

Is the early course of multiple sclerosis the same in adults and children?

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Although multiple sclerosis (MS) is predominantly a disease of young adults, approximately 5% of people with MS have their first symptoms in childhood. Pediatric-onset MS (usually defined as onset before the age of 18 years) may differ from adult-onset MS [1]. A number of retrospective studies have reported differences in MS in children with an almost exclusively relapsing disease course, higher relapse rates and slower accumulation of disability compared with adults with MS [1].

In this issue of *European Journal of Neurology*, van der Vuurst de Vries and colleagues report on a large cohort of adults and children with clinically isolated syndromes (CIS) suggestive of MS who were followed prospectively from disease onset [2]. The authors recruited patients with no previous history of neurological symptoms within six months of CIS. The patients were followed up clinically (and in some with MRI) for the development of MS, diagnosed using the McDonald 2010 criteria in adults and the International Pediatric Multiple Sclerosis Study Group [IPMSSG] 2012 criteria in children [3, 4]. The number of relapses and accrual of disability was also recorded. The authors compare the clinical features and early disease course of adults (age 18–50 years), adolescents (11–17 years) and prepubertal children (age <11 years) with CIS over a follow-up period of almost 4 years.

In keeping with previous studies, children were more likely to present with a polyfocal CIS. However, a monofocal presentation typical of CIS in adults (e.g. unilateral optic neuritis, transverse myelitis) was still more common. Adolescents (but not younger children) were more likely to have MRI evidence of dissemination in space at presentation using the McDonald 2010 criteria and were more likely to have gadolinium-enhancing lesions compared with adults. During follow-up more than half of the CIS patients were diagnosed with MS. Children aged 11-17 years were three times more likely than adults to develop MS

and the time to the second clinical attack was significantly shorter in adolescents compared with adults (9 vs 19 months).

In contrast to older children, prepubescent children (<11 years) had fewer brain MRI abnormalities at presentation, fewer gadolinium-enhancing lesions and were less likely to have cerebrospinal fluid (CSF) oligoclonal bands. Younger children were less likely to be diagnosed with MS during follow-up compared with adolescents and adults. Whether this reflects the rarity of MS in this age group, the relatively small number of prepubescent children included in the study or the need for caution in applying MRI criteria to diagnose MS in this age group (the IPMSSG criteria require two or more clinical attacks to make a diagnosis of MS in younger children) is uncertain [4]. This group were at low-risk for the development of MS, at least using prognostic markers that are well-validated in adults such as asymptomatic brain MRI abnormalities and CSF oligoclonal bands [5]. The authors did not test for MOG-IgG antibodies which are relatively common in children with first demyelinating events, particularly in younger children [6, 7]. Children with MOG-IgG antibodies are less likely to have brain MRI abnormalities and CSF oligoclonal bands, and more likely to have a non-MS disease course [6].

Given the highly-active early disease course observed in adolescents with CIS and early MS the authors advocate early initiation of disease-modifying treatment (DMT) in this group. Treatment with interferon- β , glatiramer acetate, teriflunomide and cladribine has been shown to reduce the risk of a second clinical attack and the accumulation of new MRI brain lesions in adults with CIS at high-risk for MS. None of these agents have been investigated in children in randomised controlled trials, although observational studies of interferon- β and glatiramer acetate appear to be safe and well-tolerated in children with established MS. A number of phase III clinical trials of DMT in children are underway and the results are

awaited. In the current study more than half of children with CIS were started on DMT over the first 4 years of follow-up, although children were less likely to receive treatment prior to developing clinically-definite MS compared with adults. Children who received DMT had a significantly lower annualised relapse rate compared with children who were untreated, and the annualised relapse rate was similar in both children and adults who received DMT.

The strengths of this study include the prospective design and large size. Because the study was observational MRI and other investigations were done as clinically indicated rather as part of a standardised research protocol; not all patients had spinal cord imaging (important for demonstrating dissemination in space), gadolinium-enhanced or follow-up MRI scans (important for demonstrating dissemination in time). These are important when making a diagnosis of MS using current diagnostic criteria [3, 4]. The duration of follow-up in the study was almost 4 years, and slightly shorter in children than adults. While van der Vuurst de Vries and colleagues demonstrate important differences in the early disease course of children and adults following a CIS. Further follow-up of this cohort will be required to determine how the early, inflammatory course in children influences long-term outcomes.

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