Hepatitis B virus reactivation during temozolomide administration

The purpose of a study was to clarify the clinical features of temozolomide (TMZ)-related hepatitis B virus (HBV) reactivation and to identify HBV reactivation predictive factors.

Method: We retrospectively reviewed the clinical course of 145 patients newly diagnosed or with recurrent malignant glioma treated with TMZ. Before treatment, we screened patients for HB surface antigen (HBsAg) positivity (HBV carrier) and HBsAg negativity. Patients were also screened for antibody for HB core antigen (anti-HBc) positivity and/or for HB surface antigen positivity (resolved HBV infection). The patients were monitored by HBV DNA, alanine, and aspartate aminotransaminase during and after the completion of TMZ. HBV carriers and those with resolved HBV infections with HBV reactivation received preemptive entecavir treatment. In those with resolved HBV infections, we analyzed clinical characters for the predictive factors for HBV reactivation.

Results: In one of two HBV carriers, HBV DNA turned positive 8 months after the completion of TMZ and entecavir. In four (16.7%) of 24 resolved HBV infections, HBV DNA turned detectable at completion of concomitant radiation and TMZ or during monthly TMZ. HBV DNA turned negative with entecavir in all patients without liver dysfunction. In resolved HBV infections, those with a high anti-HBc titer had significantly higher incidence of HBV reactivation than those with low anti-HBc titers (60% vs. 5.3%: $p = 0.018$).

Conclusion: Screenings, monitoring, and preemptive entecavir were important for preventing TMZ-related HBV reactivations. Anti-HBc titers could be the predictive markers for HBV reactivation in the those with resolved HBV infections [1].

A case of severe temozolomide-induced liver injury during concurrent radiotherapy treatment, at a dose level of 75 mg/m2. The aim of this case report is to focus on the problems of temozolomide-induced hepatotoxicity. In conclusion, a close monitoring of liver function tests is recommended during treatment with temozolomide [2].

Hepatitis B virus (HBV) reactivation during anticancer chemotherapy or immunosuppressive therapy in chronic carriers can lead to fatal liver failure. We report a rare case of severe HBV reactivation during postoperative radiotherapy with concomitant and adjuvant temozolomide (TMZ) for malignant glioma. A 49-year-old Japanese woman with a history of HBV carrier status with positive results for hepatitis B surface antigen presented with persistent headache due to a tumor in the left frontal lobe. The tumor was partially resected and anaplastic astrocytoma was diagnosed. Postoperative liver function was normal and radiotherapy plus concomitant and adjuvant TMZ was started. Impaired liver function became apparent just before administration of adjuvant TMZ, and acute liver failure developed. Antiviral therapy including entecavir, a nucleoside analog, led to a successful outcome and the patient survived. This case underlines the possibility of HBV reactivation due to TMZ and suggests the utility of HBV screening and antiviral prophylaxis before administration of TMZ to patients with malignant glioma [3]

A 61-year-old man with glioblastoma and positive for hepatitis B surface antigen (HBsAg) developed acute hepatitis due to hepatitis B virus (HBV) reactivation after concomitant postoperative treatment with temozolomide (75 mg/m(2)/day) and radiation therapy (60 Gy in 30 fractions). Corticosteroids were not used during chemo-radiation therapy, and grade 4 lymphocytopenia was observed. The levels of liver function tests (LFTs), including levels of aspartate aminotransferase and alanine aminotransferase, increased 5 weeks after the completion of chemo-radiation therapy, and reached the maximum levels of 1,549 IU/l (normal 13 to 33 IU/l) and 1,653 IU/l (normal 8 to 42 IU/l), respectively, after 2 weeks. At this point, serum HBV-deoxyribonucleic acid (DNA) level had increased to 630-fold over the baseline, and therapy with the antivirus agent entecavir (0.5 mg daily) was started. Over the next 2 weeks, the levels of LFTs and HBV-DNA improved. The present and previous cases suggest that grade 3/4 lymphocytopenia or grade 2 lymphocytopenia with corticosteroid use might have a significant effect on HBV reactivation. To avoid this complication, HBsAg-positive patients with glioblastoma should consult a hepatologist for initiating antivirus therapy before temozolomide treatment [4].

Fatal reactivation of hepatitis B with temozolomide [5].

Hepatitis B reactivation during glioblastoma treatment with temozolomide: a cautionary note [6].

1)
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