The potential diagnostic value of diffusion-weighted imaging in acute disseminating encephalomyelitis

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Acute disseminating encephalomyelitis (ADEM) is an immunologically mediated inflammatory demyelinating disease of the central nervous system that typically follows a viral infection or immunization, however, there are some cases in which no precipitating factor has been traced. Although the illness typically has a monophasic course, relapsing cases were reported reaching 33% in one series. It is clinically characterized by a wide range of neurological abnormalities, including fever, headache, meningism, convulsions, cranial nerve palsies, ataxia, and psychosis. There are no pathognomonic clinical or laboratory findings, and CT of the brain is usually normal. The diagnosis is made using brain MRI, which is regarded as the diagnostic imaging modality of choice, and typically demonstrates involvement of deep cerebral hemispheric and subcortical white matter, as well as lesions in the basal ganglia, gray-white junction, diencephalon, brainstem, cerebellum, and spinal cord. The objective of this study is to demonstrate the value of DWI in ADEM.

Case Report. An 11-year-old Saudi boy presented to the emergency department with history of dizziness, headache, slurred speech, and unsteady gait with a tendency to fall down on his left side with drooling of saliva from the left side of his mouth for a few days. There was history of preceded upper respiratory tract infection and fever. Neurological examination showed normal level of consciousness with full orientation to time, place, and person. Examination of the cranial nerves revealed left facial palsy resulting in facial asymmetry. The remaining cranial nerves were intact. The tone was normal in the upper and lower limbs while the reflexes were +2. There were positive plantar reflexes bilaterally with ataxic gate. The EEG and blood chemistry tests were normal. Cerebrospinal fluid (CSF) examination revealed a mildly increased protein level, a normal cell count, and an absence of oligoclonal bands and immunoglobulin G (IgG). Serological testing for common viruses, brucella, and mycoplasms were negative. The MRI showed bilateral asymmetric large extensive multifocal confluent subcortical lesions extending into the deep periventricular white matter as well as the corpus callosum, basal ganglia, and the right thalamus, sparing the cerebellum...
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Figure 1 - Axial Brain MRI at the level of the lateral ventricles, a) T2WI, b) FLAIR, and c) contrast-enhanced T1WI showing large multifocal confluent high signal intensity subcortical lesions extending into the deep periventricular white matter with beveled (lesion within a lesion) appearance and corresponding ring-like enhancement.

Figure 2 - Diffuse weighted imaging demonstrates intense high signal intensity of the white matter lesions indicating restricted fluid pattern.

and brainstem. They demonstrate iso- to hypointensity on T1 weighted images (WI), hyperintensity on T2WI and fluid attenuation inversion recovery scans (FLAIR) with a beveled (lesion within a lesion) appearance (Figure 1a & 1b). Corresponding ring-like enhancement was detected (Figure 1c). The DWI demonstrated a restricted pattern with intense high signal intensity within the corresponding lesions (Figure 2). Based on the clinical presentation and imaging findings, the diagnosis of ADEM was considered and the patient was started on large dose intravenous pulse therapy of corticosteroids. Clinically he improved with complete resolution of his neurological manifestations. The patient was discharged home on a tapering dose of oral corticosteroids. Follow up MRI carried out 11 months later, showed that the cerebral lesions had nearly resolved with minimal T2WI and FLAIR high signal intensity residual lesions with no corresponding enhancement or altered signal intensity on DWI.

Discussion. Acute disseminating encephalomyelitis is usually a monophasic disorder, often seen one to 2 weeks following a viral infection or immunization. There may be a prodromal phase of fever, malaise, headache, nausea, and vomiting. The clinical features are determined by the distribution of lesions in the CNS. Multifocal neurological signs such as hemiparesis, bilateral upper motor neuron signs, cranial nerve palsies, dysarthria, epileptic seizures, disturbances of micturition, cerebellar ataxia and/or optic neuritis are seen. Rapid progression of symptoms and signs to coma and decerebrate rigidity may occasionally occur. Rarely, ADEM may present as a persistent subtle illness in children with irritability, headaches or atypical psychiatric illness. Laboratory investigations are seldom useful in diagnosing ADEM. The CSF is usually normal, but may show lymphocytic pleocytosis and mild elevation of protein. Other markers such as oligoclonal bands, IgG, or myelin basic protein
are sometimes detectable, but are not pathognomonic. The EEG is not useful in establishing the diagnosis, although it may show delayed non-specific features of an encephalopathic process and visual evoked potentials. The final diagnosis is based on the clinical signs, time course, and imaging findings. A cranial CT scan may be normal in the early phases of the disease, whereas MRI demonstrates subtle features of ADEM at an earlier stage. The MRI is highly sensitive in detecting white matter abnormalities and is the investigation of choice in ADEM. Discrimination between ADEM and the first presentation of multiple sclerosis (MS) has important prognostic and therapeutic implications. Patients with ADEM generally recover completely, whereas those with MS may have recurrent relapses or progressive deterioration over time. No clinical feature is exclusive to either condition, but some characteristics are more commonly seen in one than the other. Brain MRI can help distinguish ADEM from MS. In ADEM, white matter lesions are typically large, extensive, and often asymmetrical involving the adjacent grey matter, in MS the plaques are typically small, circumscribed, and symmetrical in the deep white matter. Thalamic involvement is exceedingly rare in MS, but may be seen in up to 40% of patients with ADEM, making this finding a potentially useful discriminator. In ADEM, the lesions are typically of the same age, while in MS they are usually of different ages. Contrast enhancement of the lesions, which result from disruption of the blood-brain barrier, will only be seen in the new and active lesions. Most lesions on MRI, particularly those in the deep gray matter, cerebellum, and subcortical white matter resolve in 2-3 months. Acute-phase lesions of high signal intensity may be due to tissue edema rather than myelin loss, explaining their early resolution, while periventricular white matter lesions resolve later, suggesting demyelination in their pathogenesis. Some lesions on MRI persist even in complete clinical recovery.

Acute demyelinating lesions in the setting of ADEM or MS may be difficult to separate from brain tumors, atypical infectious encephalitis, stroke, and cerebral venous thrombosis using conventional MRI alone. The DWI is a sensitive test for intracellular edema, heralding ischemic infarction in the majority of cases. Areas of acute demyelination have also been identified in progressive multifocal leukoencephalopathy. The DWI may facilitate the evaluation of demyelinating disorders by the detection of acute lesions without contrast uptake, thereby facilitating treatment. Furthermore, this modern MR technique may help to obviate brain biopsy in demyelinating lesions, which is still performed in atypical cases of acute demyelination, to rule out a neoplasm or infarction.

Recent reports on DWI of ADEM cited the presence of variable patterns, increased and decreased diffusion coefficients. It has been considered that increased diffusion coefficients likely represented demyelination, while decreased diffusion coefficients reflected accumulation of inflammatory cells. In our case, high signals were evident in the periventricular and subcortical white matter consistent with increased diffusion pattern of water molecules. Up to now, it remains unresolved if diffusion abnormalities in acute demyelinating lesions are due to swelling of injured oligodendrocytes, as suggested in PLM, or if they may represent a vasculitic sub form of lesion development with ischemic cell damage.

In conclusion, ADEM is an important and treatable cause of acute CNS deterioration in children and teenagers and its diagnosis is based on clinical signs, time course, CSF, and imaging findings. Advanced MRI techniques such as diffusion is highly sensitive, and a promising tool for acute demyelination. Therefore, in patients with diagnostic uncertainty or without contrast enhancement, DWI should supplement conventional MRI before proceeding to invasive procedures such as brain biopsy.

References