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Case Report

Treating phantom limb pain: cryoablation of the posterior tibial nerve☆

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ABSTRACT

Phantom limb pain (PLP) is a complex pathophysiologic process involving both the central and peripheral nervous system for which there is no definitive treatment. The number of individuals living with amputated limbs is predicted to increase to 3.5 million by 2050, and up to 80% of these patients will have PLP. In this case report, we will demonstrate successful reduction of PLP in a patient with bilateral phantom toe pain utilizing nerve blockade and subsequent cryoablation of the posterior tibial nerves.

Introduction

Phantom limb pain (PLP) is a multifactorial pathophysiologic process first described by French physician Ambroise Pare in 1552, which refers to painful sensations perceived in amputated parts of the body. Although classically described in the extremities, PLP has been described in other portions of the body including the appendix, bladder, and teeth [1]. It is often described as sharp, burning, cramping, or stinging sensations in the missing segment and is considered a distinct entity from phantom limb sensations (sensations of position or presence of and amputated limb) and residual limb pain (pain originating in the stump after amputation). There is an estimated 1.7 million individuals living with amputated limbs which are predicted to increase to 3.5 million by 2050, and up to 80% of these patients will have PLP [2,3].

PLP is a complex pathophysiologic process proposed to involve both the peripheral and central nervous systems. Multiple theories have been proposed to explain the underlying mechanism of PLP, with cortical reorganization being the most common [4]. Literature has shown that after limb amputation, the brain undergoes cortical reorganization with adjacent representational zones in the somatosensory cortex “taking over”

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the areas initially dedicated to the amputated body part [4–7]. With this phenomenon, the affected representational zone no longer receives adequate signals from its corresponding limb and instead responds to stimulatory signals from adjacent representational zones in the somatosensory cortex, which possibly represents uncovering of dormant synaptic connections or rapid creation of new ones. Imaging studies by Flor et al have even suggested that the intensity of PLP is related to the amount of undergone cortical reorganization, which in turn may correlate with chronic pain experienced proceeding the amputation [8,9]. Other CNS related theories include visual-proprioception dissociation where the proprioceptive memories of the limb remain embedded in the subconscious, leading to continued feelings of limb position and sensation [10]. The spinal cord has also been implicated in PLP, with central sensitization occurring within the dorsal horn leading to upregulation of multiple inflammatory mediators implicated in pain signaling along with changes in the firing pattern of nociceptive neurons [11,12].

The peripheral nervous system also appears to play a role in phantom limb pain [13]. Amputees frequently develop neuromas, abnormal bundles of nerve tissue, at the site of amputation which can be seen in 13%-32% of patients. These neuromas show an increased expression of sodium channels, resulting in a hyper-excitable state with demonstrated abnormal activity following mechanical or chemical stimulation [14,15]. This is supported in literature where it was demonstrated that repetitive touching at the amputation site induces PLP, and local injection of sodium channel blockers along the peripheral nerves alleviated it [1,16,17]. Additional evidence of peripheral nervous system involvement comes from Moesker et al [2], whom demonstrated long-term reduction of PLP by cryoablating peripheral nerves. Cryoablation damages the vasa vasorum causing severe endoneural edema, eventually leading to Wallerian degeneration, while leaving the basal lamina of Schwann cells intact. This proposedly initially acts as a conduction block while allowing axonal regeneration without neuroma formation.

Multiple therapies targeting both the peripheral and central nervous system have been proposed and trialed including pharmaceuticals, mirror therapy, virtual reality augmentation, biofeedback, and even surgical interventions, though none have been shown to be completely effective at eliminating PLP [11]. Targeting the peripheral nervous system to reduce PLP is an intriguing option as it is easily accessible, can concurrently treat residual limb pain at the amputation stump, and has potential to offer patients rapid relief [18,19]. Nerve blocks performed in the sciatic nerve and brachial plexus significantly reduced the sensation of PLP in as little as 20 minutes [18,20]. Birbaumer et al demonstrated that those patients who had a significant reduction in pain post blockade of the brachial plexus also demonstrated rapid elimination in cortical reorganization in the somatosensory cortex [18]. Further support for peripheral treatments was shown by Prologo et al [2], who performed cryoablation in patients with refractory PLP and demonstrated reduction in symptoms by 37.1% at 45 days post procedure and 32.2% at long-term follow-up (defined as 95-293 days after the procedure). Moesker et al treated 5 patients with peripheral nerve cryoablation, with 3 of them demonstration significant reduction in symptoms lasting over 2.5-5 years.

Reports have demonstrated relief after local treatments involving the brachial plexus, sciatic nerve, and femoral nerve, however to our knowledge there have been no reports of treating phantom limb pain through application of regional anesthetic to the posterior tibial (PT) nerve. In this case report, we will demonstrate the safety and efficacy of bilateral PT nerve block followed by cryoablation for PLP of the toes.

Case report

Our patient is a 75-year-old male with a past medical history of coronary artery disease, aortic aneurysm, and hypertension who presented to our clinic complaining of severe pain at the sites of his multiple bilateral toe amputations. In 2016, he had a myocardial infarction and underwent cardiac catheterization, which was complicated by atheroembolization to his lower extremities. This in turn led to amputation of the left first and second toes as well as amputation of the right third, fourth, and fifth toes in 2017. He experienced continued necrosis of the residual stumps, which required revisional surgery in 2019. Since his initial operation, he reports having the sensation of burning needles at the stump sites which felt as though it extended into his now amputated toes. The pain is described as constant with the greatest intensity along the plantar surfaces and is graded as 6/10 at baseline across all stumps which worsen with walking. Ultimately, he was diagnosed with both phantom limb pain and residual limb pain. At the time of presentation to our clinic, the patient had previously attempted treatment with oral pharmaceutical therapy, however due to experiencing uncomfortable side effects and personal preferences, was aversive to continuing pharmaceutical treatment. He had not attempted any other known therapies, nor did he have prosthetics. After further discussions with the patient, it was decided that a posterior tibial nerve block would be the best initial option for pain relief.

A pain assessment was obtained prior to the start of the procedure, with the patient grading his pain as 9/10 in bilateral extremities. A screening ultrasound was performed adjacent to the amputation sites to evaluate for neuroma formation, with none identified. The posterior tibial nerves were then identified bilaterally at the level of the ankle just proximal to the medial malleolus. Under direct ultrasound guidance using an axial approach, a 22-gauge chiba needle was advanced adjacent to the posterior tibial nerve with care to ensure extravascular position. A cocktail of 6 mg of betamethasone and 0.025% bupivacaine was then administered under imaging bilaterally without complication. Immediately after the procedure, the patient graded his pain as 6/10 on the left and 4/10 on the right with cessation of the chronic burning pain at the underside of his feet. His motor function remained intact and unchanged bilaterally.

At 1-week follow-up, the patient reported 1/10 phantom pain in his toes bilaterally with slow return of the chronic burning at the base of his feet as the analgesia wore off. He reported that with the block, he was able to enjoy a more ac-

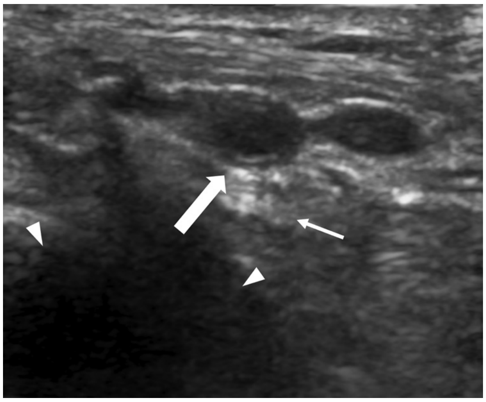

Fig. 1 – Cryoablation probe position. 75-year-old male with phantom toe pain. Gray scale ultrasound image showing tip of the needle (large arrow) adjacent to posterior tibial nerve bundle (small arrow). Medial malleolus (Arrowheads) acts as reference point for the location of the posterior tibial nerve bundle.

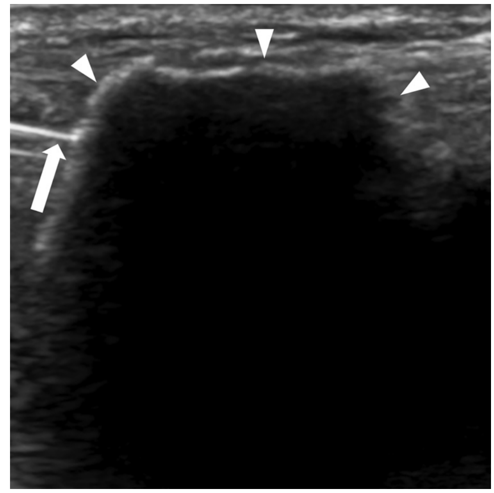

Fig. 2 – Cryoablation ice ball. 75-year-old male with phantom toe pain. Gray scale ultrasound image showing tip of the needle (large arrow) within the cryoablation ice ball (arrowheads).

tive lifestyle and do activities such as fishing, which he hadn't done in months, as well as chase around his new puppy. He also reported improvement in his ability to sleep with the nerve block- before the block, the sheets of his bed touching his feet would be so painful, it would keep him up all night. For the first time in years, he was able to get a good night's sleep.

Given the success of the nerve block, it was decided to proceed with cryoablation of the bilateral posterior tibial nerves in hopes of a more definitive treatment. Using a similar technique as the nerve block, the posterior tibial nerve was located bilaterally just proximal to the medial malleolus under ultrasound guidance, and lidocaine was administered for local anesthesia. Cryoablation probes (IceSphere, Boston Scientific) were then advanced under ultrasound guidance to the posterior tibial nerves (Fig. 1). Freeze-thaw cycles were then performed using 8 minutes of freezing, 3 minutes of passive thawing, 3 minutes of freezing, and 3 minutes of passive thawing before the probes were removed (Fig. 2). Immediately after the procedure, the patient reported absence of his phantom limb pain bilaterally with expected post-procedural pain at the site of needle insertion. The patient remained relatively pain free until the fourth postprocedural day when he developed a new 9/10 pain along the pads and dorsal aspects of his feet with different characteristics than his preprocedural pain. His phantom limb pain was still alleviated at this time. The post-procedural pain was initially managed with a steroid dose pack, anti-inflammatories, and an oral pain regiment. Unfortunately, the pain along the pads and dorsal aspects of his feet did not resolve until approximately 6 weeks post nerve ablation. Encouragingly, the patient reported significant improvement in his quality of life after immediately after the cryoablation with resolution of his phantom limb pain. He described being able to participate in his hobbies without being hindered by pain along with vast improvements in the quality of his sleep. Unfortunately, his phantom limb pain returned in full strength 6 weeks after the cryoablation procedure.

Discussion

Phantom limb pain is a complex pathophysiologic process involving both the central and peripheral nervous system that affects over 1.7 million patients. No definitive treatment has been established for phantom limb pain, however, multiple studies have shown peripheral based treatments such as nerve blocks and cryoablation in providing patients relief.

Reports have demonstrated relief after local treatments involving the brachial plexus, sciatic nerve, and femoral nerve, however to our knowledge there have been no reports of treating phantom limb pain through application of regional anesthetic to the PT nerve. The PT nerve runs in close proximity to the PT artery and vein and supplies sensory innervation to the majority of the plantar aspect of the foot. PT nerve blocks targeting pain of the foot have been shown to be successful in literature with little to no motor blockade expected when performed just proximal to the Achilles tendon [21]. Risks performing this procedure are estimated to be less than 1% and include hematoma formation, anesthetic toxicity, and damage to adjacent structures [21].

Given the distribution of our patient's pain along the dorsum of the foot and at the amputation sites of his toes, he was determined to be an ideal candidate for a posterior tibial nerve block with a positive benefit to risk ratio. Not surprisingly, he demonstrated immediate reduction in phantom pain after application of regional anesthesia without any motor deficits, which returned over the course of the following week with loss of analgesic effect. After success with temporary local anesthetic and steroid, cryoablation was attempted to create a longer lasting conduction block while allowing axonal regeneration. While initially successful, the analgesic effects for phantom toe pain of the cryoablation lasted only 6 weeks for our patient. Damaging the peripheral nervous system did prove to provide adequate analgesia, however in this case, the phantom pain returned after axonal regeneration occurred. Though this was a disappointing end result, it was not entirely unexpected given the heavy involvement of the central nervous system and cortical reorganization in the pathophysiology of phantom limb pain. Even so, it proved to be a valuable treatment for our patient. During the time when his phantom pain had subsided post block and post cryoablation, he reported vast improvements to his quality of life. He endorsed picking up hobbies he had previously abandoned such as fishing and playing outdoors with his dog. He also reported improved sleep quality, as before his cryoablation treatment, the slightest touch from his bed sheet would cause uncomfortable pain, yet post-treatment he slept virtually pain free. In this particular case, it may be beneficial to attempt a more proximal cryoablation to at the very least provide a longer period of analgesia, though it is unknown if doing so would provide more complete pain relief as the postprocedural inflammatory mediators subside. Additionally, adding other non-pharmaceutical therapy, that is, virtual reality or physical therapy with orthotics, in conjunction with peripherally based treatments could in theory provide more complete relief. Though more research is needed, we believe peripheral nerve cryoablation can be an effective and valuable therapy in providing short term analgesia to patients experiencing phantom limb pain, particularly in populations similar to our patient with an aversion to other types of pharmaceutical therapy.

Teaching point

Peripheral based nerve therapies are effective at reducing residual limb pain and phantom limb pain in patients. Cryoablation of the posterior tibial nerve is a potential viable method of pain in the lower extremity feet and digits for extended periods of time in patients with PLP.

Patient consent

Written informed consent has been obtained for the publication of this article and a copy can be produced upon request.

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