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Delayed diagnosis and worsening of pain following orthopedic surgery in patients with complex regional pain syndrome (CRPS)

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HIGHLIGHTS

- Diagnosis in 38 patients with CRPS-1 and 17 with CRPS-2 was delayed in average 4 years after symptom-start.
- Pain was worsened in 22 of 27 patients after orthopedic re-operations.
- 77% of patients with worse pain after re-operations suffered from undiagnosed CRPS.
- There is an urgent need for more knowledge about CRPS among physicians, in particular those who operate on extremities.

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ABSTRACT

Background and aims: Complex regional pain syndrome (CRPS) is a serious and disabling chronic pain condition, usually occurring in a limb. There are two main types, CRPS 1 with no definite nerve lesion and CRPS 2 with an identified nerve lesion. CRPS 1 and 2 may occur following an injury (frequently following fractures), surgery or without known cause. An early diagnosis and start of adequate treatment is considered desirable for patients with CRPS. From the clinical experience of the principal investigator, it became apparent that CRPS often remained undiagnosed and that the clinical conditions of many patients seemed to be worsened following orthopedic surgery subsequent to the initial eliciting event. The aim of the present retrospective study of 55 patients, all diagnosed with either CRPS 1 or 2, was to evaluate the time from injury until diagnosis of CRPS and the effect on pain of orthopedic surgical intervention subsequent to the original injury/surgery.

Methods: Clinical symptoms with an emphasis on pain were assessed by going through the patients' records and by information given during the investigation at Oslo University Hospital, where the patients also were examined clinically and with EMG/neurography. Alteration in pain was evaluated in 27 patients who underwent orthopedic surgery subsequent to the eliciting injury.

Results: Of a total of 55 patients, 28 women and 27 men (mean age 38.7 (SD 12.3), 38 patients were diagnosed with CRPS type 1, and 17 with CRPS type 2. Mean time before diagnosis was confirmed was 3.9 years (SD1.42, range 6 months–10 years). The eliciting injuries for both CRPS type 1 and type 2 were fractures, squeeze injuries, blunt injuries, stretch accidents and surgery. A total of 27 patients (14 men and 13 women) were operated from one to 12 times at a later stage (from 6 months to several years) following the initial injury or any primary operation because of fracture. A total of 22 patients reported a worsening of pain following secondary surgical events, while four patients found no alteration and one patient experienced an improvement of pain. None of the 22 patients reporting worsening, were diagnosed with CRPS prior to surgery, while retrospectively, a certain or probable diagnosis of CRPS had been present in 17/22 (77%) patients before their first post-injury surgical event.

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Conclusions and implications: A mean time delay of 3.9 years before diagnosis of CRPS is unacceptable. A lack of attention to more subtle signs of autonomic dysfunction may be an important contributing factor for the missing CRPS diagnosis, in particular serious in patients reporting worsening of pain following subsequent orthopedic surgery. It is strongly recommended to consider the diagnosis of CRPS in all patients with a long-lasting pain condition. We emphasize that the present report is not meant as criticism to orthopedic surgical practice, but as a discussion for a hopefully increased awareness and understanding of this disabling pain condition.

1. Introduction

Complex regional pain syndrome (CRPS) is a serious and disabling chronic pain condition, usually occurring in a limb. The clinical picture is dominated by pain and autonomic symptoms, but may also involve motor disability. There are two main types, CRPS 1 (with no definite nerve lesion and previously known as reflex sympathetic dystrophy) and CRPS 2 (previously known as causalgia) with a lesion to a major nerve, identified either clinically or by EMG/neurography. CRPS 1 is the most common type [1]. The understanding of CRPS has increased substantially in the past years [2], but the pathophysiological mechanisms are still partly unknown and controversial.

An exact estimate of the incidence of CRPS is difficult to establish, but in western countries it has been reported to be from 5.5 to 26 per 100,000 person/year [3,4]. CRPS may develop as a consequence of an injury, fractures [3,4], surgery [5], but may also occur without any known eliciting event [6]. However, relatively shortlasting CRPS may be common [7].

The diagnostic criteria of CRPS have been carefully evaluated in the recent years [8–10]. The present criteria (the "Budapest criteria") are based on a combination of subjective reports and clinical findings at the time of examination, including sensory, motor and autonomic qualities [9]. Before these redefined criteria, the diagnosis was according to IASP based on the existence of continuing pain not proportional to the inciting event, coexisting with sensory abnormalities and autonomic dysfunction at some time [11]. However, the diagnostic criteria are still debated [1,10].

An early diagnosis and start of adequate treatment is considered desirable for patients with CRPS [1,5,12]. In spite of this, patients commonly may experience a delay before diagnosis and start of therapy [1,5] or a long duration before being evaluated at a pain clinic [13].

To our knowledge, the outcome of a secondary surgical intervention for pain in CRPS has not been systematically addressed, although case stories have been published [14–16]. However, it is claimed that operations preferably should be postponed until signs are minimal [17] (see also UpToDate [18]), and, in the specialty guidelines for orthopedic practice of CRPS in the UK [1] it is stated that 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. A problem arises when CRPS has not been diagnosed.

From a clinical experience of the principal investigator it became apparent that CRPS often remained undiagnosed and thereby not treated accordingly. In addition, the clinical conditions of many patients seemed to be worsened following orthopedic surgery subsequent to the initial eliciting event. The aim of the present retrospective study of 55 patients, all diagnosed with either CRPS 1 or 2, was to go through patients' records to evaluate the time from injury until diagnosis of CRPS and the effect on pain of orthopedic surgical intervention subsequent to the original injury.

2. Methods

2.1. Material

Patients were selected from a number of >80 patients from the whole of Norway being referred to the principal investigator in the years 2004–2014 for determination of chronic medical disability for a chronic pain condition following a trauma or surgery. 55 patients with the diagnosis of CRPS type 1 or 2, either set prior to the admittance or by the principal investigator, were selected for further evaluation.

The patients who were investigated between 2004 and 2010 were diagnosed (or previous diagnosis was confirmed) according to previous IASP criteria [11], while the Budapest criteria [9] were employed for patients after 2010.

The patients were at their referral to Oslo University Hospital investigated clinically and with routine methods such as electromyography (EMG)/neurography.

2.2. Ethical considerations

The publication of results was considered by the local Ethical Committee as part of a quality improvement of a clinical material, with no necessity of an ethical approval. All patients have been examined according to ethical guidelines and the Helsinki declaration and are anonymous in the present report.

2.3. Patient's report

From the records (previous records and data from investigation at Oslo University Hospital), the following informations were assessed: details about family history, previous diseases, the actual injury, the immediate symptoms with an emphasis on all aspects of pain (character, location, intensity) as well as possible motor problems and autonomic dysfunctions. They were asked about the development of the pain condition, of results of managements (treatments including surgery) and actual and previous treatments. A statement of symptoms at the day of investigation at Oslo University Hospital was noted with details on spontaneous (ongoing and paroxysmal) and evoked pain as well as lack of motor skills and symptoms of autonomic abnormalities. The patients were also asked about the consequences of pain for work, housekeeping, leisure activities, personal hygiene and sleep.

2.4. Clinical investigation at Oslo University Hospital

Inspection of both injured and contralateral extremity was undertaken in order to look for asymmetric pathology like atrophy, discoloration of skin, trophic changes of skin (thin skin, glossy skin), involuntary movements, obvious signs of abnormal sweating and oedema. Skin temperatures (using Somedics Tempett, Hörby, Sweden) were measured at several occasions in injured (in the pain area and adjacent areas) as well as contralateral extremity during the examination which took from 2.5 up to 3 h. A clinical

neurological examination including detailed examination of motor and sensory functions was performed, with investigation of possible allodynia to light touch and/or hyperalgesia to pin-prick/pressure.

2.5. EMG/neurography performed at Oslo University Hospital

All patients were examined with EMG/neurography of the affected extremity, with either a Dantec Counterpoint, Skovlunde, Denmark or a Dantec Keypoint-apparatus, Skovlunde, Denmark with measurements of motor amplitudes, distal delay and motor conduction velocities as well as sensory amplitudes and conduction velocities of the relevant main nerves in upper or lower extremity (median, ulnar, peroneal, tibial posterior, sural nerves). EMG of appropriate muscles was performed if judged necessary for diagnosis of a nerve lesion.

2.6. Detailed history of patients undergoing orthopedic surgery subsequent to the initial injury

In 27 patients, undergoing secondary orthopedic surgery (not related to any primary operation), a detailed history of the number and types of surgical procedures as well as alterations of pain conditions was recorded. It was retrospectively (based on the patients' own reports of pain, sensory and autonomic disturbances at the investigation at Oslo University Hospital, as well as similar information from the patients' previous records) made an evaluation of whether they suffered from a probable or certain CRPS (according to the IASP criteria (before 2010) or Budapest criteria (Table 1)) before secondary operations.

3. Results

Of a total of 55 patients, 28 women and 27 men (mean age 38.7 (SD 12.3) or median 42 (27–47 25–75 percentile) at the time of injury), 38 patients were diagnosed with CRPS type 1, and 17 with CRPS type 2, the latter based on pathological findings on EMG/neurography. Mean time before diagnosis was confirmed was 3.9 years (SD 1.42, range 6 months–10 years; median 3 years (1.4–5, 25 and 75 percentile).

A total of 13 (34%) patients with CRPS type 1 and 7 (41%) with CRPS 2 were first diagnosed when examined at the Oslo University Hospital (after up to 10 years following injury). Only 50% [19] of the patients with CRPS type 1 had received treatment in forms of drugs usually employed for neuropathic pain and/or sympathetic blocks or dorsal column stimulation, whereas the majority of patients with CRPS 2 (14/17, 82%) had been treated for neuropathic pain (some even without a diagnosis of CRPS). The pain syndrome was located in the upper extremity in 26 cases and in the lower extremity in 29 patients.

3.1. The eliciting injuries

for both CRPS type 1 and type 2 were fractures, squeeze injuries, blunt injuries, stretch accidents, surgery as presented in Table 2. A total of 22 patients (a large majority men), were injured at work (fall accidents, direct trauma to a limb) whereas 12 were victims of traffic-accidents.

3.2. The characteristics of subjectively reported pain

for both CRPS type 1 and type 2 are presented in Table 3. Spontaneous ongoing pain was present in almost all patients (except for three patients in the CRPS 1- group), and evoked pain (both allodynia to light touch and hyperalgesia to pin-prick/pressure) in a large majority, whereas spontaneous paroxysmal pain was present in some, but far from all patients.

3.3. Consequences for working- and social life

45 patients (81.8%) were out of work, while nine patients (16.4%) were able to work part-time (50% or less). 19 patients (34.5%) were able to participate to some degree in housekeeping activities, while the remaining 36 patients (65.5%) needed help to all house-holding tasks. All patients reported to have given up leisure activities as well as having sleep problems. Five patients (9.0%) needed assistance for personal hygiene.

3.4. Clinical signs of autonomic dysfunctions

at the time of investigation are presented in Table 4. Altered skin temperature (≥1 °C side difference [1]) was the most prominent finding, found in 29/38 (76%) of the patients with CRPS 1 and 11/17 (65%) of patients with CRPS 2. Difference in skin temperature varied from 1 °C up to 3 °C in the affected extremity compared to the contralateral healthy side. Discoloring of skin (blue/red) was demonstrated in a certain percentage (50 and 35.3%) of both patient groups, while oedema was by far more present in the CRPS 1 group (15/38, 39.4%) as compared to the CRPS 2 group (2/17,11.7%).

3.5. Motor dysfunction

Motor dysfunction in the CRPS 1 group was present in 18 of 38 patients (47%), mostly in form of reduced strength, either in hand or foot. Motor dysfunction in the CRPS 2 group was as expected from the nerve lesion in question.

3.6. Surgery after start of CRPS

27 patients (14 men and 13 women) were operated at a later stage (from 6 months to several years) following the initial injury or any primary operation because of fracture. The patients were operated from one up to 12 times subsequent to the injury. In total, 22 of 27 patients (81.5%) experienced a worsening of pain following secondary orthopedic surgery, while four reported no alteration in pain and only one experienced an improvement (Table 5).

The five patients with either no alteration (4 patients) or improvement (1 patient) of pain, four had been operated once, one six times. Two of these five patients had been diagnosed with CRPS before re-operation and had been treated accordingly. The remaining three patients were not diagnosed and not treated, although a neuropathic pain component was suspected in one. Retrospectively, of these three patients, one patient had a certain CRPS, one a probable CRPS and in one patient it was not possible to decide the diagnosis.

3.6.1. The orthopedic surgical procedures

The orthopedic surgical procedures consisted of arthroscopies in most cases, some with synovectomies and arthrodesis. Nerve operations (neurolysis, decompression, removal of scar tissues and neuromas) were performed in eight patients, all with a serious worsening of pain (Table 5).

3.6.2. The worsening of pain

The worsening of pain in 22 patients consisted of an increase of intensity of spontaneous ongoing pain, of the development of new pain phenomena, such as new characters of ongoing pain and the occurrence of paroxysmal pain. An increase of the area of pain as well of allodynia or hyperalgesia was described by some patients

Table 1
Budapest clinical diagnostic criteria for CRPS.

1. Continuing pain, which is disproportionate to any inciting event

2. Must report at least one symptom in *three of the four* following categories
   Sensory: reports of hyperesthesia and/or allodynia
   Vasomotor: reports of temperature asymmetry and/or skin colour changes and/or skin colour asymmetry
   Sudomotor/oedema: reports of oedema and/or sweating changes and/or sweating asymmetry
   Motor/trophic: reports of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

3. Must display at least one sign at time of evaluation in *two or more* of the following categories
   Sensory: evidence of hyperalgesia (to pinprick) and/or allodynia to light touch and/or joint movement
   Vasomotor: evidence of temperature asymmetry and/or skin colour changes and/or asymmetry
   Sudomotor/oedema: evidence of oedema and/or sweating changes and/or sweating asymmetry
   Motor/trophic: evidence of decreased range of motion and/or motor dysfunction (weakness, tremor, dystonia) and/or trophic changes (hair, nail, skin)

4. There is no other diagnosis that better explains the signs and symptoms

Table 2
Eliciting injury in patients with CRPS 1 and 2.

	Fractures	Squeeze injuries	Blunt injuries	Surgery	Stretch injury	Other
CRPS 1 (n = 38)	11 (29.0%)	9 (23.7%)	10 (26.3%)	3 (7.9%)	1 (2.6%)	4 (10.5%)
CRPS 2 (n = 17)	5 (29.4%)	3 (17.6%)	5 (29.4%)	2 (11.8%)	1 (5.9%)	1 (5.9%)

Table 3
Pain characteristics in patients with CRPS 1 and CRPS 2.

	Spontaneous ongoing pain	Paroxysmal pain	Evoked pain (allodynia and/or hyperalgesia)
CRPS 1 (n = 38)	35 (92.1%) (three patients with intermittent spontaneous pain)	18 (47.3%)	32 (84.2%)
CRPS 2 (n = 17)	17 (100%)	11 (65%)	17 (100%)

(Table 5). Exact numeric scale values for intensity of spontaneous pain before secondary surgery was not available in all patients.

3.6.3. Delayed diagnosis of CRPS

None of these patients were diagnosed with CRPS prior to surgery, while retrospectively, a certain or probable diagnosis of CRPS had been present in 17/22 (77%) patients before their first post-injury surgical event (Table 5). None of the patients had received specific therapy for neuropathic pain or CRPS before surgery. In 14 patients (63.6%), the diagnosis of neuropathic pain or CRPS was made following the worsening, but eight patients (36.4%) were not diagnosed until the examination at Oslo University Hospital, often several years later. In some cases, a neuropathic pain component had been suspected, but the patients were either not referred to a pain specialist or the patient was referred to a specialist without the CRPS diagnosis being made. All patients referred to pain specialists (12 patients, 54.5%) were diagnosed with CRPS. In the remaining 2/14 patients, the diagnosis was set by a neurologist.

4. Discussion

4.1. Main findings

The main findings of the present report are that diagnosis of CRPS is delayed and that the clinical pain condition of a high number of patients is worsened following orthopedic surgery subsequent to the initial injury.

4.2. Delayed diagnosis

Although pathophysiological mechanisms, treatment of CRPS and also the diagnostic approach to CRPS may be debated, it is considered important that diagnosis is ensured in an early stage [1,5,12], in order to secure possible beneficial effects of treatment strategies for patients suffering from this disabling chronic pain disorder. In this respect, a mean delay of 3.9 years before correct diagnosis is made as found in the present retrospective study seems unacceptable, in some patients up to several years (maximum 10 years). The consequences of the chronic pain condition were for many patients catastrophic, many had been falling out of work and had a poor quality of life, as others have reported previously [19–21].

4.2.1. Budapest criteria for possible and certain diagnosis

The previous IASP criteria [11] and the renewed Budapest CRPS criteria [9], for a better definition of the condition, are based on clinical symptoms and findings (signs), making sophisticated neurophysiological investigations unnecessary.

EMG/neurography may, however, be useful, in order to distinguish an injury to a major nerve. It may be argued that it may not be necessary to decide upon CRPS 1 or 2, as treatment would be identical. However, a patient with an identified nerve lesion is in need of follow-up investigations in order to search for improvement and regeneration of the nerve. In addition, for many patients, in necessity of a determination of medical disability for insurance companies or for court cases, an exact diagnosis is required.

Table 4
Clinical signs of autonomic dysfunction at time of investigation in patients with CRPS1 and CRPS 2.

	Oedema	Discoloured skin	Altered skin temp	Trophic changes/glossy skin	Increased sweating
CRPS 1 (n = 38)	15 (39.5%)	19 (50.0%)	29 (76.3%)	6 (15.8%)	3 (7.9%)
CRPS 2 (n = 17)	2 (11.8%)	6 (35.3%)	11 (64.7%)	2 (11.8%)	1 (5.9%)

Table 5
Alteration in pain in 27 patients with secondary orthopedic surgery. Intensities of pain are values on a numeric scale from 0 to 10 on a numeric scale where 0 is no pain and 10 worst imaginable pain.

Patient range of age (years) at time of accident	Eliciting injury	Number and type of post-injury surgical procedures	Nature of worsened pain	Possible probable or certain CRPS before post-injury surgery
20–30	Fracture left tibia 2000	Three in 2006: two orth operations and neurolysis of tibial posterior	Worsening after surgery two and three, worst after the third, increase in intensity (from moderate to 9)	Certain CRPS before last operation (pain, allodynia, cold, oedema)
20–30	Blunt injury left knee in 1998	Two orth operations, 1999 and 2000	Increase of intensity of pain (from moderate to 10)	Certain CRPS from time of injury (pain, allodynia, oedema, Increased sweating, discoloured skin)
50–60	Needle in left hand's 3rd finger 2007, infection	Orth surgery later 2007, not related to infection	New pains after surgery (spontaneous ongoing and paroxysmal pain, up to 10)	Certain CRPS from time of injury (pain, oedema, discoloured skin, motor dysfunction)
30–40	Accidental squeezing of right hand 1996	Opr Carpal tunnel syndrome 1998 and Orth surgery 1999	Gradually worsened after each operation (spread of spontaneous pain, increase in intensity of spontaneous pain and allodynia)	Certain CRPS from time of injury (pain, allodynia, oedema, cold, increased sweating, discoloured skin)
30–40	Blunt injury left foot 1999	Orth surgery 2000 Opr tarsal tunnel 2002	Worsening after each opr, worst after 2002, with increase in pain area	Possible, but not certain CRPS before surgery (pain, cold)
30–40	Squeeze accident right arm 2000	Decompression ulnar nerve 2001 and two orth opr 2001 and 2002	Worsening after nerve injury, increase in intensity spontaneous pain	No certain CRPS before surgery
40–50	Fracture left foot 2000, opr same day	3 orth surgeries, last in 2001 (transplantation of bone from hip to foot)	Worsened pain after last opr (increased area and intensity of pain, up to 10 and new allodynia)	Certain CRPS from time of injury (pain, oedema, discoloured skin, increased skin temperature)
40–50	Stretch injury left foot 2003	Two orth opr, one 2005 and one 2006	Worsening after opr 2006, development of ongoing and paroxysmal pain and allodynia	Certain CRPS from time of injury (pain, allodynia, cold, oedema, discoloured skin)
20–30	Crushed left knee 2001	Opr same day, new orth opr 2002, 2005 and 2007	Worsening of ongoing pain after last opr, increase in intensity from 4 to 7–8	Probable CRPS from time of injury (pain, allodynia, oedema)
30–40	Venous stripping right leg 2002	Decompression tibial nerve later 2002	Worsened pain after last opr, increase in intensity from 2 to 4, new paroxysmal pain	Probable CRPS after initial surgery (pain, allodynia, discoloured skin, cold)
30–40	Squeeze accident left foot 2010	Orth opr six months later	Worsening of spontaneous pain (increase in intensity up to 10, and more CRPS–symptoms	Probable start of CRPS after injury, (pain, oedema, cold), full development after surgery
50–60	Fracture right arm 2002	Operated Carpal tunnel syndrome 2003	Worsening (of spont) pain after opr CTS and new pain with intensity 8	Probable start of CRPS after injury, (pain, allodynia, oedema) full development after surgery CTS
20–30	Blunt injury right knee 1986	12 orth opr from 1987–2003	Gradual worsening of pain 1987–2003, most after 2003 with new pain components and increase in area of pain, new paroxysmal pain	Possible CRPS from injury (pain, oedema)
30–40	Blunt injury left elbow 1991	Orth opr 1992 Opr decompression ulnar nerve 1996	Worsening after 1996, development of ongoing pain with intensity 10, new paroxysmal pain	Certain CRPS from injury (pain, oedema, cold, discoloured skin, tremor)
40–50	Stretch accident right arm 2004	Operated ulnar nerve elbow 2005 (had findings compatible with nerve lesion)	Serious worsening of pain, explosion, with new ongoing pain with intensity 8–9 and paroxysmal pain	Certain CRPS from time of initial accident (pain, allodynia oedema, discoloured skin, motor dysfunction)
30–40	Orth surgery 2010 (arthrodesis) right 1. toe	New orth opr 2011 and 2012	Serious worsening after both opr 2011 and 2012, with increase in intensity up to 10, new pain areas, extreme allodynia	Certain CRPS after initial orth surgery (pain, allodynia/hyperalgesia, oedema, discoloured skin)
40–50	Fracture left leg 2003	Orth opr 6 months later 2003	Worsening of spont pain after opr, up to 10 and more intense allodynia	Certain CRPS from initial accident (pain, allodynia, oedema, discoloured skin)
10–20	Squeeze accident left leg 1980	Orth opr 1981, 1982, 1984, 1998, 2000 nerve opr 1992	Acute worsening of spont pain after nerve opr 1992 (intensity up to 10) and new worsening after orth opr 1998 and 2000	Possible, but not certain CRPS from early stage (pain, oedema)
30–40	Stretch accident of right leg 2004, infection	Orth opr later 2004	Worsening after orth opr with increase in intensity spontaneous pain up to 10 and development of CRPS	Possible CRPS before orth opr (pain, oedema, discoloured skin), certain CRPS after opr
30–40	Squeeze accident right leg 2003	Opr 2004 for tumor (fat necrosis) leg	Worsening with development of allodynia	Certain CRPS from injury (pain, oedema, cold)
50–60	Blunt injury left hand 1996	Orth surgery in 1997 and 2001, and neurolysis 2001	Worsening with new pains after first opr, increase in area of pain and increase in allodynia. Increase of intensity of spontaneous pain from 4 to 8 after last opr	Certain CRPS from accident (pain, oedema, cold, discoloured skin)

Table 5 (*Continued*)

Patient range of age (years) at time of accident	Eliciting injury	Number and type of post-injury surgical procedures	Nature of worsened pain	Possible probable or certain CRPS before post-injury surgery
10–20	Fracture right foot 2003	Opr twice for fracture after accident New orth opr 2004, 2006, 2009 and 2012	Worsening after 2009, with pain at walking, worsening also after surgery 2012, with increase in intensity of ongoing pain from 6 to 10	Certain CRPS from time of initial accident (pain, oedema, discoloured skin)
10–20	Squeeze accident Right hand 2010	Orth surgery 2012	Improvement of pain	Certain CRPS from time of injury (pain, oedema, cold, discoloured skin, motor dysfunction)
20–30	Fracture right hand 2006	Orth surgery 2008	Pain unaltered	Certain CRPS from 2008, not possible to say if present earlier
40–50	Surgery L5 (screw) (2002), pain in left foot	Removal of screw 6 months later	Pain unaltered	Certain CRPS from initial surgery (pain, hyperalgesia, warm foot, discoloured skin)
50–60	Fracture right foot 2011, opr right after	New orth surgery 2012	Pain unaltered	Certain CRPS from time of injury (pain, allodynia, oedema, discoloured skin, increased sweating, motor dysfunction)
40–50	Fracture left foot and leg 2005	Several later orth opr	Pain unaltered	Probable CRPS from time of fracture (pain, oedema, discoloured skin, motor dysfunction)

4.3. Autonomic disturbances and temperature measurements

In the clinical diagnosis of CRPS, it is of extreme importance to be aware of that not all patients are presenting with all possible autonomic dysfunctions, but can still meet the criteria for the diagnosis. Not all patients present with a clearly swollen and discoloured extremity, with glossy skin. A lack of attention to more subtle signs of autonomic dysfunction may be an important contributing factor for the missing CRPS diagnosis of patients in the present report. It is strongly recommended to consider the diagnosis of CRPS in all patients with a long-lasting pain condition. In our patients, an altered skin temperature in the affected extremity was the most frequent finding, with a side difference of minimum 1 °C (often higher), which is considered significant to fulfil the vasomotor criteria [1]. A side difference in this order may not be determined without a *skin thermometer*, which we strongly recommend for all doctors working with patients with possible CRPS. In our hands, this is a simple and useful tool for a more objective determination of autonomic dysfunction. An objectification of the diagnostic criteria of CRPS [23] is wanted and in such a context, measurement of skin temperatures may be essential. However, an altered skin temperature alone is not enough for a diagnosis of CRPS and, importantly, skin temperature asymmetry in this order of magnitude is not specific for CPRS [24]. Attempts have been made to further improve the specificity and diagnostic value of skin temperature measurements in CRPS [24,25].

4.4. Eliciting injury

In the present study, the eliciting injury causing the chronic pain disorder was as described previously by others [3]; fractures and injuries of other types as well as operations. We found a larger proportion of men in the group of patients than described earlier [3,4], possibly because many of our patients had been victims of work-accidents (more men working as carpenters, industry etc.) and were admitted for determination of medical disability. We also found an equal distribution of pain in upper- and lower extremity, in contrast to previous reports in adults which found more frequent CRPS in the upper extremity [3,4]. However, lower extremity involvement is more common in pediatric CRPS [26]. In most patients, the initial injury caused the CRPS, whereas in a few patients, CRPS was developed after subsequent post-injury surgical procedures.

4.5. Worsening of pain after secondary surgery

A total of 22 (40%) patients of the whole material reported worsening of their pain after being operated from one up to 12 times following the initial injury. None of these patients were diagnosed with CRPS before these operations, and none had received specific treatment for CRPS or neuropathic pain before the surgery. Retrospectively, by an analysis of patients' reports as well as documentation in their records, based on information of pain, sensory and autonomic dysfunction, a large majority of these patients had symptoms and signs compatible with a certain or probable CRPS prior to the first post-injury surgical procedure (Table 5). We suggest that the lack of CRPS diagnosis and proper treatment before these surgical procedures may have been an important contributing reason for the worsening, for many of the patients an extreme worsening of pain.

According to the recommendation in the UK guidelines for orthopedic surgery in treatment of these patients, it is stated that surgery should be avoided on a CRPS-affected limb where possible, and where it cannot be avoided, surgery should be deferred until one year after the active process has resolved [1]. In three of the 27 operated patients (two patients with worsening of pain and one patient with unaltered pain), insurance cases evaluated retrospectively whether there had been indication for secondary orthopedic surgical, if the diagnosis of CRPS had been known beforehand. It was established that there was no indication.

4.6. Indications for post-injury orthopedic surgery

It is difficult retrospectively, in particular for a non-surgeon, to analyse the indications for the post-injury orthopedic operations. However, it seems likely that a lasting painful situation was the indication for many of the surgical procedures (i.e. arthroscopies with synovectomy, arthrodesis, and nerve decompression). CRPS was not diagnosed or treated in a large majority of these patients beforehand, and it seems plausible that these procedures were important contributing factors for the subsequent worsening of pain reported by many of our patients. However, the diagnosis of CRPS may be difficult, and the validity of the criteria in an orthopedic population can be discussed [1]. It is in any case mandatory to increase the awareness of diagnostic criteria for CRPS. We will emphasize that one patient reported a benefit after post-injury

orthopedic surgery, the same operation which in other patients resulted in a worsening, but it is impossible to speculate about the mechanisms of worsening and why some experienced worsening while others did not.

4.7. Limitations of the study

In addition to the limitations of this study due to its retrospective nature, we will emphasize that the data presented here are derived from a highly selected patient material (patients referred for determination of medical disability). We do not know how many patients with CRPS who are undergoing orthopedic surgery with a good result and what the effect of operations on CRPS patients are in general. A prospective study seems to be of interest. Anyhow, for the patients experiencing a worsening of CRPS after operations, this is a serious and disabling problem.

We strongly emphasize that the present report is not meant as criticism to orthopedic surgical practice. It is rather meant to raise a discussion about CRPS as a serious problem and to increase the awareness and understanding of this difficult pain condition. More widespread information of diagnostic criteria of CRPS is essential. Thus, delay of time for diagnosis of CRPS in children has been reduced from a mean of 12 months to 1–41 weeks, because of an increased awareness [26], leaving reason for optimism.

5. Conclusions and implications

Diagnosis of CRPS is frequently delayed and patients are often subjected to unnecessary surgery and worsening of the pain condition. There is a strong need for spread of Information about diagnostic criteria of CRPS and a more careful consideration of indication for post-injury orthopedic surgery in patients with CRPS.

Conflict of interest statement

None declared.

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