

CLINICAL VIGNETTE

Phantom Limb Pain

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Case

A 56-year-old female presented to establish care along with her annual wellness exam. She was feeling well but had prior osteosarcoma at the age of 14 with right above the knee amputation. She requested a referral for a new prosthesis as her current prosthesis was causing discomfort. In addition to osteosarcoma she has phantom limb pain, asthma and mild anxiety. She was taking gabapentin 400mg twice per day for phantom limb pain. She also had prior alprazolam and an albuterol inhaler. Family history was unknown and she did not smoke or drink alcohol.

On exam, her vital signs and general exam were normal, other than her right leg amputation with prosthesis. Her stump appeared healthy with skin intact and no erythema or ulceration. Basic labs were normal. She was referred for routine preventative screening, including mammogram and colonoscopy, with a plan for future annual wellness exam and follow up as needed.

Six months later she returned to discuss treatment of her phantom limb pain, which had worsened since her initial visit. She had her new prosthesis, which was more comfortable and not causing any pain, but felt her phantom pain was not well controlled with gabapentin. In the past she tried duloxetine and pregabalin, which were not helpful. She also used paroxetine previously, but stated it made her sleepy. I prescribed amitriptyline, but she stopped it after a month because it was ineffective regarding her pain and was causing sexual side effects. She was having increasing frequency and duration of her phantom limb pain, which was interfering with work. We discussed trying other medicines, but she requested consultation with a neurologist and is awaiting initial evaluation.

Discussion

In the mid-1500s, a French military surgeon named Ambroise Paré was the first to describe the syndrome we now call phantom limb pain (PLP).¹ In the United States, as of 2018 there were 1.7 million people living without a limb. Of these, it is estimated that 60-80% suffer from sensations in their lost limb.² Phantom pain is a painful sensation originating in a limb or organ which has been amputated or removed.² Descriptions of phantom pain vary and can be a burning sensation, shooting or aching, and most commonly affects the distal phantom limb. This may be because the distal limbs, such as fingers and toes, are represented in larger areas of the cerebral cortex.³ Phantom pain can be intermittent or constant and can vary in intensity. This pain can last from several months to years after surgery.

Ten percent will have severe pain in the amputated limb 6 months or more after surgery.⁴ If the pain lasts for over 6 months post-operatively, the chances are low that the pain will resolve without intervention.⁵

The two most common reasons for amputation include vascular disease and trauma, mostly affecting men. In fact, women are half as likely to have an amputation as a man and 42% of patients with amputation are over the age of 65.⁶

The development of phantom limb pain is multifactorial, but may be caused by three possible mechanisms arising from nerves: at the peripheral level; the spinal level; and the supraspinal level. At the peripheral level, there can be spontaneous discharge from the damaged nerves at the amputation site, or these damaged nerves can form neuromas. Neuromas are potentially more sensitive to stimuli, which can cause pain. At the spinal level, there may be anatomical reorganization of nerves in the spinal cord which leads to previously non-painful stimuli being perceived as discomfort or pain. In addition, the extreme pain from the amputation site may trigger hyperalgesia, where there is an excessive sensation of pain to various types of stimuli.⁴

At the supraspinal level there is cortical reorganization so that areas that are near each other on the anatomical homunculus can cause pain in the amputated limb.^{4,7} For example, when one area is touched, such as the face, the patient may perceive sensation in an amputated hand since these areas of sensation are adjacent in the somatosensory cortex.⁸

In addition to the above mechanisms, psychological factors such as personality, coping style and mood can contribute to the course and severity of pain, but not the occurrence of phantom pain.⁴ Other factors contributing to the risk of PLP is if the patient had pre-amputation pain and if there is residual limb pain present immediately after surgery.^{4,9} Residual limb pain is pain in the portion of the limb that remains after amputation. Those with PLP, have a higher incidence of residual limb pain post-operatively.⁴

Prevention and treatment of PLP should be a multimodal approach by an interdisciplinary team. Patient education and cognitive behavioral therapy, in addition to the surgical techniques and types of anesthesia are all important in the prevention and treatment of PLP. Severe pre-amputation and

post-amputation pain is consistently associated with increased risk of developing PLP. Thus, reduction in pain in these periods should be a goal of PLP prevention, which may require regional anesthesia. In addition, the patient's function post-operatively should be optimized and normalized to reduce the development of PLP.⁴

Regarding pharmacologic treatment of PLP, there is only limited evidence that morphine and gabapentin help reduce pain in established PLP. Intravenous ketamine can help at the time of application, but it has not demonstrated long term benefits in PLP management. The general approach has been to treat PLP as other neuropathic pain is treated. This usually includes antidepressants such as duloxetine and venlafaxine, as well as pregabalin, carbamazepine and oxycarbazepine, and cannabinoids.⁴

Sensory feedback has proven to be helpful in pain reduction. Sensory discrimination training, which includes having patients discriminate locations of electrode-stimulation on the stump may help reduce chronic pain. Visual and tactile sensory feedback using mirrors may help actually reverse the nervous system reorganization that initially took place post-operatively. Viewing one's hand in a mirror gives the patient the impression they are seeing their amputated hand and can control its motor function.⁴ In fact, functional MRI results demonstrated that patients who had mirror training had reversal of somatosensory cortex reorganization.⁷

About 25% of patients will experience telescoping which is a phenomenon where the patient perceives their amputated limb to be retracted and/or residual. Interestingly, patients with telescoping do not respond as well to mirror therapy since the limb in the mirror appears different than their perceived phantom limb.⁹

Surgical approaches can help reduce pain by giving the patient more control of their prosthesis. This is accomplished through techniques called targeted muscle reinnervation which generates functional motor units and allows for bionic reconstruction, and ultimately reversal of cortical reorganization as well. Virtual reality is also being used with mirror boxes to augment the patient experience and is a promising area of PLP treatment. In regards to prosthesis the more functionality a prosthesis has, for example, the more actual control the patient has over the prosthesis, the less PLP. Prostheses are becoming increasingly functional with advances in surgical intervention combined with rehabilitation.⁴

In August 2020, a systematic rapid review on the prevalence and incidence of PLP, phantom limb sensations and telescoping, highlights the importance of identifying particular characteristics of the patient in discussing risk and prognosis related to PLP. Characteristics include the reason for amputation, if there is pre-amputation pain present and the site of amputation. Vascular causes of amputation, which can be associated with longer courses of pain leading up to surgery, may increase risk of PLP development post-operatively.

Research is conflicting, but it seems lower limb amputations are related to worse prognosis regarding development of PLP, as compared to upper limb amputations. This review recognizes that standardized guidelines and large studies are needed provide tools to advise patients on the prevalence, incidence and prognosis regarding PLP.⁹

REFERENCES

1. **Keil G.** Sogenannte Erstbeschreibung des Phantomschmerzes von Ambroise Paré. "Chose digne d'admiration et quasi incroyable": die "douleur ès parties mortes et amputées" [So-called initial description of phantom pain by Ambroise Paré. "Chose digne d'admiration et quasi incroyable": the "douleur ès parties mortes et amputées"]. *Fortschr Med.* 1990 Feb 10;108(4):62-6. German. PMID: 2179086.
2. **Kaur A, Guan Y.** Phantom limb pain: A literature review. *Chin J Traumatol.* 2018 Dec;21(6):366-368. doi: 10.1016/j.cjtee.2018.04.006. Epub 2018 Dec 4. PMID: 30583983; PMCID: PMC6354174.
3. **Flor H.** Phantom-limb pain: characteristics, causes, and treatment. *Lancet Neurol.* 2002 Jul;1(3):182-9. doi: 10.1016/s1474-4422(02)00074-1. PMID: 12849487.
4. **Erlenwein J, Diers M, Ernst J, Schulz F, Petzke F.** Clinical updates on phantom limb pain. *Pain Rep.* 2021 Jan 15;6(1):e888. doi: 10.1097/PR9.0000000000000888. PMID: 33490849; PMCID: PMC7813551.
5. **Jackson MA, Simpson KK.** Pain after amputation. *Cont Educ Anaesth Crit Care Pain.* 2004;4:20-23. doi: 10.1093/bjaceaccp/mkh007.
6. **Ziegler-Graham K, MacKenzie EJ, Ephraim PL, Trivison TG, Brookmeyer R.** Estimating the prevalence of limb loss in the United States: 2005 to 2050. *Arch Phys Med Rehabil.* 2008 Mar;89(3):422-9. doi: 10.1016/j.apmr.2007.11.005. PMID: 18295618.
7. **Foell J, Bekrater-Bodmann R, Diers M, Flor H.** Mirror therapy for phantom limb pain: brain changes and the role of body representation. *Eur J Pain.* 2014 May;18(5):729-39. doi: 10.1002/j.1532-2149.2013.00433.x. Epub 2013 Dec 10. PMID: 24327313.
8. **Makin TR, Flor H.** Brain (re)organisation following amputation: Implications for phantom limb pain. *Neuroimage.* 2020 Sep;218:116943. doi: 10.1016/j.neuroimage.2020.116943. Epub 2020 May 16. PMID: 32428706; PMCID: PMC7422832.
9. **Stankevicius A, Wallwork SB, Summers SJ, Hordacre B, Stanton TR.** Prevalence and incidence of phantom limb pain, phantom limb sensations and telescoping in amputees: A systematic rapid review. *Eur J Pain.* 2021 Jan;25(1):23-38. doi: 10.1002/ejp.1657. Epub 2020 Sep 28. PMID: 32885523.