Clinical and genetic predictors of temozolomide-induced severe myelotoxicity in adult diffuse glioma: a case-control study

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Aims and scope

Submit manuscript

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Abstract

Purpose

Several clinical and genetic factors including single nucleotide polymorphisms (SNP) in the O^6-methylguanine-DNA methyltransferase (*MGMT*) gene are associated with increased risk of temozolomide (TMZ) induced myelotoxicity. We have previously reported substantially higher frequency of variant T allele of L84F (SNP in *MGMT* gene) in Indian patients with clinically relevant myelotoxicity compared to normal South Asian population. We now report findings from our case-control study correlating clinical and genetic factors with TMZ-induced ≥grade 3 myelotoxicity in adult diffuse glioma.

Methods

We enrolled 46 cases (≥grade 3 myelotoxicity) and 50 controls (grade 0–1 myelotoxicity) in the

present case-control study. Association of various clinical and genetic characteristics with TMZ-induced severe myelotoxicity was analysed using chi-square test and Fisher's exact test as appropriate and expressed as odds ratio (OR) with 95% confidence intervals (95%CI). For matched-pair analysis, propensity scores were estimated using logistic regression model based on baseline covariates – age, gender, platelet count, and body-surface area (BSA). Cases (n = 26 and controls (n = 26) were matched in 1:1 ratio using nearest-neighbour matching method without replacement.

Results

We found statistically significant association of TMZ-induced ≥grade 3 myelotoxicity for female gender (OR = 5.39, 95%CI: 2.25–12.94; $p < 0.001$), BSA≤1.6m^2 (OR = 3.79, 95%CI: 1.52–9.48; p = 0.005), and presence of variant T allele in L84F (OR = 5.04, 95%CI: 2.07–12.27; p = 0.001). Propensity score matching confirmed positive correlation of ≥grade 3 myelotoxicity with variant T allele in L84F (OR = 4.55, 95%CI: 1.37–15.08; p = 0.01).

Conclusions

Our case-control study reports significant association between TMZ-induced severe myelotoxicity and various clinical and genetic factors in accordance with findings from previous studies.