Clinical note

Nerve resection, crush and re-location relieve complex regional pain syndrome type II: A case report

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ABSTRACT

This case report describes the remarkable recovery of a patient with very long-standing, medically intractable and disabling, lower-limb, complex regional pain syndrome type II following the resection, crushing, and relocation of sensory nerves.

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1. Introduction

Chronic neuropathic pain due to nerve trauma (complex regional pain syndrome [CRPS] type II, or causalgia) is usually not treated by peripheral nerve section, grafting, or relocation surgery by chronic noncancer pain specialists. This appears to be due to a perception of lack of efficacy and fear of pain exacerbation or of the expectation of the inevitable return of pain. The experience of peripheral nerve surgeons is to the contrary [19]. It is time for a re-evaluation of surgical treatment in light of advances and experience in reconstructive plastic surgery and hence, the need for the publication of reports of successful surgery of this type. We selectively searched pain journals, books, and book chapters on CRPS to determine the evidence base for chronic noncancer pain specialists regarding the surgical treatment of causalgia. A few reports were found in the pain literature of the relief of upper-limb nerve causalgia by nerve section and grafting [14,27] and a report of infraorbital nerve causalgia relieved by nerve section, grafting, and relocation [37]. Here we report the remarkable case of severe, very long-standing, and intractable lower-limb causalgia with immediate and long-term relief following peripheral nerve surgery.

2. Methods

Assessment tools used in this case report were the visual analogue scale (pain, depression), numerical rating scale (pain), category scale (pain), the Hospital Anxiety and Depression scale (HADS) [40], the Pain Disability Index (PDI) (function) [6,28], the Brief Pain Inventory Interference scale (BPI-I) (function) [7], and the Short Form Health Survey (SF12v2) [36] for health-related quality of life. Figs. 1 and 2 and Supplemental Figs. 1–4 show clinical and functional impairment before surgery. We have used, in part, a qualitative narrative approach in order to capture the unique perspective of the patient and her mother. This is in the article but also online. The patient and her mother provided written permission to print unedited photographs including their faces in print and online.

3. Case report

3.1. History and examination

A 19-year-old woman from Alberta, Canada was seen by one of the authors (P.W.) in October 2010. At this time the patient presented with a 13-year history of continuous, severe, burning pain, allodynia, edema, erythema, and hair coarsening of the left lower leg following a severe inversion ankle sprain without fracture at ...
the age of 6 years after a fall from a playground climber. Prior to 2010 she had been treated with an ankle foot arthrosis brace for one month and had many nonsurgical treatments (Supplementary Table 1) in a pediatric pain clinic. At this stage, the pain was thought to be due to CRPS Type II. The sensory findings were consistently localized to the superficial peroneal nerve, and about 2 years after injury the pain was completely and repeatedly blocked by local anesthetic injections at the fibular head, performed by one of the authors (P.F.). More details of these local anesthetic and also phenol blocks are appended to Supplementary Table 1. The phenol block provided partial relief, but the residual pain was severe enough to warrant referral to Neurology.

At age 13 years (December 2004, 7 years after the initial trauma), the patient had an “arthroscopic debridement of the left ankle, lateral ligament repair and reconstruction of the joints using a screw in the left ankle” (case notes). Shortly after this operation she developed frequent severe electric shock-like neuropathic pain in the alldynic area of the left lateral ankle.

In June 2005 the screw was removed and a neurema (case notes) was resected, but with no improvement. The patient participated in a multidisciplinary pain management program beginning in 2006. The treatments included physiotherapy with a pediatric pain physiotherapist, and group and individual cognitive-behavioural therapy for pain management, pain education, relaxation training, biofeedback, and supportive counseling with a pediatric pain psychologist (T.C.). At this time, she was assessed for social and emotional functioning and was described as having difficulties with pain-related anxiety. Over the next 2 years, with continued decline in her physical functioning, the patient’s social and emotional functioning also declined. At age 18 years (2009) she was transferred to an adult pain service and participated in privately funded psychological pain management with one of the authors (T.C.). Her pain continued unabated and in the severe (7–10/10) range for all components despite the variety of medications and procedures listed in Supplementary Table 1.

During the period of 2009–2010, the patient gained 80 pounds (probably related to antidepressants and gabapentinoids), acquired benign intracranial hypertension (headaches and papilledema) attributed to the birth control pill, and acquired idiopathic thrombocytopenic purpura attributed to diclofenac. The latter 2 complications responded to treatment.

An electromyogram and nerve conduction study 18 months before the surgery described below identified absence of conduction of the left superficial peroneal nerve. Sural nerve conduction was present and symmetrical. The diagnosis by the physiatrist/electrophysiologist was CRPS type II involving one nerve (the superficial peroneal) based on this test and the clinical findings. A consultation with a neurosurgeon specializing in peripheral nerve surgery at this time concluded that there was also possible involvement of the sural nerve (due to the extent of sensory disturbance [13]).

When examined in October 2010 (P.W.), the patient reported a steady burning pain, frequent electric shocks, and extreme sensitivity of the left lower lateral leg with touch-evoked pain in the same area, all rated as severe and between 7 and 10 on a 0–10 scale (Fig. 1). She slept with her leg exposed (Fig. 2) and slept poorly because of the pain evoked by contact with the bed linens. She remained severely restricted in activities, getting about in a wheelchair for short distances at home. She moved about on her hands and knees to avoid tactile contact with the lower left leg (Supplementary Fig. 1). She could not wear shoes, socks, or long pants (wearing shorts instead) because of the aggravation of the skin sensitivity and steady, burning pain (Supplementary Fig. 2).

She wrapped her leg in ice before a shower (Supplementary Fig. 3A, B) and could not submerge the leg in a bath. An ankle foot arthrosis brace failed to provide protection (Supplementary Fig. 4). She was taking long-acting oxycodone 120 mg every 12 hours, transdermal fentanyl 25 µg/hour every 3 days, pregabalin 150 mg twice a day, amitriptyline 150 mg at night, and oral ketamine 25 mg twice daily. The area of “all pain” was over a wide area of the left lower lateral leg (Fig. 1) with an area of “deep” pain over the anterolateral ankle. She had exquisite allodynia to touch, both punctate and dynamic, and hyperalgesia to pin and cold on the left lateral lower leg (Fig. 1). Here the skin was equally dry and of the same temperature as the corresponding area on the right leg. There was no weakness of the ankle or in the limb proximally, and the reflexes were present and equal. There were no trophic changes in skin, hair or nails, or swelling. There was pain-limited restriction of left ankle movements. The diagnosis was CRPS II based in part on the previous observations of others of lower-limb erythema, edema, hair coarsening, and allodynia. The lesion was thought to lie in either the superficial peroneal plus sural nerves [13], or in the superficial peroneal nerve alone, with centrally mediated extraterritorial pain [29] extending into the territory of the sural nerve.

Consultation with 3 experienced and highly respected pain neurosurgeons in different North American centers counseled against nerve resection. The patient was then referred to a plastic surgeon in St. Louis, Missouri, USA (S.M.) based on previous success with a similar case [37].

Pain descriptors (see Dr. Mackinnon’s rating scale online) chosen just prior to surgery in St. Louis were of “throbbing,” “smarting,” “aching,” “shooting,” “stabbings,” “tingling,” and “hypersensitive.” Pain severity in the left leg “now,” “over the past month,” and “past week” was severe and 10/10 on a 0–10 rating scale where 10 means worst possible pain. A quality-of-life visual analogue scale was 10/10 and also “100% affected.” A visual analogue scale for depression was 7/10, for stress 7/10, and coping 5/10. Pain was reported to be increased by activity and by hot and windy weather. Difficulty falling asleep and remaining asleep...
were identified. Intimate personal relations were described as affected, as well as frequent suicidal rumination and inability to work and do household chores. Three wishes expressed were: 1) "to be normal and have no pain, be on no meds, and no side effects and to want my brain back," 2) "to go to school to study psychology and acupuncture," and 3) "be able to have normal relationships and to learn who I really am without meds."

3.2. Surgical procedure (Sept 28, 2011, full details online; Supplementary Figs. 5A–C, 6A & B), further details of surgical rationale and technique: http://nervesurgery.wustl.edu and references [3,4,10,19,32]

Surgery entailed resecting and cauterizing the superficial peroneal and sural nerves near the ankle, relocating the proximal nerve stumps into deep muscle around the gastrocnemius/soleus interface, and crushing both nerves [3] near the fibular head, for 30 seconds with a hemostat about 35 cm proximal to the ankle. See online description for further details.

3.3. Postoperative course

Immediately and at 12 days postoperatively, there was an absence of all neuropathic pain components (steady burning, shocks, and skin sensitivity [alldynia]), and strikingly, the patient was immediately able to wear socks and tolerate clothing and bedclothes on the lower left leg due to relief of the alldynia (Fig. 3) (Supplementary Fig. 7). She said, "It is the first time in 7 years that I have been without pain." The severe, constant, nontriggered "nerve pain" in the alldynic area was also much diminished. The predominant steady pain after surgery she described as "joint pain" slowly diminished.

At 5 months after surgery the patient was re-assessed in Toronto (P.W.). She said that since immediately after the surgery, the skin sensitivity had been gone and she had been able to wear socks, shoes, and pants. Her previous pain was replaced by a different postoperative "pressure-pain" clearly distinct from the preoperative "nerve pain" and rated at 2/10 and "mild" without medication. This pain was "0.5/10" with medication consisting of pregabalin 50 mg twice daily, amitriptyline 50 mg at bedtime, long-acting oxycodone 80 mg every 8 hours, transdermal fentanyl 100 μg/hour every 3 days, and oxycodone 50 mg every 4 hours as needed (this was used infrequently). There was a problem with withdrawal symptoms due to opioid dose reduction, and an increased opioid dose may also relate to the reduction in amitriptyline and pregabalin because of weight gain and the discontinuation of ketamine at this time. Her HADS score was 5 (no significant depression or anxiety), all BPI interference scales and PDI scales were 0–4 at most or "moderate," and the SF12v2 indicated a good health-related quality of life. There was a problem with insomnia but this was not believed to be pain-related. She was driving, going out socially, and walking 50 feet, but stopped at this distance by ankle soreness, which she felt as an ache that was unlike her previous "nerve pain." Examination revealed healed scars. There was a large area of reduced sensation to touch, pin, and cold over the lateral left leg, conforming to the superficial peroneal and sural nerve territories (Supplementary Figs. 6A & B and 8). There was no alldynia, hyperesthesia, or hyperalgesia. The skin, hair, and nails of the left leg appeared normal. A plan for gradual medication reduction was developed.

At 1 year postoperatively, the patient continued as before and could walk for 30 minutes. She remained on 10 mg long-acting oxycodone every 8 hours, celecoxib, transdermal fentanyl 100 μg/hour every 3 days, pregabalin 150 mg/day, and amitriptyline.
50 mg/day, and occasionally used short-acting oxycodone 50 mg as needed, but not daily.

Rating scales administered at 15 months postoperatively (January 2013) rated the “nerve pain” at 0/10, the ankle “joint pain” at 5/10 with walking and other activity, PDI, BPI domains were all <5 (except BPI for walking, which was 7/10), “pain relief” was 10/10, with the comment that “I do not normally have ‘nerve pain’ any more.” The HADS was 11/44 and not indicative of significant anxiety or depression. At this time she was off oxycodone, pregabalin, and amitriptyline, but continued transdermal fentanyl 25 μg/hour. Measures administered by the psychologist also indicated a significant decrease in symptoms of anxiety and depression. Her psychologist (T.C.) stated that, “psychologically, the patient is working on now adjusting to life without pain in terms of planning for her future and living with hope. The normal developmental trajectory was interrupted by the pain experience over many years. She is currently working on developmental stages her same aged ‘normal’ peers navigated four and five years ago.”

The patient continued to have complete relief of neuropathic pain symptoms at 21 months after surgery (July 2013). At this time, the “joint pain” (felt at the ankle joint area dorsally on the foot) was absent while sedentary. Walking steadily for >10 minutes also caused a rise in the “joint pain” to 6–7/10 and was relieved by stopping after about 30 minutes. She had no “nerve pain” at this time.

At 26.5 months postop, the patient had no “nerve pain” and describes “ankle pain” at 4/10 at rest, increasing to 7/10 with prolonged activity such as walking about a block, and is currently on transdermal fentanyl 12 μg/hour every 3 days with continued slow gradual withdrawal.

### 4. Discussion

We describe here a patient with intractable lower-limb CRPS II of long duration relieved by a surgical procedure.

#### 4.1. What caused this patient’s pain?

In retrospect, it is very probable that this patient had 2 kinds of pain that had co-existed at least since the time of her ankle surgery in 2004. The first kind was clearly neuropathic, with burning pain, allodynia, hyperalgesia, and electric shock-like pains. It is probable that this was subsequent to an initial injury to the superficial peroneal nerve, with possible aggravation and additional insult to the sural nerve at the time of her ankle surgery. The second pain was a musculoskeletal pain from some pathology of the ankle joint that is yet to be defined. After surgery had relieved the neuropathic pain, the patient could clearly describe this musculoskeletal pain as a deep and aching pain that was exacerbated by walking. The patient insisted that her remaining “ankle pain” was clearly different from her prior “nerve pain.”

It is probable that the patient’s neuropathic pain followed injury that interrupted axons in the superficial peroneal and sural nerves. Thus, her spontaneous pain may have been a consequence of spontaneous ectopic discharge from axotomized afferent axons [8]. Such discharge may have also initiated and maintained central changes (sensitization) that generated her allodynia and hyperalgesia. However, the ectopic discharge that caused pain and central sensitization may not have been “spontaneous” [2].

Dissection revealed that the superficial peroneal and sural nerves were trapped in scar tissue that tethered the nerves to adja-
cent structures and possibly to each other. Stump neuromas and neuromas-in-continuity are often surrounded by scar tissue that tethers them to adjacent structures. Normal axons are relatively insensitive to mechanical distortion, but axonal sprouts ending in a neuroma may acquire exquisite mechanosensitivity [5,38]. There is evidence for this in both animals [5,11,17,30,38] and man [23,24]. For example, in the chronic constriction injury model in the rat, the mid-thigh neuroma-in-continuity becomes tethered to both dorsal and ventral thigh muscle in a large mass of scar tissue. Taping the neuromatous mass or stretching it by flexing the limb causes discharge that excites nociceptive neurons in the spinal cord dorsal horn [18]. In the patient described here, the location of neuromatous scars and intraoperative observations suggest that any movement of the foot, even movement of the toes, might have caused discharge in sensory axons ending in the neuroma; a likely cause of pain. The presence of electric shock-like pain is especially suggestive of mechanical distortion of a neuroma, as this would lead to the simultaneous discharge of large numbers of abnormally mechanosensitive afferent endings in the neuroma [1]. Pain evoked by mechanical stress on a neuroma is another example of stimulus-evoked pains related to activities of daily living that may be confused with “spontaneous pain” [2].

It is noteworthy that the patient experienced immediate and complete relief of her neuropathic pain symptoms (steady burning pain, allodynia, hyperalgesia, and electric shock-like pain). This suggests that the entire neuropathic pain syndrome was dependent on neural activity originating distal to the resections. This is consistent with the observation that neuropathic pain can be temporarily eliminated by local anesthesia of a neuroma [12]. Our patient experienced immediate relief of severe neuropathic pain of 13 years duration. Such a result challenges the concept that central neuroplastic changes always become permanent and independent of a peripheral afferent drive. It is well known from many recent studies [26] that various different types of peripheral nerve injury in animal models of neuropathic pain lead to a constellation of changes not only in the affected nerves including their dorsal root ganglia but also in the dorsal horn, thalamus, and descending modulatory pathways. These central changes can include activation of glia, alterations in chloride homeostasis, changes in gene expression, up- or downregulation of various neurotransmitters and receptors, and can lead to reduced inhibition and sensitization of spinal cord dorsal horn nociceptive neurons [15,25,26,31,33,39]. There is also much evidence that in many cases these central changes, which result in mechanical allodynia and hyperalgesia and nociceptive behavior, depend on afferent activity from the injured nerve [9].

The fact that this patient’s neuropathic pain did not return after the operation (also the case for the infraorbital nerve resection patient we have described previously [37]) may be explained in 2 ways. First, it may be that spontaneous ectopic discharge was never a factor in this patient, with ectopic discharge due to abnormal mechanosensitivity the only pain generator. Animal data support the idea that axotomized axons may acquire abnormal mechanosensitivity without demonstrating spontaneous discharge [5,11,17,30,38]. Second, it may be that spontaneous discharge from a neuroma does not recur when a new neuroma forms.

4.2. Why the reluctance to operate?

In our experience, there is a general view in the community of physicians and surgeons specializing in chronic pain that surgery aimed at further denervation does not generally help neuropathic pain such as CRPS II. The belief seems to be that nerve transection runs the risk of aggravating a central sensitization component and exacerbating pain, and in the best of cases offers no more than temporary relief.

The following discussion is based on a search of books and articles in the pain literature likely to form the evidence base of pain specialists. In Mitchell’s 1872 description of causalgia, a term he coined for nerve trauma pain (now CRPS II) in Civil War soldiers [21], there is an account of median nerve resection that moderated pain in the distribution of the resected nerve. Noordenbos and Wall’s (1981) report [22] of surgical outcomes in 7 cases of pain from nerve trauma (3 upper and 4 lower limbs) emphasized the lack of satisfactory relief by nerve resection. They concluded that, “This operation should not be done in patients with this condition. Reasons are given to suggest that peripheral nerve damage induces changes in the central nervous system which are not reversed by treatment directed at the area of the original injury.” This article by 2 eminent pioneers in the pain field may have contributed to a negative view. However, details given of these 7 patients did reveal that 3/7 had some evidence of improvement.

The results of experimental studies of the consequences of nerve injury in rats probably also contributed to a reluctance to operate on CRPS II patients. First, it was shown that transected primary afferent sensory fibers ending in a stump neuroma acquired a spontaneous discharge that originated at both the end of the transected axon and in the axon’s cell body in the dorsal root ganglion [11,16,34,35]. Insertion of microelectrodes into human stump neuromas confirmed that these phenomena occurred in man and that they were present even many years after the nerve injury [23,24]. Spontaneous discharge offered a ready explanation for the persistence of spontaneous pain and dysesthesiae. It was known that exciting a neuroma is followed by the growth of a new neuroma. This may have suggested to some that one could hope for no more than partial and temporary cessation of pain-evoking spontaneous afferent discharge. It should be noted that the experimental evidence is not as clear-cut as it might seem. The appearance of spontaneous discharge in sensory axons after nerve transection is not always seen [20], and to the best of our knowledge, no one has ever demonstrated the return of spontaneous discharge after neuroma resection.

Although there are many articles in a general search, and particularly of articles found in plastic surgery journals, only a few reports of surgery for CRPS II have appeared in the pain literature in the last 2 decades. Inada et al. (2005) [14] reported 2 cases of relief of digital nerve injury pain in the hand by nerve sectioning and the use of an artificial nerve guide tube. Two of the current authors (P.W. and J.D.) and their colleagues reported (2007) the case of a youth with intractable infraorbital nerve injury pain due to orbital fracture who had gradual (unlike this patient), but eventually complete, relief (now at 9 years) after nerve resection proximal to the injury with grafting and nerve relocation [37]. Stovik et al. (2010) [27] reported on 34 patients operated on for upper-limb “neuroma pain” by nerve resection with either restoration of nerve continuity or burying of the proximal stump in bone or muscle. Nineteen of 34 (56%) reported satisfaction with the result at a mean of 22 months and with functional improvement. However, none of the 34 patients had complete resolution of “spontaneous” pain.

4.3. Conclusions

The option of peripheral nerve surgery, with or without a graft or nerve reconstitution, for patients with CRPS II needs to be more widely recognized. A surgeon skilled in nerve reconstruction and familiar with the techniques described here is essential. More details of this type of surgery are available in the additions to this article online, at http://nervesurgery@wustl.edu, and in reference [19]. Crushing the nerve proximal to the neuroma excision may be essential for a positive outcome [3,19] (see also online surgery description re: Schwann cell senescence). A search for Tinel sign(s)
before surgery may help in patient selection. It may be possible to identify a positive Tinel response even when the skin is allodynic because the localized response (electric shock-like pain) ought to be distinct from the pain of dynamically touching an allodynic area. Consideration of the involvement of more than one nerve may be important, as a wide area of allodynic skin may not necessarily be due to central sensitization. It may be critical to search for tethering by neuromatous adhesions. Involvement of a nerve(s) with a significant motor component may be a contraindication. The risk that this type of surgery may fail or even exacerbate pain is unknown, and the true outcomes of this procedure can only be known from careful, quantitative follow-up of many other cases.

Conflict of interest statement

The authors have no conflicts of interest.

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Appendix A. Supplementary data

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