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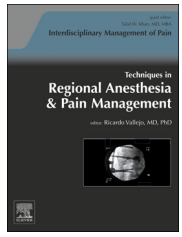

The interdisciplinary management of complex regional pain syndrome

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ABSTRACT

Complex regional pain syndrome is an ill-defined disorder typified by disproportional pain to the inciting insult in a variable setting of vasomotor and autonomic changes. The exact etiology remains unclear but likely involves augmented cytokine release affecting both peripheral and central nervous systems with concomitant psychosocial intricacies. Management of complex regional pain syndrome should encompass a systematic, interdisciplinary approach including physical and occupational therapy, psychological interventions, and oral analgesics. A thorough diagnostic evaluation should be completed before pursuing invasive treatment options, and these should be considered only in patients experiencing difficulty in progressing through a multimodal program. Collaborative therapy among a multitude of specialties should aim to facilitate reanimation and functional restoration of the affected limb.

Introduction

As the name infers, complex regional pain syndrome (CRPS) is a multifarious, painful condition that most commonly affects an extremity following a noxious event. Management of this complicated disorder can be challenging, as the pathogenesis and natural history of CRPS are incompletely characterized, and a multifaceted biopsychosocial process is invariably involved. Subsequently, an interdisciplinary treatment approach among qualified specialists is mandatory to address thoroughly all aspects of this disease. A coordinated approach targeting biomedical and psychosocial rehabilitation has been shown to augment outcomes. This article reviews the pathogenesis and diagnosis of CRPS and focuses on the multimodal, evidence-based treatments shown to optimize functional restoration.

Etiology

CRPS is a chronic and often disabling neuropathic pain syndrome typified by pain out of proportion to the inciting trauma, vasomotor changes, skin and bone abnormalities, as well as changes in motor function of the affected area. CRPS manifests itself in 2 primary forms. CRPS type 1 (formerly known as reflex sympathetic dystrophy) is not associated with obvious or known neuronal injury. CRPS type 2 (formerly known as causalgia) is associated with established neuronal injury. CRPS is usually preceded by trauma or insult, the most common being fractures, sprains, and surgery; less common insults include stroke, myocardial infarction, injections, and spinal cord injuries. Occasionally, in CRPS 1, the patient is unable to identify the initiating trauma. CRPS 2 is usually caused by high-velocity impacts or neurologic injury during a

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procedure such as syrinx during injection or neuronal transection.[1,2]

Pathophysiology

CRPS is a multifactorial disorder that involves the complex interaction of the peripheral, central, and autonomic nervous systems. Local tissue inflammation and psychological factors also play a role in the pathophysiology of CRPS.

Peripheral

Peripheral inflammation plays an important role in CRPS. Local mediators such as substance P, bradykinin, neuropeptide Y, and calcitonin gene–related peptide are elevated in patients with CRPS. After local tissue injury, these substances are released causing vasodilation, warmth, redness, and local tissue swelling. Angiotensin-converting enzyme inhibitors, which alter the metabolism of bradykinin, have been associated with the development of CRPS. Although there is an increase in local inflammatory mediators, CRPS is not associated with the classical systemic markers of inflammation such as C-reactive protein. Furthermore, there is a lack of elevation in serum leukocytes and a paucity of leukocytes in tissue biopsies of patients with CRPS. Local tissue trauma causes the release of multiple cytokines and growth factors, which sensitize peripheral nociceptors leading to allodynia and skin thickening, respectively.[2]

Central

Alterations in the central nervous system are thought to contribute to the pathophysiological changes in patients with CRPS. Central sensitization is a process that results in hyperalgesia and allodynia. Repetitive stimulation of afferent neurons causes morphologic and physiological changes in the spinal cord. The continuous release of neurotransmitters in the dorsal horn cause atrophic changes. This leads to a decrease in inhibitory neurons thus contributing to inappropriate and excessive stimulation for a given stimulus.

Central reorganization is a pattern of cortical changes associated with CRPS. Chronic sensory input is associated with a decrease in neuronal density. As would be expected, these changes are seen in the somatosensory cortex corresponding to the contralateral limb afflicted with CRPS. In contrast, the motor cortex associated with the contralateral affected limb increases in density. This is thought to result from chronic and intense positioning of the affected extremity in such a way that it decreases painful stimulation. Pathologic changes in both the sensory and motor cortexes of patients with CRPS have been shown to be reversible on resolution of CRPS.[1,2]

Sympathetic

Sympathetic dysregulation is thought to play a major role in CRPS pathophysiology. It is likely manifested through changes in vasomotor tone (temperature and skin color), hyperhidrosis, and edema. Thus, targeting the sympathetic nervous system with interventional techniques has been used in the management of CRPS. Not surprisingly, patients with CRPS are more likely to be sensitive to changes in temperature. Overall, 2 probable mechanisms are responsible for dysregulation of the sympathetic nervous system. First, patients with CRPS have increased amounts of adrenergic receptors in the affected limb when biopsied. Second, there may be an increase in the density of sympathetic afferent nerves either peripherally or centrally in the dorsal horn. This process is termed sympathetic afferent coupling. Excess sympathetic activity results in decreased blood flow to the affected area and tends to occur later on in the disease process. Changes in blood flow are thought to increase reactive oxygen species, which further enhance pain and inflammation.[1,2]

Autoimmune

There are limited data to thoroughly assess the role of autoimmunity in the pathogenesis of CRPS. Autoantibodies against autonomic receptors such as β2 and M2 have been found in patients with CRPS. These autoantibodies tend to be higher in patients with CRPS 2 as compared with CRPS 1, which may point to their role as being associated with injury with little contribution to disease. Some patients do, however, improve with intravenous (IV) immunoglobulin, thus pointing to an autoimmune cause in some patients.[1,2]

Genetics

Some genes associated with inflammation have been implicated in certain forms of CRPS. Polymorphisms in genes controlling tumor necrosis factor-α, angiotensin-converting enzyme, and alpha-1 tend to be well represented in patients with CRPS. Those with genetic polymorphisms and familial forms of CRPS tend to have earlier onsets and increased severity of disease.[2]

Psychological

Psychological factors have long been suspected to play a key role in the development of CRPS. Similar psychological profiles have been shown between patients with CRPS and those with conversion disorders. Depression has been long thought to be a risk factor for the development of CRPS; however, recent reviews and prospective studies have not supported this belief. Having an anxious personality has, however, been shown to be a risk factor for CRPS. The use of nonuniform diagnostic criteria for CRPS and numerous psychological disorders has made the study of this complex interaction difficult. A multidisciplinary treatment plan that uses counseling and cognitive behavioral therapy has been shown to improve outcomes in CRPS.[2]

Clinical manifestations

CRPS manifests as regional pain, allodynia, hyperalgesia, swelling, vasomotor and sudomotor abnormalities, motor impairment, and trophic changes. Typically, patients present after minor trauma or surgery with the injured limb feeling