity of local anesthetics. Hypotensive episodes occurred in our patient 1 hour after the total infusion of 13 mL/h of 0.32% mepivacaine with both thoracic sympathetic and cervical epidural space and initial bolus injection of 8 ml of 1% mepivacaine for sympathetic ganglions, which might have been caused by overdoses of local anesthetic. However, this transient hypotensive symptom disappeared after O2 supplementation and adjustment of infusion volume to total 10 ml/h of 0.32% mepivacaine (total 778 mg per day). The maximum dose of local anesthetics remains a controversial issue, however, and is irrelevant because toxicity is caused by the free, unbound form, and not by the total dose given or plasma peak concentration (25). The total dose of 778 mg daily infusion in our patient was more than maximum doses recommended (300 – 500 mg/ 70 kg adult). Generally recommended maximum doses are safe whenever given as single injections. However, maximum doses may or may not be safe after continuous infusion, and practitioners should closely adjust the appropriate volume of local anesthetics for continuous infusion while monitoring vital signs.

Changes of digital blood flow before and after the procedures in our patient were assessed with direct skin temperature and thermographic monitoring. In assessing skin temperature, the patient was kept under a constant room temperature setting (21 – 22°C) during the period. Although Clark et al suggested that Doppler imaging is more sensitive to perfusion changes than thermographic measurements (26), daily evaluation of skin temperature of both fingers combined with thermography was easy to assess the blood flow indirectly and repeatedly. Our patient showed an average 2 degrees increment of finger skin temperature at steady state, and 4 – 5 degrees increment immediately after the bolus injection of 4 mL of 0.5% mepivacaine through sympathetic catheters, as compared to the baseline temperature.

Conclusion

Continuous infusion of local anesthetics through the thoracic sympathetic ganglionic space can provide a significant effect on improving blood flow for wound healing of an otherwise medically refractory gangrenous ulcer of the fingertip in patients with Raynaud's phenomenon. However, more evidence is required to reliably evaluate the continuous infusion of local anesthetics through the thoracic sympathetic ganglionic space for the effective sympatholysis.

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