

Amputation of the upper extremity due to chronic, refractory CRPS: a case report

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ABSTRACT

Chronic refractory complex regional pain syndrome (CRPS) is the severest form of this condition characterised by acute pain, other painful phenomena (hyperpathia, allodynia), severe functional impairment of the affected extremity and non-responsiveness to standard treatments. This paper presents a case of a 40-year-old man suffering from this form of CRPS, in whom all treatment options, including non-standard appeared ineffective. The patient suffered from intractable pain and a completely disabled extremity was considered by him a burden,

additionally affecting his daily living. After a review of the literature and informing the patient about the potential benefits and the potential risk of failure of surgery, at the request of the patient an amputation of the upper extremity was performed at the level of $1/3$ distal arm. The postoperative course was uneventful, but amputation did not result in cessation of the pain which persisted in the residual limb. The presented case shows that limb amputation for chronic refractory CRPS may not give expected beneficial effect.

Keywords: chronic CRPS; resistance to therapy; limb amputation.

INTRODUCTION

Complex regional pain syndrome (CRPS) is a descriptive term for a complex of symptoms and signs, including pain at rest, swelling, and vasomotor instability (changes of colour, temperature and sweating), accompanied by severe functional impairment of the affected hand or a whole extremity. It is usually caused by trauma or surgery and is characterised by the presence of those symptoms and signs which are more severe than would normally be expected for the degree of the trauma of the precipitating event and extend beyond the area involved by the initial trauma [1, 2, 3].

Complex regional pain syndrome may present in 2 different clinical forms: acute/early, lasting up to 4 months and chronic/late, which may last years. Some patients develop a specific subtype of the condition called “chronic refractory CRPS” or “long-lasting therapy resistant CRPS” [4]. Chronic refractory CRPS involves almost exclusively young women and is characterised by severe pain – reaching 9–10 on the numeric rank scale (NRS), range 0–10 – and other painful phenomena (hyperpathia, allodynia), the need for regular analgesic consumption (including opioids), severe functional impairment of the affected extremity and the absence of or poor responsiveness to the treatment [5]. The causes of the progressive course, unresponsiveness to the treatment and involvement of only young women in these forms of CRPS are not known.

The author of this paper has never been able to find any standard treatment option that resulted in middle-time perspective liberation from pain experienced by chronic refractory CRPS patients treated at the author’s institution. Two non-standard treatments have been used at the author’s institution

in these patients, namely subanaesthetic intravenous ketamine infusions and continuous brachial plexus blocks with bupivacaine [6, 7]. However, the use of these treatments is limited in terms of the number of possible procedures of implantation of a catheter into the brachial plexus, and tolerance to ketamine. Therefore, some patients suffering from chronic therapy-resistant CRPS may not receive any effective analgesic therapy. Consequently, some may request amputation of the affected limb due to severe and unbearable pain, as well as infections, or extremely limited mobility. However, amputation as a treatment for long-standing therapy-resistant CRPS remains controversial [8, 9, 10]. The procedure is irreversible, associated with surgery-related complications, and may result in phantom pain. Furthermore, CRPS can recur in the residual limb or elsewhere, for instance, in the opposite limb. A study comparing CRPS patients with and without amputation found clinically relevant differences in all outcome measures, favouring the amputation group [11]. Limited data exist on the long-term effects of amputation as a treatment for long-standing therapy-resistant CRPS and little is known about the course of patients’ functioning following amputation.

This article, presents a case of a patient suffering from chronic therapy-resistant CRPS of the upper limb who underwent amputation due to intractable pain and total disability of the affected extremity.

CASE REPORT

A 40-year-old patient sustained a crush injury of his left, non-dominant hand in a work-related accident in Norway, in 2018.

Immediately after the accident he was fitted with a plaster splint at the emergency department of a hospital in Oslo, although no hand bone fracture was diagnosed during that visit.

In the next 3 months, the patient underwent 2 operations, probably due to missed metacarpal fractures (the documentation of these treatments was not available). The patient reported that infection of the operative wound occurred after the first operation, which was confirmed by bacteriological culture. The post-operative course was not uneventful and the patient's hand condition deteriorated, instead of improving. Approximately 6 months after primary injury (3 months after surgery), symptoms and signs of complex regional syndrome appeared in the patient's hand followed by the commencement of treatment according to Norwegian standards (physiotherapy; analgesic drugs, including opioids and anti-convulsants; spinal cord stimulation). That therapy proved ineffective and the state of the patient's hand gradually deteriorated. He presented at the author's institution in July 2020 (2 years after injury) with the signs and symptoms of chronic CRPS of the affected hand, such as:

- severe pain at rest of the left hand and forearm (assessed by the patient at 8–9 on the NRS),
- allodynia involving the hand and the forearm (severe pain experienced at light touch),
- total dysfunction of the left hand,
- dystonia of the hand (compulsory position of the hand in flexion of the wrist and fingers).

As the severe pain, resistant to standard analgesic therapies, was the main problem for the patient, he was proposed to undergo non-standard therapy which has been used in similar cases in the author's institution for several years, namely, implantation of the catheter for continuous anaesthesia of the brachial plexus with bupivacaine [7]. In this model, the patient regularly gives himself the anaesthetic drug through the catheter, which results in cessation of the pain for 6–8 h. It is a palliative treatment used in patients in whom all standard analgesic therapies failed.

The operation was performed in July 2020 with full success, as the patient's pain reduced significantly and he could stop taking any analgesic medication. Unfortunately, the operation did not correct dystonia and did not improve the function of the affected hand. Due to progressing flexion of the fingers, threatening with the development of decubitus and infection of the skin in the palm (Fig. 1), a tenotomy of the flexor tendons in the left forearm was performed in February 2021. This allowed partial correction of the contracture and passive extension of the fingers. The catheter implanted in the brachial plexus worked until February 2021 (6 months) when it fell out. This resulted in the recurrence of pain at the same level as at baseline. The next catheter was implanted in the brachial plexus in March 2021 and it worked for approx. 4 months. During the next several months, the patient received drug therapy with analgesics (including opioids), anticonvulsants (gabapentin, pregabalin) and antidepressives. As could be expected, this

therapy was ineffective and the patient suffered from pain at 7–8 points on NRS.



FIGURE 1. Dystonia of the left hand of the patient, before tenotomy

In October 2021, an attempt at treatment with intravenous ketamine infusions was undertaken. The use of ketamine for CRPS treatment is based on finding the role of glutaminergic N-methyl-D-aspartate receptor (NMDA) in the process of "sensitisation" in the central nervous system. A "sensitisation" is a persistent susceptibility of the central pain-projecting neurons to discharge (firing), either spontaneously or due to low-threshold peripheral stimulation. This is believed to be an underlying mechanism in neuropathic pain. Activation of the NMDA receptor by Mg^{++} ions opens calcium channels of sensory and pain pathway neurons, leading to their discharge. There is some evidence that ketamine has strong NMDA-receptor-blocking properties (antagonist) resulting in the inhibition of the central sensitisation mechanism [6]. Unfortunately, this therapy failed, as the patient just at the beginning of the first ketamine infusion reported extremely severe, unpleasant sensations and the infusion had to be stopped. It is reported in the literature, that a proportion of patients feel unpleasant sensations during ketamine infusions, such as anxiety, hallucinations and nightmares which for some of them are intractable. This was the case with our patient.

In November 2021, a third procedure of implantation of the catheter in the brachial plexus was performed; the catheter worked until March 2022 (5 months). After falling out of the catheter and the return of severe pain, the patient started to ask about amputation of the affected limb which was functionally totally disabled and was felt by the patient as a burden. This prompted the author of this paper to review the literature which showed some positive outcomes after amputation of the limbs in long-lasting, therapy-resistant CRPS. The problem was discussed with the patient in detail, and possible complications as well as failures were presented. The patient was informed that amputation of the affected limb does not warrant reduction of pain and the chance for improvement is estimated at a max. of 30%. The risk of developing another type of pain (phantom pain) in the residual limb (a stump) was also mentioned. After

discussing all these aspects, the patient upheld his decision to amputate the left upper limb.

The operation was performed under general anaesthesia and in the bloodless operative field (with the tourniquet). The upper limb was amputated at the distal $\frac{1}{3}$ of the arm, the brachial artery and vein were ligated, median and ulnar nerves were microsurgically fitted and the stump of the arm was formed. The postoperative course was uneventful and the patient was released home at day 3 post-surgery. Unfortunately, during his stay at the ward, he started to complain of the same symptoms as prior to surgery. He received a prescription on strong analgesic drugs. At the 1-month follow-up visit, the patient reported the same pain as prior to surgery and, additionally, very unpleasant phantom pain. He had also allodynia of half of the residual limb. This showed that the operation failed in terms of liberation from pain and allodynia. Considering this poor outcome, the patient was proposed to implant the next catheter in the brachial plexus, which was done in September 2022 (Fig. 2).



FIGURE 2. The stump of the arm, at 3 months after amputation. Note end of the catheter for brachial plexus analgesia

DISCUSSION

The presented case is the first in the author's experience in amputating the limb of a patient suffering from chronic refractory CRPS. Over more than 30 years of the author's involvement in the management of CRPS patients, such a dramatic decision was taken for the first time. Unfortunately, the outcome in the

presented case was bad, as surgery did not cause cessation of pain, but resulted in another unpleasant phenomenon – phantom pain. Considering the future management of the patient, he will probably receive the next implantations of the brachial plexus catheters.

LITERATURE REVIEW

Few articles in the literature concern the results of limb amputation in long-standing therapy-resistant CRPS and most of them come from the Netherlands. Geertzen et al. reported results of limb amputation in patients suffering from chronic, refractory CRPS. Over a period of 15 years (2000–2015), 53 patients have undergone amputation of the affected limb. A total of 48 patients were interviewed and physically examined. A battery of questionnaires was employed in the examination of the patients' physical and psychical condition, including World Health Organization Quality of Life to assess the quality of life, Connor-Davidson Resilience Scale to assess resilience, Hospital Anxiety and Depression Scale to assess the severity of anxiety and depression symptoms and Trinity Amputation and Prosthesis Experience Scale to assess the psychosocial processes involved in adjusting to a prosthesis. Thirty-seven patients (77%) reported an important improvement in mobility, and 35 (73%) reported an important reduction in pain following surgery. Other aspects of amputation such as deterioration in intimacy and self-confidence were reported by 13 (27%) and 11 (23%) patients, respectively. Recurrence of CRPS was observed in 22 patients (46%). Seven patients (15%) underwent a re-amputation due to recurrence of CRPS. These re-amputations mostly took place not at the institution of this author, but at other hospitals. One patient had already undergone an amputation before re-amputation, due to the recurrence of CRPS in the same limb. Of these 7 patients, 2 still had complaints and reported recurrence of CRPS elsewhere. Nine participants (19%) underwent revision surgery in the residual limb/stump for reasons other than CRPS, such as adherent scars or bone spurs. The authors conclude that amputation can be considered as a treatment for patients with severe, chronic, therapy-resistant CRPS because it can increase mobility and reduce pain, thereby improving the quality of patients' lives. However, the possibility of deterioration such as intimacy problems or lower self-confidence should be carefully considered in the decision-making process [12].

Schrier et al. reported the results of the study investigating associations between psychological factors before amputation and poor outcomes after amputation in patients suffering from chronic, refractory CRPS. A total of 33 patients underwent an amputation of the affected limb. Complex regional pain syndrome was determined to be therapy resistant if all treatments described in the Dutch guidelines for CRPS had been tried. Four of the 11 psychological factors were associated with poor outcomes. Poor social support or lower score on resilience were associated with poor outcomes regarding pain and mobility. This result could be expected since lack of social support is also a predictor of worse outcomes in patients with other

diseases with chronic pain, and patients with an amputation. The fact that social support is beneficial for many patients points in the direction of a more general principle that is not specific to CRPS. Having a psychiatric disorder or a history of a psychiatric disorder or involvement in a lawsuit have also been associated with a higher risk of recurrence. The authors conclude that amputation in patients with chronic refractory CRPS is a last option but outcomes can be disappointing, and therefore identifying risk factors associated with poor outcomes is highly relevant [13].

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