ADEM IS A CONDITION THAT CAN BE CLINICALLY AND PATHOLOGICALLY DIFFERENTIATED FROM MS AND NMO:
NO

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The incidence of ADEM is 0.4/100,000/year among those under the age of 20. There is no clear epidemiological data in the adult population. Therefore, the differential diagnosis of ADEM mainly concerns the pediatric population, when MS (0.2-0.5/100,000/year) and NMO are less frequent. A Canadian surveillance study estimated 22% of childhood acquired demyelinating syndromes to be ADEM and 76% as clinically isolated syndrome (CIS). NMO accounts for only 3-4% of pediatric cases.
Consensus criteria define ADEM as monophasic, recurrent (second episode more than 3 months after the initial one with lesions in the same area) and multiphasic (subsequent events involving different CNS areas). An estimated one-third of patients with multiphasic ADEM become diagnosed with MS later.
According to consensus criteria, rapid onset of encephalopathy is a characteristic finding in ADEM, and the clinical course is usually more rapidly progressive than in MS. However, ADEM can be also present with a more subtle disease course similar to MS. On the other hand, up to 18% of pediatric-onset MS has an initial presentation similar to ADEM: encephalopathy and seizures can be presenting symptoms in pediatric MS. Altered consciousness can occur also in adult CIS patients, initially diagnosed with ADEM. In addition, encephalopathy maybe absent in adult ADEM patients, and is less frequent above the age of 10. Encephalopathy can be also a common symptom in pediatric NMO: 45% of children had episodic cerebral symptoms including encephalopathy. Hypothalamic lesions in NMO can cause altered consciousness in adults.
Both optic neuritis and myelitis can be present in up to one-fourth of the ADEM cases, respectively, complicating differentiation from NMO. In addition, idiopathic optic neuritis can be frequently bilateral in pediatric patients, and 58% of myelitis can be longitudinally extensive. Although poor visual outcome is usually quoted as characteristics of NMO, it is more common in childhood MS in contrast to adults.
ADEM is considered to be characterized by large, enhancing MRI lesions; but small focal lesions can be also present. On the other hand, large lesions similar to ADEM can be detected in children with NMO: 66% of them can have brain lesions, which are accompanied by symptoms in 68%. Children with MS below 11 years may also present with atypical MRI features, e.g. large lesions with poorly defined borders similar to ADEM, and higher lesions burden. In adults, tumefactive MS may pose a differential diagnostic problem: only 5% of such patients met diagnostic criteria for MS prior to biopsy, and aphasia, seizures, impaired consciousness may be present similar to ADEM. Longitudinally transverse myelitis (LETM) typical of NMO can be also seen in patients with ADEM, and even in MS: in one pediatric series, only 51% of patients with LETM had NMO, but 9% had ADEM and MS, respectively.
Anti-AQP4 antibody testing can be negative in approximately 20-30% of children with NMO. Although high anti-MOG antibody levels are present in up to 30-40% of children with ADEM, it can be present also in recurrent childhood ON, in AQP4-seronegative NMO, and even in children with CIS or MS.
In ADEM, the cerebrospinal fluid may show moderately elevated cell count and protein content in up to half of the patients. Nevertheless, such abnormalities are also common in NMO relapse, and may be even present in up to one-third of acute MS relapses. Oligoclonal bands (OCB) are present in about 10-30% of patients with ADEM, which may help to differentiate this entity from MS, but oligoclonal bands and elevated IgG index are not common in NMO either. In addition, OCB is less frequent in pediatric MS.
In conclusion, although consensus criteria are present for all these nosological entities, overlapping features especially in the pediatric population may complicate differentiation.