Case Report

Complex Regional Pain Syndrome: A Case Report and Review of the Literature

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Abstract

Background: Complex regional pain syndrome (CRPS) is a rare neuropathic pain disorder associated with severe pain, muscle weakness, limb edema and hyperhidrosis. Predisposing factors include fracture, surgery, stroke and spinal cord injury. CRPS may recur in the same limb or spread to other limbs to complicate management. Case Report: A 20-year old female with CRPS Type-I had sequential spread to all four limbs despite different treatment modalities, including medical therapy, nerve block, radiofrequency ablation and surgical sympathectomy. We discuss the therapeutic challenges and reviewed recent literature on current treatment options for CRPS Type-I. Conclusion: A multidisciplinary approach is needed for effective management of CRPS, and refractory disease may respond to intrathecal baclofen with morphine.

Keywords: Complex regional pain syndrome, sympathectomy, sympathetic block

Résumé

Contexte: Le syndrome douloureux régional complexe (SDRC) est un trouble neuropathique rare associé à une douleur intense, une faiblesse musculaire, un œdème des membres et une hyperhidrose. Les facteurs prédisposants comprennent la fracture, la chirurgie, l’AVC et les lésions de la moelle épineuse. Le SDRC peut se reproduire dans le même membre ou se propager à d’autres membres pour compliquer la gestion. Rapport de cas: une femme de 20 ans atteinte du SDRC de type I s’est propagée séquentiellement aux quatre membres malgré différentes modalités de traitement, y compris une thérapie médicale, un bloc nerveux, une ablation par radiofréquence et une sympathectomie chirurgicale. Nous discutons des défis thérapeutiques et avons passé en revue la littérature récente sur les options de traitement actuelles pour le SDRC de type I. Conclusion: Une approche multidisciplinaire est nécessaire pour une gestion efficace du SDRC, et la maladie réfractaire peut répondre au baclofène intrathécal avec de la morphine.

Mots clés: Le syndrome douloureux régional complexe, sympathectomie, bloc sympathique

Introduction

Complex regional pain syndrome (CRPS) is a neuropathic pain condition affecting one or more extremities. Formerly called reflex sympathetic dystrophy and causalgia, CRPS was first described in 1872 by American physician Weir Mitchell, who observed the clinical features among civil war veterans treated for nerve injuries.¹

The International Association for the Study of Pain has classified CRPS into Type-I, which occurs without nerve injury, and Type-II, in which there is definite evidence of nerve injury.² Although still widely in use, this classification

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is falling out of favor as it is not always possible to exclude minimal nerve injury.[3]

CRPS is known to recur in the same limb and also spread to other limbs, sometimes in multiples, either spontaneously or as a result of a new trauma.[4] Herein, we report a case of CRPS Type-I which affected all four limbs in sequence, was resistant to medical therapy, and posed significant challenges to management.

**CASE REPORT**

A 20-year-old Saudi female presented to a hospital with a painful swelling of her right hand. She denied a history of trauma and was thought to have arthritis, for which she received prednisolone and naproxen. When symptoms persisted for 2 months, a neurologist diagnosed CRPS. Symptoms still persisted with prednisolone and gabapentin. Thoracoscopic sympathectomy provided relief, but painful swellings recurred in her left hand and left leg 3 weeks later.

She was referred to our center where examination revealed a swollen and tender left leg with cold and sweaty skin [Figure 1a]. Left lower limb movements were restricted by hyperalgesia and allodynia. The left upper limb showed mild edema with normal sensorimotor functions, but the right upper and lower limbs were both normal.

Investigations which included serum electrolytes, urea, creatinine, fasting glucose, liver function tests, thyroid function tests, C-reactive protein, full blood counts, clotting profile, Proteins C and S, and anti-thrombin III assays were all normal. Serum rheumatoid factor, antinuclear antibodies, double-stranded DNA, and hepatitis B and C viral screening were negative. Radioisotope bone scan showed increased tracer uptake in the left knee, but nerve conduction studies, Doppler ultrasound scans, and brain and spinal magnetic resonance imaging were all normal.

She received oral clonidine 0.15 mg daily, but left leg swelling persisted. Two weeks later, she developed another painful swelling on her right leg. A pain specialist administered computed tomography-guided bilateral lumbar sympathetic block with lignocaine, which provided relief lasting only 4–5 days even after repeating it twice.

Radiofrequency ablation of lumbar sympathetic nerves at L2, 3, and 4 levels provided no relief, and she underwent bilateral lumbar sympathectomy with phenol injections, spaced 4 weeks apart. Symptoms resolved completely at this stage [Figure 1b], but she developed urinary retention, paraparesis, and hypoesthesia below T4 levels, which improved over a course of 6 weeks. After 4 months of hospitalization, she was discharged home with no pain or swelling and muscle power of Grades 3–4/5 in the lower limbs.

Five months later, she was readmitted for the recurrence of symptoms in her right upper limb [Figure 1c]. When the stellate ganglion block provided only partial relief, she had an intrathecal infusion of baclofen with morphine, which provided sustained relief [Figure 1d] that lasted 10 months at her last visit to the outpatient clinic.

**DISCUSSION**

The clinical features of CRPS include severe pain that is disproportionate to the inciting event, allodynia, hyperalgesia, and motor-autonomic dysfunction characterized by weakness, stiffness, edema, hyperhidrosis, and changes in skin color and temperature.[2]

The major predisposing factor is a nerve lesion from trauma, fracture, or surgery, but stroke, spinal cord injury, and myocardial infarction have all been implicated.[2] While the exact pathogenesis is not well understood, there is evidence for the roles of inflammation mediated by cytokines and neuropeptides such as tumor necrosis factor-α, bradykinin, and substance P.[1,4] Other studies implicate genetic factors, circulating catecholamines, altered cutaneous innervation, central and peripheral sensitization, and brain plasticity.[5]

CRPS may start in two or more limbs simultaneously or may start in one limb and spread to other limbs. van Rijn et al. reported this phenomenon in 78 patients among 185 CRPS patients in the Netherlands.[6] The underlying mechanism has not been elucidated, but several theories have been proposed, including genetic predisposition, aberrant regulation of neurogenic inflammation, and maladaptive neuronal plasticity.[4]

The management of CRPS requires a multidisciplinary approach involving physical therapy, occupational therapy, drug treatment, and surgical interventions aimed at relieving inflammation, pain, and disability. Modalities of physical therapy include limb elevation, massage, and isometric strengthening exercise aided with adequate analgesia.

**Figure 1:** Pictures showing the patient with left lower limb edema (a) which persisted with radiofrequency ablation of lumbar sympathetic nerves but resolved after lumbar sympathectomy with phenol injections (b). Symptoms later recurred in the right hand (c) but responded to intrathecal baclofen infusion (d)
Corticosteroids are effective in relieving inflammation, while gabapentin provides short-term pain relief. However, gabapentin is less effective for pain relief in chronic CRPS, which responds more to clonidine, phenoxybenzamine, or baclofen.[5] Prolonged immobility in CRPS may cause osteopenia and osteoporosis, which is best treated with bisphosphonates.[5]

When pain persists with medical therapy, regional anesthesia with sympathetic block may provide relief, but the effect is transient. The definitive treatment of refractory CRPS is chemical or surgical sympathectomy through permanent ablation of the sympathetic chain and the stellate ganglion. This is achieved with either radiofrequency waves, ultrasound-guided phenol injections, or open surgery.[5]

Other modalities of treatment reported in the literature include spinal cord stimulation, transcutaneous electrical nerve stimulation, the use of thalidomide, N-Methyl-D-Aspartate receptor antagonists, intravenous immunoglobulin, plasmapheresis, and antioxidants, particularly Vitamin C.[5,6]

Our CRPS Type-I patient had intractable symptoms in all four limbs despite treatment regimens involving steroids, clonidine, gabapentin, sympathetic block, and sympathectomy. Beside her female gender, she lacked other risk factors for disease onset and persistence such as stroke, spinal injury, or radial fracture. Recently, Dubuis et al. detected alpha-1a adrenoreceptor antibodies in chronic CRPS patients, but this finding awaits confirmation in larger studies.[7]

While sympathetic block has a theoretical basis in CRPS, evidence of its benefits mostly come from case reports and retrospective reviews.[3] However, a randomized, controlled trial of a thoracic sympathetic block for upper limb CRPS Type-I reported significantly less pain and less incidence of depression among the treated groups.[8]

Nevertheless, our patient did not attain remission with either sympathetic block or sympathectomy, which necessitated a trial of intrathecal baclofen with morphine. This provided a complete resolution of pain lasting 10 months. In line with our experience, van der Plas et al. also reported the efficacy of intrathecal baclofen in the refractory CRPS.[9]

In conclusion, we have reported a rare form of CRPS Type-I that was intractable to various treatment regimens but finally responded to intrathecal baclofen with morphine. The rarity of CRPS and the therapeutic challenge encountered in this case informed the need for this report. Larger studies may shed more light on optimal therapies for refractory CRPS.

Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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