

COMPLEX REGIONAL PAIN SYNDROME (CRPS) REFLEX SYMPATHETIC DYSTROPHY (RSD) DIAGNOSIS AND MANAGEMENT PROTOCOL

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Abstract. Complex Regional Pain Syndrome (CRPS) / Reflex Sympathetic Dystrophy (RSD) is a relatively rare neurologic disease. In the recent years, there has been an increasing awareness about the illness. The diagnosis of CRPS (RSD) is a diagnosis by inclusion rather than exclusion. Careful history taking, neurological evaluation, and understanding the nature of the components of CRPS (RSD) spares the patient from misdiagnosis and improper treatment.

Descriptors. complex regional pain syndrome (CRPS), reflex sympathetic dystrophy (RSD).

INTRODUCTION

Complex Regional Pain Syndrome (CRPS) / Reflex Sympathetic Dystrophy (RSD) is a disease that usually starts after a relatively minor trauma. In the early stages there is a sympathetic component in the development of the disease, but with passage of time, quite frequently the somatic (non-sympathetic) nervous system becomes involved as well. It is not a disease due to simple hyperactivity of the sympathetic nervous system. It shows dysfunction of sympathetic as well as somatic nervous system in the involved regions.

ANATOMY

Normally, there are two distinct sensory nerves. The somatic and the sympathetic.

The somatic nervous system provides a variety of sensory modalities including fine touch, vibration, position sense, and well defined circumscribed pain. The sensory input terminates in the post central parietal sensory cortex of the brain where it is perceived and modulated as a conscious, clear cut, focalized, well defined sensation.

The sensory (afferent) portion of the sympathetic reflex arc, on the other hand, consists of a primitive sensory system which is not well defined, and can generate an unpleasant visceral and neuropathic pain. The pain is perceived as involving regions of the body such as upper or lower extremity. In contrast to the somatic sensory pain, the sympathetic sensory pain has a tendency to spread, and to generate referred pain (especially to paraspinal regions). Whereas the somatic sensory pain is felt in the

distribution of the nerve roots (dermatomal radiculopathy), the sympathetic nerves have a tendency to follow the arteries (for control of body temperature), and follow the small arterial branches resulting in a dermatomal distribution of the pain.

PHYSIOLOGY OF SYMPATHETIC SYSTEM

The sympathetic nervous system has three main functions.

1. Protection of internal environment of the body. Example: control of body temperature.
2. Control of vital signs (blood pressure, pulse, and respiration). Sympathetic stimulation results in cold and wet skin (temperature preservation), increased heat and circulation in the muscle and bone, and elevation of pulse and BP.
3. Modulation of the immune system by up-or down- regulating the immune system response to any distress. The hyperimmune response leads to bouts of swelling, spontaneous bruises of skin, and fever.

DIAGNOSTIC CRITERIA

The diagnosis of CRPS (RSD) is a diagnosis by inclusion rather than exclusion. The diagnostic tools consist of careful history and physical examination, triphasic bone scan (TBS), infrared thermal imaging (ITI), and other tests such as autonomic response test, or quantitative sudomotor response test (QSART).

TBS testing **is** not sensitive enough to diagnose the CRPS. It is handicapped by the fact that the abnormality may be present bilaterally making it impossible to compare right side with the left. It is also quite variable in different stages of the disease. In addition, the test is nonspecific-imitating other conditions such as arthritis or Raynaud's Phenomenon. Lee and Weeks, and O'Donoghue, et al, have reported only 55-60% sensitivity for bone scans in diagnosis of CRPS (1, 2). This means there is a 45% chance of missing the disease because the bone scan is reported as negative or nonspecific.

ITI, on the other hand, is handicapped by the fact that the test is quite sensitive causing false positive results (3). ITI is only useful to identify areas of sympathetic nerve damage-but it cannot be used as the sole tool for the diagnosis of CRPS.

CRPS can be diagnosed clinically by inclusion of a minimum of four principles (Table I) (4, 5).

According to Benarroch the sensory nerve fibers originating the sympathetic response, eventually terminate almost exclusively in the limbic system (medial frontal and medial temporal lobe regions of the brain (6). As a result, in CRPS, the patient invariably suffers from limbic system dysfunction such as insomnia, agitation, irritability, depression, poor memory, and poor judgment (Table I). Using the above

four strict criteria, other neuropathic pains such as diabetic neuropathy, myofascial syndrome, post herpetic neuralgia, etc., are excluded from the CRPS diagnosis.

Table I. Clinical Diagnosis of CRPS (RSD) The following four criteria are necessary for diagnosis of CRPS (4, 5).
<p>1. Neuropathic pain in the form of:</p> <p>a. Allodynic and hyperpathic pain elicited by simple stimuli that do not usually cause pain such as touch or breeze, and an exaggerated regional pain after simple stimulation.</p> <p>b. Hyperpathic pain: Increased sensitivity to touch (with objective sign of changes in sweating and rapid pulse in response to pain stimulation) with a tendency for secondary regional spread to the adjacent areas of the limb.</p>
<p>2. A motor response to the sensory stimulation.</p> <p>a. Vasomotor (color and temperature changes of the extremity)</p> <p>b. Motor dysfunction (flexion deformity, muscle spasm, dystonia or tremor).</p>
<p>3. Inflammation</p> <p>a. Swelling of the extremity</p> <p>b. Neurodermatitis</p> <p>c. Spontaneous bruising</p> <p>d. Swelling causing entrapment mimicking carpal tunnel, tarsal tunnel, or thoracic outlet syndrome.</p>
<p>4. Limbic system dysfunction*</p> <p>a. Insomnia</p> <p>b. Irritability and agitation</p> <p>c. Poor memory</p> <p>d. Depression</p> <p>e. Poor judgment</p>

**The fourth principle, the disturbance of the limbic system function (the marginal part of the brain responsible for mood, memory, and judgment), is essential for definitive diagnosis of CRPS (5).*

DIAGNOSIS BY NERVE BLOCK

Different types of nerve block tests such as guanethidine and phentolamine have been utilized for the diagnosis of CRPS (7, 8). However, phentolamine tests are not performed anymore. Such tests are incapable of proving or ruling out CRPS. They only prove if the pain is a sympathetically maintained pain (SMP) or a sympathetically independent pain (SIP). In CRPS, in the first few months, the pain may be almost exclusively SMP. However, with the passage of time and with application of certain treatments (such as application of ice, cast, or assistive devices), the non-sympathetic

nerve fibers become involved and the pain becomes SMP-SIP or purely SIP pain. This does not rule out the diagnosis of CRPS. The application of ice or immobilization of the extremity stimulates other mechanical or chemical sensory fibers which are independent of the sympathetic system. The harmful effect of application of ice results in cold extremity and generates a new type of pain in the form of allodynia which is transmitted by sensory nerve fibers (A-delta nerve fibers) which are not a part of the reflex arch of the sympathetic system. The immobilization stimulates the chemoreceptor sensory fibers which are also independent of the sympathetic sensory fibers. So, the simple fact that the nerve block does not get rid of the pain does not rule out CRPS in later stages of the disease.

In stage I (dysfunction), the pain is usually SMP in nature. In stage II (usually 3 months or longer after the trauma) the inflammation becomes more obvious (dystrophy) and the pain may be SMP or SIP. In stage III (atrophy), the pain is usually SIP. All of this is an academic exercise and adds confusion to the diagnosis of this baffling illness.

The clear cut staging of the disease is only applicable to the cases that have had no form of treatment. With nerve blocks and other assertive forms of treatment, the patient may rapidly move from stage III to stage II or I and the disease will be more difficult to diagnose because "the patient looks too healthy".

ETIOLOGY

CRPS is usually caused by a minor trauma. The dorsum of the foot, hand, wrist, and knee are more likely to be involved in traumatic CRPS. These areas receive sensory nerves from multiple adjacent nerves (e.g., sural and peroneal nerves over the foot or median, radial, and ulnar nerves over the hands). These watershed zones, when traumatized, stimulate the multiple adjacent nerves and result in stimulation of a wide dynamic range (WDR) of the spinal cord (9).

The reason for the minor trauma being more likely to cause CRPS is the fact that major trauma stimulates the larger somatic sensory nerve fibers which overshadow the pain impulse transmitted by the very small sensory nerve fibers (small c-fibers) involved in the transmission of the hyperpathic pain of CRPS.

One example of this phenomenon is the fact that treatment with transcutaneous electrical nerve stimulation (TENS) or spinal cord stimulator (SCS) overshadows and suppresses the hyperpathic pain of CRPS by being a stronger stimulus.

Another example is one of the worst cases of CRPS called "Venipuncture CRPS II (10)." It is due to selective nerve damage to the wall of the blood vessel. This disease fortunately is rare and happens one in several million cases of venipuncture (IV needle insertion), causes severe causalgic pain. This is one of the most severe and painful forms of CRPS, yet the only damage is in the form of injury to the small nerves in the wall of the blood vessel (10).

EMG/NCV

Electromyography (EMG) and nerve conduction velocity (NCV) are invariably normal in CRPS. NCV may be mildly abnormal and may mimic entrapment neuropathies (such as carpal tunnel or tarsal tunnel syndrome) due to the inflammation of CRPS. This only confuses the clinician and quite frequently results in unnecessary operations for such inflammatory nerve entrapments at the wrist, ankle, or elbow.

Unfortunately, NCV is frequently done only on median nerve and not on ulnar nerve. In inflammation of CRPS both these nerves have a tendency to show slowing of conduction. This fact rules out a simple "carpal tunnel syndrome". The patient undergoes unnecessary surgery with disastrous outcome of rapidly deteriorating CRPS (9).

CT AND MRI

The same phenomenon explains the fact that x-rays, CT scan, and MRI are normal in CRPS-with the exception of advanced cases of CRPS showing osteopenia. The osteopenia is secondary to vasomotor disturbance causing a reduction of circulation of the skin (cold skin) at the expense of increased circulation in the deep structures (bone and muscle) which end up causing the wash-out of the bone and muscle. This results in osteopenia spontaneous fracture of the extremity, and muscle weakness.

MANAGEMENT

Due to lack of diagnostic criteria and lack of a proper treatment plan, the CRPS becomes chronic and difficult to treat.

Even after correct diagnosis, harmful treatments-such as surgery, application of ice further aggravate and damage the nerves (5, 11).

The management should follow a clear cut plan (Table II).

Table II. Goals of Management
1. Reverse the course of the disease
2. Reduce the suffering
3. Avoid and cancel surgical procedures
4. Detoxification
5. Rehabilitate the patient
6. Avoid costly treatments
7. Add to life expectancy
8. Improving the quality of life
9. Return to work

REVERSAL OF THE COURSE OF THE DISEASE

To achieve a reversal of the course of the disease, it must be treated in a multi-disciplinary manner, in the following order of importance:

1. To mobilize the patient and to take away assistive devices such as brace, walker, crutch, cast, wheelchair, etc. The application of cast to the CRPS extremity results in disastrous deterioration in the form of tremor, atrophy of the muscles, and flexion deformity of the extremity (12, 13).

2. Immobilization due to the use of assistive devices or excessive bed rest causes aggravation of the pain by stimulation of the deep chemoreceptors which cause severe pain in the inactive extremity (14).

3. Inactivity and lack of exercise are most harmful to CRPS patients. Inactivity accelerates the deterioration of the illness, results in aggravation of the pain, inflammation of the extremity, osteoporosis, weakness and spasticity of the extremity.

HOSPITALIZATION

The CRPS patient should not be hospitalized. The prerequisite of frequent bed rest during the hospitalization will neutralize the benefit from any other form of treatment. After treatment with nerve block, the patient should be allowed no more than maximum one hour of rest and observation. Immediately afterward the patient should be treated with extensive and assertive physical therapy.

FROZEN SHOULDER

CRPS by nature results in flexion deformity and limitation of range of motion of shoulder and hip. This causes frozen shoulder (shoulder-hand syndrome). This condition should be treated with multiple trigger point injections followed by physical therapy and instruction for exercise to mobilize her shoulder. Otherwise, the disease becomes chronic and complicated by inflammation around the shoulder mimicking rotator cuff tear. Rotator cuff operation in such patients has an extremely poor prognosis.

Obviously, a remote injury to hand or elbow without direct injury cannot cause rotator cuff tear. Yet, the second most commonly performed unnecessary surgery (after carpal tunnel) in CRPS is "rotator cuff" operation -invariably on cases of hand or elbow injuries with no shoulder trauma.

PHYSIOTHERAPY

The exercise and activity should not be limited to the short periods of time the patient is under the care of the physical therapist. The patient should be instructed to be as fidgety as possible. If the patient is sitting and is in pain, they should get up and walk. If the patient is walking and is in pain, the patient should sit down. The patient should repeatedly exercise and rest as much as possible.

The patient is instructed to learn from the human heart. The human heart works 80-90 years without even two minutes of vacation at any time. If the human heart beats 60 times per minute, each worked unit is one second. Half of the work unit (half a second) the heart muscle contracting and working. The other half second, the heart muscle is relaxing. This is equal to 50% of the time the heart works and the other 50% of the time it rests. None of us are smart or lucky enough to work 50% of the time and rest 50% of the time consistently.

Reduce suffering: This is done by switching the treatment from ice and cold water to tolerable and pleasant hydrotherapy. Epsom salt and warm water bath also are quite helpful. Epsom salt (magnesium sulfate) reduces the swelling by osmosis.

Canceling unnecessary surgical procedures (e.g., sympathectomy) also reduce the suffering.

DETOXIFICATION

The second step in reducing the suffering is detoxification. Usually, long before the CRPS is diagnosed, the patient is treated with strong morphine agonist type of narcotics (e.g., Morphine, Lortab, Vicodin, Methadone, etc). Such strong agonists suppress the formation of cerebral endorphins. This causes withdrawal pain (rebound), and tolerance (gradually increasing demand for more pain medication). Even after the original injury is cured and healed, as long as the patient is on such strong pain medications, the patient will continue suffering from pain on the basis of rebound and tolerance.

This iatrogenic (treatment caused) pain should be dealt with aggressively. The morphine agonist analgesics should be switched to agonist-antagonists opioids such as Buprenorphine (Buprenex), Ultram, or Butorphanol. Buprenex has been found to be quite effective in detoxifying the patients from narcotics including Methadone, Cocaine, and Heroin (5, 15, 16). Buprenex is far less expensive than Butorphanol (Stadol) even though it is more effective.

The analgesic of choice for chronic pain is antidepressants such as Trazodone, Desipramine, or Doxepin. Desipramine is more effective than Amitriptyline (17).

Methadone, combined with sedatives (e.g., Soma, Ambien, Valium, etc.) may cause sudden respiratory arrest and death without warning. Valium, Xanax, and Halcion induce inactivity, addiction, and withdrawal agitation.

SYMPATHETIC AND NON-SYMPATHETIC NERVE BLOCKS

Nerve blocks are quite effective in reducing the suffering, mobilizing the extremity, and counteracting the pain and spasm.

In the early stages of the disease, sympathetic blocks are quite helpful. The number of blocks should be more than 1-2 blocks and definitely less than 10-12. Repetitive sympathetic ganglion blocks can cause a “virtual sympathectomy” by the needle permanently damaging the sympathetic ganglion (5, 18-20). The non-sympathetic blocks such as epidural and paravertebral nerve blocks are quite helpful in relieving the pain and spasm.

The axillary nerve block for the upper extremities and caudal block for the lower extremities are less traumatic, and quite effective.

SURGERY

In CRPS, surgery is more likely to do harm than good. There are rare exceptions when surgery helps. One example is when the patient suffers from a knee injury with

torn cartilage which makes weight bearing impossible. In such a case, surgery should be done with the coverage of pre-operative, operative, and post-operative nerve blocks.

An unnecessary operation for the so-called carpal tunnel, tarsal tunnel, thoracic outlet, or ulnar nerve entrapment syndrome due to inflammation of CRPS does nothing but accelerate the deterioration of the course of the disease. In such cases, inflammation can be counteracted by treatment with IV Mannitol, epsom salt and warm water, physical therapy, Zonalon (Doxepin cream), and nerve blocks (5).

SYMPATHECTOMY

Sympathectomy usually doesn't help the CRPS. It provides a temporary relief. If the patient's life expectancy is 5 years or less, then sympathectomy should be considered as a temporary palliative measure (9).

The reason for failure of sympathectomy in the management of the CRPS patients is the fact that the pain is not simply SMP, and the sympathectomy causes more damage than doing any kind of healing for the CRPS. Usually sympathectomy is helpful in teenagers such as soldiers or young athletes. However, teenagers by and large recover from CRPS regardless of any type of treatment. They have a rich hormonal system and an excellent healing power. There is no proof that sympathectomy has any beneficial effect in the long run among CRPS patients (9, 21-25).

CHEMICAL SYMPATHECTOMY

Chemical sympathectomy and neurectomy with phenol or alcohol causes severe chemical nerve damage and painful neuropathy with marked acceleration of pain, and spread of CRPS (2, 26).

Amputation is the most devastating and harmful form of treatment. It should be prevented by aggressive, early, assertive non-surgical treatments (5, 27, and 28).

RETURN TO WORK

The above multi-disciplinary treatments of: Physical therapy, exercise, detoxification, treatment with analgesic of choice, (antidepressants) and nerve blocks, should be followed by rehabilitation and return to work. A stressful work environment, such as an assembly line or high volume transcribing to meet deadline, or improper work station environment, should be corrected to adapt the patient to a less distressful work environment and to prevent repetitive strain injury (RSI).

Return to work is therapeutic, and beneficial to the patient's health. The physician should emphasize to the patient that avoidance of work will only deteriorate their illness.

SPREAD OF THE DISEASE

In the late stages of CRPS, due to prolonged immobilization, or improper treatment such as unnecessary surgery or application of ice, the disease shows a tendency to spread. The spread may be vertical from arm to leg (or vice versa) on the same side or may be horizontal from arm to arm or leg to leg. The spread which occurs in about 1/3 of patients is more likely to develop after surgical procedure (5, 9, 26, 29-34).

The mechanism of spread is due to the fact that at the level of the spinal cord the sympathetic input has a tendency to cross the midline to the opposite side. The second reason for spread is a chain of relay stations of the sympathetic nerves in the form of sympathetic ganglia on each side of the spine.

MOVEMENT DISORDER IN PERIPHERAL NERVE INJURIES AND CRPS

Whereas the movement disorders point to central nervous system (CNS) origin, it is becoming obvious that peripheral nerve injuries can also initiate and contribute to movement disorders. Cardoso and Jankovic reported the occurrence of Parkinsonian tremor in 9 of 11 CRPS patients who were treated with immobilization by plaster cast of the involved extremity (12).

TREATMENT OF TREMOR

Treatment with Klonopin® or Baclofen (which exert direct inhibitory effect spinal cord) is quite beneficial in CRPS patients.

Nerve blocks with alpha I and alpha II blockers (Clonidine, Hytrin, or Dibenzylidene) may be quite helpful in management of the tremor. Mobilization and prevention of inactivity are essential treatments.

Topical application of Clonidine is quite effective in relieving the extremity pain and tremor. However, the Clonidine patch should be applied to the paraspinal region of the involved nerve. Application of Clonidine patch to the area of nerve damage in the extremity causes a paradoxical aggravation of pain and tremor.

INFUSION PUMP

When all other forms of therapy fail, infusion pump can provide very good pain relief and can help the patient to return to a more useful and productive life.

Whereas systemic treatment with large doses of opioid agonists aggravate inactivity with resultant edema of extremity and aggravation of tremor, treatment with minuscule doses of opioids through intrathecal infusion pump (only 3-17mg Morphine per day) improves these complications.

The optimal dose of opioid differs among individual patients. Higher doses act similar to oral or IM Morphine causing dependence (withdrawal), tolerance, and aggravation of pain.

Dilaudid (3-8mg) in the pump is better tolerated, and more effective than morphine.

In the past few years the infusion pumps have failed quite frequently because of either too much narcotic in the pump, or simultaneous narcotic intake by mouth flooding the system, and stopping the formation of endorphins.

REASONS FOR INFUSION PUMP FAILURE

The following are some reason for infusion pump failure: *(i)* combining pump treatment with other forms of opioids, *(ii)* too little or too much pain medicine in the pump, and *(iii)* poor technique due to lack of experience.

SPINAL CORD STIMULATORS (SCS)

Spinal cord stimulators (SCS) are effective in treatment of somatic chronic pain (e.g., failed back syndrome) but do not help CRPS patients. Usually, the beneficial effect of SCS in management of CRPS is brief (a few weeks to a few months in over 70% of patients). The SCS acts as a foreign body may aggravate the CRPS pain, vasoconstriction, and inflammation in late stages of CRPS (9). Interferential surface skin stimulator is a modified form of TENS, which is a good non-invasive substitute.

ACUPUNCTURE

Acupuncture is effective in blocking the input of acute pain. Its effect lasts no more than one hour. It has no place in treatment of CRPS (9).

SUMMARY AND CONCLUSION

Early diagnosis and multi-disciplinary treatments are essential in management of CRPS. Avoidance of ice application and unnecessary surgery prevents rapid deterioration and permanent disabilities (5, 11). Return to work is an important treatment form and should be strongly encouraged. Surgery, by large, has no place in treatment of CRPS. An algorithmic approach to treatment of CRPS is outlined in (Table II).

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