Movement disorders associated with complex regional pain syndrome in children

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The aim of the present study was to review the history, clinical course, treatment, and outcome of movement disorders in children and young people with complex regional pain syndrome (CRPS). Case notes were reviewed retrospectively of children and young people who presented with movement disorders in CRPS to our tertiary paediatric pain service over a period of 13 years. Ten children with CRPS presented with movement disorders (eight females, two males). The age at first presentation with symptoms of CRPS ranged from 8 to 15 years (mean 11y 2mo, median 13y). The most common movement disorder was dystonia (*n*=8), followed by tremors (*n*=3) and myoclonus (*n*=3); two patients had all three movement disorders. The movement disorder affected mainly the lower limb (*n*=9) with a predilection for the foot (*n*=7) and was frequently initiated by minor trauma (*n*=7). Follow-up ranged from 6 months to 14 years. The outcome was variable, with good prognosis in nearly half of the cases: four children experienced complete resolution of symptoms. Two children showed a slight improvement. Four children showed no improvement. Movement disorders in CRPS are under-recognized in children. The management has to be multidisciplinary with an expertize in paediatric pain.

Complex regional pain syndrome (CRPS) is a disorder that typically affects females after minor to severe trauma to an extremity. This has been known by various names, including reflex sympathetic dystrophy and causalgia.[1–4] The current terminology of CRPS was agreed at a consensus workshop in Orlando, Florida, in 1994.[5,6]

The main characteristics of CRPS are the presence of continuing pain that is disproportionate to the inciting event, with evidence of oedema, skin blood flow changes, or abnormal sudomotor activity in the region of the pain.[7,8] The pathophysiology of CRPS is not fully understood, and there is a lack of consensus on the optimal treatment.[9,10] Physiotherapy and psychological support are the mainstay of treatment. Several pharmacological agents have been tried with variable success, including sympathetic blockade and spinal analgesia.

CRPS was considered rare among children until relatively recently. It is now understood that this may have been due to under-recognition of the disorder. Paediatric CRPS differs in many respects from adult CRPS.[11–14] There is an extremely high female preponderance in the paediatric population,[14,15] the lower limb is more often affected, and significant trauma is a much less frequent precipitating event than in adults. Children are also considered to have a better response to non-invasive treatment than adults. In children, psychological factors are thought to play a greater role.[13,15–17] Hence treatment that has been reported to be successful in adults may not necessarily apply to children.

Patients with CRPS may also suffer from movement disorders, including tremor, myoclonus, and dystonia.[18–20] The increasing awareness of the association of CRPS and movement disorders has resulted in a proposal to add this clinical category to the new criteria set.[21] The interval between onsets of CRPS and movement disorder is poorly understood, with some investigators considering a cause–effect relationship between trauma and peripherally induced movement disorder to be unlikely if the interval is greater than 1 year.[22]

To our knowledge, this is the first paediatric study looking at movement disorders and CRPS. We reviewed the patient and clinical characteristics, clinical course, treatment, and outcome of movement disorders in children and young people with CRPS.

METHOD

Patients

All patients who were diagnosed with CRPS at our tertiary paediatric pain service from August 1994 to July 2007 were identified from the database. The pain team consisted of a consultant anaesthetist, a consultant paediatric neurologist with an interest in movement disorders, psychologists, physiotherapists, an occupational therapist, and a clinical nurse specialist. International Association for the Study of Pain criteria were used to make the initial diagnosis of CRPS (Table I) The medical records of children who developed movement disorders during the course of management of their CRPS were reviewed. After consultation with the hospital clinical research committee, it was concluded that formal ethical approval was not required for the study.

Data collection

The medical records of all children who were diagnosed with CRPS and movement disorders were reviewed retrospectively for the study period. The data were analyzed using Microsoft Excel and its associated statistical package.

RESULTS

Thirty-two children were identified over the study period as having been diagnosed with CRPS (27 females, five males). Of these 32 children, 10 who developed movement disorders during the course of management were included in the study (Table II). None of these 10 children had any movement disorder before the onset of CRPS. Follow-up ranged from 6 months to 13 years, most children (n=9) being followed for more than 2 years.

Table I: Complex regional pain syndrome type I diagnostic criteria

1.	The presence of an initiating noxious event or a cause of immobilization
2.	Continuing pain, allodynia, or hyperalgesia, which is disproportionate to any inciting event
3.	Evidence at some time of oedema, changes in skin blood flow, or abnormal sudomotor activity in the region of pain
4.	This diagnosis is excluded by the existence of conditions that would otherwise account for the degree of pain and dysfunction

Demographics

Of the 10 children who had movement disorders with CRPS, eight were females. The age at first presentation with symptoms of CRPS ranged from 8 to 15 years (mean 11y 2mo, median 13y). There was no significant difference in the age of onset between males and females.

Clinical presentation

The movement disorder affected the lower limb in nine of the 10 children. There was an obvious predilection for the foot in seven patients. In one young person the wrist and hand were affected and another patient had head-nodding movements. Seven of the 10 patients reported a possible precipitating factor, six of whom had minor trauma to the same extremity and one had psychological stress in the family, including father's ill health. There was no significant past medical history in five children, two children had been receiving psychiatric care for possible eating disorders, and another three had recurrent abdominal pain that had been investigated extensively but no cause had been elucidated.

The most common symptom at presentation was severe pain in the extremity, which worsened on movement. Other symptoms were colour and temperature change in the extremity, changes in the appearance of hair and nails on the painful extremity, lack of or excessive sweating and increased sensitivity to touch.

Nine children developed movement disorders within the first year of diagnosis of CRPS (range 1–10mo). One child developed a movement disorder 16 months after the first onset of symptoms but still within 1 year after the formal diagnosis of CRPS.

Dystonia was the most common movement disorder in our cohort. Six children had isolated dystonia and a further two had dystonia in addition to other movement disorders. Isolated tremors and isolated myoclonus occurred in one patient each. Dystonia was predominantly characterized by tonic flexion posture (Fig. 1). In the majority of the patients dystonia was limited to the distal extremity and most commonly involved the foot and ankle, where it mainly comprised plantarflexion, inversion, and external rotation with clawing of toes. In two children, dystonia extended proximally to involve the knee and the hip. In nine children, the movement disorder started in the same limb as the CRPS. In the remaining child, tremors and myoclonia started in the neck but then progressed to involve the same limb where the CRPS had started.

Combinations of dystonia, myoclonus, and tremors occurred in two children. Myoclonus and tremors involved the same extremity but tended to extend proximally to legs and thighs. Myoclonia and coarse tremors of head and neck were observed in one child who also had dystonia of

Table II: Characteristics of the 10 patients with complex regional pain syndrome and movement disorders

Age at first presentation	Sex	Body parts affected	Trigger factor	Movement disorder	Outcome of pain	Outcome of movement disorder	Intervention	Total duration of symptoms
13y	F	Right foot, right knee and right hand	Walking holiday	Dystonia	Complete resolution	Complete resolution	Intravenous, oral and epidural analgesia, guanithidine block, psychotherapy, physiotherapy	18mo
14y	F	Left foot	Left fifth metatarsal fracture sustained during physical education	Dystonia	Relapsing–remitting	Relapsing–remitting	Oral analgesia, psychotherapy, physiotherapy	Relapsed after 6mo remission; three relapses in 3y
8y	F	Right knee, neck	Right knee soft-tissue injury	Tremors	Partial resolution	Partial resolution	Intravenous, oral and epidural analgesia, guanithidine block, acupuncture, ketamine, psychotherapy, physiotherapy	8y, still ongoing at the last follow-up
11y	M	Right foot	Avulsion fracture right fifth metatarsal	Exercise-induced dystonia, tremors, myoclonus	Persistent	Persistent	Intravenous, oral and epidural analgesia, guanithidine block, acupuncture, ketamine, dopamine agonists, psychotherapy, physiotherapy	6y, still ongoing at the last follow-up
11y	F	Right leg	None	Myoclonus	Complete resolution	Complete resolution	Oral analgesia,guanithidine block	7mo
13y	M	Left hand	None	Dystonia	Relapsing–remitting	Relapsing–remitting	Intravenous, oral and epidural analgesia, guanithidine block, psychotherapy, physiotherapy	11y, still relapses as an adult
13y	F	Right leg	Trivial right knee injury during netball	Dystonia	Partial resolution	Persistent dystonic posture, no functional impairment	Intravenous, oral and epidural analgesia, guanithidine block, hyperbaric oxygen, psychotherapy, physiotherapy	13y
15y	F	Right foot	None	Dystonia	Complete resolution	Complete resolution	Intravenous, oral and epidural analgesia, guanithidine block, psychotherapy, physiotherapy	8mo
14y	F	Left foot	Trivial netball injury	Dystonia	Complete resolution	Complete resolution	Oral and epidural analgesia, guanithidine block, psychotherapy, physiotherapy	17mo
13y	F	Left leg, left foot	Sprained ankle	Dystonia, tremors, Myoclonus	Persistent	Persistent	Intravenous, oral and epidural analgesia, guanithidine block, psychotherapy, physiotherapy	2y, still ongoing

the right foot. Dystonia was intermittent in these two children.

Outcome

All children and young people were treated at our tertiary paediatric pain service by our experienced pain team. The main treatment modalities were analgesics, including spinal analgesia and sympathetic blockade, intensive physiotherapy, and psychological support to the child and the family.

Four patients experienced a complete resolution of symptoms at final follow-up. Two showed a slight improvement in their dystonic posture, with some relief in pain. The remaining four showed no improvement or had worsened when last followed up, with involvement of more than one extremity in two children. Both dystonia and pain worsened in the latter group. As a result, their mobility was affected severely and three children relied largely on a wheelchair for mobility. These four children were investigated for progressive neurological disorders but had normal neuroimaging. One child in the good-outcome group had a history of a psychosomatic disorder. All children in the poor-outcome group had a history of a psychosomatic disorder. In the good-outcome group, complete resolution was achieved within 18 months of diagnosis (range 24–68wks, mean 34wks). This is in contrast to the 22 children and young people with CRPS who did not develop movement disorders, 14 of whom showed complete resolution of symptoms within the first year and the remaining eight had waxing and waning symptoms until their last follow-up within paediatric services. Thus the clinical course was more protracted and the disease duration was longer in the children and young people with CRPS who developed movement disorders than in those who did not.

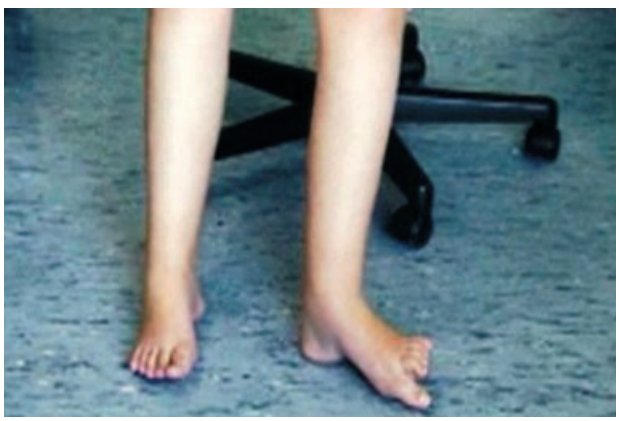

Figure 1: Dystonic posturing of left foot in complex regional pain syndrome.

DISCUSSION

CRPS is not uncommon, although it was believed to be rare in children. This is perhaps due to under-recognition of the disorder and secondary to a lack of consensus on definitive criteria for the diagnosis.

Movement disorders in CRPS have been reported widely in the adult population but, to our knowledge, our study is the first reporting movement disorders in CRPS in children and young people. This study shows that movement disorders in paediatric CRPS are similar to those reported in adults, although there are differences in the presentation of CRPS in children and adults. Of 32 paediatric patients who presented with CRPS during our study period, 10 developed movement disorders. This is much less than the 65% reported for adults from a tertiary neurology service. The high percentage in that series could have reflected referral bias, because CRPS patients with neurological symptoms would be more likely to be referred to a neurology clinic.[23]

In our study, only one child in the good-outcome group had a previous psychosomatic disorder, compared with all four in the poor-outcome group. It is plausible to conclude that a degree of psychological distress may be an important adverse prognostic indicator in children with CRPS and movement disorders. In our study, dystonia was the most common movement disorder, followed by tremor and myoclonus. We found that the children developed movement disorders in the same limb as the CRPS. Although various treatments were tried in these children, we did not find improved outcomes in movement disorders with a specific treatment. We found that CRPS in children may evolve into a disabling disorder with prominent motor involvement of one or more extremities.

There are various causes of dystonia, including genetic mutations, focal injuries to the nervous system, metabolic disorders, and exogenous toxins. The prevalence of limb-onset dystonia in primary dystonias is 2.1 per million.[24] Dystonia can be caused and treated by interventions targeting the basal ganglia. When a focal site can be identified, the most common site of injury is in the basal ganglia. However, there is increasing evidence that dystonia results from dysfunction of neural circuits rather than from dysfunction of neurones in a single nucleus. Basal-ganglia dysfunction can manifest as impaired physiological function at multiple levels of the central nervous system, such as abnormal cortical, brainstem, and spinal-cord function, even though the primary abnormality is in the basal ganglia.[25,26] Recent studies have shown that the pathophysiology of dystonia is more complex, with deficits in sensory processing and complex interactions between the basal ganglia, cerebellum, and peripheral nervous system.[27–29] Trauma and psychological stress have been reported as triggers in

genetic dystonia, such as rapid-onset-dystonia parkinsonism, but our children did not have the history and clinical phenotype of this form of parkinsonism.[30] The association of CRPS with mitochondrial disorder has been described.[31] In that series, there was a maternal pattern of inheritance of mitochondrial disorder with autonomic-related symptoms.[31] In our cases, there was no positive maternal history suggestive of a mitochondrial disorder. There was also no evidence of multi-system involvement in the four children in whom the movement disorder worsened and it seems very unlikely that children in our series had a mitochondrial disorder according to the recent criteria.[32]

In CRPS, disinhibition has been demonstrated at both a spinal and a cortical level but the sequence of involvement remains obscure.[33,34] Our findings, along with adult data, suggest the existence of a subgroup of patients with CRPS who develop movement disorders. This probably reflects the involvement of a distinct biological pathway, which may be induced by the mechanism underlying CRPS.

The relatively low incidence of CRPS in the paediatric population explains the small sample size in our study compared with adult studies. Nevertheless, as the sample has been drawn together over a period of 13 years in a tertiary paediatric pain service, we feel that the conclusions are valid. As with any retrospective study, our study has limitations. Information on the exact dates of onset is less accurate than would have been obtained with a prospective design.

This study is the largest reported paediatric series of CRPS patients with movement disorders. The clinical course of movement disorders in CRPS is not fully understood. Our study suggests that dystonia is the most common movement disorder in paediatric CRPS, similar to the results from adult studies, with the lower limb being most commonly affected. Eight children in our study had dystonia either in isolation or in combination with other movement disorders, so it is difficult to ascertain whether other movement disorders would portend any prognostic significance. Because of the small number of patients, the outcome and long-term prognosis should be interpreted with caution. Treatment in a multidisciplinary team with expertise in paediatric pain management is recommended.

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