Lesson 307: Management of the Adolescent Patient With Complex Regional Pain Syndrome

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REVIEW DATE: October, 2013

Read this article, reflect on the information presented, then go online and complete the lesson post-test and course evaluation before the termination date below. (CME credit is not valid past this date.) You must achieve a score of 80% or better to earn CME credit.

TIME TO COMPLETE ACTIVITY: 2 hours
RELEASE DATE: December 1, 2013
TERMINATION DATE: November 30, 2014

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Professional Gaps

Although most anesthesiologists and pain management specialists are aware of CRPS as a chronic condition in adults, existence and therapy in children are less well known. Only recently has the extent to which this crippling problem may occur in the pediatric population been realized.

Learning Objectives

At the end of this activity, the participant should be able to:

1. Recognize the signs and symptoms that support the clinical diagnosis of complex regional pain syndrome (CRPS).
2. Summarize the International Association for the Study of Pain (IASP) diagnostic criteria for CRPS.
3. Differentiate between CRPS types 1 and 2.
4. Recognize the differences in characteristics between adult and pediatric CRPS.
5. Describe the different stages of CRPS.
6. Review the epidemiology and theories on the pathophysiology of CRPS.
7. Understand the multidisciplinary stepwise approach to disease management.
8. Identify commonly used pharmacologic treatments available for CRPS.
9. Discuss the psychological techniques used in the treatment of CRPS.
10. Outline the prognosis for pediatric CRPS.

Case History

An active 14-year-old girl with no significant past medical history was referred to a pain center with a complaint of left foot pain of several months’ duration. The pain developed gradually without any significant history of trauma, although she vaguely recalled falling off her bike a few days before the
onset of symptoms. The pain involved the dorsal and plantar aspects of the left foot and was described as a constant, sharp, burning sensation, exacerbated by movement and light touch. She was able to ambulate initially but within days was unable to bear weight due to excruciating pain.

The patient initially presented to her pediatrician with mild swelling and severe pain involving her left foot. She reported that her foot turned purple or red for periods throughout the day. She also reported that she had difficulty wearing a shoe on the affected foot and reported difficulty with ambulation. On physical examination, the patient displayed an antalgic gait, an adaptive mechanism to reduce weight bearing on the painful extremity.

The patient’s left foot appeared erythematous with localized edema up to the level of the ankle and was markedly colder than the right. Range of motion of the ankle was limited secondary to pain. Strength was intact and equal bilaterally. Plain films of her left foot were performed and found to be unremarkable. The left ankle was then immobilized in a boot for a presumed ankle sprain. When her symptoms failed to resolve after 2 weeks, the patient was referred to an orthopedist. A magnetic resonance imaging scan was performed, which also was negative. A bone scan was then performed, which was essentially normal except for mild changes in blood flow to the affected foot.

The patient was then referred to a neurologist. Hyperalgesia to pinprick was elicited throughout her left foot but otherwise neurologic examination was unremarkable. Nerve conduction studies also were within normal limits. At that point, the patient had missed many days of school and expressed immense sadness and frustration at her pain and disability over the preceding months. The patient was referred to the pediatric pain management division for further evaluation and treatment with a presumptive diagnosis of CRPS.

**Introduction**

CRPS is characterized by persistent pain, sensory and motor impairment, and regional autonomic dysfunction. Although symptoms vary from patient to patient, the main characteristic of CRPS is the presence of pain disproportionate to an inciting event or, in some cases, the absence of trauma. The symptoms often occur in an extremity and do not follow a dermatomal distribution. Patients frequently describe the pain as sharp or burning with associated hyperalgesia (increased sensitivity to a noxious stimulus), paresthesia (abnormal sensation), dysesthesia (unpleasant abnormal sensation), or allodynia (pain from a stimulus that normally does not provoke pain). This constellation of symptoms is accompanied by evidence of findings related to the autonomic nervous system including blood flow and temperature changes, diffuse edema, increased sweating, and abnormal hair growth. If untreated, patients with CRPS can develop muscle atrophy; bony changes such as bone demineralization, and contractures may occur (Figure 1).

CRPS was first described during the American Civil War by Silas Weir-Mitchell, a student of Claude Bernard, and initially referred to using terminology such as reflex
sympathetic dystrophy (RSD), reflex neurovascular dystrophy, causalgia, Sudeck’s atrophy, neuroalgodystrophy, and shoulder-hand syndrome. These pain syndromes now are considered variants of a single medical entity.\(^4\)\(^-\)\(^6\) CRPS is a relatively new diagnosis, first published by the IASP in 1994. However, it is increasingly being recognized and diagnosed. CRPS occurs as one of two types.\(^2\) CRPS type 1, previously referred to as RSD, develops without a definable nerve lesion and accounts for a majority of cases. CRPS type 2, originally referred to as causalgia, arises in the presence of an apparent peripheral nerve lesion.

The incidence of CRPS in the pediatric population is not well defined. Once considered rare in children, probably partly due to underdiagnosis, CRPS now is thought to be both not uncommon and on the rise in this population. The peak age of onset occurs between ages 9 and 15 years,\(^1\) although CRPS has been diagnosed in children as young as age 3.

CRPS in children and adolescents differs in many respects from adult CRPS (Table 1). Pediatric CRPS appears to have a greater female-to-male sex ratio. Significant trauma as a precipitating event is seen less frequently than in adults. Pediatric CRPS has a greater propensity for lower rather than upper extremity involvement, with a ratio of 5:1, and a predilection for the foot, than does the adult form of the condition.\(^2\) Children also exhibit a better response with a more favorable prognosis using noninvasive treatment modalities\(^5\) that focus heavily on physical therapy and cognitive-behavioral therapy.

| Table 1. Adult Versus Pediatric CRPS: Several Marked Differences Have Been Identified |
|-----------------------------------|---------|---------|
| Sex predominance                  | Adults  | Children/Adolescents |
| Extremity involvement             | Upper > Lower | Lower > Upper |
| Prognosis                         | Variable | Favorable |

**Diagnosis**

CRPS remains a clinical diagnosis based on the appropriate findings on history and physical examination. However, CRPS is a difficult entity to diagnose due to clinical variability in presentation and clinical course. With these diagnostic challenges under consideration, a consensus group sponsored by the IASP was assembled to establish a set of uniform diagnostic criteria (Table 2).\(^7\)

The clinical diagnosis requires the presence of chronic pain with neuropathic characteristics that are out of proportion to an inciting event and are accompanied by evidence of autonomic dysfunction. Furthermore, it is a diagnosis of exclusion whereby orthopedic, rheumatologic, neurologic, vascular, or other diagnoses that may explain the symptoms must be excluded. Although the applicability of the IASP diagnostic criteria to pediatric cases has not been extensively studied, their use aids in awareness and recognition of the condition to more effectively diagnose CRPS and to have an effect on long-term management.
Unfortunately, no single diagnostic test for CRPS is available. Plain radiographs may support the diagnosis when findings including bone resorption, demineralization, or osteopenia are present. Three-phase bone scans also may aid in diagnosis; however, sensitivity often varies widely.

In a retrospective study of children with CRPS by Low et al, the mean time to diagnosis was 13.6 weeks. Despite increasing recognition and awareness of the disorder, delay in diagnosis from 3 months to 1 year is not uncommon. Children and adolescents on average are seen by 2.7 specialists (including the fields of pediatrics, emergency medicine, orthopedics, neurology, and rheumatology) before receiving a referral to a pain specialist. These findings become more problematic in that later diagnosis and delayed treatment almost certainly correlates with poorer outcomes.

### Stages

Historically, CRPS has been described to progress in a sequential manner that can be classified into 3 distinct stages (Table 3). Stage 1 (lasting 1-3 months) represents the acute/traumatic phase, characterized by intense burning pain at the site of injury. Stage 2 (lasting 3-6 months) involves the dystrophic phase in which the affected area along with an area of distal spread worsens in the severity of pain as well as in the degree of skin changes. Stage 3, the atrophic stage, reflects extensive irreversible structural damage. Although the stages described attempt to delineate the natural progression of the disease, not all patients will progress in this manner. In fact, most cases of CRPS tend to remain stable rather than to deteriorate progressively.

### Pathophysiology

The pathophysiology of CRPS is not completely understood. Numerous theories including central neural causes, peripheral neuropathy, and other mechanisms involving exaggerated inflammation of small nerve fibers have been implicated. CRPS also has more recently been thought to involve an abnormally prolonged and exaggerated response of the sympathetic nervous system to traumatic injury.
Management

Early reports of children with CRPS that occurred with spontaneous resolution suggested that no treatment was warranted for such a self-limiting disease. However, more recent reports suggest the use of management techniques similar to those used in adults. A multidisciplinary approach to treatment is the mainstay of clinical management of the disease. Treatment programs often involve a combination of aggressive physical therapy, pharmacotherapy with neuropathic pain medications, and biobehavioral or psychological therapies. Although definitive resolution of symptoms may not always be achieved, the main goal is to recover the child’s functional state and to minimize the degree of long-term pain and disability.

Physical Therapy

Although no single therapy has been found to be uniformly curative, physical therapy appears to be the primary modality that offers the greatest chance for resolution. Early mobilization and physiotherapy has proven beneficial in pain reduction and functional restoration. A study by Sherry et al in 1999, following 103 children in an intensive exercise program found initial resolution of symptoms in 92% of children and long-term resolution at 2 years in 88% of patients. The mean duration of exercise therapy was 14 days, a time span that decreased to 6 days over the 2-year period. Of those followed for more than 2 years, 43 (88%) were symptom-free; 15 (31%) of these patients had a recurrence, 5 (10%) were fully functional but had some continued pain, and 1 (2%) had functional limitations. The median time to recurrence was 2 months; 79% of the recurrences were during the first 6 months after treatment.

Many practitioners support the notion that all other therapies may be prescribed simply for the facilitation of a physical therapy regimen. Physical therapy goals are typically achieved through an intensive outpatient physical therapy regimen. If outpatient treatment fails, referral to an intensive multidisciplinary day rehabilitation program or to an inpatient rehabilitation program should be made. A day-hospital interdisciplinary rehabilitation approach seems effective in reducing disability and improving physical and emotional functioning and occupational performance among children and adolescents with CRPS who have failed to improve with outpatient treatment.

TENS

Transcutaneous electrical nerve stimulation (TENS) also may be beneficial in easing chronic pain by applying electrical impulses to nerve endings in an affected extremity. TENS is a noninvasive therapy that is well tolerated by children and has been shown to be extremely safe to use, making the device a worthwhile component of an initial multidisciplinary treatment regimen.

Pharmacotherapy

Medical therapy in children with CRPS has not been studied in randomized trials and is derived from experience in adults, leading to a great deal of controversy as to what constitutes appropriate drug therapy. Proponents of intensive physical therapy argue that medications are not necessary and may lead to unnecessary potential side effects. Others begin conservatively with nonsteroidal anti-inflammatory drugs (NSAIDs) and neuropathic pain medications in moderate doses to allow participation in a basic physical therapy program. Tricyclic antidepressants (ie, amitriptyline, nortriptyline, and desipramine) are prescribed widely for neuropathic pain. The chosen agent often is
selected based on the development of side effects including insomnia and anticholinergic effects. Anticonvulsants (ie, gabapentin, carbamazepine, and clonazepam) also have proven extremely effective in neuropathic pain management. Newer drugs such as pregabalin (Lyrica, Pfizer) and duloxetine (Cymbalta, Eli Lilly) have been successfully used off-label in older children and adolescents. Other classes of medications used less frequently for CRPS include \(\alpha\) - and \(\beta\)-adrenergic agonists, calcium channel blockers, systemic vasodilators, and bisphosphonates. Although opioids have been prescribed in the past for brief painful events, these drugs generally are not recommended for the treatment of neuropathic pain syndromes.

**Psychological and Biobehavioral Therapies**

CRPS is frequently a psychologically related disease process and therefore the therapeutic approach must take this aspect of the syndrome into account. A review of children with CRPS by Stanton et al found that 83% revealed evidence of “significant emotional dysfunction” on psychological testing. More recently, Logan et al reviewed children with CRPS and found that as a group, clinic-referred children with CRPS may be more functionally impaired and experience more somatic symptoms compared with children with other pain conditions. Consequently, comprehensive assessment using a biopsychosocial framework is essential to understanding and appropriately treating children with symptoms of CRPS. Patients may have coexisting psychiatric conditions such as depression, anxiety, post-traumatic stress disorder, or somatoform illness, which interfere with the motivation to improve. These findings highlight the importance of a thorough psychological evaluation in CRPS patients in order to rule out comorbid psychiatric disease or psychological comorbidities and to treat them appropriately before pursuing more invasive management.

Various psychological techniques such as cognitive-behavioral therapy (CBT) and biofeedback have been extremely useful in neuropathic pain management. CBT employs a variety of specific methods to reduce emotional distress and to mitigate the stress response, thereby reducing pain intensity. These techniques may involve the use of breathing exercises, progressive muscle relaxation, and imagery. Biofeedback, with monitoring of the body’s physiological stress response, also can be used in conjunction with CBT to direct the relaxation response through self-awareness. Relaxation-focused interventions effectively target pain management, stress reduction, school reintegration, and family functioning. Additional complementary techniques include problem solving and communication skills retraining.

Structured individual and family counseling also aids in the development of appropriate coping mechanisms. Overall, the child can be empowered to use psychological resources to manage distress and contribute to decreased pain perception.

**Sympathetic Nerve Blocks**

Sympathetic nerve blocks have gained an established place in the diagnostic and therapeutic management of intractable and recurrent pain due to CRPS. A subset of CRPS patients with sympathetically mediated pain (pain due to sympathetic efferent activity, circulating catecholamines, and increased sensitivity to \(\alpha\)-adrenergic receptors), are excellent candidates for nerve blocks with local anesthetics. An IV Bier block entails venous drainage of an extremity, proximal placement of a tourniquet for approximately 30 minutes, and injection of local anesthetic into a distal vein. This technique provides total pain relief in some patients. Other alternatives include lumbar sympathetic blocks or epidural blocks in lower-extremity cases and stellate ganglion blocks or epidural blocks for
upper-extremity involvement. Generally, continuous nerve block techniques are preferred over repeated single injections to allow for the administration of multiple doses and to minimize the number of procedures and the exposure to radiation. Regional blocks are not only effective in controlling acute pain, but also are beneficial in facilitating physiotherapy and functional rehabilitation.

**Neuromodulatory Techniques**

Children who fail to respond to the stepwise multidisciplinary approach may require more advanced techniques including spinal cord stimulation and sympathectomy, but only as a last resort if conventional therapies have been exhausted and have failed. Evidence suggests spinal cord stimulation can be helpful in adolescents with severe, incapacitating CRPS that is resistant to conventional therapy. Implantation of a spinal cord stimulator is a minimally invasive procedure, usually following trial stimulation with a temporary percutaneous device. Pain relief is achieved by electrical stimulation to the dorsal column of the spinal cord, which aims to inhibit painful input and cover the affected region with paresthesias without discomfort or motor dysfunction. Sympathectomy (chemical or surgical) also may be helpful in reducing sympathetically mediated pain, but this treatment is irreversible and generally reserved for cases involving impending loss of function. Chemical sympathectomy involves the injection of phenol into a sympathetic ganglion, aiming to destroy these nerve fibers. These procedures can prove to be problematic as patients typically get relief for a few weeks, only to have the pain return with greater intensity and covering a larger area of their body.

**Recurrence**

Although CRPS in children has an excellent prognosis, patients remain at risk for recurrence particularly in the setting of any trauma or after a planned or unplanned surgical procedure. Preoperatively, patients with a history of CRPS can benefit from consultation with a pain management physician in order to thoroughly assess pain symptoms and behaviors, implement appropriate interventions such as preoperative neuropathic medications, and coordinate with anesthesiologists to select the optimal anesthetic for the surgical procedure. Generally, elective surgical procedures on an affected extremity are postponed as long as possible, until the signs and symptoms of CRPS have resolved. For individuals requiring urgent or emergency surgery, the use of regional techniques may prove advantageous. Furthermore, the value of multimodal analgesic techniques has been well supported, as this approach targets not just the surgical site, but also mitigates central nervous system hyperexcitability. The perioperative use of *N*-methyl-*d*-aspartate receptor antagonists such as ketamine and/or methadone also may improve postoperative outcomes. Use of these techniques, in conjunction with the early use of physical therapy and rehabilitation, makes the prevention of CRPS recurrence much more feasible.

**Management of the Case Presented**

Upon thorough evaluation, a pediatric pain specialist confirmed a diagnosis of CPRS type 1. Multidisciplinary pain therapies consisting of pharmacotherapy with gabapentin, referral to physical therapy, and referral for CBT commenced immediately. Physical therapy focused on desensitization, lower-limb weight-bearing and fine motor skill retraining. Six weeks after treatment initiation, the patient reported moderate improvement of swelling and temperature changes of the foot, although significant pain was still present. At 12 weeks, the patient had full range of motion of the ankle and was able to ambulate independently. Despite continued pain, she was fully functional with no missed days of school. At 6 months, she reported resolution of pain. Three months after resolution of pain, gabapentin was slowly weaned. No recurrence of symptoms was noted at 1-year follow-up.
Conclusion

Management of CRPS in the pediatric population presents unique and significant challenges to clinicians. Effective pain management begins with the understanding of the fundamental differences between adult and pediatric CRPS and its implications on clinical course and prognosis. Awareness of the signs and symptoms of CRPS and early diagnosis are of utmost importance in the management of this potentially debilitating pain disorder. Because physical therapy is regarded as the most effective therapeutic modality in CRPS management, the clinician’s primary goal should be to develop a stepwise, multidisciplinary approach to provide adequate analgesia to facilitate the rehabilitation process. Early mobilization with intensive physical therapy, in combination with appropriate pharmacotherapy to facilitate this regimen, reduces the degree of pain and disability and subsequent development of musculoskeletal changes. Treatment begins with the least invasive modalities and advances as necessary. The potential for recurrence of CRPS also is of great concern. With this in mind, certain steps may be taken to minimize the risk for recurrence and to improve short- and long-term outcomes. Early referral to a pain specialist and implementation of a multidisciplinary therapeutic approach greatly assists children with CRPS in minimizing suffering and optimizing function.

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REFERENCES

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Post-test

1. Of the following, _____ best supports the diagnosis of CRPS.
   a. clinical history and physical exam findings
   b. laboratory testing
   c. plain radiographs
   d. 3-phase bone scan

2. _____ does not constitute one of the IASP diagnostic criteria for CRPS.
   a. Persistent pain out of proportion to an inciting event
   b. Evidence of autonomic dysfunction
   c. Exclusion of other diagnoses that may account for symptoms
   d. Evidence of bony changes such as demineralization

3. Which characteristic is more prevalent in pediatric CRPS compared with adult CRPS?
   a. Greater male-to-female ratio
   b. Greater lower extremity involvement
   c. Poor prognosis with noninvasive treatment modalities
   d. Precipitated by major trauma

4. Type 1 CRPS _____.
   a. was previously referred to as reflex sympathetic dystrophy
   b. was previously referred to as causalgia
   c. occurs in the presence of an apparent peripheral nerve lesion
   d. represents a minority of CRPS cases

5. Regarding CRPS staging, _____.
   a. stage 1 is characterized by minimal pain
   b. stage 2 is referred to as the traumatic phase
   c. stage 3 reflects extensive, irreversible damage
   d. a majority of patients follow this sequential progression
6. ____ is the primary treatment modality that offers the greatest chance for resolution of CRPS.

   a. Physical therapy 
   b. Medical therapy 
   c. Psychological techniques 
   d. Sympathetic nerve blocks

7. The class of medications successfully used in neuropathic pain management is _____.

   a. nonsteroidal anti-inflammatory drugs 
   b. opioids 
   c. steroids 
   d. anticonvulsants

8. Sympathetic nerve blocks _____.

   a. are the preferred primary treatment modality for most cases of CRPS 
   b. do not provide any benefit in acute pain control 
   c. include IV regional Bier blocks 
   d. abolish the need for an intensive physical therapy program

9. Which of the following is true regarding psychological treatment in CRPS?

   a. Psychological techniques such as cognitive-behavioral therapy are of limited value in patients with CRPS. 
   b. Coexisting psychiatric illness must be evaluated for and treated in order to be able to address long-term treatment goals. 
   c. Invasive disease management is first attempted before performing a comprehensive psychological assessment. 
   d. Patients with comorbid psychiatric illness often manage pain and distress more adeptly than those without.

10. CRPS recurrence _____.

    a. occurs at one point in all patients diagnosed with CRPS 
    b. may be precipitated by subsequent trauma 
    c. is not affected by scheduled surgical procedures 
    d. is intractable and refractory to conventional treatment