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IMAGES IN HEMATOLOGY

Subacute methotrexate-related leukoencephalopathy with stroke-like presentation

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A 20-year-old man was treated for B lymphoblastic leukemia and achieved complete remission after the first round of induction chemotherapy. Induction and the two subsequent consolidation therapy regimens were free of neurological adverse effects, although he received a total of five doses of intrathecal methotrexate (MTX). Anticancer agents (intravenous cytarabine, cyclophosphamide, pirarubicin hydrochloride, and oral mercaptopurine) were administrated with intrathecal MTX (12 mg), cytarabine (30 mg), and hydrocortisone (25 mg) on days 1 and 8 as a third consolidation chemotherapy. Eight days after the second intrathecal MTX injection, he developed sudden-onset right incomplete hemiplegia. Diffusion-weighted MRI (DWI) showed areas of high signal intensity in the white matter of the bilateral frontal lobes (Figure not shown) and the splenium of the corpus callosum (left column, Fig. 1). An apparent diffusion coefficient (ADC) map showed low signal intensity in the same lesion (middle column, Fig. 1). T1- and T2-weighted fast fluid-attenuated inversion recovery (FLAIR) (right column, Fig. 1) and magnetic resonance angiography images were unremarkable in all areas (Figure not shown). His symptoms resolved transiently the next morning; however, right complete hemiplegia, inability to vocalize, and dysphagia developed the same evening. His neurologic manifestations gradually improved within 2 days. A follow-up MRI on day+2 and day+4 after the onset of the stroke-like presentation showed new areas as well as partly reduced areas of high intensity in the white matter on DWI and of low intensity in the ADC map. FLAIR images showed a new area of high signal intensity on day+4. A follow-up MRI on day+18 demonstrated that the abnormal area had almost disappeared on DWI and the ADC map, and a residual lesion of high signal intensity was still observed on FLAIR images.

DWI provides image contrast dependent on the molecular motion of water, and has been useful in the diagnosis of cytotoxic edema secondary to acute ischemia. In ischemic stroke, decreased ADC values are correlated with irreversible brain damage, and the normalization of ADC occurs within a couple of weeks after the ischemic event. In subacute leukoencephalopathy, however, brain regions with marked hypointensity on ADC maps show rapid normalization of the ADC hypointensity. In the present case, the patient was diagnosed with subacute MTX-related leukoencephalopathy based on the fluctuating clinical course and MRI findings, which were not consistent with cerebral stroke. Although subacute MTX-related leukoencephalopathy is well recognized in childhood acute lymphoblastic leukemia, hematologists of adult or adolescent patients may be unaware of this syndrome. Our case demonstrates that sequential MRI exams including DWI and the ADC map are useful for diagnosing subacute MTX-related leukoencephalopathy.

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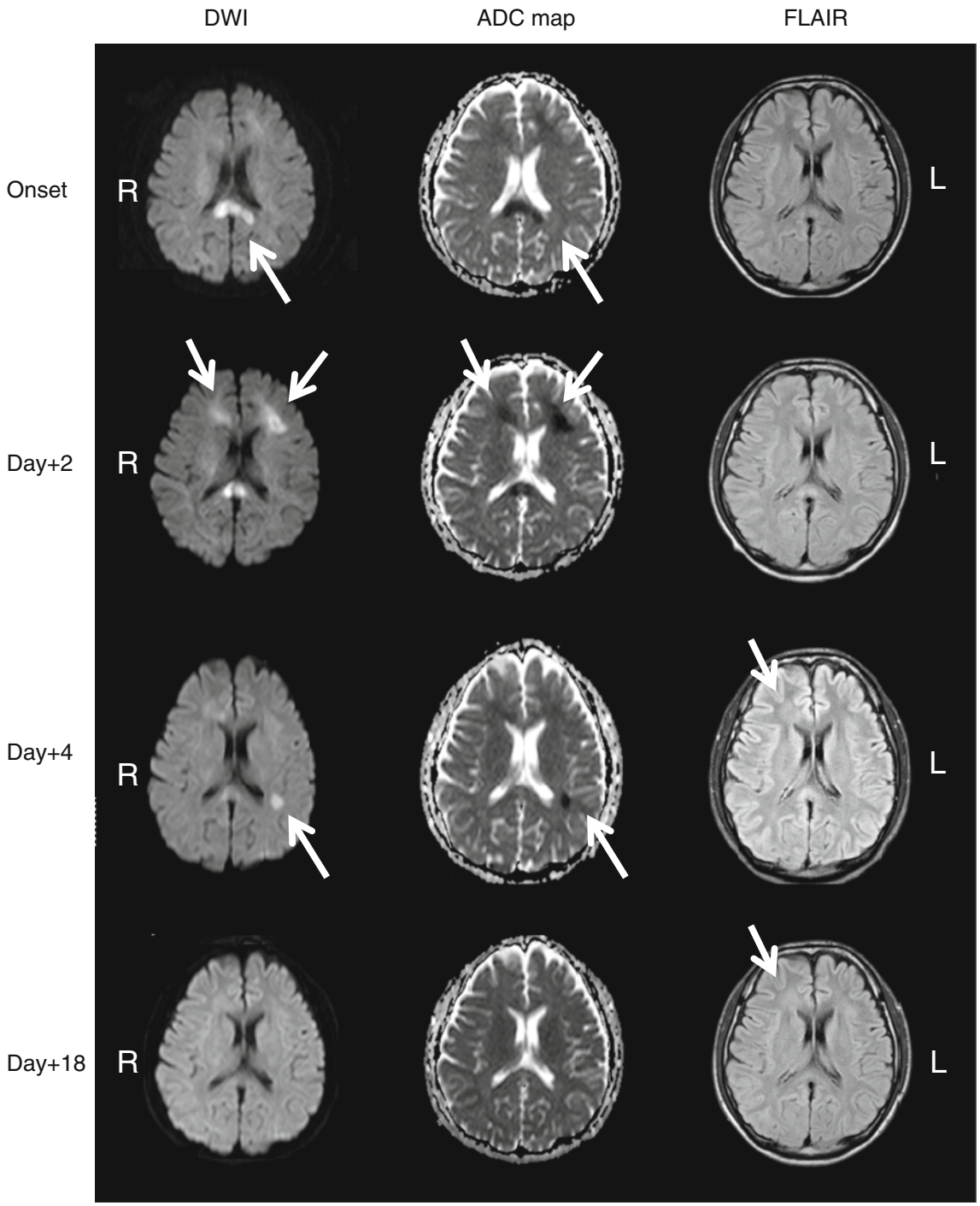

Fig. 1 Serial MRI of a patient with stroke-like syndrome after an intrathecal MTX injection. Diffusion-weighted images (DWI *left column*), apparent diffusion coefficient maps (ADC *middle column*), and fluid-attenuated inversion recovery (FLAIR, *right column*) images are shown. The *arrows* show regions with abnormal intensity

Conflict of interest None.