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Childhood chronic inflammatory demyelinating polyradiculoneuropathy: Combined analysis of a large cohort and eleven published series

Hugh J. McMillan [a], Peter B. Kang [b], H. Royden Jones [b,c], Basil T. Darras [b,*]

[a] Division of Neurology, Children's Hospital of Eastern Ontario, University of Ottawa, Ottawa, Canada K1H 8L1
[b] Department of Neurology, Boston Children's Hospital, Harvard Medical School, Boston, MA 02115, United States
[c] Lahey Clinic, 41 Mall Road, Burlington, MA 01805, United States

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Abstract

The clinical presentation, disease course, response to treatment, and long-term outcome of thirty childhood chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) patients are presented representing the largest cohort reported to date. Most children (60%) presented with chronic (>8-weeks) symptom-onset while a smaller proportion showed sub-acute (4–8 weeks) or acute ("GBS-like"; <4 weeks) onset of disease. No gender predilection was observed. The majority of patients had a relapsing (70%) versus a monophasic (30%) temporal profile. Most received initial IVIG monotherapy; 80% showing a good response. Long-term follow-up (mean = 3.8 years) was available for 23 patients; 45% were off all immunomodulatory medications, demonstrating no detectable (55%) or minimal (43%) clinical deficits. Our data were compared with 11 previously published childhood CIDP series providing a comprehensive review of 143 childhood CIDP cases. The combined initial or first-line treatment response across all studies was favourable for IVIG (79% patients) and corticosteroids (84% patients). Response to first-line plasma exchange was poor (only 14% patients improved) although it may offer some transient or partial benefit as an adjuvant or temporary therapy for selected patients. The combined long-term outcome of our cohort and the literature reveals a favourable prognosis for most patients. The combined modified Rankin scale decreased from 3.7 (at presentation) to 0.7 (at last follow-up). This review provides important data pertaining to clinical course, treatment response and long-term outcome of this relatively uncommon paediatric autoimmune disease.

Keywords: Chronic inflammatory demyelinating polyradiculoneuropathy; Intravenous immunoglobulins; Plasma exchange; Immunosuppressive agents; Treatment outcome

1. Introduction

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) may occur from infancy [1,2] to late-adulthood [3] with increasing disease prevalence seen with advancing age. Auto-reactive T-cells play a dominant role in the initial pathogenesis of CIDP, triggering an inflammatory response within sensory and motor nerves and damaging Schwann cells and the peripheral nerve myelin [4]. Children present with slowly progressive or relapsing episodes of gait ataxia, distal symmetric weakness and paraesthesiae. Diagnostic criteria differentiate CIDP from its acute counterpart, Guillain–Barré syndrome, as well as hereditary and metabolic causes of childhood polyneuropathy [5–8].

Several case series of childhood chronic inflammatory demyelinating polyradiculoneuropathy (CIDP) have been published in the literature. However, given the low prevalence of childhood CIDP (i.e. <0.5 per 100,000) [3], studies

* Corresponding author. Address: Department of Neurology, Fegan 11, Boston Children's Hospital, 300 Longwood Avenue, Boston, MA 02115, United States. Tel.: +1 617 355 8036; fax: +1 617 730 0279.
E-mail address: basil.darras@childrens.harvard.edu (B.T. Darras).

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have offered conflicting information pertaining to gender ratio, treatment efficacy and long-term outcome of this disease [1,2,9–18]. This report represents the largest case series of childhood CIDP published to date. It includes a description of disease-onset, clinical features, response to treatment and long-term disease outcome for 30 childhood CIDP patients. Data from our cohort have been combined with data from 11 previous case series (1980–2009) to provide a comprehensive review of childhood CIDP.

2. Methods

Institutional research ethics board approval was obtained prior to the start of data collection. The medical records of all patients with CIDP seen at Boston Children's Hospital (BCH) from 1989 to 2009 were reviewed.

2.1. Inclusion/exclusion criteria

Inclusion criteria included: (1) age $\leqslant$ 19.0 years old; (2) clinical history of progressive or relapsing motor and sensory polyneuropathy; (3) clinical evidence of diffuse hyporeflexia or areflexia; (4) cerebrospinal fluid white cell count $< 10\ mm^{-3}$; (5) electrophysiological studies consistent with an acquired demyelinating disorder in $\geqslant 2$ nerves. AAN research criteria [5] were used to set the electrodiagnostic criteria for an acquired demyelinating neuropathy; nerve conduction studies must have demonstrated three of the four following features: (1) reduced conduction velocity (i.e. <80% of the lower limit of normal (LLN) if the compound muscle action potential (CMAP) amplitude is >80% LLN or <70% LLN if the CMAP amplitude is <80% LLN); (2) abnormal temporal dispersion or partial conduction block. Temporal dispersion was defined as excessive prolongation of the CMAP duration with proximal stimulation compared to distal stimulation reflecting non-uniform conduction slowing; a >20% increase in proximal-to-distal CMAP duration of median, ulnar or peroneal nerves or >30% for tibial nerves was defined as abnormal. Partial conduction block was defined as a >20% drop in peak-to-peak amplitude between proximal and distal stimulation sites; (3) prolonged distal latency (i.e. >125% upper limit of normal if amplitude was > 80% of LLN or >150% upper limit of normal if amplitude was < 80% of LLN); (4) absent or prolonged F-waves (10 trials) (i.e. >120% of the upper limit of normal if amplitude was > 80% of LLN or >150% of the upper limit of normal if amplitude was < 80% of LLN. Published reference values for normal paediatric sensory and motor nerve conductions were used [19]. Nerve biopsies were not typically performed for patients meeting the above criteria.

Exclusion criteria included: (1) family or past medical history of an inherited polyneuropathy; (2) drug or toxin exposure; (3) clinical suspicion of an underlying metabolic disorder (i.e. retinitis pigmentosa, ichthyosis, hand or foot mutilation, developmental delay or regression); (4) sensory level; or (5) sphincter disturbance.

2.2. Clinical data

Patients' medical charts were reviewed to obtain the following information: (1) gender; (2) age of symptom onset; (3) time between symptom-onset and maximum disability; (4) maximum clinical deficit (using modified Rankin scale (MRS), see below); (5) clinical features at initial presentation (i.e. deep tendon reflex findings, limb/back pain, limb paraesthesiae); (6) disease course (i.e. monophasic or relapsing/polyphasic); (7) number of relapses; (8) choice and response to first-line immunomodulation therapy; (9) choice and response to all immunomodulation therapies (used at any stage of disease); (10) follow-up duration; and (11) MRS at last follow-up visit.

The modified Rankin scale (MRS) was used to quantify clinical deficit. MRS was devised as a reliable means of scoring clinical deficits after stroke [20] and has since been used to estimate clinical deficit in adult and childhood CIDP patients [9–11,13]. MRS functional scales are defined as: 0 = asymptomatic; 1 = mild symptoms that do not interfere with any work, school or extracurricular activity; 2 = slight disability (i.e. child has given up one or more activities) but is able to perform all age-appropriate personal care (i.e. dressing, eating) and complex tasks (i.e. handwriting, age-appropriate food preparation); 3 = moderate symptoms (i.e. child is still able to walk independently (may require cane or walker) but requires assistance for age-appropriate tasks (see above)); 4 = moderate-to-severe symptoms (i.e. child is unable to walk (carried by parent and/or wheelchair required) and unable to perform age-appropriate personal care); 5 = severe disability (i.e. patient is bed-ridden and requires constant nursing care), may require intubation and mechanical ventilation; 6 = death.

Cerebrospinal fluid leucocyte (WBC) count and protein were recorded for all patients. Results of magnetic resonance imaging (MRI) of the spine were recorded whenever available.

2.3. Outcomes

Clinical response to the immunomodulatory therapies (i.e. intravenous immunoglobulin (IVIG), plasma exchange (PE) or corticosteroids) was measured, both for first-line therapies and at subsequent stages of the disease. We defined a "good response" as clinical improvement to the point where the treating physician reported minimal-to-no functional impairment or limitation of activities. "Partial response" was defined as some degree of clinical improvement as judged by the treating physician; however, a change or addition of immunomodulatory treatment was necessary. "No response" was defined as either no apparent clinical improvement or clinical deterioration on a given treatment. Disease relapse was defined as a clinical deterioration not associated with weaning immunosuppressant medication and/or wearing-off effects of IVIG or plasma exchange therapy. In cases where patients could