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Letter to the Editor

Reply to the Letter, "Methotrexate myelopathy: A mimicker of subacute combined degeneration of the spinal cord"

Dear Dr. Saini,

Thank you for providing us with valuable comments regarding our manuscript entitled, "A case of subacute combined degeneration of the spinal cord due to folic acid and copper deficiency".

Indeed, the myelopathy could be attributable to methotrexate (MTX) in our patient, who received three courses of MTX. The first two courses were intrathecally administered, but the third was intravenously administered to prevent graft-versus-host disease after bone marrow transplantation. The period from the last intrathecal administration of MTX to the onset of subacute combined degeneration of the spinal cord (SACD) was about three months. Although the usual latency between MTX treatment and the onset of MTX myelopathy is thought to be about 10 days, MTX myelopathy can arise after $\geq$90 days [1]. Thus, MTX could have caused the myelopathy in our patient. Methotrexate decreases production of the active folate metabolite, dihydrofolate, by inhibiting dihydrofolate reductase. Therefore, MTX toxicity enhances the effects of a folate deficiency, and vice versa.

However, we disagree with the notion of using dextromethorphan to treat MTX myelopathy. Our autopsy findings have shown that the pathology of SACD is demyelination, not neuropathy. Since N-methyl-D-aspartate (NMDA) receptors are only found in neurons, SACD-type MTX myelopathy is unlikely to be mediated by NMDA receptors. Demyelination of SACD is caused by an S-adenosylmethionine (SAM) deficiency [2–4], and SAM is the principal methyl donor for DNA methylation, which plays a key regulatory role in myelination [4]. Both vitamin B12 and folate are essential to produce methionine, which is converted to SAM. Thus, we believe that supplementation with methionine or SAM would effectively treat SACD caused by MTX.

References

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