Complex regional pain syndrome (CRPS) is a progressive, chronic illness that is enigmatic because the mechanisms for its pathogenesis have yet to be determined. Syndromes synonymous with CRPS are reflex sympathetic dystrophy, reflex neurovascular dystrophy, causalgia, algoneuropathy, sympathetically maintained pain, clenched fist syndrome, and Sudek's syndrome.

The diagnosis of CRPS is categorized into three stages: acute, dystrophic, and atrophic. CRPS is most often precipitated by peripheral trauma (crushing injuries, lacerations, fractures, sprains, burns, or surgery) to soft tissue or nerve complexes. The pathogenesis for CRPS has been speculated as being either a disease process of the peripheral nerves, a disease process of peripheral soft tissue, or a disease process of the spinal cord.

Patients suffering from CRPS may be limited in their ability to function in a self-directed, independent fashion. A longitudinal study of CRPS on 1,348 patients revealed that 96% of the study subjects still suffer some pain and disability regardless of the duration of the disease or course of treatment. Although the primary etiology for CRPS is not clearly understood, key progress has been made in terms of establishing a psychological as well as therapeutic treatment plan once the diagnosis has been made.

Key words: Causalgia, complex regional pain syndrome (Type I and Type II), neuropathic pain, reflex sympathetic dystrophy, sympathetically maintained pain.

Introduction

Complex regional pain syndrome (CRPS) is a progressive, chronic illness that is enigmatic because the mechanisms for pathogenesis are yet to be determined. CRPS is the most recent acronym for a syndrome that has been historically most often referred to as reflex sympathetic dystrophy (RSD). CRPS has been clinically described for 127 years; however, diagnosis is elusive due to the inconsistency of presenting clinical manifestations and discordant labeling largely dependent on the field of specialization to which the patient was referred. Syndromes synonymous with CRPS are RSD, reflex neurovascular dystrophy, causalgia, algoneuropathy, sympathetically maintained pain, clenched fist syndrome, and Sudek's syndrome.1-3

A descriptive term meaning a complex disorder or group of disorders that may develop as a consequence of trauma affecting the limbs, with or without obvious nerve lesion. CRPS may develop after visceral diseases and central nervous system lesions or, rarely, without any antecedent event. It consists of pain and related sensory abnormalities, abnormal blood flow and sweating, abnormalities in the motor system, and changes in the structure of both superficial and deep tissues (trophic changes). It is not necessary that all components
are present. It is agreed that the name “CRPS” is used in a descriptive sense and not to imply specific underlying mechanisms. It is based upon the patient’s history, presenting symptoms, and findings at the time of diagnosis.3,4

Pathogenesis and diagnosis

Complex regional pain syndrome was initially described in clinical literature during the Civil War era (1860s) when the condition was diagnosed in soldiers suffering from gunshot wounds. In 1864, three U.S. Army surgeons described a group of 11 soldiers suffering from similar gunshot wounds involving peripheral nerves. The associated symptoms described for this group included hyperalgesia, allodynia, skin temperature changes, trophic changes, skin mottling, and sweating, and were categorized as “causalgia.”

Complex regional pain syndrome is most often precipitated by peripheral trauma (crushing injuries, lacerations, fractures, sprains, burns, or surgery) to soft tissue or nerve complexes. There are five major components associated with the diagnosis of CRPS. These include pain, edema, dysregulation of autonomic function, alterations in motor function, and dystrophic changes. The three-phase technique bone scan is helpful in confirming the diagnosis of CRPS for patients who fail to meet the clinical criteria for diagnosis.5,8

The pathogenesis for CRPS has been speculated as being either a disease process of the peripheral nerves, a disease process of peripheral soft tissue, or a disease process of the spinal cord. Peripheral nerve involvement has been postulated to represent a cycle of peripheral nociceptive stimulation leading to reflexive spinal cord emission of efferent sympathetic stimulation, whereas tissue injury has been speculated to produce artificial synapses between peripheral nerve fibers allowing for efferent transmission to sensory afferent fibers. The role of oxygen free radicals has also been investigated in relation to disease pathology associated with CRPS.7,9

Clinical course

The diagnosis of CRPS represents a major cause of disability for one in five CRPS patients. The precipitating injury as it relates to frequency of presentation is stratified accordingly: fractures (1-2%), postperipheral nerve injury (2-5%), myocardial infarction (shoulder-hand syndrome) (5%), hypothermic insult (trench foot) (5%), and 5% for peripheral revascularization of extremities.10

Complex regional pain syndrome is categorized into three definable yet overlapping stages: acute, dystrophic, and atrophic. The first stage (roughly 1 to 3 months) is characterized by severe, localized, burning pain, focal edema, muscle spasm, rapid growth of hair and nails, stiffness or restricted mobility, hyperesthesia, and vasospasm affecting skin color and temperature. The second stage (approximately 3 to 6 months) involves exacerbation and diffusion of pain and edema, diminished hair growth, brittle nails, deossification of bone, joint thickening, and atrophy of the muscles. The third stage implies irreversible trophic changes, intractable pain involving the entire limb, flexor tendon contractions, marked atrophy of the muscles, severe limitations in joint and limb mobility, and marked bone deossification.11,12

Causalgia

The diagnosis of “causalgia” (a widely used synonym for CRPS Type II) is considered as the most dramatic form of this illness. Affliction of this severity is in the majority of cases linked with an incomplete injury to the brachial plexus, sciatic, or median nerve. The arms or thighs are the site of insult in 80% of these cases, with rapid onset of pain (usually within the first month) following initial injury. Some authorities differentiate CRPS Type I from causalgia (CRPS Type II) based on involvement (or lack) of major nerve damage.

Patients suffering from CRPS experience profound emotional distress and behavioral changes. These patients experience pronounced pseudomotor, vasomotor, and trophic alterations. The outcome for patients symptomatic to this magnitude is favorable with early intervention utilizing sympathetic blockade. Delay in providing timely treatment may lead to osteoporosis and atrophy of the musculature that becomes refractory and amenable to temporary relief only.7,13

Exploration of symptoms

Pain. Pain associated with CRPS is classified as neuropathic, may imply diverse causal mechanisms, and will in many cases manifest away from the original site of injury. Sympathetic activation of primary afferent chains represents a “catchall” rationale for the mode of pain transmission attributed to CRPS.14 It is speculated that interaction between sympathetic activity and nociceptor sensitivity occurs due to cross-over transmission of sympathetic stimulation to pain receptors. Peripheral neural trauma results in demyelination of local nerve endings allowing for depolarization of nociceptor fibers through efferent sympathetic stimulation.9

Edema. Persistent local edema is a major component of CRPS during stages I and II. This process is thought to be mediated by cutaneous
nerve stimulation resulting in the release of the neuropeptide substance P (SP). Neuropeptide SP plays a dual role by increasing capillary permeability and promoting the release of histamine from mast cells. Subsequent vascular smooth muscle relaxation results in localized vasodilatation, increased blood flow, and extravasation of plasma to the interstitium.6

■ Movement. Dyskinesia associated with CRPS may present as muscle spasm, intention or postural tremor, weakness, hyper-reflexive movement, or the inability to initiate movement. Motor symptoms may precede the onset of pain, may appear contralaterally, and are always associated with the later two stages of CRPS. Clinical evidence suggests that there is:
1. No relationship between tremors and any specific symptom of CRPS.
2. Frequency of tremors may be reduced by weight loading.
3. The tremor is postural and presents with voluntary movement.
4. The tremor may be relieved by sympathetic blockage or remission of CRPS.6

■ Thermal response and circulatory manifestations. Alterations regarding autonomic and peripheral control of cutaneous blood flow are evident in cases involving CRPS. Vasoconstriction plays a role in thermoregulation and is mediated by the hypothalamus. This process may be inhibited when muscle receptors (which fall under medullary control) are stimulated. There are indications that following local neural insult, skin receptors may fall under medullary control. It is suggested that during the second and third stages of CRPS, observed decreases in skin blood flow may be due to increased microvascular sensitivity to circulating catecholamines. Affected extremities exhibit decreased autonomic control of thermal and arterial regulation and may initially present with skin that is warm, red, and dry, that during later stages becomes cool, pale, and cyanotic.4,6,15,16

Treatment

Early diagnosis and treatment for CRPS is essential “for establishing a cure.” The primary treatment for injuries known to be associated with CRPS is mobilization of the affected limb to reestablish normal function and active range of motion. This may be accomplished with adjunct pharmacologic support utilizing anti-inflammatory and analgesic agents. In latter stages, physical therapy modalities, such as passive range of motion, should take into consideration the possibility of restimulating or triggering the symptoms of CRPS.4

■ Anesthetic blockade. Local anesthetic blockade (such as cervical, lumbar sympathetic blocks, stellate ganglion blocks, or celiac plexus blocks) may prove diagnostically useful for differential diagnosis in cases where the presenting symptoms are masked or partially evident. Neural blockade can discriminate the source of pain whether originating from the central nervous system or the periphery. This approach may help to confirm or deny the presence of nociceptive stimulation as the precursor to pain, as well as diagram the specific pain pathway. This process of mapping the pain pathway may provide prognostic insight into potential outcomes using neurolytic or surgical denervation techniques.19

Specific information that will assist in determining treatment efficacy and/or disease pathology is when and if pain is relieved. Cessation of pain utilizing placebo may indicate psychogenic origin. Pain relief in complement with sympathetic blockade may substantiate a positive diagnosis for CRPS and demonstrate a need for further trials using sympathetic blockade. Pain relief associated with sensory blockade may indicate a source that is of somatic nociceptive origin. Pain persisting despite high spinal blockade implies that this population may not benefit from continued diagnostic evaluation using nerve block therapy. A significant subset within this group experience psychotic reactions in association with the latter modality.4,13,17

■ Pharmacologic. The benefits associated with pharmacologic intervention for chronic pain should include reduction of the patient’s perception of pain, normalization of sleep patterns, and relief from anxiety or depression. Pharmacologic intervention may include the use of tricyclics, antidepressants (inhibition of presynaptic uptake of serotonin and/or epinephrine), antipsychotics (blockade of dopamine receptors), hydroxyl radicals scavengers, or anticonvulsants (multiple sites of action).4,18

■ Psychological. Chronic pain invokes an emotional, vocational, psychological, and functional loss on the individual. Treatment for chronic pain requires assessment of the physical as well as the psychological determinants and ramifications that chronic pain represents to the patient.4,7

Research on patients suffering from CRPS has demonstrated a significant relationship between major stressful events in life (professional and/or personal loss) and the onset of symptoms. The relationship between the autonomic reflex and emotional status is raised when comparing psychological profiles of patients suffering from CRPS. A large segment of this patient population demonstrates emotional lability, depression, manic behavior, insecurity, or undue anxiety.4
Behavioral analysis should be recognized as an adjunct modality in the treatment plan for patients who have chronic pain when behavioral factors are believed to cause pain. (It is rarely effective in cases of acute tissue damage.) This endeavor serves to elicit and identify which factors increase and/or reinforce pain behavior. The patient's perception of pain may be enabled or exacerbated based on reinforcing behaviors mirrored to the patient by the individuals around him.

Conditions where the severity of pain seems grossly disproportionate to the assessed tissue damage may indicate a need for detailed inspection of the relationship between specific daily activities (postural changes, times of onset, and threshold/medication administration) and the level of pain associated with them. For example, in cases where pain manifests during daytime activities while abating at night, nociceptive pain (usually incompatible with this type of pattern) may be ruled out and environmental factors (as opposed to the tissue injury) may be indicated.

Other techniques. A transcutaneous nerve stimulator is recommended for the treatment of chronic pain associated with peripheral nerve injuries, myofascial syndromes, and stump pain. This device is a battery powered, patient operated electrical stimulator that emits a low intensity tingling or vibrating sensation. Theoretically, it is believed to supplant pain stimulus by delivering nonpain messages to the spinal cord or higher neural centers.

Numerous types of neurosurgical approaches to pain relief for CRPS patients, spanning from peripheral spinal nerves to invasive cranial procedures, have been attempted with marginal success. Techniques such as dorsal rhizotomy and percutaneous cordotomy produce effective, yet short-term pain management and therefore are rarely undertaken. Neural ablation proves to be ineffective over time and should be considered only for patients with a short life expectancy, such as in the case of terminal cancer.

Thermocoagulation of the gasserion ganglion, cryo-neural techniques, deep brain stimulation, and alcohol injection into the pituitary gland are recently developed techniques that have specific applications not consistent with the treatment of chronic pain associated with CRPS.

Conclusion

Patients suffering from CRPS may be limited in their ability to function in a self-directed, independent fashion. A longitudinal study of CRPS on 1,348 patients was conducted by Greipp and Thomas, and revealed that 96% of the study subjects still suffer pain and disability regardless of the duration of the disease. Diagnosis of CRPS is based purely on the physical examination and the personal history of the patient, regardless of whether or not symptomatic relief can be demonstrated using regional anesthesia, pharmacologic, or behavioral techniques. Although the primary etiology for CRPS is not clearly understood, key progress has been in made in terms of establishing a psychological as well as therapeutic treatment plan once the diagnosis has been made.

REFERENCES


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