Algodystrophy (CRPS) in minor orthopedic surgery

Costantino Corradini¹
Claudia Bosizio²
Antimo Moretti²

¹ Department of Biomedical Surgical and Dental Sciences, Sports Trauma Researches Center, State University of Milan c/o 1st Division of Orthopedics and Traumatology, Orthopedic Center Pini CTO - ASST Gaetano Pini, Milan, Italy
² Department of Medical and Surgical Specialties and Dentistry, Second University of Naples, Naples, Italy

Address for correspondence: Costantino Corradini, MD
Department of Biomedical Surgical and Dental Sciences, Sports Trauma Researches Center
State University of Milan c/o 1st Division of Orthopedics and Traumatology
Orthopedic Center Pini CTO - ASST Gaetano Pini
Milan, Italy
E-mail: costantino.corradini@unimi.it

Mini-review

Algodystrophy or Chronic Regional Pain Syndrome (CRPS) is a painful disorder that develops especially at upper or lower extremities of the limbs after a fracture. This syndrome is probably due to bone microvascular changes with subsequent sympathetic nervous system involvement. The pain that characterizes CRPS is spontaneous, disproportionate to the traumatic event and is associated with hyperalgesia, and a variety of autonomic and trophic disorders. This condition has a variable incidence up to 37% of the cases, increasing along with the severity of the fracture. CRPS has a higher chance of developing in women, in older individuals, in smokers, and in patients with reduced bone strength. Early diagnosis is associated with remission in 80-90% of cases. Since the typical onset of the disease is insidious over 2 weeks after surgery, a diagnostic and therapeutic delay may occur. These are the major causes of a high percentage of chronic and disabling complications leading to impaired functional outcomes. In the acute or subacute phase, infusion of bisphosphonates has proven to be the first-choice of treatment with a high percentage of remissions. Moreover, it has been suggested the utility of vitamin C in prevention of CRPS. Furthermore, in the chronic phase electroanalgesia seems to provide promising results.

KEY WORDS: complex regional pain syndrome; orthopedics; chronic pain; therapy.

Introduction

Algodystrophic syndrome or Reflex Sympathetic Dystrophy (RSD) or Complex Regional Pain Syndrome (CRPS) is a painful condition occurring particularly in foot, ankle, hand or wrist. Even if CRPS is considered an uncommon complication of orthopedic surgery, the rate of incidence after a fracture of the distal radius or hand, and distal tibia or ankle has been found to range from 1 to 37% (1-3). A prospective multicenter cohort study of 596 patients with a single fracture of the wrist, scaphoid, ankle, or metatarsal V, recruited from the emergency rooms of 3 dutch hospitals, reported CRPS in 7% of cases, and none of the patients were free of symptoms at 1-year follow-up; in the same study, intra-articular fractures, fracture dislocations, rheumatoid arthritis, or musculoskeletal comorbidities, and any psychological factors contributed significantly to the prediction of the development of CRPS (4).

This condition usually occurs after a primary surgical procedure along with the severity of the fracture, probably due to casting or bracing pressure but also to excessive distraction with an external fixator or during Open Reduction with an Internal Fixation (ORIF) (5). It has been reported that the risk to develop CRPS type I is higher in women, elderly subjects, smokers, patients with low Bone Mineral Density (BMD) and individuals with a pre-existing diagnosis of anxiety and/or depression (6).

The heterogeneity of the signs and symptoms reflects the different pathogenic mechanisms of CRPS. This syndrome may differ across patients and even within a patient over time, when there is a transition from “warm CRPS” (acute phase) to “cold CRPS” (chronic phase). The diagnosis is based on medical history and physical examination; bone scan and Magnetic Resonance Imaging (MRI) might be used as additional investigations.

CRPS is a difficult clinical entity to be managed. Symptoms might appear early symptoms (generally 2 weeks after surgery), but also several weeks later (7). Early diagnosis ensures the best outcome, that might consist in a total recovery in 80-90% of patients, preventing a long-standing or permanent disability. A successful treatment of CRPS may require a multidisciplinary and patient-tailored approach (8). In this paper we perform an overview of the scientific advances of CPRS in minor orthopedic surgery.

Pathophysiology

In recent literature, increased attention has been attributed to knowledge of pathophysiology of CRPS. It was observed increased intima-media thickness and trophic changes as well as increased sensitivity to punctate, pressure and cold stimuli in patients underwent hand surgery with cast immobilization (9-11). Also endothelial dysfunction has been reported, and in a rat model, ET-1 receptors were involved in the development of mechanical allodynia in CRPS (12).

In an animal model produced by occluding the blood flow to one hind paw for 3 hours under general anesthesia and reperfusion, the treated hind paw exhibits an initial phase of hyperemia and edema followed by mechano-hyperalgesia, mecano-alloodynia and cold-alloodynia that lasted for at least
C. Corradini et al.

1 month. The electron microscopy showed no sign of injury to myelinated or unmyelinated axons at the site of the tourniquet, but an ischemia-reperfusion injury produced a microvascular injury, slow-flow/no-reflow, in the capillaries of the hind paw muscle and digital nerves. This phenomenon initiates and maintains deep-tissue ischemia and inflammation, leading to the activation of muscle nociceptors, and the ectopic activation of sensory afferent axons due to endoneurial ischemia and inflammation. These data suggest that in a subset of patients with CRPS-I, the main causes of the abnormal pain sensations are ischemia and inflammation due to microvascular involvement in deep tissues (13).

Another experimental model suggested that the increase of vascular permeability and the intramural pressure induced cellular hypoxia and subsequent worsening of the disease, when initiating the metabolic acidosis of the tissues (14).

In this context, it is likely that the Sympathetic Nervous System (SNS) contributes to vasomotor disturbances. Subsequently, an initial triggering event can produce the release of pro-inflammatory neuuropeptides and cytokines, generating a neurogenic inflammation. Moreover, levels of IL-6, TNF-α, and the tryptase, a mast cell marker, were elevated in skin biopsies. Moderate-to-severe pain persisted for up to 1 month after cast removal (11).

In CRPS the high percentage of the CD14(+) CD16(+) monocyte/macrophage subgroup was correlated significantly compared to lower plasma levels on the anti-inflammatory cytokine interleukin IL-10 (15). This may confirm the hypothesis of neuroimmune interactions in chronic pain (16). It has been shown in a mouse model that a greater input from peripheral nociceptors alters the mechanisms of central processing during CRPS (17).

Recently, Reilly et al. (18) suggested that immunoglobulin G (IgG) from CRPS patients significantly reduced the K+ induced response of cells pre-incubated for 24h with inflammatory mediators, such as histamine, 5-hydroxytryptamine, bradykinin, and PGE2.

Moreover, a previous study showed antibodies interacting with autonomic receptors on adult primary cardiomyocytes, comparing purified serum IgG from patients with CRPS with control IgG from healthy controls, suggesting an autoimmune mechanism in this condition (19).

Wang et al. (20, 21) suggested that epigenetic modification of Dorsal Root Ganglia (DRG) neuronal gene expression might play an important role in inflammatory cytokine metabolism, neurotransmitter responsiveness, and analgesic sensitivity, key factors in the development of chronic pain. These were considered as the potential molecular bases that underlie nerve injury-associated pathogenesis of CRPS. Therefore, understanding the specific mediating factors that influence individual epigenetic differences contributing to pain sensitivity and responsiveness to analgesics has crucial clinical implications.

Clinical pattern and diagnostic criteria

The current diagnostic criteria for CRPS are based on the clinical presentation of pain and abnormal motor and somatosensory signs and symptoms, edema, and soft tissue trophic changes. The less specific symptoms of CRPS are contractures, postural abnormalities, and psychological disorders. It is worth noting that the clinical pattern of CRPS might vary among different patients and also in the same patient at different times. Distal distribution of all signs and symptoms is a key clinical feature of CRPS: disturbances propagate distally from the lesion and are described as “glove” or “sock” including all the fingers.

Sensitivity disorders and motor impairment might spread to the proximal region of the same limb but also to the unaffected limb.

Another important characteristic of CRPS is the different type of pain pattern over time, from nociceptive, after fracture and surgery, to a typically neuropathic burning pain. The hyperalgesia is the most common symptom that can be observed in patients with CRPS. The spontaneous pain, described as sharp and widespread, is localized at the extremities and occurs in the upright position. The vasomotor disturbances are common in CRPS: vasodilatation and vasoconstriction determine temperature (79-98%) and color (71-97%) differences between the limbs. Abnormal sweating (hyperhidrosis, occasionally anhidrosis) are observed in about half of patients. Edema, especially in the acute stage of the disease, is described in 55-89% of cases even if it tends to decrease in severity progressively and it may disappear completely.

The 75-88% of patients report musculoskeletal impairments, such as joint stiffness (80%) and muscle weakness (75%), with subsequent disability. Patients complain limitations in performing movements related to edema of tissue and muscle hypertonia in acute CRPS, whereas in the chronic phase, the palmar aponeurosis fibrosis has a key role in the reduction of hand functioning. Other characteristic signs of CRPS are trophic disorders, such as increased or decreased growth of hair and nails, thin and shiny skin, and soft tissue dystrophy involving subcutaneous, muscle, and bone (patchy osteoporosis).

Radiographic findings of CRPS might develop in a few weeks, more commonly 2 weeks after surgery, including subchondral and periaricular bone changes. MRI usually shows the presence of bone marrow edema, probably related to bone pain. Moreover, phase I and phase II bone scans can show hyperperfusion (warm hand) or hypoperfusion (cold and stiff hand). Altered periaricular bone remodeling can be detected also by 3-phase bone scintigraphy (TPBS), that demonstrated the highest sensitivity (69%) and specificity (75%) if performed within the first 5 months after onset of CRPS of the upper limb (23).

Treatment

The current treatment strategies for CRPS, including medications, physical therapy, sympathetic ganglion block interventions, regional anesthesia, neuromodulation, psychological support, and occupational therapy, aim to decrease pain and to improve motor function. However, the treatment of choice for CRPS remains controversial.

To the best of our knowledge, there are no high quality evidences that support the use of physical therapy for pain control in CRPS. Van de Meent et al. (24) reported a reduction in pain and motor function improvements in patients with CRPS I treated with the Pain Exposure Physical Therapy (PEPT) that consists of exercises performed in progressive load. However, a recent randomized controlled trial (RCT) did not confirm the effectiveness of this technique compared with conventional treatment to control pain in patients with CRPS (25).
In 2013, a Cochrane review suggested that physiotherapy or occupational therapy, despite the positive effects on functional improvements, were associated with no clinically important pain relief at 12-month follow-up in patients with CRPS type I (26). On the other hand, a recent study investigated the role of high-frequency repetitive sensory stimulation (HF-rSS) and low-frequency repetitive sensory stimulation (LF-rSS) in 20 patients with CRPS type I to enhance tactile performance and reduce pain intensity. Intermittent high- or low-frequency electrical stimuli were applied daily 45 min for 5 days to all fingertips of the affected hand. HF-rSS significantly improved tactile discrimination on the treated hand in 16 patients and pain relief by more than 30% was reported in only 4 patients. However, Authors suggested that longer treatment periods might be required to induce consistent pain relief (27). In this way the electro-analgesic therapy is a novel neuro-modulatory approach using electro-cutaneous nerve stimulation of no pain information that interferes with pain signals. Although randomized controlled studies on contrast of neuropathic pain by this therapy are in course, it has been shown to be effective in relieving refractory pain in some cases of CPRS (Figure 1).

In order to decrease the incidence of CRPS I after wrist fractures from 10% to 20%, vitamin C is recommended at doses of at least 500 mg daily, and should be started immediately after surgery or injury and continued for 45 to 50 days (28).

In orthopedic surgery, adequate peri-operative analgesia, reduction of operating time, limited use of tourniquet, and use of regional anesthesia are recommended for prevention of CRPS I (29). The administration of anti-nerve growth factor (NGF) before orthopedic surgery or after bone fracture attenuated skeletal pain behaviors by 40 to 70% depending on the end point being assessed. This study suggested that orthopedic surgery and bone fracture pain might be both treated by sustained blockade of NGF, even if clinical studies are still not available (30).

A previous study suggested that intravenous regional injection with ketorolac and lidocaine produced only short-term pain reduction in patients with CRPS involving the lower extremity after 4 serial injections (31).

It has been proposed also an appropriate peripheral nerve surgical strategy including a combination of joint denervation, neuroma resection plus muscle implantation, and neurolysis. Outcomes were measured in terms of decreased pain medication usage and recovery of function, and the results were excellent in 7 (55%), good in 4 (30%), and poor (failure) in 2 (15%) patients (32, 33).

The Spinal Cord stimulation (SCS) consists of production of an electrical field (biphasic pulse consisting of a pair of equal amplitude pulses with opposite polarity) on the dorsal surface of the spinal cord that blocks neuropathic pain. This
C. Corradini et al.

technique is based on the gate control theory of pain and provides significant pain relief in a majority of patients with CRPS (34).

In a recent study, Aradillas et al. performed plasma exchange therapy (PE) in CRPS patients reporting a median pain reduction of 64% following the initial series of PE (35). However, bisphosphonates (BPs) demonstrated to be the most effective treatment in reducing pain and improving physical functioning, especially in the early stages of the syndrome, with a good safety profile and tolerability. These potent inhibitors of osteoclast activity should be initiated as early as possible in the acute phase of disease. Vareena et al. demonstrated that nirodronate at dosage of 100 mg/8 ml i.v. diluted in 500 ml of saline for 2 hours in the morning 4 times in 10 days provides significant and persistent pain relief in patient with CRPS I (36).

Interestingly, Aspengren et al. reported an increase of 20% in healing at 7 weeks by distal radius fracture treated conser-

vatively in association with daily injection of an osteoanabolic drug, teriparatide; at the same time the induced periosteal mineral apposition and increased endocortical resorption were associated with an improvement in local bone geometry with significant pain reduction without any sequela (37).

However, further researches, in particular RCTs, regarding the treatment modalities are needed.

Conclusions

The prevention of CRPS following fracture of the distal radius or ankle should be one of the concerns of the ortho-

pedic surgeon, who has to choose the appropriate treatment, considering the, comorbidities and the patient habits and lifestyle. Since different several etiopathogenic mechanisms are involved in the onset and maintenance of CRPS, this is-

sue provides an opportunity to perform different therapeutic interventions. In clinical practice, when the suspicion of CRPS at the extremity occurs, prompt management is re-

quired to prevent long-term consequences. Early manage-

ment should include collaboration with other specialists, general practitioners, physical therapists, and nurses. To date, only few clinical studies have evaluated the long-term effec-

tiveness of specific therapies for CRPS.

References

1. Rewhorn MJ, Leung AH, Gillespie A, Moir JS, Miller R. Incidence of com-

3. Majuta LA, Longo G, Feakl MN, McCaffrey G, Mantyh PW. Orthopedic surgery and bone fracture pain are both significantly attenuated by sus-

4. Wüppenhorst N1, Maier C, Fretlich J, Pennekamp W, Nicolas V. Sens-

6. van de Meent H, Oerlemans M, Bruggeman M, Klopf F, van Dongen R, Oostendorp R, Frölke JP. Elevated blood levels of inflammatory mono-

7. Wang F, Stefano GB, Kream RM. Epigenetic modification of DRG neu-

ronal gene expression subsequent to nerve injury: etiological contribu-

8. Wang F, Stefano GB, Kream RM. Epigenetic modification of DRG neu-

ronal gene expression subsequent to nerve injury: etiological contribu-


Algodystrophy (CRPS) in minor orthopedic surgery

Repetitive Sensory Stimulation as Intervention to Improve Sensory Loss in Patients with Complex Regional Pain Syndrome I. Front Neurol. 2015;6:242.


