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Pediatric Complex Regional Pain Syndrome With and Without a History of Prior Physical Trauma at Onset

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Objective: To determine whether differences exist between children with complex regional pain syndrome (CRPS) who identify an inciting physical traumatic event (group T) versus those without such history (group NT).

Methods: We performed a single-center, retrospective study of children diagnosed with CRPS, 18 years old or younger, presenting between April 2008 and March 2021 and enrolled in a patient registry. Abstracted data included clinical characteristics, pain symptoms, Functional Disability Inventory, psychological history, and Pain Catastrophizing scale for children. Charts were reviewed for outcome data.

Results: We identified 301 children with CRPS, 95 (64%) reported prior physical trauma. There was no difference between the groups regarding age, sex, duration, pain level, function, psychological symptoms, and scores on the Pain Catastrophizing Scale for Children. However, those in group T were more likely to have had a cast (43% vs 23%, $P < 0.001$). Those in group T were less likely to experience complete resolution of symptoms (64% vs 76%, $P = 0.036$). There were no other outcome differences between the groups.

Discussion: We found minimal differences in children with CRPS who report a prior history of physical trauma to those who do not. Physical trauma may not play as significant a role as immobility, such as casting. The groups mostly had similar psychological backgrounds and outcomes.

Key Words: complex regional pain syndrome, trauma, childhood, outcome, cast, functional neurological disorder

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Childhood-onset complex regional pain syndrome (CRPS) differs from adult-onset CRPS in significant ways, including more typically lower limb involvement, decreased bone uptake on scintigraphy, and generally a better outcome.[1–9] Severe trauma, such as a fracture, is much more commonly mentioned as a preceding event before the onset of adult CRPS.[7] The Budapest criteria for adult CRPS requires disproportionate pain to an inciting event, usually a fracture or crush injury.[10] However, the incidence of preceding trauma in childhood-onset CRPS has widely varied. Low et al[11] and Wilder et al[12] report preceding injury in 96% and 80%, respectively, of 92 patients. Others have reported preceding injury in 40% to 54% of 171 patients.[1–3,6] In addition, psychological events, such as military deployment and family issues, have been associated with the onset of childhood CRPS.[13,14] Psychological factors and adverse life events are frequently reported in children with CRPS and other pain conditions.[6,15–19] It seemed possible that children who developed CRPS after a clear history of trauma may differ in demographic or psychological variables from those without such a history. Therefore, we studied children with CRPS with and without a preceding physical trauma history to determine whether differences exist. Variables explored include demographic, autonomic changes (cold, cyanotic, swollen, sweaty, and dystrophic skin), pain score, Functional Disability Index (FDI), Pain Catastrophizing Scale for Children (PCS-C), and self-reported psychological issues and outcomes. We hypothesized that children without a history of physical trauma would have a longer delay in diagnosis, fewer autonomic changes, more psychological abnormalities, and more coexisting and subsequent diagnoses, such as functional neurological disorder (FND) and suicidal ideation than children reporting a physical trauma preceding the onset of CRPS.

METHODS

This was a retrospective cross-sectional cohort study of patients 18 years old or younger, diagnosed with CRPS between April 2008 and March 2021 and enrolled in an Institutional Review Board approved patient registry. All patients were seen at a specialized amplified pain clinic as a part of the Rheumatology division by 1 of 3 physicians, 1 of 2 nurse practitioners, and 1 of 4 psychologists. A uniform medical record template was used. This prospective patient registry captures data from patients' initial clinic visits and subsequent follow-up visits. It includes ~96% of all new patients. CRPS was defined as pain disproportionate pain to the stimulus without other medical explanation, such as inflammation, along with at least 2 autonomic signs (cold, cyanosis, swelling, perspiration changes, and skin changes).[10,20] Patients who had CRPS could also have

diffuse or localized amplified pain, diffuse being 5 or more body parts in pain without autonomic changes and localized defined as <5 body parts in pain.[21] Minor trauma was defined as a twist, sprain, kick, pulled on or jerked, a fall without fracture, or prolonged use, such as running. Major trauma was defined as a prior fracture, surgery, or both. The traumatic event had to be in direct proximity in time (most were within days but up to a month, especially if pain followed casting) and the site of CRPS.[7] We analyzed casting without including boots, splints, and slings since only casts guarantee immobility.

Patient data included demographics, family history, medical, surgical, and psychiatric history, physical examination findings, and a review of medical interventions. Self-reported psychological variables and patient-reported outcomes included the FDI and verbal pain score (0 to 10, 10 being worse).[22] During the latter part of the study period, the PCS-C was administered to the patient and parent.[23] Data from patient questionnaires, including psychological variables, such as prior mental health diagnoses, anxiety, and depression, were abstracted into the secure Research Electronic Data Capture (REDCap) database system. Additional and confirmatory data, including that from the psychologist obtained at the clinic visits, were abstracted to create the registry database. The treatment for patients treated by our team was focused on physical and occupational therapy along with mental health therapy without specific pain medication or procedures as outlined.[6] Outcomes were determined from a chart review of the electronic medical record. Localized and diffuse amplified pains were defined as per Sherry et al.[21] Patients were said to have complete symptom resolution if they resolved all symptoms and signs of CRPS. Functional outcomes were by the patient report (including participation in physical activities, such as sports), medical evaluation (such as gait), and, when available, FDI scores (functional [0 to 12], mild disability [13 to 20], moderate disability [21 to 29] and severe disability [$\geq$30]).[22] Those with a diagnosis of FND had multiple manifestations that were tabulated as FND symptoms. All variables reported were from the initial clinic visit, and subsequent visits were only used to ascertain outcome variables.

Descriptive statistics were calculated as frequency (%) for categorical variables and median (interquartile range) for continuous variables. Wilcoxon rank-sum test and Pearson χ^2 test or Fisher exact test were used to compare continuous and categorical clinical characteristics between groups, as appropriate. P values <0.05 were considered statistically significant. All calculations were performed in *R* Statistical Software, Version 4.1.2.

RESULTS

We identified 301 patients, 167 (55%) of whom reported prior physical trauma, and 150 (90%) of these patients reported a minor trauma. Demographic variables are shown in Table 1, and both groups were similar in age, sex, and race and were typical of pediatric CRPS.[24] The vast majority were white (93%), and those self-identifying in the non-white categories were allowed to pick multiple races, so we had 22 patients identify as white Hispanic (12), black (11), Asian (3), native American/Alaska native (1), and other (10). Both groups were significantly disabled, with high FDI scores reported by the patient and parent. There was no difference between the groups in terms of duration of symptoms, allodynia, presence or number of autonomic changes, and pain intensity. There was no difference between those with and without a history of physical trauma regarding the presence of diffuse amplified pain (14% vs 10%, respectively) and areas of localized amplified pain in addition to the area of CRPS (16% vs 16%, respectively).

Those with preceding physical trauma were more likely to have been cast (43% vs 23%, $P < 0.001$). Casting, regardless of a prior history of trauma, did not predict outcome ($P = 0.622$). Although it did not reach the level of significance, more patients reporting physical trauma had received a prior nerve block (20% vs 12%, $P = 0.063$) and had CRPS involving the leg (83% vs 75%, $P = 0.067$). Only those with prior physical trauma reported being involved in a lawsuit regarding their CRPS. (6 vs 0, $P = 0.006$)

There were no differences between the groups regarding the presence of autonomic changes or the total number of autonomic changes (Table 2).

The psychological aspects are shown in Table 3. Although more patients without a history of physical trauma reported prior anxiety (28% vs 19%, $P = 0.062$), this was not significant. There was no difference in those reporting suicidality, disordered eating, malnutrition due to abdominal pain, and FND (all $P > 0.5$). FND symptoms that significantly interfered with function and were not pain-related were observed in 30% and consisted of motor stiffness (n = 33), pseudoseizures (n = 3), paralysis (n = 41), blindness (n = 2), memory loss (n = 2), loss of voice (n = 1), gait abnormalities (n = 11), tremor (n = 7), visual disturbance (n = 19), fainting (n = 3), or other/mixed (n = 37). These patients also reported severe dizziness (n = 22) and incapacitating symptoms of dysautonomia (n = 2). While FND symptoms overall were not significant between those with and without a history of physical trauma (32% vs 28%, respectively, $P = 0.5$), paralysis was more common in those who reported a history of physical trauma preceding their CRPS (17% vs 9.0%, respectively, $P = 0.035$).

The outcomes from subsequent visits are shown in Table 4. We had follow-up notes available on 259 patients (86%). The average duration of follow-up in those who reported no prior trauma was 31 months (range: 1 to 166 months), and in those reporting a trauma, 32 months (range: 1 to 160 months). Although most were fully functional and resolved their autonomic changes, a significant number reported continued pain. The last median FDI score available for those without symptoms (n = 145) was 3 (0, 7), and in those with continuing symptoms (n = 84), including pain or other clinical symptoms, such as an FND, was 12 (5.5 to 23). The last available median FDI in those reporting with (n = 135) a history of trauma was 5 (2 to 13) and without a history of trauma (n = 94) was 5 (1 to 12). Of the 259 patients, 22% reported other pain syndromes, such as abdominal pain (n = 14), head pain (n = 11), or multiple pains (n = 33), as well as subsequent episodes of CRPS (n = 14) or amplified pain (n = 51). There was no significant difference between those who reported prior physical trauma or not and the development of subsequent pain symptoms ($P = 0.6$). In addition to the clinical symptoms reported in Table 4, there were notably 2 patients without a history of trauma who were diagnosed with factious disorder and 1 with a history of trauma diagnosed with self-injury. Over half of each group had no subsequent episodes of pain, and over 70% of each group had no other clinical symptoms.

DISCUSSION

An inciting event is a requirement in the Budapest criteria for adult CRPS.[10] These criteria have not been

TABLE 1. Demographic Data on the 301 Children With CRPS

	No trauma 134 (45%); n (%)	Trauma 167 (55%); n (%)	*P*
Age	13.00 (11.25, 15.00)	13.00 (11.00, 15.00)	0.6
Sex			> 0.9
Female; n = 259 (86%)	259 (86)	144 (86)	—
Male; n = 42 (14%)	19 (14)	23 (14)	—
Pain duration (mo); n = 299	7.00 (4.00, 15.75)	9.00 (5.00, 18.00)	0.3
Race (n = 301)			0.3
White; n = 279 (93%)	122 (91)	157 (94)	—
Non-white; n = 22 (7%)*	12 (9)	10 (6)	—
Upper extremity	44 (33)	46 (28)	0.3
Lower extremity	100 (75)	139 (83)	0.067
Both extremities	23 (17)	24 (14)	0.5
Positive fracture history; n = 263	61 (55)	91 (60)	0.054
FDI patient	27.00 (15.00, 35.75)	28.00 (16.00, 35.00)	0.9
FDI parent; n = 300	25.50 (14.00, 34.00)	26.00 (15.25, 34.00)	0.8
Attending regular school	88 (66)	126 (75)	0.063
Previous cast†	31 (23)	71 (43)	< 0.001
Nerve block	16 (12)	33 (20)	0.068

*See text for details.
†Casts do not include boots, splints, or slings.
CRPS indicates complex regional pain syndrome; FDI, Functional Disability Inventory; n, number of patients.

validated for children but are generally used.[20] Children, however, frequently do not report an inciting event and, in our population, 45% did not report prior physical trauma, which is in keeping with other reports.[1–3,6,11,25,26] There were no demographic differences between these groups as well as no difference in the duration of symptoms. One would think those without a history of physical trauma would present later, but they did not. In addition, psychological factors seem to play a role in childhood CRPS.[1,16,24,27–29] We were, therefore, very interested to see whether those children without a history of prior physical trauma would have reported more psychological issues, that is, be psychologically primed, but they were not, save that there was a suggestion they reported more premorbid anxiety. Those not reporting prior physical trauma were more likely to have complete symptom resolution of their CRPS but were equally likely to those with a history of physical trauma to have subsequent chronic pain, be it CRPS or not, and other clinical outcomes, such as FND symptoms, disordered eating, suicidality, or dysautonomia symptoms. These outcomes have been documented as complicating features in children with CRPS and chronic pain.[30,31] CRPS is one aspect of amplified pain in general, so it is not unexpected that there would be an overlap of children with both CRPS and other forms of amplified pain.[32–34] Likewise, the comorbidities seen in amplified pain are not unexpected in those with CRPS.[21,35,36]

We avoided labeling those with a prior history of physical trauma as traumatic CRPS since the relationship to physical trauma is not clearly causal. All children have a history of physical trauma, and many with a recent history of physical trauma reported serval traumas preceding the onset of CRPS. The report of injury could be so mild, such as playing 3 soccer games one day without a specific event happening, that it is questionable that a physical injury, per se, occurred. Cause and effect mentality is a strong bias and may cloud the issue.[37,38] The time between the physical trauma and onset of CRPS was impossible to determine in our patient population as the pain was generally immediate and continuous, but the onset of autonomic changes was very poorly reported. Occasionally, the autonomic changes were not reported by the patient or family but were observed during the initial visit. Others have reported that the onset of CRPS after a traumatic event was very quick, within the first week and, in many cases, is immediate, such as after an injection.[7,39] As in our patients, others have reported multiple sites of CRPS.[40,41]

The reported physical trauma could be quite minimal, and only 10% of our population had a preceding major trauma, such as a fracture. One may hypothesize that the trauma led to immobilization and that the trauma itself played a role only in localizing the area where CRPS was to develop in a susceptible host. Many of the physical traumas were reported with emotionally laden language, such as being kicked "by the meanest girl" or injured by someone who "did not care." We did not include

TABLE 2. Physical Features of CRPS in 301 Children With CRPS

	No trauma; n (%)	Trauma; n (%)	*P*
Allodynia	105 (78)	139 (83)	0.3
Autonomic changes			
Cold	128 (96)	151 (90)	0.091
Color change/blue	124 (93)	148 (89)	0.3
Swelling/edema	108 (81)	142 (85)	0.3
Sweat	43 (32)	68 (41)	0.12
Hair changes	3 (2)	3 (2)	> 0.9
Skin changes	5 (4)	4 (2)	0.5
No. autonomic changes			
1*	2 (2)	5 (3)	—
2	25 (19)	30 (18)	—
3	69 (51)	80 (48)	—
4	37 (28)	48 (29)	—
5	0	4 (2)	—
6	1 (1)	0	—

*In 7 patients, 6 had a very cold extremity and 1 marked swelling. All had a history of other transient autonomic changes but not documented by us.
CRPS indicates complex regional pain syndrome.

TABLE 3. Psychological Aspects of Children* With CRPS at Presentation

	No trauma (n = 134); n (%)	Trauma (n = 167); n (%)	*P*
History of anxiety (n = 301)	37 (28)	31 (19)	0.062
Suicidality (n = 301)	11 (8)	14 (8)	>0.9
Disordered eating (n = 301)	1 (1)	3 (2)	0.6
Malnutrition (n = 301)	1 (1)	1 (1)	>0.9
FND symptoms (n = 301)	38 (28)	53 (32)	0.5
PCS-C scores			
Total score (n = 132)	30.00 (23.00, 36.00)	32.00 (26.00, 40.50)	0.3
Helplessness (n = 132)	14.00 (9.00, 18.00)	15.00 (10.50, 19.00)	0.5
Magnification (n = 132)	4.00 (3.00, 7.00)	6.00 (3.00, 8.00)	0.2
Rumination (n = 133)	12.00 (10.00, 14.75)	13.00 (10.00, 15.00)	0.6

*Psychological variables ascertained at initial evaluation by history, and examination by the physician and psychologist.

CRPS indicates complex regional pain syndrome; FND, functional neurological disorder; n, number of patients; PCS-C, Pain Catastrophizing Scale for Children.

psychological trauma, although frequently, psychological trauma accompanied physical trauma, such as being taken by ambulance after a motor vehicle accident or it occurred in isolation, such as a father being deployed to a war zone.[13] The role of psychological trauma, including adverse childhood events, should be further explored.

It makes sense that those reporting a history of physical trauma were more likely to be cast. The cast may have contributed to the CRPS since immobilization is deleterious in CRPS, albeit probably unavoidable in cases of true fractures, but not all casts were placed for documented fractures, but for suspected Salter I fractures or due to the degree and persistence of pain. We did not have specific data on the duration of casting or if the pain was reported while in the cast. It makes sense to limit casting to when necessary, especially for patients without a history of trauma. It may be helpful to encourage the movement of the limb, fingers, or toes as much as possible while in a cast. Patients with a history of physical trauma may have prompted more invasive treatment, such as nerve blocks, rather than opting for physical and occupational therapy, which could possibly exacerbate a true injury.

The fact that we could find minimal differences between these groups may indicate that physical trauma is not a driving force in most children with CRPS. Those with spontaneous CRPS have all the features of CRPS with the same autonomic changes, degree of pain, amount of dysfunction, and allodynia. Those with a history of physical trauma may fare worse, and it may be due to innate differences in the condition, early casting, and possibly more invasive therapy upfront.

There was no difference between the groups and subsequent other clinical outcomes, such as other pain targets, FND symptoms, suicidality, disordered eating, and dysautonomia symptoms. We had a few patients with multiple somatic symptoms, self-injury, and factitious disorder. These outcomes need to be appreciated and monitored in this population of children.

There are limitations to this study. It is a single-center study, and the results may not be generalizable. Since we are a quaternary referral center, some of the cases may be more severe than is typical. Several patients were only seen once and did not have therapy or further care with us. The outcome data are limited to what were in the medical record, and care could have been sought elsewhere. Many of the measures were self-reported, including the history of physical trauma and psychological comorbidities, which introduces an unknown degree of bias. Patients would report an injury in an adjacent body location to the area of CRPS and think it related, whereas we did not. We did not administer specific questionnaires to assess anxiety and depression. As this was not a treatment study, we did not select the patients who were treated in our outpatient, day hospital, or hospital treatment programs.

TABLE 4. Outcome in Children Seen for CRPS

n = 269	No trauma; n (%)	Trauma; n (%)	*P*
Complete resolution of symptoms	92 (76)	95 (64)	0.036
Fully functional n = 259	118 (98)	137 (93)	0.069
Pain outcomes (n)	114	145	0.6
Another CRPS episode	8 (6)	6 (4)	—
Diffuse amplified pain	14 (12)	19 (13)	—
Localized amplified pain	8 (7)	10 (7)	—
Abdominal pain	3 (3)	11 (8)	—
Head pain	5 (4)	6 (4)	—
Multiple pains	18 (16)	15 (10)	—
No subsequent pain symptoms	58 (51)	78 (54)	—
Other clinical outcomes			>0.9
FND symptoms	13 (11)	17 (12)	—
Disordered eating	1 (1)	1 (1)	—
Dysautonomia symptoms	3 (3)	8 (6)	—
Multiple of the above	8 (7)	11 (8)	—
No subsequent symptoms	85 (75)	103 (71)	—

CRPS indicates complex regional pain syndrome; FND, functional neurological disorder; n, number of patients.

CONCLUSIONS

A physically traumatic inciting event may be less important in children with CRPS, and the differences between those with and without such a history are minimal on the surface. A history of physical trauma may predispose one to get a cast, and maybe more invasive therapy and less of a chance for resolution of all symptoms, but most still achieve full function.

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