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Editorial

Complex regional pain syndrome

Peri-operative triggers

This editorial refers to Perioperative factors affecting the occurrence of acute complex regional pain syndrome following limb bone fracture surgery: data from the Japanese Diagnosis Procedure Combination database, by Sumitani Masahiko *et al.* Rheumatology 2014: doi: 10.1093/rheumatology/ket431, on pages 1186–93.

Complex regional pain syndrome (CRPS) is a pain syndrome with a characteristic clinical presentation. CRPS has previously been known by many different descriptive terms including reflex dystrophy syndrome and causalgia. The cause of CRPS is unknown and effective treatment is often suboptimal. The resultant morbidity may be very significant [1, 2]. In this issue, Masahiko *et al.* [3] report a well-conducted study of a specific subgroup of CRPS. They have identified novel risk factors relating to deep tissue ischaemia following surgical repair of peripheral fractures, providing new insights into one of the triggers of CRPS.

The clinical phenotype of CRPS has been better defined over the last few decades and the Budapest diagnostic criteria for CRPS capture these essential clinical features [4]. A modification of this benchmark was used in the Masahiko *et al.* study [3], defining patients as having continuing pain disproportionate to the inciting event, and the report of at least two symptoms and at least two signs reflecting sensory (dysaesthesia), sudomotor (sweating), oedema, motor (stiffness, involuntary movements) or trophic (bone, muscle, skin) abnormalities [5]. These features define a clinical condition that is characteristic yet variable in individual components. Like other pain phenotypes, such as fibromyalgia, the components of CRPS each exist on a continuum [6]. Thus there are distinctive core features, such as pain, swelling, sweating, motor or trophic abnormalities, each of which may be mild or severe, contributing to a variety of presentations, all of which are recognized as CRPS.

A range of non-traumatic causes, including some cerebrovascular conditions or exposure to certain drugs, may associate with CRPS [2]. However, the majority of cases of CRPS are triggered by mild to moderate trauma to a peripheral limb, such as fracture (~45% of all CRPS), sprain (~18%) or elective surgery (~12%) [7]. CRPS affects the arm in ~60% of cases and the leg in ~40% of cases [7]. It is noteworthy that even immobilization of a limb in healthy volunteers can induce mild CRPS [8]. Historically, most studies examined patients with CRPS of different causes and duration.

In this clinically useful study the authors analysed the Japanese Diagnosis Procedure Combination database, identifying 185,378 patients who had open reduction and internal fixation (ORIF) of a peripheral bone fracture [3]. They found 39 patients developed CRPS during their in-patient stay, with a median of 8 days for upper limb fracture and 31 days in hospital for fractures of the lower limb. Hence this study examined one common cause, that of limb bone fracture, one common treatment, that of ORIF and one common phase of the illness, that of the acute phase of CRPS, where pain, tenderness, swelling and vasomotor change dominate. A higher rate of CRPS was found in upper limb fractures compared with lower limb or multiple fracture groups and rates in males were comparable to those in females, in contrast to the usual female predominance in the literature [2]. Most importantly, a longer duration of general anaesthesia associated with increased risk of CRPS.

The study [3] has some caveats. There may be confounding issues with regard to application of the diagnostic criteria, as these were collected retrospectively. Associated nerve injury, itself a potential cause of CRPS, was found in the patients. There may have been microneural injury associated with fractures, however, multifracture patients, where a higher incidence of neural trauma might be expected, did not have an increased rate of CRPS. There was no information regarding the specific factors of the injury or background psychosocial factors, both of which are likely to be relevant to the onset of CRPS. The individual clinical components of the CRPS were not reported.

However, the association of acute CRPS with duration of general anaesthesia in this context is important. The concomitant use of regional anaesthesia, such as spinal, epidural or peripheral nerve procedures, did not alter this finding. This might imply that nociceptive input at the time of the ORIF was not the triggering nociceptive stimulus. Since, in Japan, it is standard practice to apply tourniquet inflation to reduce blood loss with ORIF, it is likely that the duration of anaesthesia is a surrogate for the duration of limb ischaemia in the operative field. Reperfusion subsequent to prolonged ischaemia causes hyperalgesia, allodynia, hyperaemia and oedema [9]. Therefore deep tissue ischaemia with resultant neurogenic inflammation may be the relevant trigger for the development of CRPS in this setting [10].

Many other mechanisms contribute to the subsequent clinical phenotype of CRPS, including ongoing neurogenic inflammation, vasomotor dysfunction, central sensitization and maladaptive neuroplasticity [1]. Additionally, other factors, including genetic and psychological factors, may increase vulnerability to CRPS and also sustain the mechanisms that maintain CRPS. CRPS is well named.

The findings of this study suggest that factors related to peripheral deep-tissue ischaemia have an important potential triggering role in CRPS. Awareness of increased rates of CRPS in this clinical context will facilitate early diagnosis and probably better management outcomes for this important disorder. It will also allow for further targeted research into the cause of CRPS.

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