Complex Regional Pain Syndrome (CRPS) with Resistance to Local Anesthetic Block: A Case Report

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We present a case of complex regional pain syndrome (CRPS) Type 1 in a 12-year-old girl. The patient did not respond to the usual therapeutic modalities used to treat CRPS, including physical therapy, lumbar sympathetic block, epidural local anesthetic block, intravenous lidocaine infusion, or other oral medications. Of note is the fact that, during epidural block, the patient demonstrated a resistance to local anesthetic neural blockade in the area of the body involved with the pain problem. The mechanism of this resistance could be related to the changes in the dorsal horn cells of the spinal cord, secondary to activation of N-methyl-D-aspartate receptors, which may play a role in the pathophysiology of this pain syndrome.

Keywords: Anesthesia, local; complex regional pain syndrome; pediatrics; reflex sympathetic dystrophy.

Introduction

Complex regional pain syndrome (Type 1), also known as reflex sympathetic dystrophy (RSD), has been reported to occur in children. With appropriate treatment, the usual course of the disease in children seems to be relatively benign. Therapeutic modalities that yield gradual resolution of symptoms include aggressive physical therapy, nonopioid analgesics, sympathetic nerve blocks, and behavioral modification.1–3

We report a case of CRPS in a 12-year-old girl, who did not respond to the usual treatment modalities. This case was remarkable due to a resistance to local anesthetic, limited to the area of the patient’s body where the pain was localized, when injected through an epidural catheter.

Case Report

A 12-year-old previously healthy girl was referred to the chronic pain service for evaluation. The child presented with the history of a fall 5 months before our initial examination, with soft tissue injury to the right ankle. There was no radiographic evidence of any bony injury. One week later, she started to complain of worsening pain and some numbness in the right big toe. An orthopedic surgeon found a mass over the area of the saphenous nerve. At biopsy the mass turned out to be necrotic fatty tissue.

The patient’s symptoms worsened with time. Swelling and a blotchy cyanosis developed over the right foot extending up to the midcalf. The foot turned cold and weight bearing provoked severe pain. Motion at all joints in the foot and ankle was severely limited. Her pain was of a continuous and burning nature. In addition, she had episodes of sharp stabbing pain, accompanied by spasms in the calf and foot. The patient could not wear socks or shoes due to severe pain. Her sleep was interrupted at night when her foot brushed against the covers. On a scale
of 0 to 10, her average pain was rated between 8/10 and 10/10. The orthopedic surgeon had prescribed hydrocodone 7.5 mg plus acetaminophen 750 mg on an as needed basis for severe pain and a course of physical therapy, which was unsuccessful due to increased pain with any manipulation of the foot.

The child appeared to be emotionally stable with no history of psychological problems or any evidence of chronic pain behavior. Examination revealed a healthy well-developed girl weighing 52 kg, with a swollen, cyanotic, and cold right foot and ankle with significant hyperesthesia and allodynia. Maximum tenderness was over the area where the orthopedic surgeon had biopsied the mass on the medial aspect of the ankle. Motion was restricted at all joints in the foot and ankle due to severe pain. No weight bearing was possible on the right foot. Strong arterial pulses were palpable in both lower extremities. A diagnosis of CRPS (Type 1) or RSD was made, based on the history and physical examination, and a therapeutic plan formulated.

This plan consisted of starting the patient on a course of gabapentin, which was increased from 100 mg three time a day (tid) to 300 mg tid, and amitryptiline 10 mg per day. The hydrocodone was replaced with tramadol 50 mg tid. A series of lumbar sympathetic blocks also was planned. Intravenous (IV) regional blocks (Bier blocks) with bretyllium or ketorolac also were considered, but it was felt that the patient would not be able to tolerate the procedure at that time due to the severe pain in the foot. Psychological evaluation of the child was recommended to the parents. Physical therapy was planned to be restarted, once the pain had been adequately controlled with sympathetic blocks.

Pharmacologic therapy provided minor relief of the patient’s symptoms over a 2-week period, and the patient subsequently was scheduled to receive a lumbar sympathetic block. This procedure was carried out with light sedation in the prone position at the level of the second lumbar vertebra. The block caused a temperature elevation in the right foot from less than 29°C (below the minimum temperature of the skin probe), to 37°C. The color of the foot improved dramatically as the temperature rose. Pain relief was minimal, the pain score decreasing from 10/10 to 8/10. The patient initially refused to have a repeat block due to the discomfort of the procedure, but after further discussion it was decided to attempt another block 3 days later with deep sedation. However, again, there was minimal pain relief despite a dramatic increase in temperature.

Because of failure of the lumbar sympathetic blocks, an epidural local anesthetic block was administered through a catheter placed at the level of L2–L3 under deep sedation. After recovery, she received a total of 15 mL lidocaine 0.5% through the epidural catheter, resulting in a temperature rise of 5°C in the right foot. However, the patient experienced no pain relief from this block.

It was decided to proceed with administration of bupivacaine 0.25% through the epidural catheter. A total of 20 mL was injected in 5-mL increments over a period of 15 minutes, which resulted in a sensory block up to T4 dermatome. The patient still complained of pain in her right foot and ankle. On examination, her foot still had intact sensory function up to the midcalf where her pain began. Above this level, she had complete sensory loss. In her left lower extremity, she had a complete sensorimotor block. She was able to discriminate between the temperature of an alcohol wipe and a cotton swab applied to the area of her right foot and ankle. The patient also did not report any decrease in her pain symptoms.

We postulated that the problem probably was due to hypersensitivity that had developed in the dorsal horn of the spinal cord. She was scheduled for a trial lidocaine infusion, possibly followed with a ketamine infusion, in an attempt to decrease the sensitivity in the dorsal horn. She received lidocaine 250 mg over a 10-minute period through an IV placed in her right upper extremity. This dose produced minor symptoms of toxicity with perioral tingling and some slurring of speech, but no change in symptoms. Subsequently, ketamine 10 mg was infused slowly, causing considerable sedation but no change in pain levels. After recovery from the ketamine, a bolus of fentanyl 25 μg IV was given, without any effect. At this time, the patient seemed to become more uncomfortable, developing severe spasms in her foot.

The patient was subjected to further psychological evaluation, which was normal. She then became an inpatient to receive a continuous lumbar sympathetic block for 5 days, with accompanying physical therapy. At discharge, the patient’s pain score had decreased from 10/10 to 7/10. Weight bearing with crutches now was possible. The patient continued treatment with intensive physical therapy and pharmacotherapy with gabapentin and amitriptyline. Currently, she is doing well, with pain scores ranging between 3/10 and 4/10, and she has increased her daily activities considerably.

Discussion

The development of localized resistance to the sensory effects of local anesthetics in the course of therapy of CRPS has not been reported to date, and is the rationale for presenting this case. In addition to the etiology, pathophysiology, and treatment of CRPS, the possible etiology of this resistance is reviewed.

CRPS (Type 1) has been defined as a complex pain problem with accompanying signs of sympathetic dysfunction (previously known as reflex sympathetic dystrophy) subsequent to minor trauma and which may even occur in the absence of trauma. The hallmarks of this problem1 include severe burning or stabbing pain with allodynia and hyperesthesia (especially to cold sensation), accompanied by movement disorder (painful or stiff joints) and muscle spasms. In the early stages, there may be swelling and increased skin temperature, with redness or cyanosis. This situation usually gives way to decreasing skin temperature with pallor and dystrophic changes of the skin. There may be hair loss, slowed nail growth, and increased sweating in the area. If untreated, this condition may lead to an atrophic, painful, and useless extremity. In some cases, as the disease progresses, the pain may spread

to other extremities or to areas of the body not previously involved in the disease process. Psychological dysfunction may predispose certain individuals to develop CRPS.\textsuperscript{5}

Diagnostic tests used to confirm the presence of CRPS may include thermographic techniques,\textsuperscript{6} triple phase bone scan,\textsuperscript{7} systemic administration of alpha-blockers,\textsuperscript{8} regional anesthetic techniques\textsuperscript{9} such as stellate ganglion block, lumbar sympathetic block, and differential epidural and spinal block, and regional IV block with alpha-blockers.

The pathophysiology of CRPS remains an enigma. Many theories focus on peripheral mechanisms, whereas others surround spinal cord dysfunction.\textsuperscript{10} Peripheral changes seen in CRPS\textsuperscript{11} may include neural membrane or receptor dysfunction\textsuperscript{12} in the area of injury and in surrounding areas, which increases their sensitivity to neural mediators, such as norepinephrine, prostaglandins, serotonin, substance P, and histamine, which may be present in the area of injury. Central theories include increased sensitivity and dysfunction of wide dynamic range (WDR) neurons,\textsuperscript{13} which are the second-order sensory neurons in the dorsal horn of the spinal cord. Activation of N-methyl-D-aspartate (NMDA) receptors\textsuperscript{14,15} on the WDR neurons may cause sensory dysfunction with hyperalgesia and allodynia. WDR neurons in surrounding dermatomes, sympathetic neurons in the lateral horns of the spinal cord, and motor neurons may be activated with consequent spread of pain, hyperalgesia and allodynia, sympathetic hyperactivity, and muscle spasm.

Therapy of CRPS should be started as early as possible, involving multiple modalities. Physical therapy\textsuperscript{16} plays the most important role in the treatment of CRPS. As the disease process continues, it is extremely important to continue physical therapy to maintain function in the affected extremity. When the patient, because of severe pain, cannot tolerate physical therapy, other modalities, such as pharmacologic intervention and regional anesthetic techniques, should be used in conjunction with physical therapy to decrease pain.

Pharmacologic interventions\textsuperscript{17–20} include the use of antiepileptic drugs, antidepressant medication, systemic or regional use of alpha-blockers, nonopioid and opioid analgesics, and NMDA-receptor blockers. A variety of regional anesthetic techniques\textsuperscript{21–25} have been used to treat CRPS. A number of sympathetic and somatic nerve blocks to the area involved are extremely useful in controlling the symptoms. If pain relief from these procedures does not last for a reasonable duration of time, a continuous block technique for 3 to 5 days can be carried out as an inpatient procedure for longer lasting pain relief. Intravenous regional anesthesia (Bier block)\textsuperscript{26–31} using phenoxybenzamine, reserpine, guanethidine, bretylium, and ketorolac may be equivalent to local anesthetic sympathetic block in treating CRPS. Intravenous infusion of lidocaine\textsuperscript{28–35} has been used to relieve neuropathic pain that fails to respond to other modalities of treatment. In our patient, we tried a combination of some of these therapeutic approaches without much success.

The interesting feature that prompted us to report this case is that there seemed to have developed a resistance to local anesthetic blockade localized to the area of pain. Epidural block gave rise to anesthesia (both sensory and motor) from the T4 dermatome down to the sacral dermatomes. However, the area where the pain was localized escaped blockade and sensation remained intact to light touch, pressure, pinprick, and temperature.

It could be argued that the patient had an anatomical anomaly in the epidural space,\textsuperscript{36} which prevented the local anesthetic drug from affecting the involved nerve roots. On reviewing the history and physical examination, we felt that this situation was unlikely.

In general, if a patient fails to gain pain relief in the presence of an otherwise effective somatic epidural block, it is presumed that there is either a central nervous system (CNS) lesion or a psychosomatic disorder.\textsuperscript{37} We have observed three patients in our pain center in whom a diagnostic differential epidural block did not yield complete pain relief in the presence of a high level of somatic blockade. These patients, who lacked any evidence of CNS disease, were thought to have some degree of psychosomatic pain disorder and consequently were referred to a psychologist for evaluation. On evaluation, two of the three patients had psychobehavioral problems that were responsible for their pain and that improved with further therapy. The other patient refused psychological evaluation. In this case, there was no evidence for either CNS or psychosomatic problems.

Chronic neuropathic pain is known to cause changes in the CNS leading to resistance to various modalities of treatment. Many of these changes are due to the “wind-up” phenomenon seen when NMDA-receptor channels open and release excitatory amino acids, such as glutamate, which may be present in the area of injury. Central theories include increased sensitivity and dysfunction of wide dynamic range (WDR) neurons,\textsuperscript{13} which are the second-order sensory neurons in the dorsal horn of the spinal cord. Activation of N-methyl-D-aspartate (NMDA) receptors\textsuperscript{14,15} on the WDR neurons may cause sensory dysfunction with hyperalgesia and allodynia. WDR neurons in surrounding dermatomes, sympathetic neurons in the lateral horns of the spinal cord, and motor neurons may be activated with consequent spread of pain, hyperalgesia and allodynia, sympathetic hyperactivity, and muscle spasm.

In conclusion, this report is presented to stimulate further efforts to elucidate this phenomenon of resistance to local anesthetic block that was observed in this patient.
Questions that need to be addressed are: is this phenomenon caused by the chronic pain syndrome, and if so, what is the exact mechanism of this problem and what could be done to reverse this phenomenon. It also raises questions about the conclusions we draw from various procedures we perform such as the "differential epidural block," which has been used in the diagnosis of chronic pain problems.

Many physicians who practice pain management are faced with patients who seem to be resistant to the usual modalities of treatment and continue to suffer in spite of all efforts to relieve their suffering. We are sure that continuing research into the pathophysiology and pharmacology of CNS will bring relief to these unfortunate people in the future.

References


