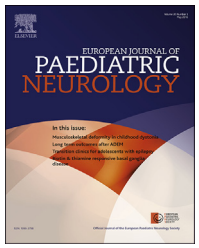
Official Journal of the European Paediatric Neurology Society



Original Article

Progression to musculoskeletal deformity in childhood dystonia

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ARTICLE INFO

Article history:
Received 23 September 2015
Accepted 7 February 2016

Keywords:
Dystonia
Contracture
Spasticity
Childhood
Deformity

ABSTRACT

Aim: Dystonia is a movement disorder characterized by involuntary muscle contractions, resulting in abnormalities of posture and movement. Children with dystonia are at risk of developing fixed musculoskeletal deformities (FMDs). FMDs cause pain, limit function and participation and interfere with care. We aimed to explore factors relating to the development of FMD in a large cohort of children with dystonia.

Method: The case notes of all children referred to our Complex Motor Disorder service between July 2005 and December 2011 were reviewed. Data from 279 children (median age 9 years 10 months, Standard Deviation 4 years 2 months) with motor disorders including a prominent dystonic element were analyzed. Parametric accelerated failure time regression was used to identify the factors related to development of contractures.

Results: FMDs were present at referral in more than half (n = 163, 58%) of cases. Three quarters (n = 120, 74%) of children with FMD had deformities around the hip, and 42% had spinal deformity (n = 68). Compared to pure primary dystonia, FMD onset was earlier with a diagnosis of secondary or heredodegenerative dystonia, and a mixed spastic–dystonic phenotype (all $p < 0.001$). FMD onset was also earlier with increasing Gross Motor Function Classification System (GMFCS) level ($p < 0.001$). The effect of aetiological classification was lost when controlling for GMFCS level and motor phenotype.

Interpretation: Children with secondary or heredodegenerative dystonia are at greater risk of progression to FMD compared to primary dystonia, likely due to more severe dystonia within these groups. Children with additional spasticity are at particular risk, requiring close monitoring.

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http://dx.doi.org/10.1016/j.ejpn.2016.02.006
1090-3798/

Dystonia is characterized by "*sustained or intermittent muscle contractions causing abnormal, often repetitive, movements, postures, or both*".[1] Dystonia has most commonly been classified on an aetiological basis as "primary", "primary-plus", "secondary" or "heredodegenerative".[2] In primary dystonia, dystonic movements are the only abnormality, in the absence of any exogenous cause and with normal neuroimaging. In Primary-plus dystonia other abnormal movements are present.[3] Secondary dystonia is a symptomatic disorder, arising due to a disease processes affecting the brain, often with additional neurological features. Heredodegenerative dystonias are those arising in the context of progressive neurodegeneration. Secondary dystonias are more common in childhood.[4,5] Whilst a move away from this terminology has recently been proposed,[1] it remains a useful way to classify dystonias from diverse aetiologies into groupings with common features for comparative work.

Dystonia in childhood can interfere with all domains of the International Classification of Functioning, Disability and Health (ICF) framework,[6,7] including impairment, activity and participation, with significant implications for future adult life.

In general, hypertonic movement disorders are associated with the development of fixed musculoskeletal deformity (FMD). FMDs cause pain, limit function, impair sleep and create difficulties with care. Without effective intervention, progression of FMD and worsening impairment of function will occur,[8–10] though the rate of this progression varies for each individual. Cerebral palsy (CP) has been the focus of much of the work around FMD development, which has been related to increasing impairment of function.[11,12] Most studies have focused on patients with predominantly spastic motor disorders (the most common motor phenotype in CP), with only small numbers of children with dystonic CP included. Large studies of FMD in children with dystonia are absent. We aimed to explore which clinical factors were related to the development of FMDs in a group of children and young people (CAYP) referred to our supra-regional complex motor disorder service (CMDS).

1. Method

All CAYP assessed by our CMDS between June 2005 and December 2012 were considered for inclusion in this study. Our service offers a supra-regional referral service for CAYP with dystonic motor disorders, primarily with view to assessment for suitability for ITB/DBS. Demographic/clinical characteristics were extracted from patient case notes. Details of musculoskeletal examinations performed by three of the authors were reviewed (MK and JL, Paediatric Neurologists with >10 years of experience, and KT, a Clinical Specialist Paediatric Physiotherapist with >10 years of experience working with children with complex neurodisability). Clinical features of CAYP in this cohort have previously been reported.[5,7]

A pragmatic definition of FMD was used: Fixed deformity of a limb/joint impairing function due to contracture (i.e. permanent tightening of non-bony tissue) and not due to active contraction, restricting daily activity/participation and/or impairing the delivery of care whether through a direct restriction of movement or secondary to pain/discomfort. When present, FMDs were categorized on the basis of body region affected into i) hip, ii) spine or iii) peripheral. Deformity at multiple regions was recorded when present.

Details of CAYP diagnosis and aetiological classification were recorded. Motor-phenotype was classified as i) pure dystonia, ii) mixed dystonia–spasticity, iii) dystonia–choreoathetosis, iv) dystonia–myoclonus, v) dystonia with prominent tremor, or vi) dystonia–parkinsonism. CAYP deemed to have a purely spastic motor phenotype were excluded.

The Gross Motor Function Classification System (GMFCS)[13] was used to classify motor function. This scale has been validated for children with CP, and so should be considered "GMFCS equivalent" as not all children in this study had this diagnosis. For 132 patients dystonia severity had also been assessed using the Burke–Fahn–Marsden Dystonia Rating Scale (BFMDRS).[14] Videotaped BFMDRS evaluations were scored by 2 clinicians, not blinded to other clinical/demographic details.

Statistical analysis was performed using the R language for Statistical Computing, version 2.15.2 (R Foundation for Statistical Computing, Vienna, Austria), and the survival package, version 2.36–14 (Terry M. Therneau, Mayo Clinic, Rochester, USA).[15] Age of FMD onset was considered to be interval censored between the age of onset of dystonia and age of referral to our service for CAYP with FMD at referral and right-censored at age of referral for CAYP without FMD at referral, based on the assumption of eventual progression to FMD over time.[8,9] Parametric accelerated failure time models using the log-normal distribution were fitted to identify which clinical factors led to an earlier or later onset of FMD. A parametric approach was chosen to give greater power to the analysis of the interval-censored observations. An accelerated failure time model was used both because the assumptions of a proportional hazards model were not met and because accelerated failure time models are more robust to model misspecification.[16,17] The log-normal model was chosen because it provided the best fit of 6 models considered. Modelling assumptions were checked using diagnostic plots and relevant statistics. Median event times, 95% confidence intervals and p-values were calculated. Aetiological classification, motor-phenotype, GMFCS level and age of dystonia onset were used as covariates in the models – both in univariate and in multivariate models. Small subgroups of less than 20 patients (e.g. patients with Dystonia–Myoclonus, Dystonia–Choreoathetosis, Dystonia tremor, or Dystonia–Parkinsonism motor-phenotype) were merged together to produce sufficiently large groups for statistical modelling.

The study was registered as an audit with Guy's and St Thomas' NHS Trust. Since the data were not personally identifiable, consent was neither required nor obtained. Data were permanently anonymized and handled according to Caldicott principles and the requirements of the Data Protection Act.

2. Results

Case notes were available for 294/320 (92%) CAYP referred to our service between July 2005 and December 2011, 15 of whom