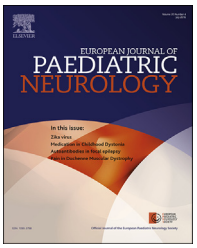
EUROPEAN JOURNAL OF PAEDIATRIC NEUROLOGY XXX (2016) 1–9

Official Journal of the European Paediatric Neurology Society



Original article

Multiple sclerosis in Belgian children: A multicentre retrospective study

Helene Verhelst [a,*], *Liesbeth De Waele* [b,c], *Nicolas Deconinck* [d], *Berten Ceulemans* [e], *Barbara Willekens* [f,g], *Rudy Van Coster* [a]

[a] *Department of Paediatrics, Division of Paediatric Neurology, Ghent University Hospital, Ghent, Belgium*
[b] *KU Leuven, Department of Development and Regeneration, Campus Kulak Kortrijk, Kortrijk, Belgium*
[c] *Department of Paediatric Neurology, University Hospitals Leuven, Leuven, Belgium*
[d] *Department of Paediatric Neurology, Hôpital Universitaire des Enfants Reine Fabiola (U.L.B.), Brussels, Belgium*
[e] *Department of Neurology-Paediatric Neurology, Antwerp University Hospital, University of Antwerp, Belgium*
[f] *Department of Neurology, Antwerp University Hospital, Edegem, Belgium*
[g] *Department of Neurology, Translational Neurosciences, Faculty of Medicine and Health Sciences, University of Antwerp, Belgium*

ARTICLE INFO

Article history:
Received 14 December 2015
Received in revised form
28 July 2016
Accepted 17 October 2016

Keywords:
Multiple sclerosis
Paediatric multiple sclerosis
Childhood
Adolescence

ABSTRACT

Background: Although the diagnosis of multiple sclerosis (MS) in the paediatric population remains challenging, paediatric-onset MS is increasingly recognized worldwide.
Methods: We report on the clinical and biochemical features of a Belgian multicentre cohort of paediatric MS patients in a national retrospective descriptive study.
Results: Twenty one paediatric MS patients from four Belgian University Hospitals were included. In nine patients, onset of MS was before the age of ten years which makes the study cohort of special interest. We report a higher incidence of acute disseminated encephalomyelitis (ADEM)-like first MS attacks and an overall higher proportion of polysymptomatic episodes than in adult and most paediatric cohorts reported in the literature. The clinical presentation in our cohort was rather severe with high median EDSS-score during the first clinical manifestation and barely more than half of our study patients showing full recovery after their first clinical manifestation. Also, a significant proportion of children in our cohort has severe disease progression despite disease modifying therapy and 9.5% of patients showed transition to secondary progressive multiple sclerosis during adolescence.

Abbreviations: ADEM, acute disseminated encephalomyelitis; ADEMON, acute disseminated encephalomyelitis followed by optic neuritis; AQP4, aquaporine 4; CMV, cytomegalovirus; DIS, dissemination in space; DIT, dissemination in time; EBV, Epstein-Barr virus; EDSS, Expanded Disability Status Scale; HSV, herpes simplex virus; MDEM, multiphasic disseminated encephalomyelitis; MOG, myelin oligodendrocyte glycoprotein; MRI, magnetic resonance imaging; MS, multiple sclerosis; NMOSDs, neuromyelitis optica spectrum disorders; ON, optic neuritis; pMS, paediatric multiple sclerosis; RRMS, relapsing remitting multiple sclerosis; SPMS, secondary progressive multiple sclerosis; VZV, varicella-zoster virus.

* *Corresponding author*. Universitair Ziekenhuis Gent, Administratieve Pediatrie, De Pintelaan 185, 9000 Gent, Belgium. Fax: +32 3329 3839.
E-mail addresses: helene.verhelst@ugent.be (H. Verhelst), liesbeth.dewaele@uzleuven.be (L. De Waele), Nicolas.DECONINCK@huderf.be (N. Deconinck), Berten.Ceulemans@uza.be (B. Ceulemans), Barbara.Willekens@uza.be (B. Willekens), rudy.vancoster@ugent.be (R. Van Coster).

http://dx.doi.org/10.1016/j.ejpn.2016.10.005

Conclusion: An early and correct diagnosis of paediatric MS is essential to start early adequate treatment. As illustrated by our study cohort, current treatment options in childhood are unsatisfactory.

1. Introduction

Multiple sclerosis (MS) is one of the most important human immune-mediated demyelinating disease.[1] The disease usually starts in young adulthood. Only about 2–10% of all MS patients experience their first clinical symptoms before the age of 18 years.[2] The childhood form with first symptoms starting before the age of 10 years even occurs less frequently and probably accounts for less than 1% of all MS cases.[2,3] Diagnosing MS in the paediatric population remains challenging and many questions about the clinical course, aetiology and relationship with other childhood demyelinating diseases remains unanswered.

In this study, we present the clinical and biochemical features of a Belgian multicentre cohort of paediatric MS (pMS) patients.

2. Materials and methods

Nine paediatric neurology units in Belgium were contacted and invited to participate to a national retrospective descriptive study on pMS. Eight paediatric neurology units principally agreed to participate but four centres did not have pMS patients in follow-up. Finally, data were recorded from: Ghent University Hospital, University Hospitals of Leuven, Hôpital Universitaire des Enfants Reine Fabiola (Brussels) and Antwerp University Hospital.

2.1. Inclusion and exclusion criteria

Patients in whom the diagnosis of pMS was made before their 18th birthday according to the in 2013 revised criteria of the International Paediatric Multiple Sclerosis Study Group[4] and who were in follow-up at any of the participating centres were included. All patients or their legal representatives gave written informed consent to the study. Patients with follow-up duration of less than six months were excluded.

2.2. Patient recruitment and data collection

After identification of eligible cases, a comprehensive set of clinical and investigative data organized in a structured questionnaire was collected for each patient. First, the questionnaire was filled out by the treating physicians, all paediatric neurologists with experience in treating children with neuroimmunological diseases. Subsequently, the data were reviewed by the principal investigator, also a paediatric neurologist with experience in treating children with neuroimmunological diseases and especially with MS, and if necessary treating physicians were contacted to clarify or to complete missing data. Neuroimaging was reviewed by the treating paediatric neurologist, the principal investigator, a paediatric radiologist and a neuroradiologist.

2.3. Operational definitions

According to the International Paediatric Multiple Sclerosis Study Group two pMS types can be distinguished: the childhood form with onset before 10 years of age and the adolescent form with onset between 10 and 18 years of age.[4] Disability status was assessed by a paediatric neurologist with the Expanded Disability Status Scale (EDSS)[5] at each relapse and in remission between relapses. Due to the small sample size of the study cohort we decided not to perform statistical analysis.

3. Results

Twenty one pMS patients were enrolled in the present study (Ghent University Hospital: 7 patients, University Hospitals of Leuven: 6 patients, Hôpital Universitaire des Enfants Reine Fabiola (Brussels): 5 patients, Antwerp University Hospital: 3 patients). All were diagnosed with relapsing remitting MS (RRMS). Median follow-up period was 53 months with a range of 6–141 months.

3.1. Demographics

All pMS patients were Caucasian, 20/21 were born in Belgium. Median age at onset was 11 years (range 2–15 years), median age at diagnosis 12 years (range 6–15 years). In 9/21 patients (43%) onset of MS was before the age of 10 years (childhood group) and in 12/21 patients (57%) onset was between 10 and 18 years of age (adolescent group). The female/male ratio in the total study group was 1.33/1, and 0.8/1 and 2/1, respectively, in the childhood and adolescent group.

Two pMS patients also suffered from an autoimmune disease other than MS (1 Crohn's disease and 1 diabetes mellitus), one patient had a family history of MS and 5 patients had a family history of another autoimmune disease (3 rheumatic diseases, 1 Crohn's disease and 1 Graves' disease). Immunological status before disease onset was recorded if available. Epstein-Barr virus (EBV) antibodies were positive in 14/15, cytomegalovirus (CMV) antibodies in 7/14, herpes simplex virus (HSV) antibodies in 5/13, varicella-zoster virus (VZV) antibodies in 9/10 and parvovirus B-19 antibodies in 2/3. Four

Please cite this article in press as: Verhelst H, et al., Multiple sclerosis in Belgian children: A multicentre retrospective study, European Journal of Paediatric Neurology (2016), http://dx.doi.org/10.1016/j.ejpn.2016.10.005