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Case report

Very early phantom limb pain following amputation of a lower extremity: Case report[☆]

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ABSTRACT

This is a case of a patient with very early occurrence (18 h) of phantom limb pain (PLP) following amputation of a lower extremity. The clinical data prior to the event, the pathophysiology, the clinical manifestations and the treatment of the phantom limb pain are described. A literature review on the current status of the PLP etiology and any analgesia interventions that may control its occurrence and intensity was performed and a description is given of the timely interventions affecting the outcome.

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Miembro fantasma doloroso muy temprano luego de amputación de la extremidad inferior. Reporte de caso

RESUMEN

Se presenta el caso de un paciente con aparición muy temprana (18 h) de miembro fantasma doloroso (MFD) luego de la amputación de la extremidad inferior. Se describen los datos clínicos preexistentes al evento, la fisiopatología, las manifestaciones clínicas y el tratamiento para el MFD. Se realiza una revisión de la literatura sobre el estado actual de la etiología del MFD y las intervenciones analgésicas que puedan controlar su aparición e intensidad. También se describen intervenciones que pudieran modificar dicho desenlace para el presente reporte de caso con una aplicación oportuna.

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Palabras clave:

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Introduction

Pain following the amputation of an extremity may present as phantom limb pain (PLP), stump pain, or both.¹ The prevalence of PLP has been reported in 30% and up to 80% of patients.²⁻⁴ This is a frequent and debilitating disease following surgery that affects the patient's quality of life and rehabilitation.

The onset of PLP is variable. Most cases present from the third week post-amputation, but some cases have been reported as early as the fifth postoperative day.^{5,6}

Several risk factors for the occurrence of PLP have been described, including the intensity of pre-amputation limb pain with a statistically significant association.^{7,8} Recently, the intensity of post-operative pain has also been identified as an associated factor.⁹ Additionally, other risk factors have been described, such as postoperative radiotherapy and lower extremity amputation.

The abovementioned risk factors for PLP may coexist. Pre-existing limb pain may increase in duration and severity if the patient requires multiple surgical procedures, attempts for limb salvage or when the limb becomes infected prior to amputation.

This case report describes a very early onset of lower extremity PLP and possible contributing factors to PLP based on a literature review.

Case report

A 19-year-old male patient was admitted to our hospital following a complex left leg trauma as a result of a motorcycle accident involving vascular lesions and soft tissue avulsion. The patient required a series of reconstructive surgical procedures in an attempt to salvage the limb. Initially the patient experienced somatic postoperative pain associated with the first vascular and reconstructive surgical interventions. The pain was clearly localized and continued at the surgical bed, and improved in the first few hours after the surgical attempts to salvage the limb. The pain was managed with systemic opioids prescribed by the treating physicians, in addition to oral acetaminophen and NSAIDs administered in 3-5 days cycles. During the last few weeks the pain became resistant to tramadol, so patient-controlled analgesia (PCA) was started for pain associated with surgical lavage. The patient underwent several lavage and debridement procedures of necrotic tissue but failed to control the leg infection. Two months later the patient was scheduled for below the knee amputation. The patient received general anesthesia, 2 mg/kg propofol anesthetic induction, fentanyl 2 mcg/kg, rocuronium 0.6 mg/kg and sevoflurane maintenance and oxygen at therapeutic doses. The anesthesiologist attending the amputation procedure did not use regional or neuroaxial techniques in the patient. The analgesia during recovery was based on morphine at salvage doses of 0.05-0.1 mg/kg/bolus every 5-10 min in the post-anesthesia recovery room. In the first 6 h after surgery the patient described his pain as continued, moderate to severe, in the stump area. The acute pain specialists were consulted for the first time after surgery, because the patient developed phantom limb pain

18 h after amputation. The PLP was described as severe, pressure-type pain, in addition to other neuropathic pain descriptors such as lancinating, cramp-type pain in the absent foot.

Perioperative stump pain and concomitant phantom pain were managed in the hospital floor with a higher titration dose of intravenous morphine with poor response. Morphine was continued during the next 6 h and a multimodal therapy was initiated with a 0.15-mg/kg bolus of intravenous ketamine followed by 0.15 mg/kg/h infusion. The phantom limb pain decreased down to 4/10 in the verbal numerical pain scale. When the patient tolerated the oral route, neuromodulator treatment was added with amitriptyline and pregabalin to control moderate to severe pain episodes, both in the stump as in the phantom limb. After three days the agent was switched to slow release oral oxycodone and stable doses of amitriptyline (50 mg/day) and pregabalin (300 mg/day). The ketamine infusion was stopped after 7 days and the patient was then discharged with an oral multimodal analgesia regimen and continued outpatient follow-up in the pain management clinic.

Discussion

Acute postoperative pain following amputation of an extremity is usually somatic in nature and mainly affects the stump. After several days or months, neuropathic pain may present in the stump and/or phantom limb pain that complicate the patient's rehabilitation and could be interrelated.¹⁰ In this case, we observed PLP for a short period of time after surgery (18 h), associated with acute postoperative stump pain.¹¹

Very early occurrence and severe intensity of PLP associated with perioperative somatic pain may be the onset of a chronic pain syndrome with a stronger impact on the patient's quality of life.

There are physician-modifiable risk factors for the presence of PLP. The severity of the acute operative pain is the strongest risk factor associated with chronification of post-surgical syndromes such as PLP, post-thoracotomy syndrome, inguinal post-herniorrhaphy syndrome, among others.¹²

In a prospective study of 56 patients scheduled for lower limb amputation, Nikolajsen et al., reported that phantom limb pain was more frequent in patients with pre-amputation pain.⁷

While pre-amputation pain is a well known risk factor for PLP, we hypothesized that it is not just the intensity, but also the duration of prior pain in the amputated limb that contribute to phenomena such as central sensitization and amplification of the receptive fields that promote earlier occurrence of PLP.¹³ Both high and low frequency C-fiber persistent nociceptive stimuli are associated with long term potentiation (LTP), a phenomenon related to hippocampal changes for the establishment of memory and to persistent pain in animal models.^{14,15}

The inflammation that usually co-exists in this type of patients as a result of repeated surgical stimuli and occasionally as a response to infection, may also increase long term potentiation,^{16,17} and theoretically be linked to earlier memory establishment.

While the pathophysiology of PLP is complex, there are some practical clinical approaches that may theoretically affect this phenomenon. Studies on pre-emptive PLP measures such as the use of ketamine or epidural anesthesia, *inter alia*, have shown variable results or pose methodological difficulties.¹⁸

A recent clinical trial by Karanikolas et al. studied whether the optimization of analgesia, both in the pre- and post-operative period of patients undergoing lower extremity amputation, reduced the incidence of postoperative and phantom limb pain at 6 months in 65 patients. In all groups the intervention started 48 h prior to surgery and continued for 48 h after surgery (with on-demand analgesia regimens or epidural), resulting in a lower incidence of phantom limb pain with optimized perioperative analgesia as compared to the control group.⁹ Therefore, the infusion of ketamine at analgesia doses (0.1–0.2 mg/kg/h) has shown to reduce post-amputation pain and the severity of PLP.^{19,20} Similarly, we observed a reduction in early PLP with ketamine administration – an effect some researchers have associated with NMDA receptor blockers, a phenomenon related to the development of LTP and central sensitization.^{21,22} On the other hand, the value of drugs such as gabapentinoids and tricyclics for PLP is recognized^{23,24} but their oral titration is usually slower and therefore we suggest extending ketamine administration for up to seven days. At the indicated doses, no significant psychotropic effects were observed.

So it may be concluded that according to the most recent evidence,⁹ early implementation of measures such as regional block or epidural analgesia, if planned prior to surgery, were able to change the rapid evolution to PLP in this case. In isolation, these measures do not provide for good outcomes in reducing the frequency of chronic postoperative pain, since the concept behind preventive analgesia includes systemic drugs such as NSAIDs and ketamine.

Conclusion

Early presentation of PLP in this report may be attributed to longer pre-existing pain and inflammation prior to the amputation, based on the central sensitization models described in the literature. Moreover, the occurrence of such chronic severe intensity, post-surgical pain, is associated with severe perioperative pain, a condition that may be avoided with axonal blockade techniques and preemptive multimodal analgesia that were not planned by the anesthesiologist in this particular case. Postoperative management with neuromodulators and the preventive or therapeutic use of antihyperalgesic agents such as ketamine, are both interventions aimed at changing this outcome.

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Conflicts of interest

The authors have no conflicts of interest to declare.

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