CHAPTER 7

Update on Complex Regional Pain Syndrome Diagnosis and Management

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INTRODUCTION

Complex regional pain syndrome (CRPS) is an uncommon and poorly understood debilitating condition that has been described in both the podiatric and general medical literature. CRPS is a painful neurological condition that is associated with progressively worsening spontaneous regional pain. There is no dermatomal distribution. CRPS has now replaced other terms such as Sudeck's atrophy, reflex sympathetic dystrophy, algodystrophy, fracture disease, and causalgia. CRPS can develop after major trauma or surgery and has a variable course progression that can sometimes be self-limiting with mild symptoms or can develop into chronic disease. Future research is needed to further understand CRPS.

EPIDEMIOLOGY AND PATHOPHYSIOLOGY

The incidence of CRPS is approximately 20-26 per 100,000 people annually and can occur within a few months of any extremity injury or surgical procedure (1). The incidence disparity between women and men is as high as 71% and 29%, respectively (2). The peak age at onset is between 45 and 55 years (3). Patients with asthma, osteoporosis, migraines, or hematological disorders are at a higher risk due to the fact they take angiotensin-converting enzyme (ACE) inhibitors (1). Other population variables associated with CRPS include Caucasian race, higher median income, and a history of depression, headache, or drug abuse. Patients with hypothyroidism, or who are diabetic or obese have lower rates of CRPS (3).

CRPS is thought to be caused by post-traumatic hyperactivation of small nerve fibers. This abnormal nerve fiber activation leads to central sensitization, which is a process where the central nervous system increases any peripheral impulses (1). Studies have shown that low-dose ketamine treatments can downregulate central sensitization, which leads to a reduction of CRPS pain (4). Now it is clear that the nerve fiber hyperactivation is caused by immune processes in patients (1). Most CRPS patients have autoantibodies that are specific in their serum. Studies have demonstrated that when the autoantibody is transferred to mice, it elicits a CRPS picture that has been restricted to the paw, which confirms an autoimmune origin (3). The exact pathogenesis of why CRPS patients produce these autoantibodies is still unknown, but there has been some progress in identifying genotypes that convey that vulnerability (1).

DIAGNOSIS

There is no diagnostic gold standard for CRPS, however a thorough history and physical examination are critical for appropriate diagnosis and management of these patients. Currently, the new International Association for the Study of Pain (IASP) criteria are the most frequently used clinical diagnostic criteria for CRPS. The IASP criteria are based on clinical as well as patient-reported signs and symptoms. (5). CRPS can be differentiated between CRPS type I (without an obvious nerve lesion) and CRPS type II (with a verifiable nerve lesion). At first presentation, approximately 70% of patients report a warm subtype with an increased skin temperature at symptom onset, whereas the remaining 30% report a cold subtype. Trauma typically precedes clinical symptoms. Table 1 shows the Budapest diagnostic criteria, which present clinical diagnostic criteria to help identify patients with CRPS.

Instrument-based investigation may be beneficial if there are doubts concerning the differential. These include repeated measurements of skin temperature, magnetic resonance imaging and radiographs of each extremity, and 3-phase bone technetium scintigraphy in acute CRPS. Quantitative sensory testing (QST) is not suited for CRPS diagnosis because it primarily describes pain symptoms, which are not specific. A typical QST pattern (thermhypaesthesia, mechanical hyperalgesia, and pressure hyperalgesia) may support a CRPS diagnosis, particularly in the distal joints that were not affected directly by trauma and are sensitive to pressure pain. The CRPS severity score can also be utilized to grade the severity of CRPS and help monitor the disease course (Table 2) (6).

Pain is the most important clinical symptom. The pain can be permanent or fluctuating and most often occurs in the deep tissue. This pain symptom increases through movements and during temperature changes. In chronic and severe cases of CRPS, allodyna is a hallmark feature. Sensory deficits include hypoesthesia and impairment of thermal perception in a glove or stocking-like pattern. All patients have decreased muscle strength and most have

Table 1. Budapest Diagnostic Criteria For CRPS

Clinical diagnostic criteria for CRPS

- Continuing pain, which is disproportionate to any inciting event
- Must report at least 1 symptom in 3 of the 4 following categories:
  - Sensory: Reports of hyperalgesia and/or allodynia
  - Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry
  - Sudomotor/Edema: Reports of edema and/or sweating changes and/or sweating asymmetry
  - Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor and dystonia) and/or trophic changes (hair, nails, and skin)
- Must display at least 1 sign at the time of evaluation in 2 or more of the following categories:
  - Sensory: Evidence of hyperalgesia (to pinprick) and/allodynia (to light touch and/or deep somatic pressure and/or joint movement)
  - Vasomotor: Evidence of temperature asymmetry and/or skin color changes and/or asymmetry
  - Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry
  - Motor/Trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, and dystonia) and/or trophic changes (hair, nails, and skin)

There is no other diagnosis that better explains the signs and symptoms

Adapted from reference 8.

movement-induced pain. Contractures can develop fairly quickly. Trophic changes may be found on the skin (ulcers), nails, and hair. In chronic cases, patients have reported that their extremity feels thicker. All patients display a change in their skin color that varies from reddish in patients with warm CRPS, to a blueish color in those with cold CRPS (6).

TREATMENT AND MANAGEMENT

A multidisciplinary approach is recommended for the management of CRPS. The main goals of therapy are to restore function to the affected limb, decrease pain and disability, and improve the quality of life while minimizing side effects and toxicities. Treatment is more effective when started early in the course of disease. Referral to a pain management specialist with experience in CRPS management is appropriate in patients with progressive symptoms and signs of CRPS, as well as patients with chronic/severe forms. Initial management of CRPS includes patient education, physical and occupational therapy, a psychosocial assessment, and symptomatic pain management, typically beginning with low-risk pharmacotherapy.

Table 2. CRPS severity score CSS

Self-reported symptoms

Continuing disproportionate pain
Allodynia or hyperalgesia
Temperature asymmetry
Skin color asymmetry
Sweating asymmetry
Asymmetric edema
Trophic changes
Motor changes

Signs observed on examination

Hyperalgesia to pinprick
Allodynia
Temperature asymmetry
Skin color asymmetry
Sweating asymmetry
Asymmetric edema
Trophic changes
Motor changes

Adapted from reference 8.

Participating in physical and occupational therapy can be facilitated by explaining that CRPS-associated pain symptoms does not indicate tissue damage in the hyperalgesic area but arises from an unknown cause. It is important to stress the importance of working to regain use of the affected limb while also recognizing the difficulty of doing so due to ongoing pain. Physical and occupational therapy is considered to be the first line treatment for CRPS. Physical therapy can be performed twice daily at home for patients in all stages of CRPS. This should ideally begin before limitation of movement occurs in order to maintain the patient's current range of motion and prevent any contractures from arising. Resting splints can be utilized to prevent progressive joint contractures. General therapeutic methods of physical and occupational therapy include general exercise/strengthening, gait retraining, transcutaneous electrical nerve stimulation, hydrotherapy, edema control strategies, and relaxation techniques.

Psychosocial and behavioral therapy can be used in CRPS patients. A clinical psychologist should be consulted if a patient has CRPS longer than 2 months duration at presentation, insufficient response to a treatment, or if a patient has a suspected comorbid psychological or psychiatric disorder. The goals of psychosocial and behavior management include identifying any psychological factors contributing to a patient's pain and disability, treating anxiety/depression, considering needs to family and caregivers, identifying and addressing internal factors (counter-productive behavior patterns) or external influences (family dynamic), and providing a problem-

solving and goal-oriented approach to reduce barriers and promote healthy functioning. A skilled hypnotherapist can also be helpful for patients with heightened arousal and in whom exercise is otherwise impossible.

In terms of the pharmacologic approach, the goals of pain management are to allow active participation in a rehabilitation program and to restore both motion and strength of the affected extremity. The key to success is to use whatever works to reduce pain so patients can tolerate physical therapy. For patients with early CRPS, this approach encompasses one or more of the following agents: an NSAID such as ibuprofen or naproxen, neuropathic pain medications such as gabapentin or pregabalin, a course of bisphosphonate treatments, and/or topical lidocaine or capsaicin cream. The total duration of pharmacotherapy is individualized. Pharmacotherapy is generally continued as long as patients have a significant symptom burden, do not have intolerable side effects and appear to be deriving a symptomatic benefit.

In patients with refractory pain, there are a few interventional options. Interventional procedures for the treatment of pain related to CRPS include trigger and tender point injections, regional sympathetic nerve blocks, spinal stimulation, epidural clonidine, and chemical/mechanical sympathectomy. Patients who are receiving noninvasive therapy and are not improving are candidates for increasingly invasive treatment, allowing 2 weeks for improvement before proceeding to the next treatment (7). Amputation in patients with CRPS may be indicated due to chronic/severe pain, extremity dysfunction, gangrene, infections, or ulcers. A majority of patients will report a reduction in pain along with improvements in mobility and sleep following amputation of the affected limb. Many patients will still exhibit pain and symptom recurrence in the residual extremity (8).

FUTURE TREATMENT AND MANAGEMENT

The scope of finding new or existing agents to target the different disease mechanisms of CRPS will continue to grow, as our understanding of CRPS pathophysiology develops.

There are several emerging treatments for the future of CRPS patients. Certain cancer drugs possess anti-inflammatory and immunomodulatory effects that have shown promise in alleviating CRPS since many of these patients display systemic elevation of proinflammatory cytokines. Hyperbaric oxygen therapy has also been thought to be useful due to its antinociceptive effect. Botulinum toxin A can provide pain relief in neuropathic pain. Although there has yet to be a currently successful or gold standard treatment for patients with CRPS, years of research has provided the field of medicine many valuable lessons. Given the complex nature of this syndrome, the future of CRPS treatment may lie in combination therapy along with a multidisciplinary approach (8).

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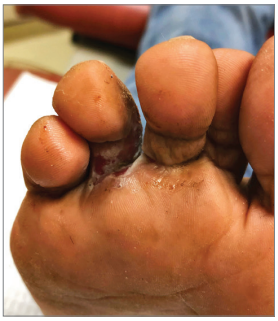

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