Aspects of current management

COMPLEX REGIONAL PAIN SYNDROME

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Complex regional pain syndrome (CRPS), previously termed reflex sympathetic dystrophy (RSD) comprises abnormal pain, swelling, vasomotor instability, contracture and osteoporosis. It used to be considered a rare, sympathetically mediated, devastating complication of injury, seen mainly in psychologically-abnormal patients. Modern research has changed this view and this article summarises current understanding within an orthopaedic context.

Terminology

The condition has numerous synonyms (Table I) and recently the International Association for the Study of Pain (IASP) suggested a new nomenclature, complex regional pain syndrome (CRPS, Table II),^{1,2} which deliberately avoids suggesting the aetiology or the site. The diagnostic criteria of the IASP have not been universally adopted,³ and a different approach may be more relevant for the orthopaedic surgeon (Table III).^{4,5} CRPS is subdivided into type 1 where there is no causative nerve damage (RSD) and type 2 where there is (causalgia).

Clinical features

CRPS is a biphasic condition characterised by early oedema with late contracture and joint stiffness.⁶ The sites of predilection are the hand or foot, although the syndrome is increasingly recognised in the knee.⁷⁻⁹ The elbow is rarely involved, whereas shoulder disease is common and some cases of frozen shoulder are probably of CRPS.¹⁰ The hip may be affected in pregnancy.

CRPS begins up to a month after the precipitating trauma. As the direct effects of injury subside, a new diffuse, unpleasant, neuropathic pain arises.¹¹ Spontaneous or

Table I. Synonyms for complex regional pain syndrome

Complex regional pain syndrome
Reflex sympathetic dystrophy
Sudeck's atrophy
Causalgia
Minor causalgia
Mimo-causalgia
Algodystrophy
Algoneurodystrophy
Post-traumatic pain syndrome
Painful post-traumatic dystrophy
Painful post-traumatic osteoporosis
Transient migratory osteoporosis

Table II. Diagnostic criteria for CRPS type 1 and 2² proposed by the IASP

CRPS type 1 (reflex sympathetic dystrophy) and type 2 (causalgia)

1. Type 1 is a syndrome that develops after an initiating noxious event and type 2 is a syndrome that develops after a nerve injury
2. Spontaneous pain or allodynia/hyperalgesia occurs which is not limited to the territory of a single peripheral nerve and is disproportionate to the inciting event
3. There is or has been evidence of oedema, abnormality of skin blood flow, or abnormal sudomotor activity in the region of the pain since the inciting event
4. This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction

Table III. Suggested criteria for the diagnosis of CRPS within an orthopaedic setting

The diagnosis is made clinically by the finding of the following abnormalities:

Neuropathic pain	Non-dermatomal, without cause, burning with associated allodynia and hyperpathia
Vasomotor instability and abnormalities of sweating	Warm red and dry, cool blue and clammy or an increase in temperature sensitivity. Associated with an abnormal temperature difference between the limbs
Swelling	
Loss of joint mobility	
Joint and soft tissue contracture	

These clinical findings are supported by:
Radiographic evidence of osteoporosis after three months
Increased uptake on bone scintigraphy early in CRPS

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©2003 British Editorial Society of Bone and Joint Surgery
doi:10.1302/0301-620X.85B8.14673 \$2.00
J Bone Joint Surg [Br] 2003;85-B:1100-6.

Fig. 1

A patient with early CRPS type 1 affecting the right leg. Note the swelling of the leg and the discoloration of the shin.

Fig. 2a

Fig. 2b

The late phase of CRPS. Fig. 2a – Detail of the thumbs of a patient with late CRPS type 1 of the right hand. There is spindling of the digit particularly distally. The nail is excessively ridged and is discoloured. Fig. 2b – The hand of a patient with late CRPS type 1, who is trying to make a fist. Note the digital spindling and extension contractures with loss of joint creases.

burning pain, hyperalgesia (increased sensitivity to a noxious stimulus), allodynia (pain provoked by innocuous stimuli, such as gentle touch) and hyperpathia (the temporal and spatial summation of allodynia) are common but not universal.¹ Pain is unremitting, although sleep is often unaffected, worsening and radiating with time. Vasomotor instability (VMI) and oedema dominate the early phase (Fig. 1), although this is less marked with more proximal CRPS. In the classical presentation, the limb is initially dry, hot and pink but soon becomes blue, cold and sweaty. Oedema is marked and loss of joint mobility is due to swelling and pain. Passing into the late phase, VMI recedes, the oedema resolves and the limb atrophies (Fig. 2). The skin is thin and the joint creases and subcutaneous fat disappears. The hairs become fragile, uneven and curled, while the nails are pitted, ridged, brittle and discoloured brown. The palmar and plantar fascias thicken and contract causing Dupuytren's disease.¹² The tendon sheaths constrict with triggering and increased resistance to movement. Muscle contracture combined with adherence of the tendons leads to their reduced excursion. The joint capsules and collateral ligaments become shortened, thickened and adherent, causing joint contracture.

Bone involvement is universal with increased uptake of isotope on bone scanning in early CRPS (Fig. 3). This was originally thought to be peri-articular, suggesting arthralgia.^{13,14} However, CRPS does not cause arthritis and recent studies have shown generalised hyperfixation.^{15,16} Increased uptake is not invariable in children.¹⁷ Later, the bone scan returns to normal and there are radiographic features of rapid bone loss including visible demineralisation with patchy, subchondral or sub-periosteal osteoporosis, metaphyseal banding and profound bone loss (Fig. 4).¹³ Despite the osteoporosis, fractures are uncommon.

Incidence

Severe, chronic CRPS is uncommon with a low prevalence (<2%) in retrospective series.¹⁸⁻²² However, prospective

Fig. 3

Changes in CRPS in the bone scan. The delayed phase of a bone scan of a patient with early CRPS type 1 of the lower leg. There is increased uptake throughout the affected region. The bone scan will usually revert to normal after six months.

studies show that mild CRPS occurs after 30% to 40% of fractures and surgical trauma, such as total knee replacement,^{5,23-29} when evidence for it has been actively sought. Although these cases resolve substantially within a year,^{25,26,29,30} some features, particularly stiffness, remain suggesting that CRPS may be responsible for significant long-term morbidity even when mild.^{26,31}

Aetiology

CRPS may occur after a particular trauma, while an identical stimulus in a different limb does not produce it. The incidence is not altered by the method of treatment and open reduction and internal fixation does not abolish it.²⁷ It is unclear whether the severity of the injury or the quality of the reduction of the fracture alter the incidence.^{5,25} There is, however, an association with excessively tight casts³² and there may be a genetic predilection.³³⁻³⁷ The following aetiologies have been proposed.

Psychological abnormalities. A psychological cause for chronic pain was first suggested by Breuer and Freud³⁸ but the concept that CRPS is primarily psychological is unsupported.³⁹ Studies of pre-morbid personality show no con-

Fig. 4a

Fig. 4b

Radiographic features of CRPS. Fig. 4a – Oblique radiograph of a patient with CRPS type 1 of the foot. There is patchy osteoporosis with accentuation of the osteoporosis beneath the joints. Fig. 4b – Profound osteoporosis in a patient with late severe CRPS type 1 affecting the hand.

sistent abnormality.^{40,41} Most patients are normal,⁴² although emotional lability, a low pain threshold,⁴³ hysteria,⁴⁴ and depression⁴⁵ have been noted. There is an association with antecedent psychological stress⁴⁶⁻⁵⁰ which probably exacerbates pain in CRPS, as in other diseases.⁵¹ It seems likely that the severe chronic pain of CRPS causes depression and that a 'Sudeck' type of patient who develops CRPS is at risk of a poor outcome because he/she will not mobilise in the presence of pain.

Abnormal pain. Pain is normally caused when an intense noxious stimulus activates high-threshold nociceptors. It prevents tissue damage. The neuropathic pain of CRPS has no such function and arises without an appropriate stimulus. However, injured peripheral nerve fibres undergo cellular

changes which cause usually innocuous tactile inputs to stimulate the dorsal horn cells via A- β fibres from low-threshold mechanoreceptors, causing allodynia in CRPS 2.^{52,53} Similar dysfunction of the C-nociceptors explains causalgia. Furthermore, axonal injury prevents transport of nerve growth factor to the cell body where it is essential to normal nerve function.^{11,54} In CRPS 1, covert nerve lesions with artificial synapses have been postulated,⁵⁵ but these 'epheses' have not been demonstrated histologically and are unnecessary, since cytokines and inflammatory mediators, released by the initial trauma, can sensitise nociceptors which then respond to normally innocuous thermal and mechanical stimuli.¹¹

Abnormalities of the sympathetic nervous system (SNS).

Abnormalities in blood flow in the skin, temperature regulation, sweating and trophic changes, which are features of SNS dysfunction, are integral to CRPS. However, SNS activity is not normally associated with pain.^{56,57} In CRPS, some pain, termed sympathetically maintained pain (SMP), is dependent on the SNS and spontaneous pain and allodynia may be relieved by stellate ganglion blockade⁵⁸ and then restored by noradrenalin injection.^{59,60} There is also an abnormal difference in cutaneous sensory threshold between the limbs, which is reversed by local anaesthetic sympathetic chain blockade^{61,62} (although not by intravenous guanethidine),³⁰ while increasing sympathetic activity worsens pain.⁶³ The key to the abnormal SNS activity lies in the body's reaction to injury. After partial division of a nerve, injured and uninjured somatic axons express α -adrenergic receptors⁶⁴ and sympathetic axons come to surround the cell bodies of sensory neurons in dorsal root ganglia.^{11,65,66} These changes, which may be temporary,^{59,67,68} make the somatic sensory nervous system sensitive to circulating catecholamines and noradrenalin released from post-ganglionic sympathetic terminals.

Abnormal inflammation. CRPS is associated with extravasation of macromolecules,⁶⁹ reduced oxygen consumption⁷⁰ and other inflammatory changes,⁷¹ while infusion of free radical donors causes a CRPS-like state in animals.⁷² Amputated human specimens show basement membrane thickening consistent with overexposure to free radicals.⁷³ These considerations suggest that CRPS is an exaggerated local inflammatory response to injury.^{74,75} If this is the case, CRPS may represent a local form of the systemic free radical disease that causes adult respiratory distress syndrome and multiple organ failure after severe trauma. An alternative explanation is a primary capillary imbalance causing stasis, extravasation and local tissue anoxia.⁷⁶⁻⁷⁹

Immobilisation. Undue immobilisation has been proposed as a cause of CRPS⁸⁰⁻⁸³ and features of CRPS, except pain, are seen after immobilisation in a cast.⁸⁴ Activity dependent gene function is common in the nervous system¹¹ and CRPS is associated with an abnormality of motor function which is often overlooked. In a prospective study of 829 patients, 95% reported motor abnormalities, varying from weakness to inco-ordination and tremor.⁸⁵

CRPS type 1 appears to be associated with a 'neglect-like' phenomenon in which the patients find difficulty in initiating movement or accurately directing it.⁸⁶ Pain avoidance behaviour in response to allodynia may exacerbate changes of disuse since normal tactile and proprioceptive inputs are necessary for correct processing of central nerve signals.⁸⁷ Indeed, it has been suggested that abnormal mobility is the entire cause, due to loss of integration between sensory input and motor output, in a manner akin to seasickness.^{88,89}

Investigations and differential diagnosis

CRPS is a clinical diagnosis (Table III) and there is no single diagnostic test. The classic case is obvious and the direct effects of trauma, fracture, cellulitis, arthritis and malignancy are common alternative diagnoses. The patient is systemically well, normal on general clinical examination, with no abnormal biochemical markers or indices of infection.

The radiographic appearances and bone scans are discussed above. CRPS does not cause arthritis and the joint space is preserved. Sudeck's technique of assessing bone density by taking radiographs of two extremities on one plate remains useful, but densitometry is not usually helpful.⁹⁰ A normal bone scan without radiographic evidence of osteoporosis virtually excludes adult CRPS. The temperature difference between limbs is greater in CRPS than other pain syndromes,^{91,92} but this is not usually applied in an orthopaedic context. MRI shows early bone and soft tissue oedema with late atrophy and fibrosis, but is not diagnostic.

Management

A bewildering array of treatments have been proposed but scientifically constructed studies are few⁹³ and uncontrolled investigations are particularly unreliable. Most patients are sensible people, concerned at the development of inexplicable pain, but the occasional 'Sudeck' patient fares poorly and should be treated vigorously. Early treatment gives optimal results, so a high index of clinical suspicion must be maintained. It is not reprehensible to have caused a case of CRPS through surgery or non-operative management of injury. However, delay in diagnosis and treatment may contribute to a poor outcome.

Treatment of CRPS is no longer concentrated on manipulation of the sympathetic nervous system but on functional rehabilitation of the limb to break the vicious cycle of disuse.⁹⁴ The initial treatment from the orthopaedic surgeon is by reassurance, excellent analgesia and intensive, careful physiotherapy avoiding exacerbation of pain. Non-steroidal anti-inflammatory drugs may give better pain relief than opiates. Immobilisation and splintage is generally best avoided, but if used, joints must be placed in a safe position and splintage is a temporary adjunct to mobilisation. If the

patient does not respond rapidly, a pain specialist should be involved and treatment continued on a shared basis. Second line treatment is often unsuccessful and many patients are left with pain and disability. Further options include centrally acting analgesic medications, such as amitriptylene, gabapentin or carbamazepine; regional anaesthesia; the use of membrane stabilising drugs, such as mexilitene; sympathetic blockade; desensitization of peripheral nerve receptors with capsaicin; transcutaneous nerve stimulation or an implanted dorsal column stimulator. Behavioural therapy may be necessary in children. Where the knee is affected, epidural anaesthesia and continuous passive motion may be appropriate.⁸

The role of surgery is limited. Where CRPS is caused by a surgically correctable painful lesion, such as median nerve compression at the wrist, operation may abort it but should be undertaken cautiously in the presence of active disease. Surgery is rarely indicated to treat fixed contractures which usually involve all of the soft tissues. Surgical release must therefore be radical and expectations limited. Surgery for contracture should be delayed until the active phase of CRPS has completely passed. Ideally, there should be a gap of at least a year since the patient last experienced pain and swelling.

Amputation of a limb affected by severe CRPS should be approached with great caution. Dielissen et al⁹⁵ reported a series of 28 patients who underwent 34 amputations in 31 limbs. Surgery was usually performed for recurrent infection or to improve residual function. Relief of pain was rare and unpredictable, neither was infection always cured nor function universally improved. CRPS often recurred in the stump, especially if the amputation level was symptomatic at the time of surgery. For this reason only two patients were a prosthesis.

Generally, surgery represents a painful stimulus which may exacerbate CRPS or precipitate a new attack. This risk must be balanced carefully against the proposed benefit. The risk of surgically precipitated recurrence is greatest when the same site is operated upon in a patient with abnormal psychology in the presence of active disease, and lowest when these conditions do not apply. Surgery must be performed carefully with minimal trauma and excellent post-operative analgesia. Ideally, the anaesthetist will have a particular interest in the treatment of CRPS.

Conclusion

Far from being a rare disease of abnormal patients, CRPS is emerging as a major feature in avoidable morbidity within orthopaedic practice. Research in the final decades of the last century has set the stage for a better understanding of the condition. Further appropriate studies should now elucidate the aetiology and produce simple, rational treatments which will eradicate this scourge from the orthopaedic patient.

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