Complex regional pain syndrome (CRPS) in orthopaedics: an overview

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Abstract

Complex regional pain syndrome (CRPS) is a debilitating and painful condition in a limb, occurring most often after trauma and surgery, and associated with nerve, skin and bone abnormalities. The condition is poorly understood, often diagnosed late and national recommendations are not yet generally integrated into standard practice. Whilst signs and symptoms generally improve within 6 months of onset, many patients have long-term pain and disability, and the costs of managing chronic pain and disability are substantial. This paper provides an overview of the latest understanding of CRPS and national guidelines, explains how to make a diagnosis, describes initial treatment and controversies in orthopaedic care and explores the implications of CRPS to the orthopaedic team.

Keywords complex regional pain syndrome; CRPS; immune system

Introduction

Case vignettes

Case 1: You review a 60-year-old, fit and healthy man at 5 weeks following non-operative management of a simple distal radius fracture. He reports having felt 'claustrophobic' in the cast from day 1 and has had the plaster changed on three occasions. On examination out of plaster, the patient has disproportionate pain, allodynia to light touch throughout the hand and he cannot make a full fist. There are no temperature changes, but there is colour and swelling asymmetry and the patient withdraws the hand every time you approach him. What will you do next?

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Case 2: You have successfully performed a metatarsal osteotomy to treat hallux valgus in a 45-year-old healthy woman. On review at 4 weeks, she complains of high-intensity burning pain and sensitivity throughout her foot and has more limited foot and ankle movement than you would expect. Radiographs show mild localized osteoporosis around the metatarsophalangeal joint (MTPJ) and no signs of mechanical failure of the fixation. On examination, there is mild, mottled bluish discolouration throughout the foot, which also feels cooler than the other side. In general, she does not like anyone handling her foot. When you check the consent form, CRPS is not listed amongst possible complications. How will you inform your patient about her diagnosis?

What is complex regional pain syndrome (CRPS)?

CRPS is a debilitating, painful condition in a limb, associated with sensory, motor, autonomic, skin and bone abnormalities.[1] CRPS replaces all other terminology such as 'Sudeck's atrophy', 'reflex sympathetic dystrophy', 'algodystrophy', 'fracture disease' and 'causalgia', which are now considered outdated and misleading.[2]

CRPS often arises in orthopaedic practice, because orthopaedic doctors see patients after trauma or surgical intervention. Any trauma or operation to a limb, usually distal, can trigger CRPS; the type or magnitude of the trauma or surgery is of less importance.

Whether CRPS should be considered a rheumatic or a neurological disorder is not clear. With pain being the predominant issue, and in the absence of actual tissue destruction, CRPS is best classed as a 'pain condition'; CRPS is classed as 'chronic primary pain' in the new World Health Organization International Classification of Diseases, 11th revision (WHO ICD-11).

What causes CRPS?

CRPS is a disease caused by post-traumatic regional hyperactivation of small nerve fibres. This abnormal nerve fibre activation leads to profound 'central sensitization', a process in which the central nervous system (CNS) augments any peripheral impulses. We understand this role of the CNS from clinical studies involving low-dose ketamine treatment which, by down-regulating central sensitization, can temporarily reduce CRPS pain, albeit with side effects.[3]

It is now clear that this nerve fibre hyper-activation is caused by an immune process in susceptible patients. Most patients with CRPS have specific autoantibodies in their serum, which upon transfer to hind limb-injured mice elicit a CRPS-like picture restricted to the injured paw, confirming an auto-immune origin.[4] The pathogenetic antibody mechanism, or why patients produce these antibodies is yet unknown, but some genotypes are speculated to convey vulnerability.[5,6]

Classification

Traditionally, two types of CRPS have been described: Type 1 without, and Type 2 with a nerve injury, which is typically caused by the same trauma that triggers the CRPS. For clarity, the nerve injury in Type 2 is not a consequence of CRPS.

Budapest diagnostic criteria for chronic regional pain syndrome (A to D must apply)

A. The patient has continuing pain which is disproportionate to any inciting event			☐
B. The patient has at least one sign in two or more of the categories			☐
C. The patient reports at least one symptom in three or more of the categories			☐
D. No other diagnosis can better explain the signs and symptoms			☐
Category		**Sign (you can see or feel a problem)**	**Symptom (the patient reports a problem)**
1. 'Sensory'	*Allodynia* to light touch and/or temperature sensation and/or deep somatic pressure and/or *Hyperalgesia* (to pinprick)	☐	Hyperaesthesia does also qualify as a symptom ☐
2. 'Vasomotor'	Temperature asymmetry and/or skin colour changes and/or skin colour asymmetry	☐ If you notice temperature asymmetry: must be >1°C	☐
3. 'Sudomotor/oedema'	Oedema and/or sweating changes and/or sweating asymmetry	☐	☐
4. 'Motor/trophic'	Decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair/nails/skin)	☐	☐

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Table 1

The predominant management of the CRPS for both types is the same, and the distinction therefore has little benefit to a clinician; however the nerve injury itself is addressed as per usual practice for nerve injury management.

How common is CRPS?

The incidence of CRPS in Europe is estimated as 20–26/100,000 person-years - similar to the incidence of rheumatoid arthritis.[7] Transient CRPS has been reported as a relatively common occurrence early after wrist fractures (incidence up to 32.2%).[8] CRPS can occur within a few months of any limb injury or surgery, but the incidence may have been overestimated in some published research when diagnostic criteria were not strictly applied[9]; not every complex limb pain is CRPS (see making a diagnosis section).

Females (3:1 ratio), and patients with asthma, osteoporosis, migraines, or rheumatological disorders are at higher risk, as are patients taking angiotensin-converting enzyme (ACE) inhibitors.[10] CRPS can rarely affect children and it sometimes affects adolescents.

CRPS can sometimes start in two limbs concomitantly, usually after bilateral limb trauma; in 5–10% of cases CRPS can spread to additional limbs, often without additional trauma.[11]

The overall socio-economic implications of CRPS are exorbitant. For example in Switzerland, the average overall cost of a distal radius fracture that is complicated by CRPS is about 25 times that of the costs of an uncomplicated fracture.[12]

Making a diagnosis

CRPS is a diagnosis of exclusion and the Budapest criteria (Table 1)[13] as adopted by the International Association for the Study of Pain (IASP) now supersede other criteria; their use is recommended in the UK.[2] The use of a single set of diagnostic criteria allows consistency and a shared language.

The Budapest criteria identify symptoms and signs subdivided into four categories: i) sensory; ii) vasomotor; iii) sudomotor/oedema and iv) motor/trophic. Other conditions, such as infection, failure of fixation, nerve compression or malignancy may have some features of CRPS and should therefore be carefully excluded. Fortunately, in orthopaedic practice, patients often have 'barn door CRPS', readily identifiable using the Budapest criteria. If an orthopaedic surgeon does not feel confident to diagnose CRPS, then it is reasonable to ask a pain specialist to verify the diagnosis.

Signs such as swelling, sweating, colour and temperature changes, and hair/nail growth changes generally reduce with time, although pain and motor symptoms can persist longer. Theoretically, for patients who earlier had documented CRPS limb signs and then later lost some of these signs, a diagnosis of CRPS according to the Budapest criteria may not be possible any more despite ongoing, unchanged spontaneous pain. In practice, this situation is rare, because most patients with persistent CRPS initially have, and also later retain, both motor and sensory signs (Table 1) and report additional symptoms. A reduction of signs is in itself not defined as 'recovery'. Where pain persists, the condition is considered to be still active.

A more challenging scenario is where patients never received a Budapest diagnosis and their clinical signs were never documented by any healthcare professional. Earlier diagnostic criteria for CRPS were looser, and the presence of fewer signs, or indeed the report of symptoms only was acceptable. A specific category has been created to somehow capture these patients (CRPS not otherwise specified, CRPS-NOS). The diagnostic specificity and sensitivity of CRPS-NOS is poor – no research has been conducted in this group; this category is best avoided wherever possible in orthopaedic practice. Note that although CRPS with reduced signs over time as outlined in the previous paragraph is currently also termed 'CRPS-NOS', this terminology for that subtype is expected to soon change.

The physical signs and symptoms of CRPS as listed in the Budapest criteria (Table 1) distinguish it from other neuropathic pain problems. The prognosis may also be different from other neuropathic pain and care should be taken to recognize this early.

Additional symptoms

Many patients with CRPS have a constellation of additional symptoms not included in the Budapest criteria. These symptoms are often difficult for patients to explain and are best summarised as body dysmorphic and 'neglect-like'. Typically, patients experience their limb as being different in size or shape, or in an altered spatial location. Patients can also develop an abnormal cognitive/emotional relationship with their limb, characterized by alienation, dislike and disgust, anger and neglect, and some may even have a wish for immediate amputation. These symptoms, likely caused by a shifted representation of the affected limb in the sensory cortex,[14] are transiently present more often after any, even uncomplicated, limb injury than clinicians may recognize,[15] but are even more common and more long-lasting in CRPS. These symptoms are bewildering and distressing; patients may fear they 'go mad', and that they are not being believed. This fear can lead to lack of communication, and it can be salutary if the healthcare professional signals that they understand what their patient goes through.

Management of CRPS

The British Orthopaedic Association[16] recommends early diagnosis and the local establishment of an agreed care pathway for patients with CRPS, as does the Royal College of Physicians (RCP).[2]

Perhaps one of the most useful and simple interventions is to ensure there is at least one 'CRPS champion' within any practice area. This position has been successfully established in some UK clinics as part of their acute CRPS care pathways, and a physiotherapist may often be ideally placed to undertake this role.[17] The CRPS champion's role is to keep the team updated with evidence-based practice, being the 'go to' person when CRPS is suspected, and acting as a link between different professionals involved in patient care to ensure care pathways are effective.

A four-pillared management approach is recommended: this includes pain relief; physical and vocational rehabilitation; patient information and education to support self-management; and psychological intervention. The first three pillars can be delivered in orthopaedic practice.[2]

Pain relief

A protocol for first-line medication should be agreed locally and generally includes simple analgesia, including weak opiates, with the addition of neuropathic pain medication from 3 to 4 weeks, or sometimes earlier, to facilitate rehabilitation. A sample protocol is provided in the orthopaedic section of the UK guidelines (Figure 1). While there is little evidence that these medications are effective in reducing the actual CRPS pain, they might treat secondary musculoskeletal pains and/or any remnants of trauma-related pain. The individual response should be assessed repeatedly, and medications stopped if found ineffective.

Physical and vocational rehabilitation

Early referral to physiotherapy and/or occupational therapy (PT/OT) is vital. For simple cases PT/OT will be the most important intervention required, especially if there is expertise within the therapies department. Prolonged immobilization and reducing functional activity as a treatment are not recommended and may be harmful even though this may feel intuitively right when a patient has had a fracture. General guidance is to only immobilize if necessary and not beyond the normal timescale for the particular injury. Early function, attention to the injured limb and gentle exercise should be encouraged from first contact. Interestingly, the benefits of this important management strategy can be modelled in rodents, where painful sensitivity after experimental tibia fracture resolves much quicker when the stabilized limbs are being exercised.

There are a number of novel physical therapies such as graded motor imagery and mirror visual feedback that can help patients with CRPS; all therapies are focussed on restoring function as soon as possible to normalize the sensory-motor feedback loop.

Patient information and education

Many patients will utilise the internet and social media following their initial diagnosis and may see horrible stories representing extreme subtypes. It is important to reassure patients that the difficult-to-bear initial pain will in all likelihood improve, and that they can help their progress by adhering to gentle physiotherapy. Information should therefore include the usually benign nature of the condition.

Other methods of treatment

Local blocks or regional blocks as a treatment for CRPS are still frequently employed although good randomized controlled trial evidence is lacking. Blockade of interleukin-1 will prevent or revert transferred CRPS ('tCRPS') in mice, indicating that immune treatments may also be of use in treating patients, and this is an area of ongoing research interest.

What is the typical disease course?

About 80% of patients with CRPS will get substantially better within the first 6–12 months after trauma due to a natural resolution process. However they often report lesser ongoing pain or partial loss of function for many years, and only about a third of patients consider themselves fully recovered at 6 years.[7] About 15–20% of patients will have persistent symptoms for many years and may never fully recover.[18]

It is not yet possible to clinically predict how patients will recover, however it is likely that this rare latter group of patients that do not recover at all has fundamentally a different disease, which cannot be prevented or shortened even with excellent early treatment. A new subclass designation for this group is being considered.

Rarely, patients can present with 'relapsing-recurring' CRPS, with remission periods varying between months and years.[1]

Since early rehabilitation in established CRPS very likely shortens the disease course, a late diagnosis contributes to a protracted course.

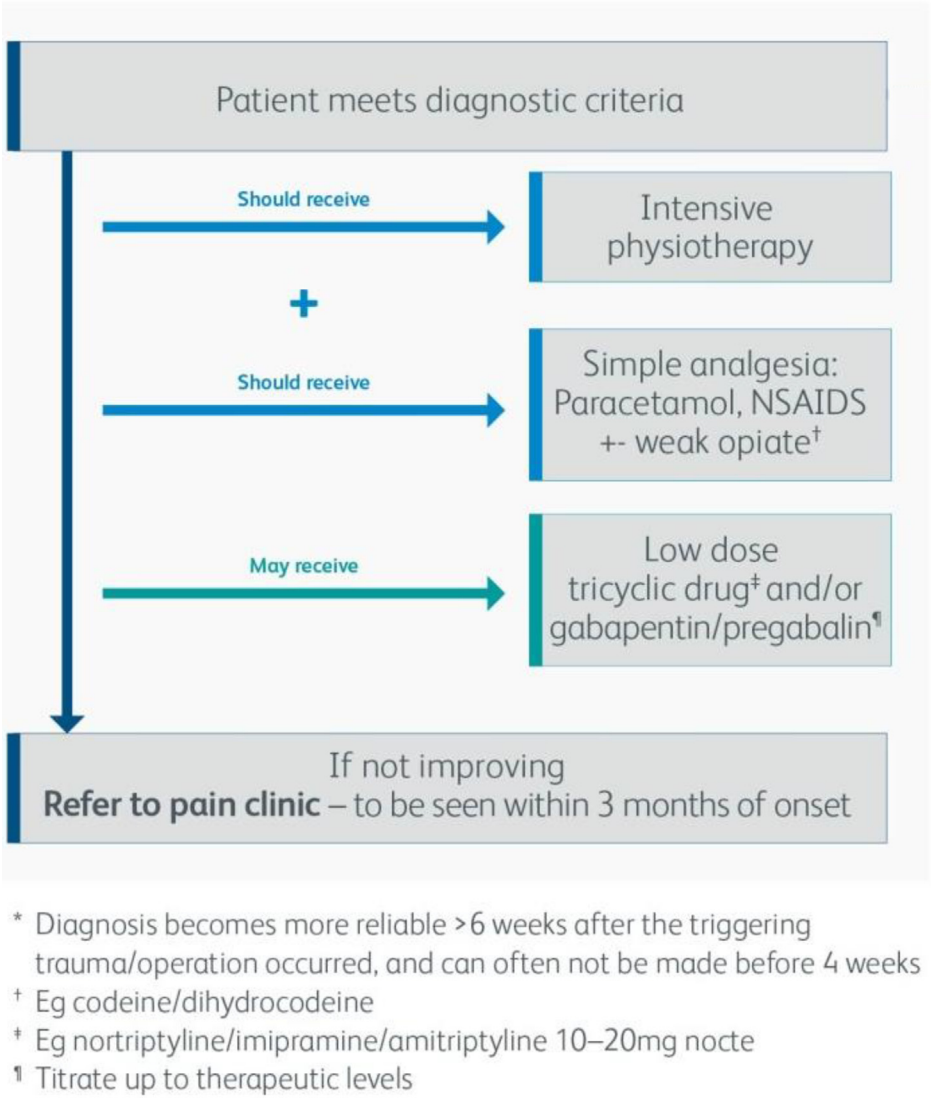

Figure 1 Sample protocol for first-line management of chronic regional pain syndrome (CRPS). Reproduced from reference 2 with permission. © 2018 Royal College of Physicians. IASP, International Association for the Study of Pain; NSAIDS, non-steroidal anti-inflammatory drugs.

Uncommon subgroups of CRPS

About 5% of patients will develop CRPS in another limb (spread) and about 10% of patients with persistent CRPS may develop widespread pain, which may have in some a neuropathic character similar to the CRPS pain, or alternatively such widespread pain can also have a musculoskeletal character such as in fibromyalgia syndrome. One other, peculiar, rare presentation is the 'shoulder-hand syndrome', with neuropathic pain and sensitivity in the shoulder, and typical CRPS signs, but usually no pain, in the ipsilateral hand.

Some patients develop tremors or myocloni in the affected limb, or occasionally fixed dystonia.

Some patients develop small blisters, which spontaneously erupt and then heal; others can develop skin ulcerations, which get infected and require antibiotic treatment; this is very rare.

Orthopaedic surgeons must be aware of the existence of these subgroups, and support patient management by recognizing the need for onward referral.

Can CRPS be prevented?

There is preliminary, but persuasive, evidence that CRPS after a wrist fracture is often preventable by establishing early, simple rehabilitative measures.[17] In animal fracture models, those animals which exercise early recover earlier and have less pain; this is likely mediated through exercise-induced anti-inflammatory effects. Maintaining normal sensory-motor feedback loops may also help to maintain limb representation in sensorimotor cortex and help prevent central sensitization.

Tight or restrictive plasters and disproportionate pain beyond a few days from injury/surgery are well recognized as risk factors for CRPS. When these problems occur, they should be addressed as soon as possible (See Box 1).

Psychological aspects of CRPS

Several decades ago the existence of a 'CRPS personality' was proposed, but this is now obsolete[19] and current evidence

Key elements of successful chronic regional pain syndrome preventative intervention in orthopaedics

1. Do not immobilize excessively or unnecessarily
2. Ensure casts/splints or boots are well fitting and comfortable, avoid over-flexion of wrist in cast, smooth sharp edges and ensure there is no restriction to unaffected joints
3. Encourage patient to return to clinic if any concerns
4. Encourage hourly gentle exercises to control swelling in elevation, e.g. grip-release, toe flexion/extension
5. Encourage light function and attention to limb whilst in cast/splint or boot
6. All verbal information given should be supported with a patient information leaflet and visual reminders such as posters in clinics to help reinforce points 2, 3, 4 and 5
7. All advice given should be recorded in patient notes
8. Recognize 'at-risk patients' e.g. high level of pain beyond a few days and/or lack of engagement with limb
9. Patients reporting tight and/or restrictive casts should **always** have this cast changed
10. Patients requesting repeated change of cast or reporting 'claustrophobia in cast' should trigger immediate referral to specialist physiotherapist within clinic

Box 1

suggests that psychological distress is generally not a risk factor for the development of CRPS. Having CRPS, as with any severe chronic pain is stressful and many patients will develop secondary psychological co-morbidity such as anxiety or depression. This should be recognized and treated as with any other condition (e.g. depression in a patient with diabetes).

Whether or not psychological factors constitute a risk in CRPS-subgroups, or contribute to the perpetuation of CRPS has not yet been clarified.

Rarely people self-induce signs with the aim of making their limb appear as though they have CRPS. Methods have been described[20] and clinicians should be cautious of this. While such actions may occasionally be employed to gain benefits in a medico-legal context, in very rare cases serious psychiatric 'factitious disorder', may be present, where patients create symptoms to gain medical attention.

Surgery in patients with CRPS

Operating on a CRPS-affected limb

Elective surgery on a limb previously affected by CRPS should be delayed where possible until acute signs of CRPS have clearly improved and stabilized. Waiting for a period of a year after the CRPS onset should generally achieve this. Based on the limited evidence available, it is thought that the rate of operation-triggered recurrence of CRPS is less than 15%, with most recurrent cases being mild.[21,22] If surgery on an affected limb is unavoidable, this should ideally be performed by a surgeon with experience in operating on patients with CRPS and with an anaesthetist who is also a pain specialist, and patients should be told about the risks involved.

Operating in a non-CRPS affected area in a patient with a history of CRPS

There is a dearth of high-quality evidence in this area. Anecdotal reports suggested that complications such as poor wound healing following orthopaedic surgery in patients with CRPS may be more common, even if conducted in unaffected areas.

Some recent evidence suggests that patients with a history of CRPS may be at higher risk to develop CRPS following operations in previously non-affected limbs.[23] However, this should be regarded as preliminary, and it is important that such preliminary results do not indiscriminately scare surgeons from performing otherwise useful operations. Patients should however clearly be counselled about their potentially higher risks.

Amputation to reduce pain or to improve function from CRPS

Orthopaedic surgeons may be asked to refer for or perform amputation for CRPS due to pain, deformity or chronic infection secondary to CRPS. This area is extremely complex, and multidisciplinary input is mandatory.

Based on current evidence, the RCP CRPS guidelines[2] do not recommend amputation, but recognizing the importance of patient autonomy and the pressure sometimes applied to surgeons, offer detailed guidance.

The decision to refer for amputation should be made by a multidisciplinary expert team including a pain specialist, pain-psychologist, and a pain specialist physiotherapist. The referral should always be to a tertiary rehabilitation team with experience in this area, and not to a single-surgeon service. Patients and their families should be made aware that the amputation is unlikely to improve their pain, and that CRPS may recur in the stump or in another limb. Amputation may be considered in cases of intractable infection of the affected limb that cannot be controlled with antibiotics. Prosthesis use may not be possible and patients should be made aware that ulceration might recur in the stump after amputation. Except in immediate emergencies, involvement of the outlines multidisciplinary team is essential.

Operating to reduce nerve compression in a patient with CRPS type 2

There is preliminary evidence that surgery for neuropathic pain attributed to nerve compression (confirmed by nerve conduction studies) might also improve CRPS symptoms in the distribution of that nerve.[24]

Are patients with a chronic pain condition other than CRPS more likely to develop CRPS after elective limb surgery?

This is a complex area in which few data exist, and which is outside the scope of this review. The issues include: i) does a patient suffer from chronic pains in limbs or other body parts? ii) is elective limb surgery in a patient with non-CRPS limb pain mainly aimed at reducing pain? iii) did the patient have past operations aiming to reduce their pain, and what was the outcome?

Pragmatically, it is our opinion, that assessment before elective orthopaedic limb surgery with the main indication of reducing pain should include an assessment for other chronic pains, and a clear recognition of the outcomes of any previous elective

Top tips for an orthopaedic surgeon regarding CRPS

1. Include CRPS as a potential complication when counselling patients for elective limb surgery, or after injury
2. Recognize 'at-risk' patients after trauma or elective limb surgery, and earn to recognize the early signs and symptoms of CRPS
3. Use the Budapest diagnostic criteria: put a poster on the wall in your clinic as a visual reminder
4. Foster 'CRPS champions' in your practice: these may be physiotherapists or other healthcare professionals who can support care pathways and keep the team updated
5. Design a care pathway to meet BOAST for patients with early CRPS within your fracture and elective clinic practice. If you are commissioned to provide care you are commissioned to provide appropriate care pathways
6. Institute early referrals to physiotherapy and the pain team and agree first-line medications for CRPS locally
7. Use the RCP CRPS guidelines to inform best practice

BOAST, British Orthopaedic Association standards for trauma; CRPS, chronic regional pain syndrome; RCP, Royal College of Physicians.

Box 2

operations aiming to reduce pain. Patients may, for example suffer from other types of chronic pain, such as fibromyalgia, a common widespread pain condition (2–8% of the population affected) which is associated with other symptoms such as irritable bowel and fatigue. We anticipate that the routine assessment for, and recognition of these issues will lead orthopaedic surgeons to develop their practice over time as appropriate.

Informed consent and shared decision-making

Since CRPS is rare and can be devastating, it is a prime example of those conditions which since the Montgomery ruling deserves renewed consideration as a material risk.[25] It appears now rarely acceptable to not explain this risk in some detail, or to assume that the patient understands the implications when they are told this only at the day of the operation.

While explaining the risk and sequelae of CRPS is always important, it is perhaps even more urgent with potential aggravating factors such as previous CRPS. Patients do not always volunteer information about their past pain history and it is the responsibility of a surgeon to seek this relevant information. Close questioning about the medications currently prescribed can also point to undisclosed chronic pain conditions, and the need for appropriate counselling (see above).

In patients who develop CRPS following surgical intervention after acute trauma, it is difficult to determine which event – the trauma or the surgery – accounted for the development of the CRPS. Patients should be counselled that both events are risk factors for CRPS.

Finally, it is worth noting that surgical technique is not to blame if a patient develops CRPS – it is an expected risk, though a patient may not perceive it in that way. The importance of informed consent therefore cannot be stressed enough.

We would also suggest from anecdotal evidence that as recent information about the beneficial effects of early rehabilitation[17] filters through into the medicolegal system, there will be an increasing number of cases claiming damages from delayed or inadequate functional rehabilitation following surgery or trauma.

Case vignettes: answers

Case 1

The patient has a number of risk factors for CRPS: recent injury, feeling 'claustrophobic' in cast, a number of plaster changes and a fear of touch. He fulfils category A, B, C and probably D and therefore meets the Budapest CRPS Diagnostic Criteria (Table 1). Current evidence suggests immediate referral for PT/OT and review of medication to facilitate rehabilitation. It is not known at this stage if this will be a mild, transient CRPS or will progress to a chronic state. Further review is recommended within a month to monitor progress and adjust medication. Communication with the patient's GP is essential to facilitate timely titration of appropriate analgesia and to consider neuropathic pain medication if needed. Making the GP aware of RCP CRPS guidelines can be helpful. If there is no progress onward referral to a pain specialist within 3 months of onset is recommended.

Case 2

The patient has had a trauma (surgery) which puts her at risk of CRPS. She fulfils category A, B, C and D and therefore meets the Budapest CRPS Diagnostic Criteria (Table 1). It is important to acknowledge your concerns with the patient in a manner that does not heighten fear, anxiety and apprehension. Failure to list CRPS in the list of complications should be acknowledged as full and honest disclosure to the patient. At this stage there is good reason to believe that with appropriate PT/OT and medication to facilitate rehabilitation it is most likely that her symptoms will improve. Normalizing function is the goal. It is also important to explain that only a few patients go on to have long-lasting pain and reduced function despite the appropriate therapy. (See Box 2) ◆

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