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LETTER TO THE EDITOR

MGMT promoter methylation status in anaplastic meningiomas

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To the Editor:

Anaplastic meningioma [World Health Organization (WHO) grade III] is characterized by aggressive biological behavior and recurrent tumor growth [1]. Radiation therapy is commonly employed after both total and subtotal resection, but effective chemotherapeutic regimens are lacking [2]. Hypermethylation of the O^6-methylguanine-DNA methyltransferase (MGMT) promoter is an important prognostic marker and also predicts response to therapy with alkylating agents (e.g., temozolomide) in patients with malignant gliomas [3]. While in benign meningiomas (WHO grade I) MGMT promoter methylation is rare or absent [4, 5] and temozolomide lacked efficiency in a small series of grade I meningiomas refractory to treatment [6], in anaplastic meningiomas, i.e., those neoplasms most likely to be considered for adjuvant treatment, MGMT methylation status has only been assessed in one and three cases, respectively [4, 5] and the role of temozolomide remains unclear. We thus aimed to examine MGMT methylation status in a large series of anaplastic meningiomas.

Formalin-fixed paraffin-embedded tissue samples from all anaplastic meningiomas diagnosed from 1989 to 2009 were retrieved from the archives of the Institute of Neuropathology, Münster. In addition, available samples of formerly grade II or recurrent grade III tumors of these patients were also retrieved. All samples were reviewed neuropathologically according to WHO criteria [1]. After isolation and bisulfite conversion (EZ DNA Methylation-Gold Kit; Zymo Research, Orange, CA), DNA from representative tumor material was subjected to methylation-specific polymerase chain reaction (PCR) as described previously [7]. Controls included clones representing methylated and unmethylated bisulfite converted DNA [8] as well as enzymatically methylated human genomic DNA (Zymo Research).

Using the above approach, a total of 55 samples from 30 patients could be examined. The median age of the 17 females and 13 males was 66 years (range 33–92 years). Eighty-five percent of the tumors were of supratentorial location. As shown in Fig. 1, MGMT promoter methylation status was negative in all cases except for a single specimen. This 57-year-old male suffered from recurrent grade III meningioma, showing hypermethylation of the MGMT promoter region on repeated analyses. Using the same methodology, MGMT promoter methylation status was positive in 90 out of 194 malignant astrocytic tumors (46%, data not shown).

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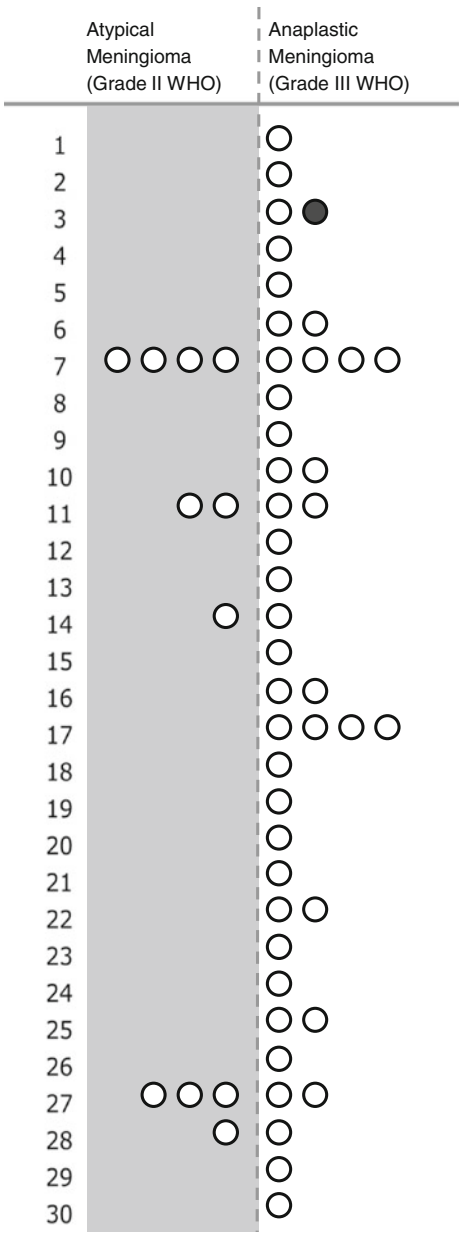

Fig. 1 MGMT promoter methylation status (● positive; ○ negative) in 30 patients harboring anaplastic meningioma. Also shown is the MGMT promoter methylation status of 14 recurrences as well as 11 atypical meningiomas that had been diagnosed earlier in these patients

The absence of MGMT promoter methylation in the vast majority of cases in this large representative series of anaplastic meningiomas extends previous observations in benign and atypical meningiomas showing absent [4] or low extent [5] of MGMT methylation. In contrast to astrocytic tumors, where a higher proportion of hypermethylated samples is encountered in malignant neoplasms as compared with low-grade astrocytomas [9], in meningiomas the proportion of methylated samples seems to be very low and unrelated to grade of malignancy. Even though the role of alkylating agents in the treatment of anaplastic meningiomas remains to be determined in future clinical trials, our data provide no rationale for the determination of MGMT methylation status in this context.

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