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Complex regional pain syndrome: new concepts regarding diagnosis and treatment

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Resumen

Antecedentes: Los autores presentan una revisión crítica sobre el cuadro clínico, el diagnóstico, clasificación y tratamiento del síndrome de dolor regional complejo, discutiendo todos los métodos de tratamiento y haciendo hincapié en que la reabilitación debe ser empleada con el fin de obtener un mejor resultado. Aspecto psicológico debe ser discutido en el tratamiento y también se anima equipo multidisciplinario para participar en él.

Palabras clave: El síndrome de dolor regional complejo, dolor, causalgia, atrofia de Sudeck.

Abstract

Background: The authors presented a critical review about the clinical picture, diagnosis, classification and treatment of complex regional pain syndrome, discussing all methods of treatment and emphasizing that the reabiltation must be employed in order to obtain a better result. Psychological aspect must be involved in the treatment and also multidisciplinary team is encouraged to take part on it.

Key words: Complex regional pain syndrome, pain, causalgia, Sudeck athrophy.

Introduction

The complex regional pain syndrome is an uncommon form of chronic pain that usually affects an arm or a leg, after any injury or trauma. Complex regional pain syndrome typically develops after an injury, but are also possible as cause after surgery, stroke or heart attack, but the pain is out of proportion to the severity of the initial injury.

CRPS describes a diversity of painful conditions following trauma, coupled with abnormal regulation of blood flow and sweating, trophic changes, and edema of skin[22,49].

Alternative names for CRPS in the literature include reflex sympathetic dystrophy (RSD), algodystrophy, causalgia, Sudeck atrophy, transient osteoporosis, and acute atrophy of bone[55]. In 1995, a consensus conference grouped these disorders under a single heading of CRPS.

The excruciating pain and diverse autonomic dysfunctions in CRPS are disproportionate to any inciting and recovering event. CRPS type I is formerly identified as “reflex sympathetic dystrophy[22,49].

The cause of complex regional pain syndrome isn’t clearly understood. Treatment for complex regional pain syndrome is most effective when started early. In such cases, improvement and even remission are possible[54].

The importance of this topic is beyond any doubt the classification and the treatment, reason of debates in the literature.

Literature review

Signs and symptoms

Signs and symptoms of complex regional pain syndrome may include: continuous burning or throbbing pain, usually in your arm, leg, hand or foot, sensitivity to touch or cold, swelling of the painful area, changes in skin temperature - at times your skin may be sweaty; at other times it may be cold, changes in skin color, which can range from white and mottled to red or blue,changes in skin texture, which may become tender, thin or shiny in the affected area, changes in hair and nail growth, joint stiffness, swelling and damage, muscle spasms, weakness and loss (atrophy), and decreased ability to move the affected body part.

Symptoms may change over time and vary from person to person. Most commonly, pain, swelling, redness, noticeable changes in temperature and hypersensitivity (particularly to cold and touch) occur first.

Over time, the affected limb can become cold and pale and undergo skin and nail changes as well as muscle spasms and tightening. Once these changes occur, the condition is often irreversible.

Complex regional pain syndrome occasionally may spread from its source to elsewhere in your body, such as the opposite limb. The pain may be worsened by emotional stress.

There is compelling evidence that patients with CRPS may develop movement disorders (MDs) including loss of voluntary control, bradykinesia, dystonia, myoclonus, and tremor.

These MDs may occur early in the disease course and occasionally precede the onset of the more typical features of CRPS[2,3,5,50].

Findings from different studies indicate that 9-49% of the CRPS patients may develop MDs[2,3,5,19,50]. The prevalence of MDs increases as the disease duration lengthens[63,65].

Many cases of complex regional pain syndrome occur after a forceful trauma to an arm or a leg, such as a crush injury, fracture or amputation. Other major and minor traumas - such as surgery, heart attacks, infections and even sprained ankles - also can lead to complex regional pain syndrome. Emotional stress may be a precipitating factor, as well.

It's not well-understood why these injuries can trigger complex regional pain syndrome, but it may be due to a dysfunctional interaction between your central and peripheral nervous systems and inappropriate inflammatory responses[49]. (Figure 1a, 1b, Figure 2).

If complex regional pain syndrome isn't diagnosed and treated early, the disease may progress to more disabling signs and symptoms. These may include:

- **Tissue wasting (atrophy).** If you avoid moving an arm or a leg because of pain or if you have trouble moving a limb because of stiffness, your skin, bones and muscles may begin to deteriorate and weaken.
- **Muscle tightening (contracture).** You also may experience tightening of your muscles. This may lead to a condition in which your hand and fingers or your foot and toes contract into a fixed position.

A set of research criteria derived from the results of the previously mentioned factor analysis and external validation, later corroborated in a revalidation study, was developed in order to provide such a test [Harden, bruel, harden]. These adapted criteria grouped all CRPS traits into one of the four statistically derived factors described earlier (pain/ sensation, vasomotor, sudomotor/edema, motor/trophic Table 1; In light of evidence from the Galer et al. [Galer, and Harden et al. and Bruehl et al. studies[7,17,18,19]], which demonstrated that objective signs on examination and patient-reported symptoms both provide valuable but nonidentical data, the adapted research criteria required the incidence of signs and symptoms of CRPS for diagnosis.

Physiopathology

The traditional specificity theory of pain perception holds that pain may involve a direct transmission system from somatic receptors to the brain[37].

Patients with chronic pain conditions such as complex regional pain syndrome or fibromyalgia typically describe a diverse range of somatosensory changes, with cortical and thalamic involvment[35].

The amount of pain perceived, moreover, is thought as consequence of direct injury as well as proportional to the extent of injury, however we mean currently that the pain is regulated by more complex mechanisms.

Clinical and experimental evidence shows that noxious stimuli may sensitize central neural structures involved in pain perception.

We can emphasize that important clinical examples of these effects shall include amputees with pains in a phantom limb that are similar or identical to those felt in the limb before it was amputated, and

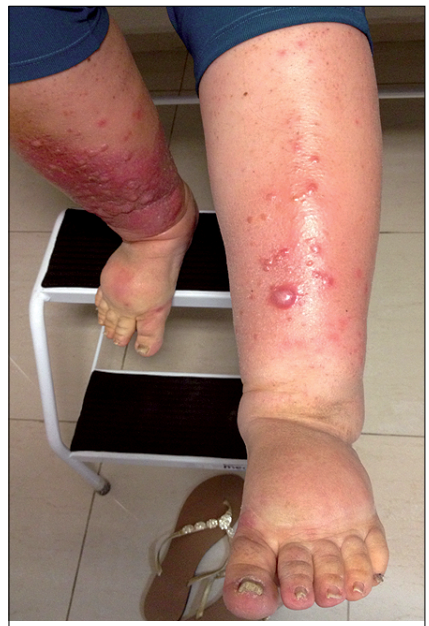

Figure 1a. Secondary infection to Streptococcus causing CRPS.

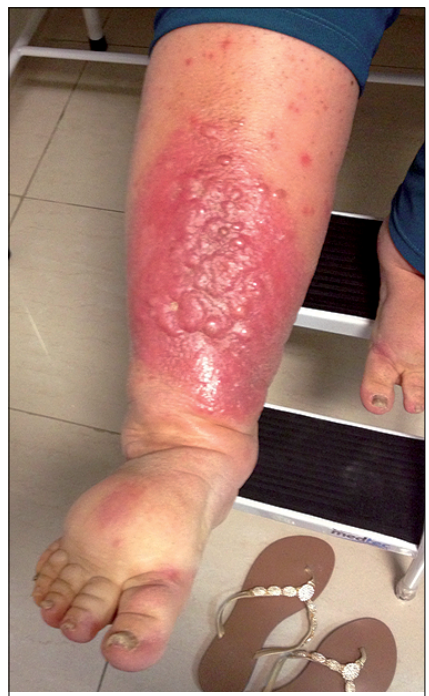

Figure 1b. Secondary infection with extensive progression and CRPS

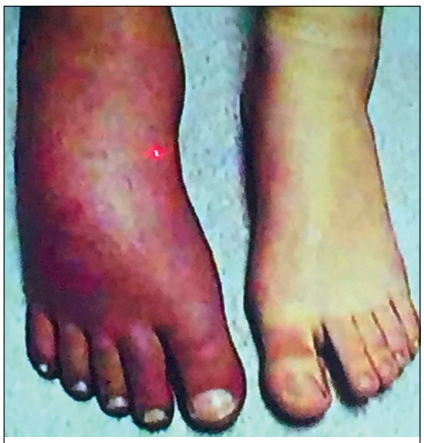

Figure 2. Classic complex regional pain syndrome showing clearly the difference of color between the affected limb and the normal.

Table 1.
Original International Association for the Study of Pain (Orlando) diagnostic criteria for complex regional pain syndrome

1) The presence of an initiating noxious event or a cause of immobilization
2) Continuing pain, allodynia, or hyperalgesia with which the pain is disproportionate to any inciting event
3) Evidence at some time of edema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain
4) This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction

patients after surgery who have benefited from preemptive analgesia which blocks the surgery-induced afferent barrage and/or its central consequences[37].
There is enough experimental evidences of these changes. It is illustrated by the development of sensitization, wind-up, or expansion of receptive fields of CNS neurons, as well as by the enhancement of flexion reflexes and the persistence of pain or hyperalgesia after inputs from injured tissues are blocked[37].
It seems to be evidente and salient from the material presented that the perception of pain does not simply involve a moment-to-moment analysis of afferent noxious input, but rather involves a dynamic process that is influenced by the effects of past experiences[37].
Sensory stimuli act on neural systems that have been modified by past inputs, and the behavioral output is significantly influenced by the "memory" of these prior events[37].
An increased understanding of the central changes induced by peripheral injury or noxious stimulation should lead to new and improved clinical treatment for the relief and prevention of pathological pain.
Compelling evidence suggests that in CRPS, different mechanisms may play a role.
Similarities between the classical symptoms of inflammation and the clinical features of CRPS have led several investigators to suggest that inflammation must play an important role in the syn- drome[41,55, 60,61].
Tissue injury stimulates C and Ad-fibers of sensory nerves, which causes the release of the inflammatory neuropeptides substance P and Calcitonin-gene-related-peptide from the afferent nerve endings[6].
These neuropeptides may induce local vasodilatation and increased capillary permeability causing edema and an increase of skin blood flow, a process known as neuro-genic inflammation[6,20].
Indeed, several studies confirmed that this mechanism is involved in the perturbed regulation of inflammation in CRPS[3,4].
Because neurogenic inflammation is initiated by sensory nerves, it remained unclear how MDs may evolve in CRPS. However, nociceptive neurons in the dorsal horns of the spinal cord may become sensitized (central sensitization) by peripheral tissue or nerve injury[70,71].
In central sensitization, there is an increased sensitivity of spinal neurons, despite a lack of change of afferent input. As a result, pain becomes chronic and non-noxious stimuli become painful[70,71].
On a molecular level, central sensitization is associated with changes in the release of neuropeptides, neurotransmitters, and aspartate receptors in particular[70,71]. It seems unlikely that central sensitization only involves pathways that deal with the perception of pain and not those that mediate a response to pain. Indeed, two lines of research now show that central sensitization may influence spinal motor circuitry. First, findings from a recent study suggest that the induction of central sensitization causes a spinal learning deficit with respect to simple motor responses to shock[13].
Second, cutaneous afferents which mediate neurogenic inflammation are also linked to spinal interneuronal circuits that mediate nociceptive withdrawal reflexes (NWR)[14].
Animal models of neurogenic inflammation have shown that SP released at the dorsal horn of the spinal cord, enhances NWRs[42,70].
In withdrawal reflexes, flexor muscles play a prominent role, and interestingly, in dystonia of CRPS there is a conspicuous involvement of flexor postures, which may hint towards the involvement of spinal motor programs that mediate NWRs[63].
Neurophysiological studies have shown that central disinhibition is a key characteristic of central nervous system involvement in CRPS patients with and without dystonia[12,27,28,29,34,51].
Both SP-sensitized NWRs in animal models and dystonia in CRPS patients respond to baclofen, a gamma-aminobutyric acid (GABA) B receptor agonist which enhances spinal GABA-ergic inhibition on neurons of the spinal cord[45,63].
Collectively, findings from different sources of research suggest that peripheral tissue or nerve injury may induce central sensitization, which is associated with spinal changes that may contribute to the development of MDs.
In CRPS, there is a conspicuous tendency for dystonia to spread to other extremities. In two studies, 37 and 67% of the CRPS patients had two or more extremities affected by dystonia[48, 61].
Recent studies of neuropathic pain, in both animals and patients, have established a direct relationship between abnormal thalamic rhythmicity related to Thalamo-cortical Dysrhythmia (TCD) and the occurrence of central pain. Here, this relationship has been examined using magneto-encephalographic (MEG) imaging in CRPS Type I, characterized by the absence of nerve lesions[67].
The localization of such abnormal activity, implemented using independent component analysis (ICA) of the sensor data, showed delta and/or theta range activity localized to the somatosensory cortex corresponding to the pain localization,

and to orbitofrontal-temporal cortices related to the affective painperception. Indeed, CRPS Type I patients presented abnormal brain activity typical of TCD, which has both diagnostic value indicating a central origin for this ailment and a potential treatment interest involving pharmacological and electrical stimulation therapies[67].

Studies through evoked potential and magnetic transcranial stimulation shows that the presence of pain and other CRPS symptoms may induce lasting changes in motor cortical plasticity, as it also does in the sensory córtex[28].

Krause et al, 2006[b29] demonstrated that the comparison between a group of patients with short- and long-term (chronic) duration of complex regional pain syndrome type I (CRPS I) motor cortical and a controll normal group, using a transcranial magnetic stimulation (TMS) mapping method showed an asymmetry which was absent in healthy subjects. Such motor cortical representation asymmetry can be considered an effect of altered sensomotor cortical representation[29]. We mean that other point must be considered as the increased use of the unaffected hand and the presence of pain as cortical influencing variables. The phyiopathology remains still controversial and speculative.

Studies with trascranial eletrostimulation and eletroneneuromigraphy suggest that the disease mechanisms of CRPS1 do not typically affect the direct neural circuit between sensory and motor cortex and that normal sensorimotor interaction is occurring via this route[59].

Classification

In some people, signs and symptoms of complex regional pain syndrome go away on their own. In others, signs and symptoms may persist for months to years. Treatment is likely to be most effective when started early in the course of the illness.

Complex regional pain syndrome occurs in two types, with similar signs and symptoms, but different causes[8,47]:

- **Type 1.** Also known as reflex sympathetic dystrophy syndrome, this type occurs after an illness or injury that didn't directly damage the nerves in your affected limb. About 90 percent of people with complex regional pain syndrome have type 1.
- **Type 2.** Once referred to as causalgia, this type follows a distinct nerve injury.

We can exemplify stating that coronary catheterization using a transradial approach has become a common procedure, as the risks of local complications are low and this procedure affords relatively expeditious postprocedural patient mobilization. Access site complications-such as radial artery spasm, hematoma, and compartment syndrome-have been reported in the literature; however, cases of complex regional pain syndrome (CRPS) of the hand related to the procedure are extremely rare[8,47].

Diagnosis

Diagnosis of complex regional pain syndrome is based on a physical exam and your medical history (Table 1 and Table 2). There's no single test that can definitively diagnose complex regional pain syndrome, but the following procedures may provide important clues:

- **Bone scan.** This procedure may help detect bone changes. A radioactive substance injected into one of your veins permits viewing of your bones with a special camera.
- **Sympathetic nervous system tests.** These tests look for disturbances in your sympathetic nervous system. For example, thermography measures the skin temperature and blood flow of your affected and unaffected limbs.

Other tests can measure the amount of sweat on both limbs. Dissimilar results can indicate complex regional pain syndrome.

- **X-rays.** Loss of minerals from your bones may show up on an X-ray in later stages of the disease.
- **Magnetic resonance imaging (MRI).** Images captured by an MRI device may show a number of tissue changes.
- **fMRI, LEP, PET CT.** The study of pain integration, in vivo, within the human brain has been extremely improved by the functional neuroimaging techniques available for about 10 years. Positron Emission Tomography (PET), as well as complemented by laser evoked potentials (LEP) and beyond any doubt functional Magnetic Resonance Imaging (fMRI) can now a days produce maps of physiological or neuropathic pain-related brain activity [Laurent]. Several studies using PET demonstrated pain-related activations in thalamus, insula/SII, anterior cingulate and posterior parietal córtices. Activity in right pre-frontal and posterior parietal cortices, anterior cingulate and tha-lami can be modulated by attention (hypnosis, chronic pain, diversion, selective attention to pain) and probably subserve attentional processes rather than pain analysis. As far as we know responses in

Table 2.
Clinical diagnostic criteria for complex regional pain syndrome

1) Continuing pain, which is disproportionate to any inciting event
2) Must report at least one symptom in three of the four following categories Sensory: Reports of hyperalgesia and/or allodynia Vasomotor: Reports of temperature asymmetry and/or skin color changes and/or skin color asymmetry Sudomotor/Edema: Reports of edema and/or sweating changes and/or sweating asymmetry Motor/Trophic: Reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
3) Must display at least one sign* at time of evaluation in two or more of the following categories Sensory: Evidence of hyperalgesia (to pinprick) and/or allodynia (to light touch and/or deep somatic pressure and/or joint movement) Vasomotor: Evidence of temperature asymmetry and/or skin color changes and/or asymmetry Sudomotor/Edema: Evidence of edema and/or sweating changes and/or sweating asymmetry Motor/Trophic: Evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)
4) There is no other diagnostic

insula/SII cortex probably subserve discriminative aspects of pain perception while SI cortex is particularly involved in particular aspects of pain discrimination (movement, contact.) In patients, neuropathic pain, angina and atypical facial pain result in PET abnormalities whose significance remain obscure but which are localized in thalamus and anterior cingulate cortices suggesting their distribution is not random while discriminative responses remain detectable in insula/SII[31].

Functional activation of brain regions are thought to be reflected by increases in the regional cerebral blood flow (rCBF) in PET studies, and in the blood oxygen level dependent (BOLD) signal in fMRI. rCBF increases to noxious stimuli are almost constantly observed in second somatic (SII) and insular regions, and in the anterior cingulate cortex (ACC)[43]. Generally speaking, abnormal pain evoked by innocuous stimuli (allodynia) has been associated with amplification of the thalamic, insular and SII responses, concomitant to a paradoxical CBF decrease in ACC[43]. Imaging studies of allodynia should be encouraged in order to understand central reorganisations leading to abnormal cortical pain processing. A number of brain areas activated by acute pain, particularly the thalamus and anterior cingulate, also show increases in rCBF during analgesic procedures[43]. Drugs or stimulation induced analgesia are associated with normalization of basal thalamic abnormalities associated with many chronic pains. We mean that is necessary to investigate the significance of these responses, their neuro-chemical correlates (PET), their time course, the individual strategies by which they have been generated by correlating PET data with LEP and fMRI results, are the challenges that remain to be addressed in the next few years by physicians and researchers[31].
Electromyography may show any abnormalities in CRPS regarding nerve conduction, however thermography of the forearm showed temperature discrepancy between both forearms, which confirmed the diagnosis of CRPS[24].

Treatment approach

Prompt diagnosis and early treatment is required to avoid secondary physical problems associated with disuse of theaffected limb and the psychological consequences of livingwith undiagnosed chronic pain[20,68].
Many current rationales in treatment of CRPS (such as topical agents, antiepileptic drugs, tricyclic antidepressants, and opioids) are mainly dependent on efficacy originate in other common conditions of neuropathic pain[22].
An interdisciplinary setting with comprehensive approach (pharmacologic, interventional, and psychological in conjunction with rehabilitation pathway) has been proposed as protocol in the practical management of CRPS[22,23].
Improvement and even remission of complex regional pain syndrome is possible if treatment begins within a few months of your first symptoms. Often, a combination of various therapies is necessary. One specialist physician will tailor the patient's treatment based on his specific case. Treatment options include:
We shall emphasize that patient has to look for:

- Early referral to physiotherapy and encouraging gentle movement as early as possible, may potentially prevent progression of symptoms[40].
- Except in mild cases, patients with CRPS are generally bestmanaged in specialist pain management or rehabilitation programmes.
- An integrated interdisciplinary treatment approach is required, including the four 'pillars of intervention.

Medications

We can use various medications to treat the symptoms of complex regional pain syndrome:

- **Pain relievers**. Over-the-counter (OTC) pain relievers - such as aspirin, ibuprofen (Advil, Motrin IB, others) and naproxen (Aleve) - may ease pain and inflammation.
  Stronger pain relievers must be prescribed if OTC ones aren't helpful. Opioid medications may be an option. Taken in appropriate doses, they may provide acceptable control of pain.
- **Antidepressants and anticonvulsants**. Sometimes antidepressants, such as amitriptyline, and anticonvulsants, such as gabapentin (Gralise, Neurontin), are used to treat pain that originates from a damaged nerve (neuropathic pain)[23].
- **Corticosteroids**. Steroid medications, such as prednisone, may reduce inflammation and improve mobility in the affected limb.
- **Bone-loss medications**. Your doctor may suggest medications to prevent or stall bone loss, such as alendronate (Fosamax) and calcitonin (Miacalcin).
- **Sympathetic nerve-blocking medication**. The sympathetic block is widely used for treating neuropathic pain such as complex regional pain syndrome (CRPS). However, single sympathetic block often provides only short-term effect[26]. Injection of an anesthetic to block pain fibers in your affected nerves may relieve pain in some people. There remains a scarcity of published evidence and a lack of high quality evidence to support or refute the use of local anaesthetic sympathetic blockade (LASB) for CRPS. From the existing evidence, it is not possible to draw firm conclusions regarding the efficacy or safety of this intervention, but the limited data available do not suggest that LASB is effective for reducing pain in CRPS[39,66]. Kim et al 2016, believe that a continuous sympathetic block is a considerable option before performing neurolysis or radiofrequency rhizotomy and even after spinal cord stimulation (SCS) implantation[26,66]. In face of CRPS of upper limb for instance, we shall instigate immediate treatment and supports the notion that stellate ganglion blockade is preferable to upper limb intravenous regional anaesthetic block for refractory index finger pain, or hand associated[21].
- **Intravenous ketamine**. Studies show that low doses of intravenous ketamine, a strong anesthetic, may substantially alleviate pain. However, despite pain relief, there was no improvement in function.

Therapies

- **Applying heat and cold**. Applying cold may relieve swelling and sweating. If the affected area is cool, applying heat may offer relief in 4 to six weeks. The combination of all local terapies seems to be useful in sciatic causalgia after ac-

etabular fracture[56].

- **Topical analgesics**. Various topical treatments are available that may reduce hypersensitivity, such as capsaicin cream (Capsin, Capsagel, Zostrix) or lidocaine patches (Lidoderm, others).
- **Physical therapy**. Gentle, guided exercising of the affected limbs may help decrease pain and improve range of motion and strength. The earlier the disease is diagnosed, the more effective exercises may be.
- **Transcutaneous electrical nerve stimulation (TENS)**. Chronic pain is sometimes eased by applying electrical impulses to nerve endings. Electrical stimulation applied directly to a single peripheral nerve can provide sufficient relief ofpain, improve patient outlook, improve lasting sleep, release the individual from addictive narcotic pain medication, and restore a psychological sense of well-being[9]. Clinical, intractable pain in the upper extremity that often resulted from neuroma, direct injury to a peripheral nerve, or repetitive operative insults to a peripheral nerve that has compressive neuropathy is currently treated by direct stimulation of the nerve[9].
- **Biofeedback**. In some cases, learning biofeedback techniques may help. In biofeedback, to learn to become more aware of your body so that it is possible to make the patient relax his body and relieve pain.
- **Epidural Catheter with anesthetical agents for upper and inferior limb pain** - placed an epidural catheter and 2 infraclavicular catheters under general anesthesia and ran continuous infusions of local anesthetic and morphin the epidural catheter (ropivacaine 0.1% and preservative-free morphine [20 µg/mL] at 8 mL/h) and ropivacaine 0.1% 6 mL/h in each infraclavicular catheter[10].
- **Spinal cord stimulation**. It is inserted electrodes along the spinal cord. A small electrical current delivered to the spinal cord results in pain relief[26,69]. Effective pain relief was obtained in 60 to 80% of patients with FBSS and CRPS Type I. Furthermore, these patients had significant improvements in quality of life (QOL) and a significantly greater chance of returning to work than patients who did not undergo SCS[32]. The use of SCS in patients with inoperable angina (that is, refractory angina pectoris) resulted in significant decreases in chest pain and hospital admissions as well as increased exercise duration, with less morbidity than with open procedures that were performed for pain control only. Patients with inoperable PVD also demonstrated significant improvements in pain relief, QOL, and limb mobility[32].

The evidence suggested that spinal cord stimulation SCS was effective in reducing the chronic neuropathic pain of (faliled Back Pain Surgery Syndrome FBSS and CRPS type I and II[69]. For ischaemic pain, there may need to be selection criteria developed for critic limb ischemia (CLI), and SCS may have clinical benefit for refractory angina short-term. Further trials of other types of neuropathic pain or subgroups of ischaemic pain, may be useful[52]. For neuropathic pain for several etiologies in upper and lower limb, even caused by infectious diseases as Lyme, the SCS may be an ideal indication[36].

Preoperative evoked potencial (sensitive motor) SSEPs provide an objective prediction of patient outcome after SCS. Sindou et al, 2003 suggest that if a patient's central conduction time - CCT is abolished or significantly altered, the patient should not undergo SCS[53].

Brush-evoked allodynia may be a significant negative prognostic factor of SCS treatment outcome after 1 year in chronic CRPS-1[62]. In one third of CRPS-1 patients, SCS treatment fails to give significant pain relief and 32-38% of treated patients experience complications[64]. A high level of pain catastrophizing in patients with CRPS-I is not a contraindication for SCS treatment[30].

An economic interesting analysis of costs based on the randomised controlled trial showed a lifetime cost saving of approximately 58,470 (60,800 US dollars) with SCS plus physical therapy compared with physical therapy alone. The mean cost per quality-adjusted life-year at 12-month follow-up was 22,580 (23,480 US dollars) [Taylor]. SCS appears to be an effective therapy in the management of patients with CRPS type I (Level A evidence) and type II (Level D evidence). Moreover, there is evidence to demonstrate that SCS is a cost-effective treatment for CRPS type I[58]. The Figure 3 shows the types of electores usually used for SCS.

Figure 3. Electrode used for spinal cord stimulation also may be used direct in nerves with lower voltage, tripolar 5-6-5 (Meditronic, USA). The Lamitrode from-Saint Judge, Abott, USA and Resume, Meditronic, USA are used for this purpose.

- **Peripheral nerve direct stimulation.** Temporary implant of the StimRouter device resulted in both pain reduction and reduced use of oral opioid pain medication during the 5-day stimulation period. The results suggest that permanent implant of the StimRouter System may be safe and effective for treating chronic peripheral neuropathic pain[11]. In University of Regina, Canada, few devices were implanted direct in the Sciatic nerve rami of L4 and S2, with good results using low voltage [Unpublished data]. His stimulation parameters were less than 1 mampere, < 1 volt, pulse width between 30-60 mSec and frequency of 60 and 120 HZ. [Figures 4a, 4b, 4c].
- **Intrathecal clonidine and/or opioid.** Intrathecal clonidine was of limited utility for most patients. It may be of benefit for subset(s) of patients, but in the literature, the duration of relief is typically < 18 months. Hydromorphine and morphine also can be used with better results[1]. It can be used trhough cateter or pump. The use of long-term intrathecal drug delivery for the treatment of intractable pain or intolerable medication adverse effects has expanded to include the

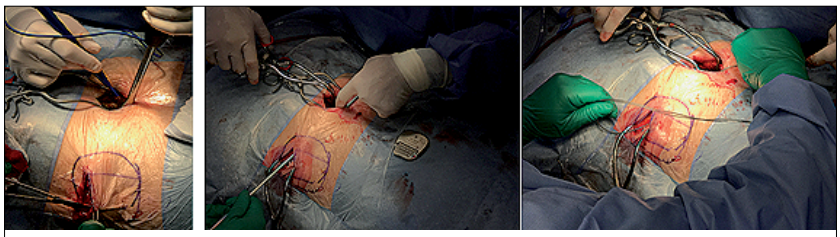

Figure 4a. Surgical view approching spinal cord for implation of electrode.

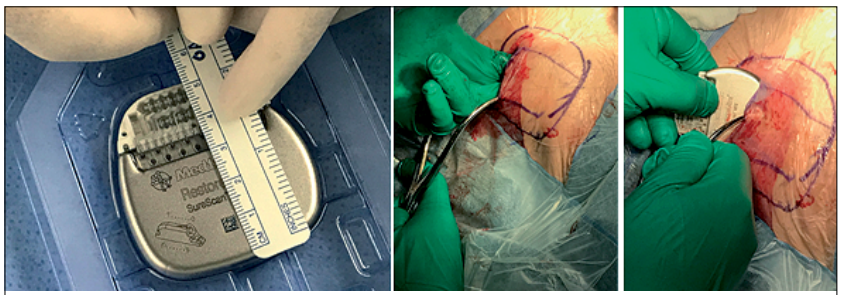

Figure 4 b. Mesurement of the size of generator (battery- Restore, Surescan, Meditronic, USA)), dissection of a small pierce for implantion of generator, inserption of the genetrator in the hypodermic cavity.

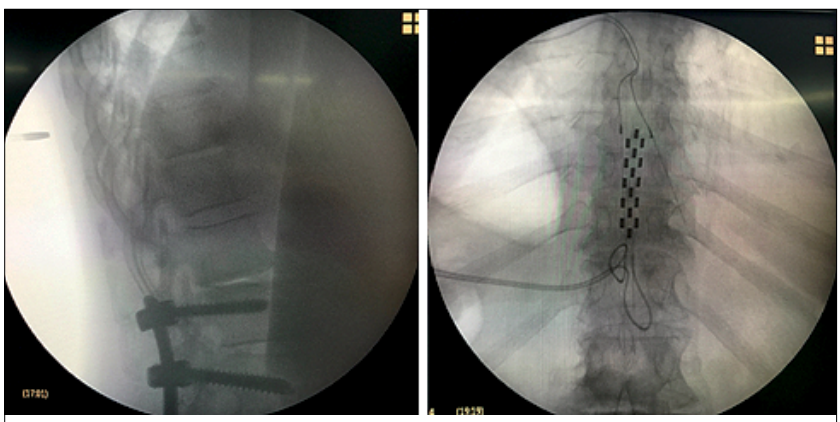

Figure 4c. Pre-operative XR showing the screws of arthrodesis in a female patient with CRPS in inferior limbs, and XR showing the extention as well as the electrode implanted in thoracic spine.

treatment of patients with chronic or cancer-related pain. Important considerations for the use of intrathecal drug therapy include the appropriate selection of patients, delivery systems, and medications, as well as potential complications of therapy as infection, lesion of nerve roots and quality-assurance measures necessary to ensure patient safety[15,57]. We prefer use the intrathecal drugs when the spinal cor and direct nerve stimulation fail, because we mean that the results of neuromodulation after the chronic use of opioid will reduce the eficacy of neuromodulation methods, because the patient will became dependente on such drugs, even with the stimulation reliefing the pain. However, we prefer central neurostimulation after such intrathecal devices deliverying opioids.

- **Motor cortex stimulation.** The effects of spinal cord stimulation (SCS), deep brain stimulation (DBS) of the thalamic nucleus ventralis caudalis (VC) and motor cortex stimulation (MCS) are indicated patients with phantom limb pain and CRPS type II[25]. The effects of MSC is still controversal, but seems to be superior when compared with DBS results [Katayama]. For deafferatation pain the MCS may be usefull showing relief of pain when it is indicated[46].
- **Dual stimulation with spinal cord stimulation and motor cortex stimulation.** Eventually may be used in refractary cases in CRPS type II, but is an excetional indication for treatment[33].
- **Deep Brain Stimulation.** Electrical intracerebral stimulation (also referred to as deep brain stimulation [DBS]) is a tool for the treatment of chronic pain states that do not respond to less invasive or conservative treatment options. Careful patient selection, accurate target localization, and identification with intraoperative neurophysiological techniques and blinded test evaluation are the key requirements for success and good long-term results. Electrodes were implanted in the somatosensory thalamus and the periventricular gray region. The best long-term results were attained in patients with chronic low-back and leg pain, for example, in so-called failed-back surgery syndrome. Patients with neuropathic pain of peripheral origin (such as complex regional pain syndrome Type II) also responded well to DBS. Disappointing results were documented in patients with central pain syndromes, such as pain due to spinal cord injury and poststroke pain[44].

Mirone et al, 2008[36] report on the use and follow-up of direct peripheral nerve stimulation of the median nerve for the treatment of iatrogenic complex regional pain syndrome (CRPS) in 56-year-old woman presented with CRPS type II in the right forearm and hand, which had started after multiple carpal tunnel surgeries and had lasted for 2 years. They observed that the visual analogue scale (VAS) score was 8-10 out of 10 and after a successful 15-day trial of median nerveperipheral nerve stimulation via a quadripolar lead in the right carpal tunnel space, they inserted an implantable pulse generator in the right infraclavicular space. The authors conclude that VAS score decreased to 1-2 out of 10 and the patient regained the ability to

sleep. The interesting about their repor tis that after 36 months of follow-up, the patient was still experiencing good pain relief without other treatment. They also conclude that peripheral nerve stimulation is easy to use in pain management and could offer a valid treatment option for iatrogenic CRPS type II[38].

Recurrences of complex regional pain syndrome do occur, sometimes due to a trigger such as exposure to cold or an intense emotional stressor. Recurrences may be treated with small doses of antidepressant or other medication.

Living with a chronic, painful condition can be challenging, especially when - as is often the case with complex regional pain syndrome - your friends and family don't believe you could be feeling as much pain as you describe. Share information from reliable sources about complex regional pain syndrome with those close to you to help them understand what you're experiencing.

Take care of physical and mental health patients by following these suggestions:

- Maintain normal daily activities as best you can.
- Pace yourself and be sure to get the rest that you need.
- Stay connected with friends and family.
- Continue to pursue hobbies that you enjoy and are able to do.

If complex regional pain syndrome makes it difficult for you to do things you enjoy, ask your doctor about ways to get around the obstacles.

The patients have to Keep in mind that their physical health can directly be affected their mental health. Denial, anger and frustration are common with chronic illnesses. It is critical to continue physical therapy and psychological support after discharge from the hospital[10].

At times, they may need more tools to deal with their emotions. A therapist, behavioral psychologist or other professional may be able to help them put things in perspective. The psychologist also may be able to teach them coping skills, such as relaxation or meditation techniques.

Sometimes joining a support group, where they can share experiences and feelings with other people, is a good approach.

The following measures may help the patients reduce the risk of developing complex regional pain syndrome:

- **Taking vitamin C after a wrist fracture.** Studies have shown that people who took a daily minimum dose of 500 milligrams (mg) of vitamin C after a wrist fracture had a lower risk of complex regional pain syndrome compared with those who didn›t take vitamin C.
- **Early mobilization after a stroke.** Some research suggests that people who get out of bed and walk around soon after a stroke (early mobilization) lower their risk of complex regional pain syndrome.

There are no randomized controlled studies of physical therapy, occupational therapy, or oral pharmacotherapy in treatment of MDs in CRPS[16]. Splints or plaster casts are often ineffective or may even worsen the dystonic postures of CRPS[16]. Benzodiazepines and high doses of baclofen may be beneficial in the treatment of dystonia and spasms in patients with CRPS but the extent of improve- ment is rarely described. Also, no controlled studies exist on the use of botulin toxin in dystonia in CRPS-I patients [Gerztein]. One study reported on the beneficial effects of intrathecal baclofen therapy in a small number of patients with CRPS-I and dystonia [van hilten]. However, given the complexity of this treatment, it should only be considered for patients with CRPS-I if dystonia is a major problem and conventional therapy has proven ineffective[16].

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