ADEM IS A CONDITION THAT CAN BE CLINICALLY AND PATHOLOGICALLY DIFFERENTIATED FROM MS AND NMO: YES

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Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating condition which may present in pleiotropic ways with a combination of encephalopathic symptoms suggesting a diffuse disorder of the central nervous system and with multifocal symptoms suggesting an inflammatory demyelinating disease (e.g. optic neuritis, hemiparesis). It may also involve the spinal cord. ADEM is thought to be akin to postvaccinial encephalomyelitis, a monophasic illness and represent an immune-mediated reaction to a myelin antigen, typically due to an exogenous exposure to a mimicking antigen, either vaccinial or infectious.

Neuroimaging is usually consistent with an extensive though multifocal CNS demyelinating disorder. Some use the term ADEM to refer to any acute or subacute CNS disorder with diffuse and/or multifocal white matter abnormalities as ADEM. Such indiscriminant use of this diagnostic terminology should be discouraged and is the major reason why some argue that it is not a reliabl diagnosis. There is, unquestionably, a broad differential diagnosis of ADEM, including but not confined to

1. Acute tumefactive and other fulminant forms of MS and NMO,
2. Infectious encephalopathies (e.g. HIV or CMV),
3. Neoplastic (gliomatosis cerebri, lymphoma),
4. Vasculitis and vasculopathy (e.g. Susac syndrome),
5. Genetic (adrenoleukodystrophy, metachromatic leukodystrophy and newer recognized leukodystrophies such as adult onset leukodystrophy with neuroaxonal spheroids).

Although the rules distinguishing ADEM from acute MS and other CNS demyelinating disorders are indistinct and imperfect, a combination of clinical, radiological and when required pathological findings is able to exclude other causes of leukoencephalopathy and suggest ADEM as the most likely cause[1, 2].

The diagnosis is suspected under the following circumstances:

1. The symptoms occur following an infection
2. The symptoms include encephalopathy, especially when severe, and associated with coma
3. The MRI findings are diffuse, extensive and generally symmetric and multifocal
4. The MRI findings include involvement of the basal ganglia
5. Longitudinally extensive spinal cord lesions are present

When all are present, especially in a child, these findings predict lack of relapse and monophasic course, the usual gold standard for retrospective accuracy of the initial diagnosis, they are imperfect. Individually, each of these characteristics may occur in patients with MS. Furthermore, it is unclear whether ADEM may be correct in the absence of any one or more of the above characteristics and the minimum requirement for a confident diagnosis of ADEM is not well established.

Pathological findings may be highly suggestive. While biopsy is usually unnecessary when patients have an expected course and recover smoothly, a biopsy may help differentiate ADEM from fulminant MS in the face of ongoing and recurrent symptoms, particularly when severe or life threatening. In ADEM, perivenous demyelination in sleeves surrounding small veins but without confluent demyelination and diffuse infiltration of macrophages is typical; inflammatory cells tend to be concentrated in a perivenous distribution. In contrast, in fulminant MS, extensive sheets of macrophages admixed with astrocytes, with occasional Creutzfeldt cells and confluent demyelination is the typical pathology. In a study of biopsies performed of CNS demyelinating disease, there was a strong correlation between pathological findings of ADEM and clinical features that distinguish ADEM from MS[3].

Diagnostic algorithms have been developed to permit a comprehensive evaluation stratified on the level of clinical certainty[4]. These algorithms clarify the role of biopsy for cases with atypical features for MS or suggestive features of other competing diagnoses. In such cases, biopsy should be considered relatively early when less invasive testing has failed to establish a diagnosis. Biopsy may lead to a clear diagnosis of acute disseminated encephalomyelitis in many patients, although issues with sampling bias and overlap of pathologies (combined perivenous and confluent demyelination) may lead to continued confusion.

Clinical and radiological followup remains the gold standard for accurate diagnosis. However, current understanding of ADEM and diagnostic guidelines supplemented with use of contemporary neuropathology allows for a reasonably accurate diagnosis, differentiation from mimics and prediction of clinical course.

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