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Letter to the Editor

Methotrexate myelopathy

Keywords: Intrathecal methotrexate; Myelopathy; SACD

Dear Sir,

We read with great interest the article by Nakamura et al. on subacute combined degeneration of the spinal cord (SACD) due to folic acid and copper deficiency in a child with T-cell acute lymphoblastic leukemia [1]. Authors have aptly discussed the possible etiology for SACD and attributed it to folic acid and copper deficiency. However, we would like to raise a few concerns and discuss other possibilities, particularly methotrexate myelopathy (MM).

Besides leukoencephalopathy, intrathecal methotrexate has been associated with myelopathy [2]. MM may be necrotizing or demyelinating and is similar to SACD in clinico-radiological presentation. Hence, the route of methotrexate administration (especially intrathecal) in the index case should be specified. MM probably occurs due to a complex interplay of direct toxic effects, elevated homocysteine, and folate antagonism. Irreversibility of SACD, despite folate and vitamin B12 supplementation, might be a clue towards MM. MM should also be considered in cases with associated white matter changes in brain parenchyma and elevated homocysteine in presence of normal vitamin B12 and folate levels. Authors have rightly pointed that folate and copper levels in the index child were not very low as described in previous patients. Therefore, the possibility of etiology being multifactorial (MM, folate and copper deficiency) is high.

Dextromethorphan, an antagonist of N-methyl-D-aspartate receptors (activated by elevated homocysteine), is thought to be beneficial in methotrexate related neurotoxicity and may be tried in patients with MM [3]. Also, screening patients for low folate levels before methotrexate administration may be considered, although it may lead to "folate over-rescue" and reduction in the anti-neoplastic activity of methotrexate [4].

Other possible etiologies include chemotherapeutic agents- cytosine arabinoside, nelarabine etc and radiotherapy. Also, it would be important to know the general anesthetics used during appendectomy. Nitrous oxide administration may also be associated with SACD [5].

Author contribution

PM prepared the initial draft of the manuscript and reviewed the literature.

LS – critical review of the manuscript and reviewed the literature, edited the final version of the manuscript.

Declaration of interest

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