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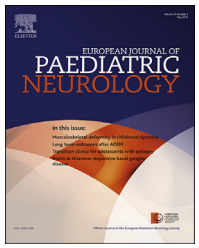

Original Article

Long-term motor, cognitive and behavioral outcome of acute disseminated encephalomyelitis

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ABSTRACT

Objective: The purpose of this study was to evaluate the long-term motor and neurocognitive outcome of children with acute disseminated encephalomyelitis and to identify prognostic risk factors.

Methods: The study included 43 children who were hospitalized due to acute disseminated encephalomyelitis during the years 2002–2012. The children underwent full neurological examinations, along with comprehensive neurocognitive and behavioral assessments.

Results: Twenty-six (61%) children had different degrees of neurological sequelae after a mean follow-up of 5.5 ± 3.5 years. The most common residual impairment included attention-deficit hyperactivity disorder (44%), behavioral problems (32%), and learning disabilities (21%). Five (12%) children had a full-scale IQ of 70 or less, compared to 2.2% in the general population.

Conclusions: Neurocognitive sequelae were found even in children who were considered as fully recovered at the time of discharge. Risk factors for severe neurological sequelae were older age at diagnosis and male gender. We suggest neuropsychological testing and long-term follow-up for all children with acute disseminated encephalomyelitis, even in the absence of neurological deficits at discharge.

Abbreviations: ADEM, acute disseminated encephalomyelitis; ADHD, attention deficit hyperactivity disorder; CBCL, child behavior check list; CI, confidence interval; CNS, central nervous system; EDSS, expanded disability status scale; EEG, electroencephalography; ICU, intensive care unit; IQ, intelligence quotient; MS, multiple sclerosis; OR, odds ratio.

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1. Introduction

Acute disseminated encephalomyelitis (ADEM) is an acute, usually monophasic, immune-mediated inflammatory disorder of the central nervous system, characterized by multifocal neurological signs and symptoms and encephalopathy, along with the presence of multifocal demyelinating lesions on neuroimaging studies.[1] While the etiology is not fully understood, ADEM is commonly preceded by immunization or by viral infection, suggesting an autoimmune response to myelin basic protein.[2] Although usually monophasic, some children may develop either recurrent or chronic disease, such as multiple sclerosis.

Data regarding long-term outcome for patients diagnosed with ADEM prior to the steroid era suggest that spontaneous improvement was seen over several weeks in most children, with 50–70% of patients experiencing full recovery.[3,4]

Previous studies on long-term neurologic outcomes in children with ADEM showed complete remission of symptoms in approximately 60–90% of patients.[5–7] In the majority of these studies, data were determined by using clinical follow-up assessments at outpatient clinics[8–11] and structured questionnaires[5] that focused mainly on motor sequelae and the possibility of predicting multiple sclerosis. Only a few small case studies used standardized cognitive and behavioral tests.[12–15] Previously reported neurological sequelae include motor deficits, cognitive and behavioral problems.[15,16] Up to 30% of patients had a recurrent or multiphasic course.[17]

Information regarding prognostic factors of ADEM in children is sparse. One study reported a greater vulnerability to cognitive dysfunction and behavioral problems among ADEM patients diagnosed prior to age five.[12] Optic nerve involvements at presentation[18] and antecedent viral infection[5] have also been suggested as indicative of a poor outcome.

The aim of the present study was to evaluate the long-term sequelae of ADEM in children and to look for predictors of long-term morbidity. This study is distinctive because it combines genuine motor assessment with an objective neurocognitive performance and behavior evaluation in a relatively large group of children. This information can help in offering guidance, as well as emphasizing important aspects for future follow-up.

2. Materials and methods

2.1. Study population

The medical records of children and adolescents, aged one month to 18 years, admitted to Meyer Children's Hospital in Haifa, Israel, during the years 2002–2012 with a final diagnosis of ADEM were reviewed. The hospital is the main tertiary center in the north of Israel and serves a population of 280,000 children. Patients are referred either directly from pediatricians or pediatric neurologists in this case, or from other smaller medical centers that lack either a pediatric neurologist or a pediatric intensive care unit. The diagnosis of ADEM was based on the international consensus clinical criteria according to the International Pediatric Multiple Sclerosis Study Group. These include a first polyfocal, clinical CNS event with presumed inflammatory demyelinating cause, encephalopathy that cannot be explained by fever, and abnormal typical brain MRI findings during the acute phase (3 months).[19] Children with any underlying neurological, systemic or metabolic diseases were excluded from the study. Children eventually diagnosed as having MS, or children that developed a clinical picture suggestive of neuromyelitis optica (Devic disease) were not included in the study. All eligible patients were contacted by letter and then by telephone to ask whether they would be willing to participate in the study.

Sixty-one patients fulfilled the criteria for ADEM. Of those, five children were eventually diagnosed as having multiple sclerosis and were excluded, eight declined to be assessed, and five could not be located. There was no difference between the children regarding age at onset, gender, and presenting symptoms.

Written informed consent was obtained from the parents during the follow-up meeting. The study was approved by the institutional ethics committee.

2.2. Data collection

A structured form was used to obtain data from the patients' hospital records regarding presenting symptoms and signs, laboratory examinations, EEG and neuroimaging studies, and clinical findings at discharge. Outcome at discharge was classified for all subjects. Good outcome was defined as having no neurological sequelae. Moderate outcome was defined as having minor to moderate sequelae, including altered behavior or clinical signs not affecting functions. Poor outcome was defined as having severe neurological sequelae that impaired everyday functions.

2.3. Clinical, motor and neurocognitive assessment

All the children were interviewed and underwent a thorough neurological examination by a pediatric neurologist during the follow-up visit. A structured questionnaire was used to obtain information from parents regarding comorbid illnesses, medications, behavioral problems, school performance, and ability to perform daily activities.

The functional degree of neurologic disability was assessed using the Kurtzke functional systems and Expanded Disability Status Scale (EDSS).[20]

The Kaufman brief intelligence test[21] was used to assess intelligence. This is a standardized validated test that yields three scores: verbal, nonverbal, and the overall score, known as the IQ composite. The mean age-based standard score for each test is 100 with a standard deviation of 15. Scores lower than 2 standard deviations from mean were considered as retardation. Scores between 1 and 2 standard deviations from mean were considered as borderline intelligence.

The diagnosis of attention deficit hyperactivity disorder (ADHD) was based on the Diagnostic and Statistical Manual of Mental Disorders IV criteria.[22] Clinical evaluation was performed by a pediatric neurologist, using interviews with the parents and child, and examination during the visit. In addition, attention and behavior were measured using the Conners' Parents Rating Scales-Revised.[23]