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Temozolomide-induced myelodysplasia.

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Abstract

A patient who had received temozolomide (TMZ) as a single agent in treatment of malignant glioma developed therapy-induced myelodysplasia (T-MDS). TMZ is an orally active imidazotetrazine which methylates guanine residues in DNA, ultimately causing single and double-strand DNA breaks leading to apoptotic cell death. TMZ does not chemically cross-link DNA and is considered a nonclassical alkylating agent, similar in structure and activity to dacarbazine. Observations on this patient, and on similarly treated others, suggest that the cumulative dose threshold (CDT) for TMZ that predisposes to T-MDS and which may potentially lead to acute myeloid leukemia (T-AML) is around 18000 to 20000 mg/sq m. Although the incidence of T-MDS and the predisposing CDT of TMZ may differ from that of other potentially leukemogenic compounds currently and formerly used as chemotherapeutic agents, all alkylating agents, including TMZ, should be considered potentially leukemogenic when administered long term.

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