Neurogenic Edema from Complex Regional Pain Syndrome Resulting in Fulminant Infection Necessitating Below Elbow Amputation

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Abstract

Keywords

- amputation
- carpal tunnel syndrome
- complex regional pain syndrome
- infection
- neurogenic edema

We report a case of severe upper extremity complex regional pain syndrome type 1 (CRPS-1) and neurogenic edema that ultimately led to a medically necessary below-elbow amputation. The patient presented with a history of remote bilateral carpal tunnel release complicated by debilitating and recalcitrant bilateral CRPS-1. Following years of severe neurogenic edema of the left upper extremity, the patient had full-thickness skin sloughing on the dorsum of her hand due to massive edema. This subsequently led to maggot infestation of the soft tissues of the left hand ultimately necessitating amputation. We present the case as an illustration of an extreme case of neurogenic edema, a potential physical manifestation of CRPS-1. The case presented discusses upper extremity amputation as an end treatment option for CRPS-1, though in this case amputation was primarily indicated secondary to medical necessity.

Introduction

Complex regional pain syndrome type 1 (CRPS-1) is an infrequent yet debilitating complication of upper extremity surgery or minor trauma.¹ The physical manifestations of CRPS are well described in the literature though much regarding underlying causality and pathophysiology remains uncertain.² Edema of the affected extremity—whether neurogenic or vasogenic in nature—is among these defined physical characteristics of CRPS.^{2,3} This can clinically range from mild intermittent swelling to severe persistent swelling of the affected extremity. Risk factors and prevention of severe disease states are not well described.^{4–7} Additionally, treatment modalities are extensive—though potentially unsatisfactory—and include medical management, physical therapy, psychological therapy, neuraxial intervention, and additional attempts at neuromodulation.⁸ Though more common in the lower extremity, amputation has also been reported as an extreme end intervention to recalcitrant CRPS with good results.^{9–11}

Case Report

We present the case of a 31-year-old woman who underwent a below-elbow amputation after a severe case of neurogenic edema and infection associated with CRPS-1. The patient is an otherwise healthy woman who underwent bilateral open carpal tunnel release 12 years prior to presentation at our clinic. Following surgery, she reported worsening hypersensitivity and pain in bilateral hands. Her symptoms initially began in her left hand but within several weeks affected both the hands, though the left significantly more severe than the right. Her symptoms persisted with a remitting and relapsing pattern of pain, hypersensitivity, and episodic swelling.

She was initially managed for almost 2 years by her index surgeon with an extended course of opioid pain medication. She met International Association for the Study of Pain (IASP) criteria for the diagnosis of bilateral upper extremity CRPS-1^{3,12,13} and was ultimately referred to an anesthesiology pain management clinic for treatment. She never returned for further follow-up with her index surgeon. The patient remained under the care of

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Fig. 1 Clinical photographs of massively edematous and infected left upper extremity at time of presentation.

the same pain management clinic for nearly 10 years. During this period, she underwent aggressive medical management with varied combinations of opioids, neuroleptic medications, steroids, and antidepressant medications. She additionally underwent multiple peripheral nerve blocks, epidural injections, intravenous (IV) bisphosphonates, placement of intrathecal morphine pump, ketamine infusions, and placement of a spinal cord stimulator.

Throughout this time, she continued to experience swelling and worsening hyperesthesia in the bilateral hands, left much more severe than the right. The extreme sensitivity in her left upper extremity eventually necessitated sleeping with the arm dangling to avoid contact with bedding. All treatments ultimately provided no lasting improvement, and she was discharged from pain management.

The neurogenic edema in her left upper extremity continued to worsen, and within 1 year, she sustained full-thickness skin sloughing on the dorsum of her left hand. The episodic swelling and hypersensitivity in her right hand continued, though these symptoms were minor and manageable in comparison to those

in the left upper extremity. She presented at this time to an outside tertiary care center where she underwent initial debridement of the left hand wound followed by split-thickness skin grafting, which failed in the early postoperative period.

Several months later, she presented to our institution with a massively edematous left upper extremity and maggot-infested left hand (►**Fig. 1**). The patient was offered a below elbow amputation, which she elected to undergo. A preoperative X-ray and magnetic resonance imaging (MRI) demonstrated massive soft tissue swelling and edema (►**Fig. 2**). Prior to the planned surgical date, she presented to the emergency department with sepsis and was taken urgently for amputation. Histopathology results were consistent with diffuse inflammatory process without evidence of malignancy or other disease. Deep cultures from the specimen were positive for methicillin-susceptible *Staphylococcus aureus*.

Her immediate postoperative course was without medical complication, and she was off narcotic pain medication within 2 weeks. Her wound healed without issue (►**Fig. 3**). For nearly 1 month postoperatively, she experienced coping

Fig. 2 Preoperative AP and lateral plain radiographs (A) and coronal and sagittal magnetic resonance images (B) demonstrating massive soft tissue swelling and edema.

Fig. 3 Clinical photograph of left upper extremity 3 months after amputation with well-healed stump and minimal swelling.

issues regarding the amputation and refused to look at her upper extremity. Though this improved, we recommended psychiatric evaluation for further treatment. She agreed to this and was diagnosed with adjustment disorder. She experienced excellent improvement in her coping symptoms through cognitive behavioral therapy and medical management. At 6 months postoperatively, she was fitted for a prosthesis. She continued to follow with a psychiatrist for 1 year postoperatively for ongoing assistance with coping.

At her last follow-up in our clinic, she was over 1 year from time of amputation and she had returned to her normal activities as a mother and wife. She stated that though she had some limitations to her activity given her amputation, she had far fewer limitations than she did prior to amputation, when she had to carefully avoid contact of the edematous, hypersensitive upper extremity with all objects and surfaces. She continues to wear a prosthesis and is able to use the extremity to assist the right hand with light tasks both with and/or without the prosthesis donned. Her symptoms in the right upper extremity remain mild and have continued to improve.

Discussion

We present a patient with a 12-year history of severe, bilateral upper extremity CRPS-1. This case highlights the uncommon finding of severe neurogenic edema that can be seen in association with CRPS-1. There is a paucity of the current literature demonstrating examples of such profound associated edema. We believe in this case that it was a combination of extreme neurogenic and dependent edemas from patient

disuse and positioning that led to massive swelling skin breakdown, infection, and ultimately amputation. Though much is unknown, the underlying pathophysiology of CRPS-1-related edema has been attributed to a sustained and dysregulated proinflammatory state.^{14–16} In this model, it is injury to and perpetuated activation of C- and A-delta sensory nerves, which results in the release of substance P and other inflammatory peptides.¹⁴ This leads to a state with increased vascular permeability, protein extravasation, and even further neuropeptide and inflammatory release.^{14,15} In addition to resulting pain and hyperesthesia, this pathway provides basis for some of the profound physical manifestations of CRPS-1.

An additional consideration regarding causality in our case is that this represents a factitious disorder. This has been previously reported in patients carrying a chronic diagnosis of CRPS-1.¹⁷ Though certainly a possibility, we found nothing in our patient's history such as previous psychiatric diagnoses or behavior patterns to suggest that this was the cause. Additionally, the patient had a long history of bilateral upper extremity symptoms with the left as presented being profoundly more involved than the right. Though never witnessed in our clinic, she continues to have occasional swelling and hyperesthetic symptoms in her right hand. We feel that this case represents sequelae from the severe neurogenic edema potentially seen with CRPS-1 rather than a factitious disorder.

Prevention and treatment options for CRPS-1 remain a topic of much discussion. Additionally, the risk factors for developing CRPS-1 following trauma or surgery are not well understood.^{5–7} The incidence of CRPS-1 following elective carpal tunnel release has been reported between 3 and 9%.¹⁸ We did not find any cases in the literature describing a similar severity of CRPS-1-related symptoms following carpal tunnel syndrome. Several studies have shown higher prevalence in females as well as in those with depression, anxiety, and high initial pain scores.^{5,6,19} Similar variables have also been associated with a worse prognosis and more severe disease state.^{5,6} Furthermore, a delayed diagnosis has been associated with poor outcomes and poor response to treatment.^{5,19} In our patient, the initial diagnosis of CRPS-1 was not made until over 1 year following the index procedure. This potentially late diagnosis and initiation of treatment could certainly have been one factor contributing to her severe presentation. Additionally, a multidisciplinary approach including physical therapy, psychiatry, and pain management has been shown beneficial in patients demonstrating symptoms of CRPS-1.^{5,20,21} Our patient was managed exclusively by her index surgeon for nearly 2 years prior to an outside referral for treatment. This also presents another plausible explanation for her severity of symptoms and poor response to treatments once initiated. There was some early evidence that vitamin C administered postoperatively was beneficial in preventing upper extremity CRPS-1²² though subsequent trials have failed to show a benefit.²³ Similarly, other modalities have failed to demonstrate consistent results in helping prevent CRPS-1.²³ Despite this, early diagnosis of CRPS-1 and treatment of coexisting conditions such as depression and anxiety remain important strategies in preventing progression of symptoms to more extreme states.

The literature is replete with case reports and small patient cohorts with CRPS-1 that have responded to a variety of conventional and nonconventional treatments.⁸ The primary target of many of these medical interventions are attempts at neuromodulation—both centrally and peripherally. Our patient presented was treated extensively with opioids, topical ointments, antidepressants, antiepileptics, bisphosphonates, steroids, spinal cord stimulator, sympathetic ganglion block, and ketamine infusions. Though she experienced short-lived relief from several of these interventions, she ultimately had continued clinical decline.

In cases of refractory CRPS-1, amputation presents a viable end-treatment option. In this case, it was ultimately a presentation of ascending infection and sepsis that warranted urgent amputation of the extremity. Elective amputation has been well described in the literature with good results as an extreme, end intervention for recalcitrant CRPS-1.^{9–11} Krans-Schreuder et al reported favorable outcomes with a series of 22 patients who underwent extremity amputations for recalcitrant CRPS-1. The same study reported a recurrence risk of 24% in the remainder of the amputated extremity.⁹ Upper extremity amputation is not without potentially serious psychological, psychosocial, and functional implications.^{24,25} Coping issues are experienced by nearly all patients,²⁴ and functional limitations are generally more significant than lower extremity amputation.²⁵ In this patient, amputation served to address an urgent medical crisis as well as provide an acceptable solution for a long-standing problem. Furthermore, this case continues to underscore the potentially severe and progressive physical manifestations of CRPS-1. Despite the body of research surrounding the topic, much remains unknown in terms of pathophysiology and ultimate efficacy of prevention and treatment.

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Conflict of Interest

None.

References

- de Mos M, Huygen FJ, van der Hoeven-Borgman M, Dieleman JP, Ch Stricker BH, Sturkenboom MC. Outcome of the complex regional pain syndrome. *Clin J Pain* 2009;25(07):590–597
- de Mos M, de Bruijn AG, Huygen FJ, Dieleman JP, Stricker BH, Sturkenboom MC. The incidence of complex regional pain syndrome: a population-based study. *Pain* 2007;129(1–2):12–20
- Harden RN, Bruehl S, Stanton-Hicks M, Wilson PR. Proposed new diagnostic criteria for complex regional pain syndrome. *Pain Med* 2007;8(04):326–331
- Bean DJ, Johnson MH, Kydd RR. The outcome of complex regional pain syndrome type 1: a systematic review. *J Pain* 2014;15(07):677–690
- Allen G, Galer BS, Schwartz L. Epidemiology of complex regional pain syndrome: a retrospective chart review of 134 patients. *Pain* 1999;80(03):539–544
- Petersen PB, Mikkelsen KL, Lauritzen JB, Krosgaard MR. Risk factors for post-treatment complex regional pain syndrome (CRPS)—an analysis of 647 cases of CRPS from the Danish Patient Compensation Association. *Pain Pract* 2017. Doi: 10.1111/papr.12610
- Savaş S, İnal EE, Yavuz DD, Uslusoy F, Altuntaş SH, Aydın MA. Risk factors for complex regional pain syndrome in patients with surgically treated traumatic injuries attending hand therapy. *J Hand Ther* 2017. Doi: 10.1016/j.jht.2017.03.007
- Cossins L, Okell RW, Cameron H, Simpson B, Poole HM, Goebel A. Treatment of complex regional pain syndrome in adults: a systematic review of randomized controlled trials published from June 2000 to February 2012. *Eur J Pain* 2013;17(02):158–173
- Krans-Schreuder HK, Bodde MI, Schrier E, et al. Amputation for long-standing, therapy-resistant type-I complex regional pain syndrome. *J Bone Joint Surg Am* 2012;94(24):2263–2268
- Midbari A, Suzan E, Adler T, et al. Amputation in patients with complex regional pain syndrome: a comparative study between amputees and non-amputees with intractable disease. *Bone Joint J* 2016;98-B(04):548–554
- Geertzen JH, Rietman JS, Smit AJ, Zimmerman KW. A young female patient with reflex sympathetic dystrophy of the upper limb in whom amputation became inevitable. *Prosthet Orthot Int* 1997;21(02):159–161
- Stanton-Hicks M, Jänig W, Hassenbusch S, Haddox JD, Boas R, Wilson P. Reflex sympathetic dystrophy: changing concepts and taxonomy. *Pain* 1995;63(01):127–133
- Merskey H, Bogduk N. Classification of Chronic Pain: IASP Task Force on Taxonomy. 2nd ed. IASP Press: Seattle, Washington: IASP Press; 1994:40–43
- Parkitny L, McAuley JH, Di Pietro F, et al. Inflammation in complex regional pain syndrome: a systematic review and meta-analysis. *Neurology* 2013;80(01):106–117
- Weber M, Birklein F, Neundörfer B, Schmelz M. Facilitated neurogenic inflammation in complex regional pain syndrome. *Pain* 2001;91(03):251–257
- Fischer SG, Zuurmond WW, Birklein F, Loer SA, Perez RS. Anti-inflammatory treatment of complex regional pain syndrome. *Pain* 2010;151(02):251–256
- Taskaynatan MA, Balaban B, Karlidere T, Ozgul A, Tan AK, Kalyon TA. Factitious disorders encountered in patients with the diagnosis of reflex sympathetic dystrophy. *Clin Rheumatol* 2005;24(05):521–526
- MacDonald RI, Lichtman DM, Hanlon JJ, Wilson JN. Complications of surgical release for carpal tunnel syndrome. *J Hand Surg Am* 1978;3(01):70–76
- Bean DJ, Johnson MH, Heiss-Dunlop W, Lee AC, Kydd RR. Do psychological factors influence recovery from complex regional pain syndrome type 1? A prospective study. *Pain* 2015;156(11):2310–2318
- Rome L. The place of occupational therapy in rehabilitation strategies of complex regional pain syndrome: comparative study of 60 cases. *Hand Surg Rehabil* 2016;35(05):355–362
- Veizi IE, Chelimsky TC, Janata JW. Complex [corrected] regional pain syndrome: what specialized rehabilitation services do patients require? *Curr Pain Headache Rep* 2012;16(02):139–146
- Zollinger PE, Tuinebreijer WE, Kreis RW, Breederveld RS. Effect of vitamin C on frequency of reflex sympathetic dystrophy in wrist fractures: a randomised trial. *Lancet* 1999;354(9195):2025–2028
- Evaniew N, McCarthy C, Kleinlugtenbelt YV, Ghert M, Bhandari M. Vitamin C to prevent complex regional pain syndrome in patients with distal radius fractures: a meta-analysis of randomized controlled trials. *J Orthop Trauma* 2015;29(08):e235–e241
- Grunert BK, Smith CJ, Devine CA, et al. Early psychological aspects of severe hand injury. *J Hand Surg Br* 1988;13(02):177–180
- Tennent DJ, Wenke JC, Rivera JC, Krueger CA. Characterisation and outcomes of upper extremity amputations. *Injury* 2014;45(06):965–969