Peripheral Nerve Stimulation in Complex Regional Pain Syndrome: A Relationship of Pain and Dermatology

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Introduction

Complex regional pain syndrome (CRPS) is a chronic pain condition that typically presents with allodynia and hyperalgesia resulting from central and peripheral neurovascular dysfunction.[1] In addition to pain, diagnosis is based on other clinical findings, including skin and hair changes, swelling, and joint stiffness, with early diagnosis and management paramount for quality of life and medical costs.[2] Treatment consists of multiple integral modalities targeting these changes, including physical and pharmacological treatments. More recently, the use of neuromodulation interventions, including peripheral nerve stimulation (PNS), has burgeoned in CRPS care.[2,3] Despite this growth, the full mechanism for PNS is continuing to be elicited, with multiple theories between the gate-control hypothesis, peripheral effects, or central influences still being debated.[4] While most literature reports the improvement of CRPS pain with PNS, this case highlights the successful treatment of CRPS pain reduction in addition to the corresponding reversal of pathognomonic dermatological symptoms, furthering discussions of peripheral and central influences in PNS mechanisms of actions.

Case

A female patient in her 30s with Ehlers-Danlos syndrome, Parsonage-Turner syndrome of the left shoulder, and chronic pain after a left labral repair 5 months prior presents to the pain clinic with left shoulder and upper arm pain. The pain was localized to the anterolateral upper extremity extending to the posterior left shoulder. Other symptoms included shiny-erythematous skin, edema, temperature differences, hair loss, and diffuse allodynia. Prior evaluations included multiple physician specialists including an allergist, neurologist, physical medicine & rehabilitation, psychiatry, and orthopedics. Other medical, familial, and psychiatric histories were non-contributory. Physical exam was notable for the symptoms reported. Diagnostic studies, including lab drawings, MRI imaging, and electrodiagnostic exams, were inconclusive. This patient met the CRPS diagnostic criteria set forth by the Budapest criteria and was referred to the pain management department for evaluation and treatment of the left upper extremity.

Pharmaceutical treatments trialed included varied combinations and titrations of gabapentin 900 mg three times daily (TID), pregabalin 50 mg TID, duloxetine 60 mg daily, tizanidine 2 mg four times daily (QID) as needed (PRN), 10 mg baclofen TID, cyclobenzaprine 10 mg TID PRN, methylprednisolone 4 mg daily, 4% lidocaine patches, nortriptyline 10 mg daily, amitriptyline 25 mg daily, cannabinoid cream, high-dose vitamin C, turmeric, low-dose naltrexone 4.5 mg daily, diphenhydramine 25 mg TID, acetaminophen 650 mg QID, hydrocodone-acetaminophen 650/10 mg QID PRN, and oxycodone 5 mg QID PRN. Physical and interventional modalities trialed included serial stellate ganglion blocks, intravenous ketamine infusions, transcutaneous electrical nerve stimulation (TENS), red light therapy, ice, heating pads, physical therapy, and graded motor imagery therapy.

Despite extensive workup and refractory symptoms, the CRPS diagnosis of the left arm prompted a discussion of the risks and benefits of interventions, including spinal cord stimulation (SCS) and PNS. She proceeded with ultrasound-guided implantation of a PNS at the left infraclavicular brachial plexus at the posterior cord and at the left axillary nerve (Image 1). She tolerated the procedure well and noted that the PNS resulted in 85% pain relief and improvement of skin color changes at her two-week follow-up (Image 2). The patient reported continued improvement of pain and complete resolution of dermatologic symptoms at her four-month follow-up. She has weaned off opioids while the stimulator was in place, reporting drastic improvement in quality of life.

Discussion

With two distinct subtypes (Type 1 (idiopathic) and Type 2 (causalgia)), CRPS presents as a continuum of 3 stages (acute, dystrophic, and atrophic) with worsening progressions of sensory, autonomic, sudomotor (edema, diaphoresis), trophic/dermatologic, and vasomotor (temperature) abnormalities.[1] This symptom heterogeneity correlates to three proposed pathways: aberrant inflammatory mechanisms, vasomotor dysfunction, and maladaptive neuroplasticity. In this patient and her CRPS, chronic disease immune-mediated inflammatory responses induce pro-inflammatory cytokine activation, sensitizing central and peripheral pain signals in a continuous cycle.[1] Her recent surgical history amplifies cytokine signaling, with direct damage to peripheral nerves during surgery influencing neuroplasticity, edema, and pain signal pathways.[1] Additionally, her Parsonage-Turner syndrome – which can be influenced by connective tissue disorders (i.e., Ehlers-Danlos) or trauma (i.e., surgery) – can further induce inflammatory responses, serving as a potential catalyst to exacerbate symptoms.[5]

Despite the gate-control theory, which is known to promote analgesia, the full mechanism of PNS is still largely unknown; newer studies have suggested potential PNS mechanisms via peripheral modulation with inflammatory responses and pain signal sensitization, and central modulation with neuroplasticity.[4,6] It is through these potential mechanisms that this case and discussion on CRPS pain and dermatologic lesions are unique. Previous studies report on the analgesic benefits of PNS on CRPS[3]; reports on the dermatologic changes, however, are limited. For this patient, PNS adequately reduced her analgesic consumption and pain by 85%. Dermatologic presentations, however, are extensions of the allodynia, serving as a physical demarcation of the disease.[7] Immune-mediated inflammatory responses promote vessel

permeability and vasodilation, inducing the pathognomonic vasomotor warmth, swelling, and erythema that was seen in this patient. The drastic improvement in her skin provides empirical support for the proposed PNS mechanism of peripheral and central modulation of inflammatory swelling, warmth, and erythema. The additional benefits of analgesia along that previous demarcation also suggest local pain signal sensitization and neuroplasticity.

References

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Figures and Legend

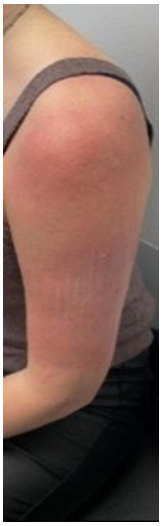
Image 1: Pre-PNS CRPS dermatological presentation

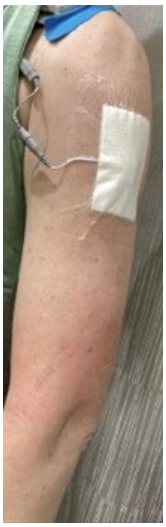
Image 2: Post-PNS CRPS dermatological presentation

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The patient provided informed consent for us to report this condition for educational purposes.