

# Why so many Recurrences of Complex Regional Pain Syndrome among Children?

Berthelot S, Giquello C, Folliot V, Bures E and Nouri M

Pain Department at the Haut-Anjou Hospital, France

## Abstract

**Introduction:** Paediatric Complex Regional Pain Syndrome (CRPS) is still relatively unknown. A higher rate of recurrences than for adult patients has been theorized [1]. This study aimed to study those recurrences for children treated for CRPS at the hospital center of Haut-Anjou, Mayenne, France.

**Methods:** This study was retrospective, using medical records of patients between 0 and 18years old treated for a CRPS at the pain ward of the hospital center of Haut-Anjou, between September 2002 and April 2022.

**Results:** 13 of the 22 patients included in this study presented a recurrence. No significant impact of the psychological state of the patients was showed. Patients that presented a recurrence had a significant higher pain score at the beginning of the treatment.

**Discussion:** As discussed in other studies, a high recurrence rate was found in this study [2]. CRPS optimal treatment is still unknown. An interdisciplinary treatment seems to be important, with physiotherapy, psychotherapy, pain management and parental involvement [3]. Continuous regional anaesthesia could be a pain management solution [4]. Parental information to be conscious of their involvement in their child's care could be a way to help treating CRPS, maybe even reduce recurrence rates.

**Limits:** The small sample size of this study, and the retrospective use of data makes the results of this study difficult to extrapolate to the general paediatric population.

**Conclusion:** This study's results indicate a higher recurrence rate of paediatric CRPS. A large scale prospective study would be interesting to further investigate this issue.

## Introduction

Studies on paediatric Complex Regional Pain Syndrome (CRPS) are few [5]. Its prevalence is considered to be low, but possibly underestimated by lack of diagnosis. Recent studies have found a female, with a higher prevalence of lower limb cases than in adult cases [6]. A higher importance of psychological factors is also presumed in the syndrome's expression and its resolution, with no concrete evidence yet [2]. Faced with the failure of oral treatments, physiotherapy, electrotherapy, tenacious paediatric CRPS has been treated at the Haut-Anjou Hospital by use of perineural catheters, with spectacular results. However, were noticed high recurrence rates, which have also been mentioned in some studies [7].

This study aimed to evaluate the recurrences rate of CRPS in paediatric patients, and to try and identify risk factors of those recurrences.

## Methods

This study has been approved by the examination committee of the Hospital Center of Haut-Anjou, Mayenne, France. It is a retrospective study, using medical records included in the database of the Medical Information Department of the hospital. Were used medical records of paediatric patients having been treated for a CRPS at the pain department of the Hospital Center of Haut-Anjou between September of 2002 and April of 2022.

Initial evaluation of each patient was done by the same pain specialist doctor within the ward. Each patient had beforehand gotten treatment from a physiotherapist.

CRPS' diagnosis was made through the examiner's clinical experience using the Budapest criteria [8,9] and sometimes with the help of additional imaging results.

Pain evaluation was made through a numeric scale. The psychological impact was evaluated using the Hospital Anxiety and Depression scale the patients had filled with their legal guardians before the initial consultation [10].

Each patient was treated according to a weekday hospitalization schedule, with introduction of a perineural catheter for pain management adapted to the pain localisation, coupled with increased physiotherapy work. For at least two five-day sessions, patients therefore were treated by Ropivacaine through the catheter, at a 0.2mg/mL flow rate, in an infusorelastometric pump, allowing for mobility [4,11]. Additional boluses could be administered if needed. Flow rate was also adjustable.

In case of a recurrence of the CRPS, care was adapted to every patient, with, if needed, renewal of perineural catheter use.

To be included in this study, patients had to have been diagnosed with CRPS, to be treated at the CPMW for this same CRPS, and to be younger than 18years old at the time of the first evaluation.

**\*Correspondence to:** Dr. Sarah Berthelot, Pain Department of the Hospital Center of Haut-Anjou, France, E-mail: sarahberthelot.7@gmail.com

**Keywords:** CRPS, paediatric, recurrence

**Received:** March 16, 2024; **Accepted:** May 21, 2024; **Published:** May 24, 2024

**Table 1.** Characteristics during the first assessment (n = 22)

Characteristics	n (%)
<b>Age, mean (SD) (y)</b>	13.2 (2.8)
<b>Genre</b>	
Male	4 (18.2)
Female	18 (81.8)
<b>Localisation</b>	
Upperlimb	5 (22.7)
Lowerlimb	18 (81.8)
<b>Triggering factor (trauma)</b>	
Present	20 (90.9)
Absent	2 (9)
<b>Initial cold presentation</b>	19 (86.4)
<b>Delay before treatment, mean (SD) (m)</b>	5.6 (4.9)
<b>Anxiety score (HADs), mean (SD)</b>	9.5 (4.2)
Score below or equal to 7	7 (31.8)
Score between 8 and 10 included	3 (13.6)
Score equal or higher than 11	10 (45.4)
<b>Depression score (HADs), mean (SD)</b>	7.1 (4.1)
Score below or equal to 7	12 (54.6)
Score between 8 and 10 included	2 (9.1)
Score equal or higher than 11	6 (27.3)
<b>Pain Intensity (NP), mean (SD)</b>	7.1 (1.3)
Missing data:	
Delay before treatment n=1 ; pain intensity n=1, anxiety score n=2, depression score n=2	
One patient presented two separate concomitant localisation ;	
NP =numeric scale, HAD = Hospital Anxiety and Depression scale	

No exclusion criteria were enforced during this study.

Data was collected by going through the physical paper files of the patients, after establishment by the MID of a list of the patients corresponding with the inclusion criteria. Data was extracted from the scales and self-evaluation documents filled by patients, reference letters from specialists and general practionners, medical and paramedical consultation notes, and additional notes taken by the referring nurse during telephonic check-up made between consultations.

Extracted data included demographics, including sex, age at the first consultation, schooling, medical and familial history.

Data about CRPS included length of symptom before the first consultation, context surrounding the first apparition of those, and localisation of the pain. DN4 scales and numeric scales were also extracted. Mobility impact and use of technical aid was also taken into consideration.

HAD scale was used to evaluate psychological impact at the time of the first consultation and at the follow-up consultation.

The psychological state of patients was also interrogated by the pain specialist during the first consultation, using clinical knowledge. Proposition of a psychological consult was included in the data extracted, associated with execution of psychological care.

Occurrence of CRPS recurrencehaving needed a new consultation at the center was noted, as well as the localisation of this recurrence, time between the two CRPS events. There was no data about the psychological state of the patients during the recurring events.

Descriptive statistics were calculated for demographic data, psychological and pain characteristics, and for recurrences data.

Comparison between patients with no recurrences and those with recurrences was made using Student test via BiostaTGV. A p-value <0.05 was considered as statistically significant.

## Results

Data extraction allowed for the inclusion of 22 patients having been treated at the center between September 2002 and April 2022 for CRPS having needed a hospitalisation for care because of a loud clinical impact.

Demographics collected from the initial consultation are presented in (Table 1).

One patient presented in the same time upper limb and lower limb CRPS.

13 of the 22 patients, amounting to 59% of patients, included initially exhibited a recurring event of CRPS, two patients having been lost to follow-up after initial care. Among those 13 patients, 84.6% were female. Only one patient exhibited a recurring event in a different localisation than the initial event, representing 7.7% of patients.

On average, time between the two events was 18.7+/-10.2months, one patient having presented two recurrences, respectively 18months and 30months after the first episode.

Psychological state of patients was evaluated both by the HAD scale and by the clinical experience of the pain specialist administering the first evaluation. The initial evaluation highlighted for nine patients a complex familial situation, and for two patients school absenteeism. One patient had been a victim of sexual assault several months prior to the first CRPS symptoms.

Clinical evaluation coupled with results of the HAD scale had optionally led to psychological care, data being presented in (Table 2).

During a recurring event, psychological care could be again offered if mental health issues were suspected. Psychological care was never mandatory. One patient refused this offered care both during initial treatment and during the recurring event treatment.

A conversion disorder was diagnosed for one patient following psychological care. Another patient was enrolled in psychiatric care at the same time of the CRPS care for unrelated symptoms. One patient was being treated for anxiety and self-harm prior to the CRPS care.

**Table 2.** Psychological characteristics

Psychological care	Patients without recurrence (n=9)	Patients with recurrence (n=13)
<b>Offered</b>	1 (11.1)	8 (61.5)
During initial treatment	1 (11.1)	4 (30.7)
Accepted	1 (100)	2 (50)
Refused	0 (0)	2 (50)
Duringrecurrences	-	5 (38.5)
Accepted	-	2 (40)
Refused	-	3 (60)
Missing data :		
Two patients lost to follow-up		
One patient from "with recurrence" group had been offered psychological care both during initial treatment and during the recurrence's treatment		

**Table 3.** Comparison between patients with and without recurrences

	Without recurrences (n=9)	With recurrences (n=13)	p
Age, in years, mean (SD)	12.6 (3.9)	13.1 (2.3)	0.79
Genre			
Male	2 (28.6)	2 (15.4)	
Female	5 (71.4)	11 (84.6)	
Treatment delay, in months, mean (SD)	4.8 (3.5)	6.4 (6)	0.48
NS before treatment (SD)	6.4 (0.9)	7.6 (0.9)	0.01
NS after treatment (SD)	1.8 (1.7)	2 (2.2)	0.87
Anxiety score (HADs) before treatment (SD)	7.7 (3.1)	11 (4.1)	0.07
Score ≥ 11 (%)	2 (22.2)	8 (61.54)	
Anxiety score (HADs) after treatment (SD)	3.3 (1.5)	6.1 (3.8)	0.11
Depression score (HADs) before treatment (SD)	6.6 (4.6)	7.75 (4)	0.58
Score ≥ 11 (%)	2 (22.2)	4 (30.8)	
Depression score (HADs) before treatment (SD)	1 (1)	2.6 (2.2)	0.13
Missing data :			
Two patients were lost to follow-up			
With recurrences group : delay before treatment n=1, NS before treatment n=1, NS after treatment =3, Anxiety before treatment =1, Anxiety after treatment =4, Depression before treatment =1, Depression after treatment =4			
Without recurrences groupe: NS after treatment =1, Anxiety after treatment =4, Depression after treatment =4			

Comparison between the two groups “with recurring event” and “without recurring event” is presented in (Table 3).

Only one significant difference was demonstrated, after data analysis via Student testing, involving pain intensity evaluation via Numeric Scale, at the first evaluation.

## Discussion

Studies emphasize a lack of knowledge of CRPS presentation in paediatric patients [2,9]. Algodystrophy incidence among children is low, estimated as 1.2/100 000. It is less studied than among adults. The average age upon diagnosis is similar to the one we found in this study. It is also noted a majority of lower limb cases, especially involving the foot. The patients' sample having been treated for CRPS in the chronic pain ward of this hospital leads towards the same results, although the majority involving the ankle. A predomination of female patients was observed, as noted in previous studies. Moreover, as mentioned in literature, CRPS can be triggered after minor trauma, without any identified nerve damage. In some cases, no trauma is even to be recalled. As also shown in previous studies, most of the patients included in this study presented straight away a cold CRPS presentation [12,13].

Recurrences rate is barely talked about, even though it has been mentioned in other studies. In this study, 59% of patients presented a recurrence, confirming the impression of frequent recurrences in paediatric CRPS. This rate is higher than for adult patients, which challenges the idea of a rather good prognosis for this paediatric syndrome. This could be caused by increased delay of treatment for paediatric patients, or by CRPS being more rebellious in children. However, this rate might have been increased compared to reality, the patients being treated at the pain ward being those having had unsuccessful prior attempts at treatment.

Diagnosis delay for children is often considered to be elongated compared to adult patients presenting CRPS. Several reasons have been

theorized, as such as the more insidious presentation of symptoms for children, the initial cold chronic phase, the lack of seriousness put into a child's pain complaint, the lack of knowledge about CRPS from primary care providers [14,15]. In case of doubt concerning the diagnosis, imaging can help, although no gold standard has been recognized.

Despite sometimes extensive delay until care, a significant impact on recurrences risk was not demonstrated in this study. Although attempts of reducing this delay have been put in place, in part by educating primary and secondary care providers to this pathology, there hasn't been an increase in the number of paediatric patients treated for CRPS at the pain ward.

Only statistically significant result of this study, using a very small sample, was related to the pain intensity, which was highest during initial assessment for the patients having later presented a recurrence. It had already been suggested in previous studies. It therefore seems appropriated to beware of those patients, although the threshold of pain intensity is yet to be determined [16].

As theorized in adults, yet to be demonstrated, psychological pain is presumed to have a part in the developing of paediatric CRPS, maybe even in a more prominent way than for adults [17]. Neuropsychological functions affected are separated in three distinct groups, non-independent: altered corporal representation, decrease lateralised spatial cognition, altered superior cognitive functions non spatially lateralised. It has been shown that a number of those symptoms can be associated with a larger disturbance of parietal function. In several studies have been shown the existence of anxiety in children diagnosed with CRPS, who often have a favourable social background, but find schooling stressful, with sometimes the presence of learning disabilities. Some studies have found recent emotional trauma prior to the beginning of symptoms. Although some patients showed an anxious proclivity, it isn't a significant risk factor of recurrences. Same goes for depression issues.

Some studies, as well as this one, raise the question of an inappropriate investment of the familial entourage of the young patient. Pillemer and Micheli identified psychological risk factors of complications for sport injuries in children [18]. Were cited overinvestment in education, familial stress, under or overinvestment of one or more of the parents.

Treatment in weekday hospitalisation allowed for a change of the patient usual environment, which could impact those inappropriate investments. For one of this cohort's patients, an underinvestment of the father towards the patient, in favour of her siblings, had been shown. Identification of this allowed for adjustment, and acceleration of clinical progress. Considering those constataions, it could be interesting to alert parents about those investment issues, if existing, as soon as the beginning of care.

Paediatric CRPS needs interdisciplinary care, involving physiotherapy, psychotherapy, and pain-control. Physiotherapy coupled with occupational and cognitive-behavioural treatment is the most acclaimed option [3].

This treatment plan has several setbacks. First, as observed in this study, psychological care isn't always accepted by patients. Several reasons can be thought of, stigmatisation of psychological issues for one, or time constraints, because of the child's schedule, or his parents. Some patients lived in this study more than an hour away from the hospital where the care was provided. Some patients took part in hypnotherapy sessions, of which the efficacy in this situation is still to be studied.

Physiotherapy treatment also has its setbacks. First off, the difficulty of accessibility to a physiotherapist, who are few and even fewer educated on CRPS treatment. Physiotherapeutic care for CRPS in children is also to be discussed. Moseley protocol is largely used for adults, although sometimes criticised [19]. As of yet, no studies have been conclusive towards a more appropriate treatment protocol for children. Establishment of a list of CRPS-trained physiotherapists could help in the better and quicker treatment of patients.

Pharmaceutical treatment must be kept for unresponsive patients. No guideline for paediatric patients has been established. Several patients in this study had been treated by PREGABALINE and GABAPENTINE, prior to their initial assessment in the pain ward, with no effect. Those drugs had sometimes been prescribed for long periods. Although a few studies had had encouraging results with those drugs, little to no efficacy is seen in reality [1]. A Canadian study recently showed frequent use of drugs in paediatric CRPS, with PARACETAMOL and NSAIDS in first line, and anti-epilepsy drugs in second [20].

Continuous regional anaesthesia was used in this study and can be an option to facilitate sustained rehabilitation when failing because of the pain felt by young patients. Continuous regional anaesthesia's efficacy has been proved in paediatric type I CRPS, by notably allowing a more efficient physiotherapy. Studies' results tend towards an improvement in mobility recovery [21]. Unlike in this study, motor blocks were more significant. Future studies could clarify regional anaesthetic use in CRPS' treatment, and its specificity. Ambulatory technical feasibility of this treatment is still being studied, although limits of an ambulatory technic could again be the lack of extra-hospital health professionals [22].

Several other technics have been thought of: electropuncture, oxygen and ozone treatment, rTMS (repetitive Transcranial Magnetic Stimulation), vagal nerve stimulation. One meta-analysis taking interest in rTMS showed promising results in adult patients with CRPS [23].

CRPS is a public health matter, with significant costs. Quality of life is also greatly impacted, with amputation being an option in the more severe cases. Although prognosis is better amongst children, a high recurrence rate can impact important formative years. A clear line of treatment and the identification of recurrences' risk factors is necessary. Long time impact of paediatric CRPS also needs to be studied. Parents' information about the risks of recurrence and the need to keep a steady involvement with the patients could be part of the treatment.

Some limits are important to note in this study. The small sample size has impacted the comparability of the two groups of participants, which makes those results hard to extend to the entire paediatric population suffering from CRPS. The delay in treatment can also be attributed to the localisation of the study, this area lacking physicians. This study being retrospective, data was non-homogenized, especially for treatment having been given prior to the initial consultation at the center. All patients were evaluated by the same medical team, which is appreciable, CRPS' diagnosis being subjected to clinical experience.

Use of the HAD scale is also a limit, this scale having been created for adult patients. Children having been helped by their parents; answers might have been influenced. Several scales are currently under examination for psychological assessment in children. The Behaviour Assessment System for Children seem to be an interesting tool but has yet to be translated for French speaking population.

This study has used a single cohort of patients from 0 to 18yo. Recent data in studies show that CRPS could be different in children or in teenagers. A comparative study of recurrences in those two groups is yet to be made.

## Conclusion

This retrospective study, using a small sample, described demographic and psychologic characteristics of paediatric CRPS. As shown in previous studies, patients are mainly female, around 13years old, with a lower limb initially cold CRPS. Despite the small sample size, this study showed a high recurrence rate, with initial pain intensity being the only significant factor. Those results have yet to be confirmed by a large-scale study. Steady parental involvement could be a way of diminishing this rate.

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