Complex Regional Pain Syndrome (CRPS)

Santhanam Suresh and Antoun Nader

Keywords

Complex regional pain syndrome (CRPS), types I and II • CRPS pathophysiology • Treatment goals of CRPS • Comorbidity in CRPS • Algorithm for management

Definition

The term Complex Regional Pain Syndrome (CRPS) is a pain disorder in which the pain is disproportionate to the initial inciting injury. The disorder is complex because it involves multiple organ systems with abnormal blood flow, sweating abnormalities, trophic changes, and fine motor impairment. The pain distribution tends to be regional (not dermatomal), and is not limited to the area initially affected (Rand 2009). The pathophysiology of CRPS is not entirely understood. The pain can be sympathetically-maintained (responsive to sympathetic interventions) or sympathetic-independent (Gibbs et al. 2008; Wilson 1999). The diagnosis is excluded by the presence of a condition that would otherwise account for the degree of pain and dysfunction. According to the International Association for the Study of Pain (IASP), CRPS is divided into two categories based on the absence of a recognizable nerve injury (CRPS type I, formerly known as reflex sympathetic dystrophy) or the presence of a proximal nerve injury (complex regional pain syndrome type II, formerly known as causalgia) (Bruehl et al. 1999). It is often seen in teenage girls and has a greater predeliction for the lower extremity in children when compared to adults (Wilder et al. 1992). Unlike the adult population where there is workman’s compensation etc., the main red flag in children is school absenteeism.

Clinical Features

1. Somatosensory abnormalities: Persistent pain is the essential feature of CRPS. It is characteristically disproportionate to the initiating event with often no dermatomal distribution to an individual nerve. It is frequently reported as a burning sensation, usually spontaneous, mostly felt at the distal extremity in the dependent...
position. Typically, joint movements and movement of the extremity exacerbate the pain. Mechanical and thermal allodynia (pain out of proportion to the inciting event) to cold more often than heat, and hyperalgesia are frequently present. In addition, 50% of patients with chronic CRPS Type I develop hypoesthesia and hypoalgesia in the same body quadrant or the whole half body of the affected site (van Bodegraven Hof et al. 2010) with increased mechanical and thermal threshold on the affected side. These patients have a longer period of illness, greater pain intensity, and a higher tendency to develop somatomotor changes (Walton et al. 2010). The pain can be described as sympathetic maintained (SMP) or sympathetic independent (SIP) based on the positive or negative effect of selective blockade of the sympathetic nervous system or blockade of adrenoreceptors. Therefore, SMP is a symptom in a subset of patients and is not essential for the diagnosis of CRPS.

2. **Autonomic and trophic abnormalities**: Autonomic abnormalities and trophic changes are present at some time during the course of the disease (Bruehl et al. 1999; Stanton-Hicks 2000). Swelling is found in almost all patients. It is usually exacerbated by evoked pain. Sudomotor abnormalities, frequently hyperhidrosis, are very common. Temperature asymmetry of more than 1° is present in 30–80% of patients. Three distinct vascular regulation patterns are identified in relation to the duration of the disorder.

(a) In the early acute stage, the affected limb is usually warmer, skin perfusion values are higher, and norepinephrine concentrations in the venous effluent from the affected area are low. In addition, sympathetic vasoconstrictor neurons are difficult to activate.

(b) In the intermediate stage, temperature and skin perfusion tests may be either high or low depending on the sympathetic activity.

(c) In the chronic stage, the limb is colder, skin perfusion test values are low, and norepinephrine concentrations remain low in the affected side. Passing into the chronic stage, the edema resolves; and the limb atrophies with muscle contracture, constriction of the tendon sheaths and joint stiffness. Abnormal skin (thin, glossy), nail (brittle and discolored), and hair growth (fragile, uneven, curled) may be present. Bone involvement is frequent. Initially, increased isotope uptake on bone scanning is found. Later, there is rapid and profound bone loss with patchy demineralization. Although this is commonly seen in adults, this finding may not be commonly seen in children (Schurmann et al. 2007).

3. **Somatomotor abnormalities**: Motor symptoms, although not included in the definition, are frequently present and can be noted in the intermediate and the chronic phase of the disease. Weakness of all muscles in the affected area is present in approximately 70% of patients. In addition, patients may present with postural or action tremors and dystonia and myoclonus (Agrawal et al. 2009). Typically, small, precise movements are impaired. Nerve conduction studies may reveal sensory changes in over 46% of cases with chronic CRPS type I (Rommel et al. 2001).

4. **Psychological abnormalities**: Most patients have a normal psychological profile although the incidence of fixed psychogenic dystonia has been described in adolescents (Majumdar et al. 2009). In addition, there is prone to be significant family dynamics that may alter the clinical scenario necessitating the need for family therapy in some instances. Most of the children with CRPS type I are athletic and have major impetus for improvement of symptoms to participate in their sport; this can also change the psychological milieu in these children. An association with previous psychological stress, however, has been noted. A low pain threshold, emotional lability, and depression are usually present.

**Pathophysiology**

A number of hypothetical mechanisms for the disease have been described. A recent study looking at fMRI (functional magnetic resonance imaging) in children who had active symptoms of CRPS
when compared to children who did not have active symptoms revealed alterations in fMRI images when the children were in the active phase of CRPS suggesting that there may be altered neuronal circuits while in an active state of CRPS (Lebel et al. 2008). In the peripheral nervous system, the continuous barrage of noxious stimuli sensitizes the small polymodal A-δ and C-fibers, leading to hyperalgesia. In the spinal cord, there may be sensitization of the wide dynamic range neurons that occurs after intense peripheral stimulation of A-δ and C fibers. In addition, the activity of the low threshold A-β mechano-receptor fibers is altered, which may induce a state of hyperalgesia and allodynia. There is also growing evidence that the sympathetic nervous system is involved, especially when the pain or autonomic components are relieved using sympathetic blocks. In the acute stage of the syndrome, there is functional inhibition of cutaneous sympathetic vasoconstrictor activity leading to increased vascularity and hyperemia of the area. In the chronic stage, after the initial inhibition, secondary end-organ supersensitivity is manifested by increased vasoconstriction, reduced skin temperature, and enhanced sudomotor activity. The sympathetic-mediated pain may be maintained by pathologic coupling of sympathetic and afferent activity either in the periphery, between sympathetic fibers and C-fibers, or in the dorsal root ganglia. Central nervous system alterations, probably in the cortex and thalamus, may also play a role in CRPS, especially in patients with extensive sensory deficits; however it is not clear whether changes in the CNS are primary abnormalities or secondary to pain (Walton et al. 2010).

**Non-pharmacological Approaches**

Non-pharmacological approaches to the management of CRPS have been traditionally used in all instances. We use a variety of techniques including psychological interventions, biofeedback, hypnosis, and complementary interventions including massage and acupuncture.

**Psychological measures:** After a thorough psychological evaluation, the patients are evaluated for changes in family dynamics as well as the presence of any comorbid psychological problems including but not limited to anxiety and depression. We use several measures including visual-guided imagery as well as relaxation techniques in addition to other interventions including hypnosis for managing pain. Other techniques used for managing children and adolescents include the use of biofeedback therapy as an adjuvant to pain management (Linkenhoker 1983).

**Physical therapy:** Physical therapy measures including but not limited to active and passive motion and to facilitate recovery. This is the most important part of recovery from CRPS in children and adolescents. This has been addressed in this book in the chapter on interventional pain management. Other modalities in physical therapy that can help in managing pain in CRPS include heat therapy, ultrasound therapy, as well as the application of a TENS (Trancutaneous Electrical Nerve Stimulation) unit (Lee et al. 2002). A study in children demonstrated the efficacy of TENS in children with CRPS type 1 (Kesler et al. 1988). This is routinely introduced in children for managing pain
as an initial intervention for managing CRPS type 1 (Fig. 16.1).

Pharmacotherapy: Pharmacological management of CRPS type I is used commonly again to facilitate the ability to participate in physical therapy. The most common pharmacotherapy includes tricyclic antidepressants, anticonvulsants, as well as other interventions including SSRIs and SNRIs. This is still an evolving management therapy since the major side effects of pharmacotherapy especially sedation and somnolence are carefully avoided to allow the child to participate in regular activities.

(a) Tricyclic antidepressants: This is the most common pharmacological intervention used in children and adolescents. Clinical experience has demonstrated the efficacy of tricyclic antidepressants for the management of pain following CRPS in children and adolescents (Stanton-Hicks et al. 1998). Tricyclic antidepressants may have a propensity to prolong the QT interval, hence a screening EKG is obtained to rule out the potential for prolonged QT syndrome in which case the medication is avoided (Olgun et al. 2009). Amitriptyline may cause drowsiness especially in children who are school bound, hence we use nontriptyline which has less anticholinergic effects as well as possibly less sedation. Rarely imipramine and desipramine are used in pain clinic settings.

(b) Anticonvulsants (ACD): ACDs are used for managing pain in children and adolescents. Carbamezepine or oxycarbezine was used extensively in the past for managing neuropathic pain (Lalwani et al. 2005) until the gabalins were compounded. The introduction of voltage-gated calcium channel blockers like gabapentin as well as pregabalin has provided the clinician with a better modality for pain control. Side effects include potential for allergic reactions as well as the potential for weight gain with continued use of this drug.

(c) SSRI and SNRI: The use of SSRIs and SNRIs are controversial in the management of pain in children. Although there has been no direct correlation with potential benefits from the use of any of these drugs, there is an association with depression in these children and the beneficial effects may be the effect of these drugs on depression. In our own clinical setting, we have had great benefits from the use of duloxetine, an SNRI in the clinical setting of CRPS type I, we are able to provide pain control while we are able to decrease the incidence of weight gain (Meighen 2007).

(d) Opioids: Opioids are very rarely used in the setting of CRPS type.
Occasionally in patients with severe pain, opioids are used to facilitate physical therapy. However, with the introduction of nerve blocks, this therapy has been reserved for severely refractory CRPS type I.

**Interventional Techniques**

(a) *Intravenous Regional Anesthesia:* This is our first approach to the treatment of CRPS type I. A combination of local anesthetic with a non-steroidal anti-inflammatory medication such as ketorolac has been shown to have significant advantages in children and adolescents with CRPS type I (Suresh et al. 2003). In our experience, we have noted that it may not be worthwhile performing more than four blocks. We often find that it is best to move down the algorithm to perform either a continuous peripheral nerve block or a sympathetic nerve block in this setting (Fig. 16.1).

(b) *Central neuraxial blocks:* The placement of central neuraxial catheters are placed for providing pain relief for pain control to provide analgesia for physical therapy. We resort to tunneling indwelling epidural catheters and leave the catheter in place for 7–10 days. This has demonstrated to be an effective mechanism for managing pain without the side effects of opioids etc. that can cause somnolence.

(c) *Peripheral nerve blocks:* The use of peripheral nerve blocks has now become the major first-line intervention in this setting. A study from France demonstrated the efficacy of continuous nerve blocks in CRPS type I (Dadure et al. 2005). We have demonstrated the efficacy of peripheral nerve catheters in children for pain control with a home management program. A dilute local anesthetic solution with the addition of an α-2 adrenergic agonist can be more effective in managing CRPS type I. Randomized controlled trials support the use of steroids, amitriptyline, and gabapentin. In addition, regional and neuraxial techniques play an important role in diagnosis as well as treatment, especially in sympathetically mediated pain (SMP). As discussed earlier, the diagnosis of SMP is established by determining the magnitude of pain relief achieved with an appropriate sympathetic block. However, the results of local anesthetic blocks should be interpreted with caution as the adequacy of the sympathetic block in SMP must be demonstrated simultaneously with the degree of pain relief obtained. Measuring changes in skin blood flow, skin temperature, or skin resistance on the involved extremity usually assesses the adequacy of a sympathetic block. This is especially important when the goal is diagnosis of SMP. Infection is the most feared complication of long-term catheter implantation. Infection, if it occurs, is usually local and is superficial to the deep fascia. It therefore readily responds to antibiotic treatment. If a spinal or paraspinous infection is suspected, the catheter should be removed and neurological consultation and spine imaging are required.

(d) *Sympathetic blocks:* Stellate ganglion blocks for upper extremity CRPS type I or lumbar sympathetic blocks for lower extremity CRPS type I are performed for managing pain (Nordmann et al. 2006; Yucel et al. 2009). Stellate ganglion blocks are placed using ultrasound guidance in children. This has been described in detail in the chapter on radiographic imaging for pain in this book. Lumbar sympathetic blocks are performed with the use of fluoroscopy or CT guidance.

(e) *Spinal Cord Stimulation:* Neuro-modulation in children is a much more uncommon intervention in children. This is something that we resort to as a later intervention in children and adolescents and not resorted to until all other modalities have failed. The use of neuromodulation especially for peripheral nerves may be a much more advantageous intervention than central neuromodulation. All these interventions need further recommendations after more controlled trials are performed in children (Olsson et al. 2008).
Conclusion

CRPS Type I and II are well recognized entities in children and adolescents. We feel that the current armamentariums for the management of CRPS has to be further researched. Multicenter prospective randomized trials should be performed in children and adolescents and future algorithms should be created for managing children with CRPS type-1.

References


