Neurotoxic Effects of Intrathecal Methotrexate

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Clinical Image

A 9-year-old girl with history of acute lymphoblastic leukemia (pre-B cell) presented with an acute onset left sided weakness. The brain MRI (Figure 1) revealed a DWI lesion with ADC correlate in the right parietal lobe. Over the next 24 hours her weakness progressed to involve the right side. A repeat MRI was done which revealed bilateral parietal lobe DWI lesions (Figure 2). An MRA of head and neck was done and did not reveal any significant stenosis or occlusion. She had received intrathecal methotrexate one week prior to presentation. A working diagnosis of methotrexate induced neurotoxicity was made and she was treated with dextromethorphan. The next day her symptoms had nearly resolved and she was almost back to her baseline.

Methotrexate related neurotoxicity is rare, but can develop from 5 to 14 days after treatment and symptoms may include headache, nausea, emesis, lethargy, altered mental status, blurred vision, aphasia, hemiparesis and seizures [1]. The MRI findings can include DWI lesions within cerebral deep white matter corresponding to the symptoms of hemiparesis. The contrast studies may not reveal any enhancement.

Figure 1: Brain MRI, axial DWI and ADC showing a DWI lesion with ADC correlate.

Figure 2: Brain MRI, axial view DWI/ADC 24 hours after the first MR.
The treatment options include aminophylline, leucovorin [1] and dextromethorphan [2]. Methotrexate therapy is known to increase both plasma and CSF homocysteine which is directly toxic to vascular endothelium. In addition, methotrexate and its metabolites are excitatory agonists of the N-methyl-D-aspartate (NMDA) receptor. Dextromethorphan, a noncompetitive antagonist of NMDA receptor can help resolve the symptoms [2].

References