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CASE REPORT

Effect of Transcatheter Arterial Microembolization on Phantom Limb Pain Persisting for 17 Years

Masahiko Shibuya[1] · Masayoshi Yamamoto[2] · Yuji Okuno[1]

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Abstract Phantom limb pain is a frequent consequence of the amputation; currently available treatments are far from satisfactory. The present report describes a case in which transcatheter arterial microembolization had a remarkable curative effect on phantom limb pain persisting for 17 years. The patient began feeling phantom limb sensations and brief intermittent pain following lower limb amputation above the knee in 2001. The frequency, intensity, and duration of the pain increased over time, and it was resistant to conservative treatments. Following transcatheter arterial microembolization in 2018, patient immediately experienced marked improvement. The pain has been infrequent, much less intense, and did not interfere with daily life 6 months posttreatment. Transcatheter arterial microembolization could be an alternative treatment option for phantom limb pain.
Level of Evidence IV, Case Report

Keywords Arterial embolization · Phantom pain · Phantom limb pain · Abnormal neovessels · Embolization

✉ Yuji Okuno
how_lowlow@yahoo.co.jp

1 Musculoskeletal Intervention Center, Okuno Clinic., 7-8-4, Roppongi, Minato-ku, Tokyo, Japan

2 Department of Radiology, Teikyo University Hospital, Tokyo, Japan

Introduction

Although the frequency and intensity of phantom pain decrease over time, approximately 5–10% of amputees continue to experience severe intractable and disabling phantom pain for many years after amputation [1]. Of the large number of different treatments that have been suggested, those currently available for chronic phantom limb pain are far from satisfactory [2].

Studies have shown that angiogenesis may contribute to chronic pain by enabling the growth of new sensory nerves along their path [3]; these two phenomena are closely related. In fact, histopathological studies have demonstrated the existence of abnormal neovessels with accompanying nerve fibers from painful conditions including osteoarthritis [4] and overuse injuries such as tendinopathy and enthesopathy [5].

Based on the hypothesis that the increased number of blood vessels and accompanying nerves is a possible source of chronic pain, transcatheter arterial microembolization (TAME) has been used for treating pain associated with osteoarthritis, adhesive capsulitis, and lateral epicondylitis resistant to conservative treatment [6–8]. Herein, we describe, to the best of our knowledge, the first case wherein TAME was performed on phantom limb pain persisting for 17 years.

Case

A 46-year-old male sustained life-threatening hemorrhage and other injuries in May 2000 after being thrown from his motorcycle consequent to a head-on collision with a car. He had a right mid-femoral compound fracture and severe injury below the knee. The patient showed no syncope or disturbance in consciousness postaccident and has not received any treatment for brain damage. Conservative treatment with seventh regenerative therapy was performed from May 2000 to February 2001. However, his wound healing was unfavorable, and it was concluded that further conservative therapy would not enable him to walk again. Therefore, the patient agreed to lower limb amputation 15 cm above the knee, performed in February 2001.

In August 2001, the patient simultaneously began feeling phantom sensations when prosthesis was attached to the amputated area below the femur, regardless of whether he was wearing it or not. He recognized that the phantom sensations were indistinctly existent at only the fifth toe of his phantom limb. At the same time, he experienced intermittent phantom limb pain that felt like sharp pricking/lancinating sensations and burning. The phantom pain attacks lasted from a couple of seconds to 1 min, two or three times a day. He took loxoprofen sodium for the pain, but the effect was limited. The frequency and intensity of his pain attacks increased in 2010 from approximately 3 to 5 on the numeric rating scale of phantom limb pain. In 2011, sciatic nerve and root blocks were administered once a month for pain, and their effect was observed to be limited. In 2014, he began taking pregabalin and tramadol hydrochloride for pain, but they were not effective. Mirror visual feedback was performed several times with no effect. The shooting pain became stronger in 2016 without a trigger in an event of an attack. The pain lasted 2–3 h every night and was sometimes accompanied by uncontrollable motion of the remaining limb. Use of a fentanyl transdermal patch from the end of 2017 was not effective. At this time, his numeric rating scale scores were 7–10 when the pain came. When he visited our clinic in February 2018, there was no obvious abnormality in the appearance of the stump aside from mild tenderness, and TAME was selected for treatment. Available treatment options and potential risks, benefits, and outcomes of TAME were explained to the patient and subsequently, a written informed consent was obtained from the patient.

Procedure

Under local anesthesia, percutaneous retrograde contralateral (left side) femoral artery access was obtained using a 3-F introducer sheath (Super Sheath Medikit Co, Ltd, Tokyo, Japan). A 3-F Judkins right 2.5 angiographic catheter that was moved distally to the right superficial and deep femoral artery. Digital subtraction angiography, following injection of 3–5 mL of iodinated contrast medium (Hexabrix, Guerbet LLC.), enabled imaging of the right femoral artery. Embolization was sequentially performed in each arterial branch using a 1.7-F Asahi Veloute microcatheter (Asahi Intecc Co., Ltd.), by injecting imipenem/cilastatin sodium [IPM/CS; Primaxin IV, Merck & Co., Inc.]. A suspension of 0.5 g of IPM/CS in 7 mL of iodinated contrast agent was prepared by agitating for 10 s and then injected into the patient in 0.5-mL increments. The IPM/CS embolic agent was selected on the basis of a previous report of transcatheter arterial embolization of refractory painful tendinopathy and enthesopathy [9]. IPM/CS is a slightly water-soluble crystalline compound that forms small particles that exert an embolic effect when suspended in contrast agent. During the injection of the contrast agent or IPM/CS, the patients experienced pain, itching, or heat sensation related to the vessel where the contrast was injected (called "evoked pain"). This finding was useful to identify the artery responsible for the pain during the procedure. As the stump contains granulation tissue, which contains the perfusion-rich tissue, distinguishing between normal and abnormal neovessels is rendered difficult using angiography. Thus, the injection of IPM/CS was performed based on the location of evoked pain. Particularly, after selective angiography of each branch, 0.5 ml of IPM/CS was injected and the patient was asked to specify whether he feels pain at the location where he usually feels pain. If he felt the pain at the usual location, the perfusion area of the selected branch was held responsible for the pain. IPM/CS was injected until the blood flow stasis to the targeted branch was observed. In this case, we injected IPM/CS twice (total 1.0-ml increments) in each branch as shown in Fig. 1. Hemostasis was achieved with 10 min of hands-on pressure.

The patient was discharged the same day and immediately felt marked improvement in his phantom limb pain. Although lancinating pain recurred once a day, numeric rating scale scores improved to 1–2. He started clearly recognizing the fifth toe, along with toes, of his phantom limb after TAME. Swelling at the stump of the patient's phantom limb had improved, and the size of the equipment reduced at 6 month. The patient resumed his hobbies of diving and paragliding thereafter. There was no evidence of the tissue necrosis, dermal ulcers, or peripheral paresthesia in any embolized territory during 6-month follow-up.

Discussion

The present report describes a case of phantom limb pain persisting for more than 17 years, which was treated by TAME and followed up for 6 months. Although the pain was resistant to other treatments, including mirror visual feedback therapy, TAME reduced the frequency and intensity of phantom limb pain.

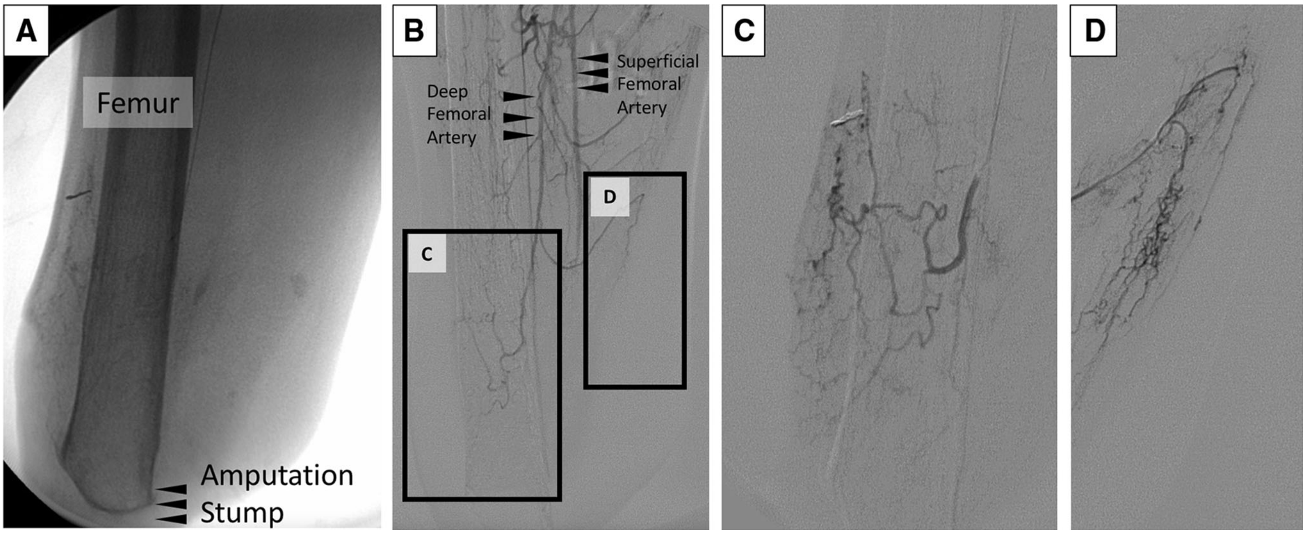

Fig. 1 **A** Image of the right femoral region including the amputation stump. **B** Angiography of the common femoral artery revealing the superficial femoral artery and deep femoral artery. The amputation stump region was primarily perfused by the deep femoral artery. **C** Microcatheter at the tip of the deep femoral arterial branch revealing the angiogram details at the area of the lateral side of the femur (corresponds to left black box in B). **D** Angiography revealing the vessel distribution of the medial side of the femur (corresponds to right black box in B)

The mechanisms underlying phantom limb pain can be categorized as peripheral, spinal, and supraspinal, and interactions between these mechanisms are thought to contribute to phantom limb pain. Ectopic discharge from a stump neuroma has been hypothesized as an important peripheral factor of phantom limb pain. Sumitani et al. classified pain in two categories based on its origin in this condition and described different treatment methods depending on the origin of the pain [10]. Deep pain (e.g., cramp-like taut twisting) derives from the higher-order cognitive processes of the central nervous system, such as disagreement between the intention of exercise and actual feeling, whereas superficial pain (e.g., pricking, shooting, and sticking) derives from the hyperexcitability and firing patterns of neurons in pain pathways. It is thought that hyperexcitability of pain pathways causes inappropriate rearrangement of visual body perception in the transient somatosensory area (S1).

In this case, the phantom pain could have occurred due to inappropriate rearrangement of visual body perception in the transient somatosensory area (S1) as only the fifth toe was idly recognized; this perception may have led to phantom limb pain. The patient described phantom pain as sharp pricking/lancinating sensations with burning; these were categorized as superficial pain. Therefore, TAME might be effective for this type of phantom pain.

The mechanism was exemplified by the mild tenderness of the patient's stump. IPM/CS injection into the deep femoral artery branch around the stump was able to reproduce the pain, indicating that these vessels likely corresponded to part of the pain pathway. Thus, we posit that TAME suppresses neuronal hyperexcitability by decreasing the level of inflammation, thereby reducing the phantom pain.

Mirror visual feedback mainly affects deep pain, which was nonexistent in the present case, and this supports a previous hypothesis [10]. However, further verification is necessary to confirm this notion.

Compliance with Ethical Standards

Conflict of interest The authors declare that they have no conflict of interest.

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