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LETTER TO THE EDITORS

Defining metronidazole-induced encephalopathy

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Dear Sirs,

Metronidazole is commonly used and generally safe. Central nervous system (CNS) toxicity associated with metronidazole has been known since 1970s. Sørensen et al. again raised awareness of this complication with their systematic review [1]. We have several concerns on Sørensen et al.'s review to more precisely define metronidazole-induced CNS toxicity and encephalopathy.

First, we doubt that the term "encephalopathy" used by Sørensen et al. correctly describes this entity. Encephalopathy is a term that describes a diffuse brain disorder that presents with an altered level or content of consciousness, and is occasionally accompanied by seizures. However, cerebellar dysfunction is the most common manifestation of metronidazole-induced CNS disorders; altered mental status and seizures are much less common [2]. The term "metronidazole-induced encephalopathy" should thus be used more selectively.

Second, Sørensen et al. listed "polyneuropathy" as a manifestation of metronidazole-induced CNS toxicity. They used the term to name paresthesia such as a burning or tingling sensation on limbs in some cases, which is a typical presentation of metronidazole-induced 'peripheral' neuropathy. It is thus not a CNS symptom but a concurrent complication. Hence, polyneuropathy should be left out from the list of manifestations of this entity in Sørensen et al's study.

Third, the inclusion criteria of cases in Sørensen et al.'s study are unclear. For example, Sørensen et al. excluded a case of 55-year-old man who developed acute mental status change alone [3], though this case met their inclusion criteria. Further, magnetic resonance imaging (MRI) is not diagnostic for patients with altered mental status or convulsive seizures due to metronidazole, because they do not always have abnormal MRI findings [2]. Sørensen et al. excluded cases that had symptoms but did not undergo (MRI), and should have underestimated altered mental status or convulsive seizures due to metronidazole. We are concerned that Sørensen et al. excluded clinically relevant cases that could paint a clearer picture of the spectrum of metronidazole-induced CNS toxicity.

Finally, metronidazole-induced CNS toxicity can be classified as three types: altered mental status, convulsive seizures, and cerebellar dysfunction. We proposed this classification in our systematic review of metronidazole-induced CNS toxicity in 2011 [2]. Our review has served as a core reference to highlight metronidazole-induced CNS disorders in clinical practice guidelines, reviews, and textbooks [4–15]. Although our taxonomy has thus been extensively utilized, Sørensen et al. treated our review as a case report and failed to credit our taxonomy properly. Clinicians should be aware of this triad (altered mental status, convulsive seizures, and cerebellar dysfunction) as potential manifestations of metronidazole-induced CNS toxicity.

Compliance with ethical standards

Conflicts of interest All authors declare that they have no conflict of interest.

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

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