Complex regional pain syndrome (CRPS)

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Complex regional pain syndrome (CRPS) is a syndrome characterised by a non-dermatomal distributed, severe, continuous pain in the affected limb and is associated with sensory, motor, vasomotor, sudomotor, and trophic disturbances[1].

When there is tissue damage like after trauma or surgery, we experience pain which will subside once the healing process is completed without many features of autonomic dysfunction. In CRPS we see that the pain is not only disproportionate to the injury but is also associated with changes related to autonomic dysfunction.

CRPS is mostly precipitated after trauma or surgery. Upper limbs are more commonly affected than lower limbs[1]. The incidence is 5-26 / 100,000[2]. CRPS can occur in anyone at any age, with mean age of diagnosis peaking at 40-50 years[2]. It is reported 3-4 times more frequently in females than in males[2]. Less than 10% of patients with CRPS report no causal injury or trauma[2].

There are two types of CRPS, type 1 where there is no distinct demonstrable nerve lesion, and type 2 where a demonstrable nerve lesion is present.

The available evidence suggests that transient CRPS is common after limb fractures and orthopaedic operations (up to 25% of cases)[3]. The pain improves in most cases and CRPS lasting longer than a few months is an uncommon condition (the overall prevalence is less than one in 1,500), although even a transient episode of CRPS may give rise to long-term disability due to structural and/or functional changes[3].

Pathophysiology

The pathophysiology is multifactorial with the most commonly accepted one described as exaggerated inflammatory response with autonomic nervous system dysfunction.

Different pathophysiologies include[2]:

- Hyperactivity of the sympathetic nervous system and vasomotor disturbance.
- Neurogenic inflammation.
- Deep tissue microvascular pathology.
- Autonomic dysregulation and small fibre neuropathy.
- Central processes including cortical reorganisation.
- Genetic predisposition.
- Psychological factors contributing like Depression, PTSD etc.

Differential diagnosis[3]

- Infection (bone, soft tissue, joint or skin), orthopaedic mal fixation.
- Joint instability.
- Arthritis or arthrosis, bone or soft tissue injury (including stress fracture, instability or ligament damage), compartment syndrome, neural injury (peripheral nerve damage, including compression or entrapment neuropathy, or central nervous system or spinal lesions).
- Thoracic outlet syndrome (due to nerve or vascular compression), arterial insufficiency (usually after preceding trauma, atherosclerosis in the elderly or thromboangiitis obliterans (Buerger's disease),Raynaud's disease, lymphatic or venous obstruction, Gardner–Diamond syndrome, brachial neuritis or plexitis, erythromelalgia (may include all limbs) and self-harm.

How do we diagnose CRPS?

It is a clinical diagnosis as there is no single test which can confirm CRPS. It is diagnosed as pain developing after an initial inciting event with allodynia or hyperalgesia out

of proportion for the inciting event. This would include evidence of skin changes, sudomotor dysfunction, or oedema and the absence of any other cause which would otherwise explain the presenting signs and symptoms.

Budapest criteria for diagnosis of CRPS[1]

This is considered as continued pain that is disproportionate to any inciting event or there is no other diagnosis which explains the patient's signs or symptoms.

The patient must report at least one symptom in three of the following four categories and at least one sign in two of the following four categories:

1. **Sensory:** allodynia and or hyperalgesia.
2. **Vasomotor:** temperature asymmetry and or skin colour changes / colour asymmetry.
3. **Sudomotor:** oedema and / changes in sweating / sweating asymmetry.
4. **Motor or trophic:** decreased range of motion and / motor dysfunction and / changes in hair and nail.

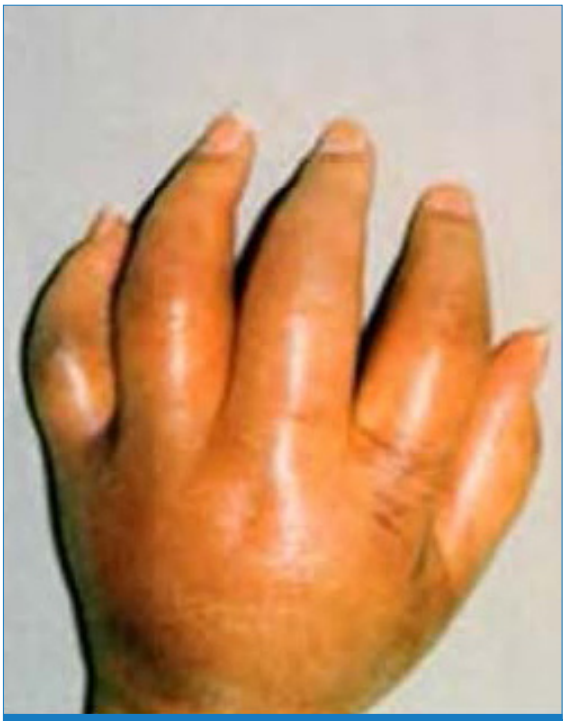
Clinical features[4]

Unprovoked or spontaneous pain that can be constant or fluctuate with activity. Excess or prolonged pain after use or contact. Burning or pins and needle sensation, or as if the affected limb was being squeezed.

Allodynia, in which light touch or normal physical contact is very painful. Hyperalgesia where severe or prolonged pain after a mildly painful stimulus such as a pin prick.

Changes in skin temperature, skin colour, or swelling of the affected limb. The injured arm or leg may feel warmer or cooler than the opposite limb. Skin on the affected limb may change colour, becoming blotchy, blue, purple, grey, pale, or red. These skin symptoms typically fluctuate as they indicate abnormal blood flow in the area.

Changes in skin texture over time. Insufficient delivery of oxygen and nutrients can cause skin in the affected limb to change texture. In some cases, it becomes shiny and thin, in others thick and scaly.



CRPS of the left hand.

Changes in sweating and nail and hair growth. On the affected limb, hair and nails may grow abnormally rapidly, or not at all. Patches of profuse sweating or no sweating may occur. All are under neural control and influenced by local blood circulation.

Stiffness in affected joints. Reduced movement leads to reduced flexibility of tendons and ligaments. Tight ligaments or tendons sometimes rub or pinch nerves to provide an internal cause of CRPS in people who do not have external injuries.

Muscle atrophy. In affected limbs, bones that receive signals from the damaged nerves rarely become affected. However, most patients report reduced ability to move the affected body part often resulting in disuse osteopaenia visible on a plain X-ray. This is usually due to pain and abnormalities in the sensory input that help coordinate movement. Rarely patients report abnormal movement in the affected limbs, fixed abnormal posture like dystonia and tremors or jerking. These can reflect secondary spread of disturbed neural activity to the brain and spinal cord. Most resolve by themselves during healing, but some people require orthopaedic surgery to lengthen contracted tendons and restore normal flexibility and position.

> "There is no single test which can confirm CRPS. It is diagnosed as pain developing after an initial inciting event with allodynia or hyperalgesia out of proportion for the inciting event."

Management of CRPS

Prompt diagnosis and early treatment are considered best practice in order to avoid secondary physical problems associated with disuse of the affected limb and the psychological consequences of living with undiagnosed chronic pain[3].

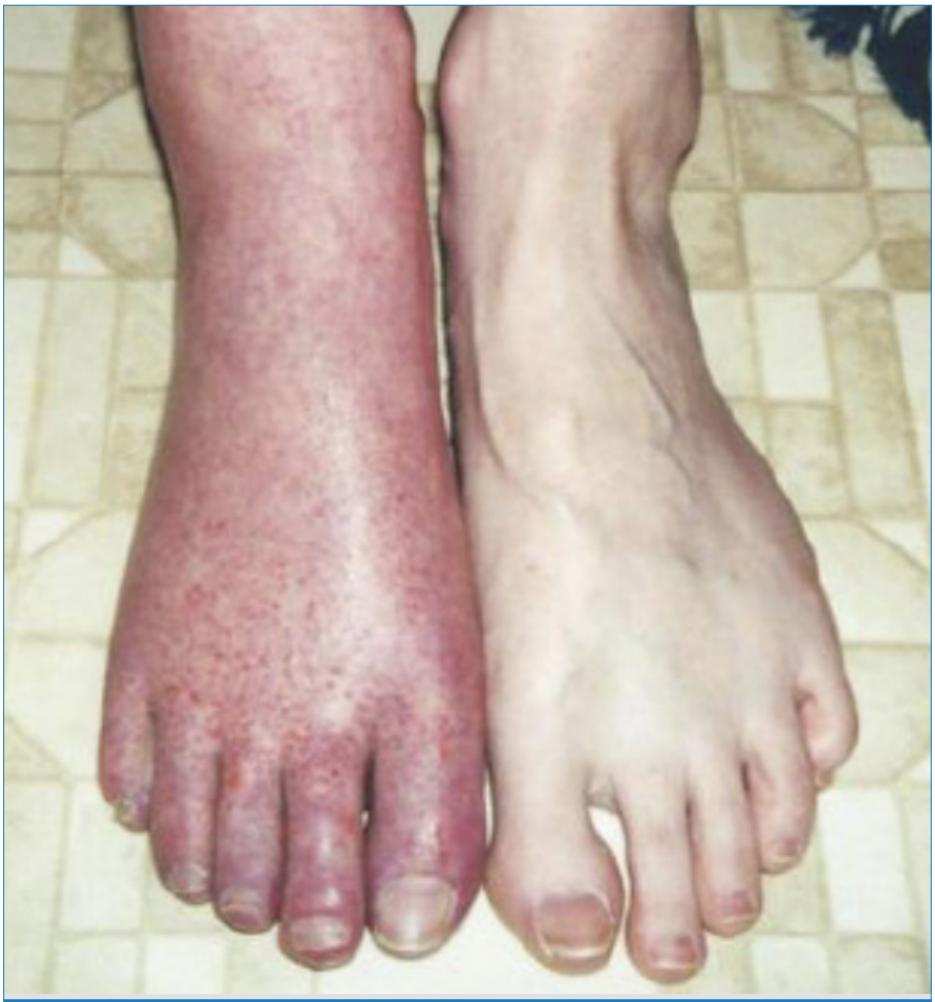
Practitioners can support patients by providing a clear diagnosis, information and education about the disease, helping to set realistic goals and, where possible, involving the patient's partner and/or other family members[3].

Physical/occupational/psychological therapy[1]: A multidisciplinary approach including rehabilitation with physical therapy (PT), occupational therapy (OT), and psychological therapy. Because of the extremity pain in CRPS, patients tend to avoid the use of the affected limb and generate fear associated with the pain. With the use of PT and OT, the goal is to have the patient improve the function and the range of motion of the extremity and achieve reduction in pain and increased mobility.

With severe pain, patients will experience significant emotional distress. Psychological therapy can be helpful to assist patients with coping mechanisms for pain, relaxation training, thermal biofeedback and graded exposure therapy.

The role of PT, OT and psychological therapy is to improve function, mobility, quality of life and the ability to manage one's own pain. In CRPS, these therapies should be utilised early and are considered by many pain specialists to be the first-line treatment[1].

Neuropathic pain medications: The basis of using neuropathic pain medications to treat CRPS is based on their usefulness in treating other neuropathic conditions. >>



Right foot of an individual with complex regional pain syndrome.

RCTs in children with CRPS have shown improvement in pain and sleep with Amitriptyline and Gabapentin[1].

Anti-inflammatory medications: Non-steroidal anti-inflammatory medications with their anti-inflammatory action has a role in the acute phase of the syndrome[1].

Bisphosphonates: Pamidronate (single 60 mg intravenous dose) should be considered for suitable patients with CRPS less than six months in duration as a one-off treatment[3].

Spinal cord stimulator (SCS): There is good evidence to support the use of SCS in CRPS[1]. It should be considered early and not as a therapy of last resort. Dorsal Root Ganglion (DRG) stimulation[1] may prove to be the more superior neuromodulation option for CRPS, as DRG can target specific painful areas of the limbs.

Recommendations for orthopaedic surgeons[3]

Orthopaedic surgeons should be aware of the diagnostic criteria for CRPS. They should be aware that CRPS may never fully resolve and that it often severely reduces patients' quality of life and may be associated with increased psychological distress. They should be aware that the diagnosis of CRPS can be made in patients who have only had a minor soft tissue injury. It may even occur without a traumatic event. A diagnostic checklist for use in an orthopaedic setting should be available in orthopaedic departments, including outpatient departments and plaster rooms. Physiotherapy and/or occupational therapy, unless contraindicated, should be initiated immediately when CRPS is suspected. The orthopaedic team should initiate early treatment with simple analgesic drugs. Orthopaedic surgeons may initiate treatment with other drugs useful for neuropathic pain, such as tricyclic antidepressants (amitriptyline, nortriptyline or imipramine) and anticonvulsants (gabapentin or pregabalin), but the GP or pain specialist is usually best placed to arrange the follow-up required for drug titration and monitoring. An early referral to prevent chronicity and its detrimental effects is recommended.

Amputation in CRPS[3]

Amputation may be considered in rare cases of intractable infection or fixed deformity of the affected limb. Surgery should be avoided on a CRPS-affected limb where possible and be deferred where it cannot be avoided until one year after the active process has resolved. Surgery may be indicated in CRPS type 2 when there is an identifiable remediable nerve lesion (for example certain cases of neuropathic pain due to either nerve compression by scar tissue, neuroma formation or peri-operative nerve injury, such as through a needle stitch) but should be undertaken only when the expected benefit from pain reduction outweighs the risk of exacerbation. Where surgery on an affected limb is necessary, this should ideally be performed by a surgeon with experience in operating on patients with CRPS and an anaesthetist who is also a pain specialist[3].

Key learning points

1. CRPS is a clinical diagnosis and other causes of pain (e.g. infection) should be excluded.
2. Budapest criteria is useful in establishing diagnosis.
3. Early commencement of physiotherapy and medical treatment (e.g. neuropathic agents) can improve outcome.
4. When considering surgery for Type 2 (nerve injury) there should be a thorough discussion of pros and cons with the patient.
5. Early referral to the pain service for medication titration, pain interventions and consideration of a spinal cord stimulator.
6. Amputation is an option in the presence of infection or fixed deformities but warrants careful discussion with the patient and a multi-disciplinary input. ■

References

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