LETTER TO THE EDITOR

Drug-induced cholestatic hepatitis: how late can it occur even after the cessation of the culpable drug?

Dear Editor:

We read with interest the study performed by G. Sarganas et al., entitled “Severe sustained cholestatic hepatitis following temozolomide in a patient with glioblastoma multiforme: case study and review of data from the FDA adverse event reporting system,” recently published in *Neuro-Oncology*. The authors first presented a 51-year-old man who was admitted to their center with glioblastoma multiforme. He was hospitalized for about 2 weeks after craniotomy and then discharged. About one month after the craniotomy, he underwent chemotherapy with temozolomide. About 1 and a half months later, the patient began to complain of nausea and vomiting, and after evaluations were performed, the diagnosis of cholestatic hepatitis due to temozolomide was confirmed for him.

Although, as the authors declared, cholestatic hepatitis induced by temozolomide has previously been reported, there is a point the authors may have missed. Evaluation of the patient’s history reveals that the patient had been on paracetamol for postoperative pain within the 2 weeks between the craniotomy and discharge from the hospital (1000 mg 3 times per day). Although this therapy had been stopped at discharge and the patient was asymptomatic for about 2 months after its cessation, there is a point about the hepatotoxic medications that should not be forgotten. Drugs that produce predictable liver injury, such as paracetamol, usually do so within a few days and are generally a result of direct liver toxicity of the parent drug or its metabolites. However, unpredictable events manifest as overt or symptomatic disease and can occur with intermediate (1–8-week) or long (1-year) periods of latency even after cessation of the culpable medication. The authors have also not mentioned anything about the patient’s drug history while he was on chemotherapy. How do they know that the patient had not been consuming paracetamol or similar medications for pain? How could they exclude the diagnosis of paracetamol-induced cholestatic hepatitis? Thank you for this interesting study.

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References

