

Prolonged and severe thrombocytopenia with pancytopenia induced by radiation-combined temozolomide therapy in a patient with newly diagnosed glioblastoma—analysis of *O*⁶-methylguanine-DNA methyltransferase status

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Abstract We report a case of a 51-year-old woman with newly diagnosed glioblastoma multiforme (GBM) who was treated with surgery followed by the standard concomitant temozolomide (TMZ) and radiotherapy (RT). Although TMZ is generally safe and well-tolerated, she developed a sudden onset of prolonged and severe thrombocytopenia as the most prominent event of pancytopenia during the combined treatment, leading to discontinuation of the combined therapy. Thrombocytopenia lasted for more than 2 months with intensive, intermittent platelet transfusions. A bone marrow aspiration and biopsy performed after recovery of severe suppression still revealed reduced number of megakaryocytes. *O*⁶-methylguanine-DNA methyltransferase (MGMT) analyses showed methylated MGMT promoter in GBM, but unmethylated promoters in both peripheral blood leukocytes and bone marrow cells. This is the first report suggesting the irrelevance of MGMT status of normal hematopoietic cells to TMZ-induced severe thrombocytopenia and pancytopenia.

Keywords Temozolomide · Pancytopenia · Thrombocytopenia · Glioblastoma · *O*⁶-methylguanine-DNA methyltransferase · Combined radiochemotherapy

Introduction

Temozolomide (TMZ) has been considered as the current standard chemotherapeutic agent in combination with radiotherapy (RT) for management of patients with glioblastoma multiforme (GBM) [1]. TMZ is generally safe and well-tolerated at continuous daily dose of 75 mg/m² during external beam radiotherapy for total 60 Gy, fractionatedly delivered in 6 weeks. The incidence of grade 3 or 4 myelosuppression, the dose-limiting toxicity, is relatively uncommon, being reported to occur in only 4% of patients [1]. TMZ is an alkylating agent giving rise to methylation at the *O*⁶-position of guanine in DNA, thereby exerts antitumor effects in tumor cells. However, this lesion is effectively repaired by a DNA repair enzyme *O*⁶-methylguanine-DNA methyltransferase (MGMT) and a close relationship between MGMT status and sensitivity to TMZ has been demonstrated in GBM [2]. Here we report a case of GBM treated with the standard TMZ and RT regimen, who developed a sudden onset of prolonged and severe thrombocytopenia as the most prominent event of pancytopenia during the treatment, together with an analysis of MGMT status in hematological system.

Case report

A 51-year-old Caucasian woman with an unremarkable past medical history presented with a sudden onset of

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