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LETTER TO THE EDITOR

Methotrexate neurotoxicity due to drug interactions: an inadequate folinic acid effect?

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Keywords Methotrexate · Neurotoxicity · Drug interaction folinic acid.

Dear Sir,

Forster et al. [1] are to be congratulated on their detailed and thorough review of possible reasons why a patient developed neurotoxicity after intrathecal (IT) methotrexate (MTX) therapy with concurrent nitrous oxide. They were suspicious that this neurotoxicity could have been caused by a direct drug interaction leading to increased methotrexate (MTX) plasma (and/or CSF) concentrations or interference with the same metabolic pathways as MTX. However, as they note, neurotoxicity is not directly related to the dose of MTX used. The episode of neurotoxicity occurred after the fifth dose of IT MTX, which raises the question as to whether this patient also received systemic MTX. Aur et al. [2] noted that encephalopathic reactions developed almost exclusively in patients receiving five or more doses of intrathecal methotrexate and more than 40 mg/m^2 weekly of intravenous methotrexate. One aspect of methotrexate neurotoxicity not discussed in the manuscript is the significance of folinic acid in the prevention of neurotoxicity. Recently, more attention is being payed to the connection between neurotoxicity following systemic MTX and the folinic acid rescue dose given [3–5]. The neurotoxicity due to an increase in MTX CSF levels in this case, due to systemic MTX, if it was given, or an interaction with the nitrous oxide may have been a result of inadequate folinic acid available for "rescue". This potential for neurotoxicity should be appreciated, since it is easily avoided by folinic acid rescue.

Compliance with ethical standards

Conflict of interest Nothing to declare.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

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