A 13-year-old girl with acute lymphoblastic leukemia (ALL) achieved complete remission after induction according to the TPOG ALL 2002-HR protocol [1]. On the 9th day after the 2nd high-dose methotrexate (HDMTX), progressive right hemiparesis with headache, dysphagia, dysarthria, and emotional disturbances were noted. Magnetic resonance imaging (MRI) of brain showed high intensity in bilateral centrum semiovales on diffusion-weighted image (DWI) and low intensity on apparent diffusion coefficient (ADC) maps (Web Fig. 1a – 1d). Findings on fluid attenuated inversion recovery (FLAIR) images were much less prominent. Dexamethasone and aminophylline were administered; symptoms resolved soon. A recurrent episode of similar symptoms but with more intense severity and left hemiparesis occurred after the 3rd HDMTX. MRI (Web Fig. 1d - 1f) illustrated extension of hyperintense on DWI and hypointense on ADC maps with new lesions in the right side. Increased intensity on FLAIR images was now evident. Administration of leucovorin with dexamethasone and aminophylline improved the condition gradually. Considering the risk of her ALL, HDMTX with intrathecal chemotherapy was resumed as the schedule despite the residual leg weakness. To prevent recurrence, four doses of dexamethasone were administered before HDMTX and an additional dose of leucovorin was given six hours before the schedule. No related side-effects occurred after the 4th course. She is now in complete remission without neurological sequelae. Follow-up MRI (Web Fig. 1g - 1r) showed resolution of hyperintensity on DWI and hypointensity on ADC maps. The high intensity on FLAIR images was most prominent 3 months after the second episode. As resolved slowly thereafter, it remained evident in the absence of a clinical correlate.

HDMTX is the mainstay during consolidation for children with ALL [2], and leukoencephalopathy is rare in these patients who receive MTX at a dose of 1-5 g/m² [3]. From 2002 to 2013, we treated 1,620 children with ALL with the TPOG ALL 2002 protocol, which included four courses HDMTX (2.5 g/m² or 5 g/m²) during consolidation phase. Only two patients without delayed MTX clearance had leukoencephalopathy, and only the present patient experienced two episodes.

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