

Unusual radiographic presentation of methotrexate-induced leukoencephalopathy involving the internal capsule

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DESCRIPTION

A man in his early 20s with very high-risk B-cell acute lymphoblastic leukaemia on chemotherapy presented to emergency department (ED) as a stroke-code activation for acute onset of focal neurological deficits of left-sided weakness and unsteady gait. He developed symptoms 2 hours prior to ED presentation. On examination, he had left lower facial weakness and left hemiparesis that was more pronounced in the distal musculature. He also had a wide-based unsteady gait, positive Romberg and left-sided hyper-reflexia. The patient received recent administration of intrathecal (IT) and intraventricular (IV) methotrexate 9 days prior as part of his treatment regimen.

MRI performed in the ED less than 4 hours from symptom onset revealed an area of restricted diffusion in the posterior limb of the right internal capsule on diffusion-weighted and apparent diffusion coefficient sequences without other areas of T2-fluid attenuated inversion recovery (FLAIR) signal abnormality (figure 1) and normal MR angiography (not shown). The patient's clinical presentation, MRI findings and recent history of administration of high-dose IV and IT methotrexate was most suggestive of methotrexate-induced leukoencephalopathy. He was started on a cocktail treatment regimen of leucovorin, dextromethorphan, pyridoxine and folic acid with complete resolution within a few days and was discharged with a normal neurological examination.

Strokes involving the internal capsule typically present with persistent symptoms of contralateral mixed sensorimotor deficits. However, in cases of methotrexate-induced leukoencephalopathy, symptoms are generally transient and self-resolve within a few days. In addition, T2 FLAIR lesions are not expected to appear on MRI in vascular strokes presenting less than a 6-hour time frame from symptom onset. A pathognomonic feature of methotrexate toxicity is the appearance of both DWI and correlated T2 FLAIR lesion, as seen in our patient's case.

Neurotoxic effects of methotrexate and its radiological findings have been well established, especially in the young adult cancer population. Clinically, symptoms usually present within 2–14 days of methotrexate administration in acute onset methotrexate leukoencephalopathy. The typical radiologic findings of methotrexate toxicity in the brain are restrictive diffusion signals of a bilaterally asymmetric distribution crossing multiple vascular territories. However, unilateral and alternating lesions may also be seen. It can affect the centrum semiovale, with initial sparing of the subcortical U fibres. These lesions tend to be transient and disappear with symptom resolution.^{1,2}

Methotrexate is a folate antagonist and is a competitive inhibitor of dihydrofolate reductase in the folic acid cycle. In addition, certain neurotoxic metabolites accumulate such as adenosine in the cerebrospinal fluid (CSF) as well as homocysteine

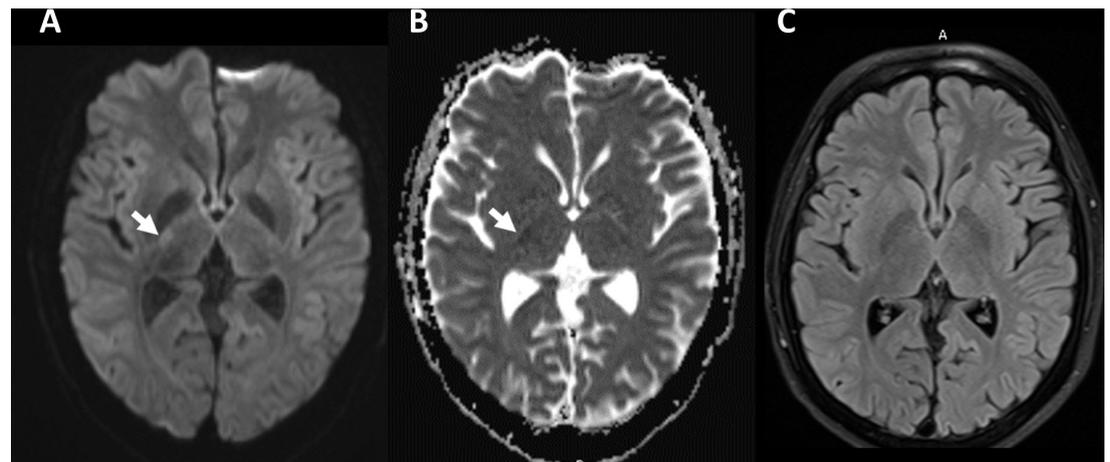


Figure 1 MRI features of atypical methotrexate-induced leukoencephalopathy. MRI demonstrates a small area of restricted diffusion in the posterior limb of the right internal capsule on diffusion-weighted (arrow) (A) and apparent diffusion coefficient sequences (B) without abnormalities on T2-fluid attenuated inversion recovery sequence (C).



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in the CSF and serum. Treatment of methotrexate toxicity involves the neutralisation of these toxic metabolites as well as reversal of folic acid cycle inhibition through administration of both folic acid and high-dose folinic acid. Aminophylline and dextromethorphan therapies act on the antagonistic properties of adenosine and homocysteine, respectively, to reduce the toxic molecules and thereby treat methotrexate toxicity.^{3 4}

We report an atypical radiographic presentation of methotrexate toxicity involving the posterior limb of the internal capsule (PLIC). PLIC lesions can be seen in acute and chronic hepatic encephalopathy, heroin toxic leukoencephalopathy and inhaled heroin (chasing the dragon) toxicity. However, this is not a usual finding in methotrexate leukoencephalopathy

Learning points

- ▶ Methotrexate toxicity should be considered in the differential of a patient presenting with recent administration of high-dose intraventricular and/or intrathecal methotrexate with new focal neurological symptoms.
- ▶ Typical presentation of methotrexate toxicity on MRI includes asymmetric distribution of restriction diffusion signals crossing multiple vascular territories; classically, involving centrum semiovale and initial sparing of subcortical U fibres.
- ▶ Atypical radiologic findings of diffusion restriction signal and/or T2/fluid-attenuated inversion recovery hyperintensity of the posterior limb of the internal capsule may be associated with methotrexate-induced leukoencephalopathy.

and although subtle, correlated with the patient's clinical presentation.

The atypical neuroradiographic findings as reported in this case will raise awareness for clinicians to recognise both typical and atypical radiologic findings of methotrexate toxicity that may lead to early recognition and changes in management.

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Case reports provide a valuable learning resource for the scientific community and can indicate areas of interest for future research. They should not be used in isolation to guide treatment choices or public health policy.

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