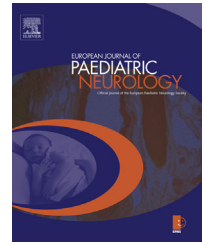




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Original article

Multiple sclerosis in children and adolescents. An important differential diagnosis of acute neurological disease



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ABSTRACT

Aim: Multiple sclerosis (MS) has traditionally been considered a disease of adults. However, in recent years, there have been numerous reports about the disease occurring in childhood and adolescence. The purpose of this article is to document Norwegian experience of this population based on clinical observations and neuroradiological findings.

Methods: Children and adolescents diagnosed with MS at the Department of Child Neurology, Oslo University Hospital, between 1 January 2004 and 1 May 2012 were included. Gender, previous diseases, age, symptoms at first attack, spinal fluid findings and cerebral magnetic resonance tomography (MRI) findings were recorded. The course of the disease, treatment and sequelae was noted.

Results: The study includes 18 patients who received MS diagnosis. Median age at onset was 10 years and six months. The presenting symptoms and MRI findings varied. Almost all patients were treated with steroids in the acute phase and later with interferon-beta. Some patients were treated with natalizumab when there was lack of efficiency of interferon-beta. Seven patients developed permanent, moderate sequelae in terms of motor, sensory, or cerebellar symptoms. Nine patients had cognitive difficulties and 11 specified increased fatigability.

Conclusion: MS in children and adolescents is a disease with varying acute neurological symptoms and findings. The patients were treated with the same medicines as adults with MS and tolerated it well. We found that cognitive sequelae and fatigue were common also in this young age group.

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1. Introduction

Multiple sclerosis (MS) is a chronic, inflammatory, demyelinating disease of the central nervous system (CNS) which commonly presents in early adulthood. Signs and symptoms vary widely depending upon the location of the affected nerve fibers. Some of the most common clinical manifestations include central weakness, sensory changes, cerebellar symptoms such as ataxia, and visual problems including optic neuritis. Brainstem affection may present with double vision or facial nerve palsy.

MS is being increasingly diagnosed in children and adolescents. This is probably due to a combination of improving awareness of the diagnosis, greater use and availability of MRI in pediatric neurology and a potential true increasing incidence in this age group. It has previously been demonstrated that 2–5% of patients have onset of symptoms before 16 years of age.¹ A more recent study estimated that symptoms may be present in 10% of patients before 18 years of age.² A relapsing-remitting (RRMS) pattern of disease, is seen in over 90% of cases of MS in children and adolescents.³

In adults, the main treatment strategy is the prevention of attacks with disease modifying, immunomodulatory therapies. Prophylactic treatment with Beta interferons (INF- β), reduces the frequency of relapses by approximately 30%.⁴ Natalizumab, a monoclonal antibody, reduces incidence of relapses by 70%.⁵ Until recently, these medications have been used with a degree of caution in the pediatric population, in part because of concern about their impact on growth, puberty and an immature immune and central nervous system. This trend is now changing, however and pediatric neurologists are adopting a more aggressive approach (6,7). Preliminary experience with immunomodulatory therapy in children is good and these medications appear to be safe and well tolerated in children showing similar efficacy to adult studies.^{6,7}

It is our experience that pediatric MS is seldom recognized by general paediatricians and family doctors. The purpose of this article is to document and share a Norwegian experience based on clinical observations and neuroradiological findings from our own patient material.

2. Materials and methods

This retrospective study included 18 children and adolescents who were all under 16 years of age when they were diagnosed with MS from the period 1 January 2004 to 1 May 2012. All patients were referred by their local hospitals to the Department of Child Neurology, Oslo University Hospital for a second opinion. Written, informed consent was obtained from all families for participation in this study, and the study was approved by the Regional Ethics Committee. Clinical assessment was carried out by at least one of the authors. Additional information was obtained from the referring hospital's medical notes and discharge letters. Telephone interviews have also been conducted where necessary to obtain updated information about the patients.

The following information was recorded:

- Gender, previous medical history and health status, age at the first attack and the initial diagnosis (Table 1).
- Clinical neurological signs and symptoms at the time of disease onset (Table 1).
- Spinal fluid findings included the number of cells, total protein, and the presence or absence of oligoclonal bands.
- The results of neuroradiological MRI studies. In most cases, this included brain MRI. In some cases, this included MRI of the spinal cord and neuroradiological studies from the local hospital. All MR images were evaluated by the same experienced neuro-radiologist.
- Medical therapy and disease progression, including the frequency of relapses with both acute care and following commencement of preventive treatment and persisting neurological sequelae including any cognitive problems.

All of the patients included in this study were rediagnosed according to the McDonald criteria. All patients were thoroughly investigated to exclude other potential diagnoses.

3. Results

In total, 18 patients, 14 girls and four boys were included. The patients had varying degrees of disease progression. All patients had RRMS. Earliest age at symptom onset was three years and four months; the earliest age at the time of diagnosis was four years and five months in the same patient. Median age onset of symptoms was 10 years and six months. The follow-up time for patients ranged from two months to nine years with a median follow-up time of three years and one month.

Because of the introduced obligatory criteria of encephalopathy, only three of the patients got ADEM diagnosis (patient nr. 1,12,13). Two children, the first with symptoms of reduced balance and sensibility disturbance for 12 months and the second with symptoms of headache and double vision for 7 months before admission, were diagnosed with MS following the first in-patient/hospital assessment.

Of the remaining 13 patients, 12 were diagnosed with Clinical isolated syndrome (CIS), the 13 with unspecified convulsions. One of the CIS patients was diagnosed with an isolated optic neuritis. Optic neuritis was also given as an additional diagnosis in four other patients, that is to say, a total of five patients had optic neuritis at onset of symptoms.

Infection, preceding the first attack was recorded based on patient report in five patients (nr. 1, 5, 13, 14,16). Two of these were in the ADEM group. Initial presenting symptoms and findings varied from patient-to-patient but were dominated by pyramidal dysfunction with motor paresis in 10, cerebellar symptoms with ataxia, dysdiadochokinesia, dysarthria and/or nystagmus findings in six, sensory disturbances with paresthesia or reduced sensibility in seven and neuro-ophthalmological findings with optic neuritis, oculomotor paresis or double vision in nine patients. Three of the children were encephalopathic (Table 1).

Seven patients have moderate sequelae in terms of motor, sensory, or cerebellar symptoms. Cognitive impairments have

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