Acute Demyelination in Children

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There is increased recognition of pediatric demyelinating diseases, such as multiple sclerosis (MS), neuromyelitis optica (NMO) and acute demyelinating encephalomyelitis (ADEM)\(^1\)-\(^3\). Current topics regarding these diseases in pediatric patients are reviewed.

**Multiple sclerosis**

MS is the most common autoimmune inflammatory demyelinating disease of the central nervous system. MS typically affects young adults between 20 and 40 years of age, but 2-5% of all MS patients experience the initial onset before age 16\(^4\). As in adults, females are more affected\(^1\), but no female predominance is seen in young children\(^5\),\(^6\). Most pediatric MS patients present with a relapsing remitting course, and the time from onset to secondary progression is longer than in adults.\(^1\),\(^5\)

The international diagnostic criteria for MS (McDonald Criteria) were revised in 2010 (published in 2011)\(^7\). MRI criteria for demonstration of dissemination in both space and time have been simplified for application to pediatric patients, as well as for Asian and Latin American populations\(^7\).

MRI features of pediatric MS resemble those for adults MS, but children tend to have fewer lesions. Many pediatric MS patients thus did not meet the MRI criteria for dissemination in space of the former (2005) version of the McDonald criteria\(^8\),\(^9\). Ill-defined, large lesions, often involving the central gray matter, are more commonly seen in young children\(^5\). MRI is an invaluable diagnostic tool for MS in both children and adults, but lacks specificity to distinguish ADEM from the first attack of MS\(^5\).
Neuromyelitis optica

NMO is a disease characterized by severe optic neuritis and transverse myelitis that affects children as well as adults\textsuperscript{10}. Some controversy remains regarding whether NMO is a subtype of MS or a distinct entity, but NMO is now considered distinct from MS, since anti-aquaporin 4 (AQP4) antibody (also known as NMO IgG), has been identified as specific for this disease, \textsuperscript{11-13}. AQP4 is a dominant water channel in the central nervous system densely expressed on foot processes of astrocytes\textsuperscript{14}. Pathologically, astrocytes are primarily destroyed and demyelination is secondary in NMO\textsuperscript{14}.

Median age at onset is 39 years old (10 years older than with MS), and 90\% of patients are females\textsuperscript{13}. Approximately 60\% of NMO patients show brain lesions on MRI in both adults\textsuperscript{15, 16} and children\textsuperscript{17}. NMO brain lesions show a predilection for periventricular regions, medulla oblongata (area postrema), hypothalamus and pyramidal tracts\textsuperscript{13, 16, 18, 19}. Typical spinal cord lesions are vertically long (\(\geq 3\) vertebral bodies) and involve the center (gray matter) of the spinal cord on axial images\textsuperscript{13, 20}.

Differentiating NMO from MS is extremely important, because therapeutic strategies differ between these diseases. Indeed, NMO patients may show severe deterioration of symptoms on administration of interferon beta\textsuperscript{21}. The 2010 revision of the McDonald criteria emphasizes the importance of excluding NMO from MS, and AQP4 serum testing is recommended to facilitate differentiation\textsuperscript{7}. Clinical and radiological findings of pediatric NMO patients may also overlap with ADEM. In such cases, AQP4 testing aids in the distinction\textsuperscript{17}. Other autoimmune disorders, such as systematic lupus erythematosus, Sjögren syndrome and rheumatoid arteritis\textsuperscript{17}, and posterior reversible encephalopathy syndrome\textsuperscript{22} may coexist with NMO.

Pediatric NMO patients show similar MR appearances to adult patients\textsuperscript{3, 17}, although children tend to exhibit more diencephalic, brainstem or cerebral hemispheric lesions\textsuperscript{15}. Brain lesions in NMO predominantly involve the periventricular regions, medulla, midbrain, thalamus and hypothalamus\textsuperscript{3, 17}. Longitudinally extensive spinal cord lesions are also characteristic.
Acute demyelinating encephalomyelitis

Historically, the term ADEM had been applied inconsistently, but the International Pediatric MS Study Group recently proposed defining ADEM as a first episode of inflammatory demyelination with polyfocal neurological deficits implicating involvement of multiple sites of the central nervous system accompanied by encephalopathy\textsuperscript{2,23}. ADEM more commonly affects young children under 10 years of age\textsuperscript{5,23}. ADEM is frequently, but not always, preceded by an infectious episode. ADEM may recur or be multiphasic, but is not associated with a lifelong disorder characterized by an ongoing demyelinating process\textsuperscript{2}. Cases with more than two events are extremely suspicious for MS\textsuperscript{2}.

Typical ADEM lesions are large (>1 to 2 cm), multifocal, and located in the supratentorial or infratentorial white matter and central gray matter\textsuperscript{2}. Periventricular lesions are less frequent in ADEM than in MS\textsuperscript{24}. However, in general, MRI findings alone are insufficient for the diagnosis of this disease\textsuperscript{2}. Acute hemorrhagic encephalomyelitis is a rare, severe form of ADEM, in which MRI depicts hemorrhages in large demyelinating lesions\textsuperscript{25}.

Callen et al.\textsuperscript{24} proposed the following criteria to distinguish a first attack of MS from monophasic ADEM: 1) absence of a diffuse bilateral lesion pattern; 2) presence of black holes; and 3) presence of two or more periventricular lesions. These criteria (Callen MS-ADEM Criteria) are currently considered to be the best criteria, offering the combination of high sensitivity and specificity\textsuperscript{26}.

References
*Ann Neurol* 2011;69:292-302