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Authors' Reply to "Pituitary Atypical Adenoma or Carcinoma Sensitive to Temozolomide Combined with Radiation Therapy: A Case Report of Early Identification and Management"

Yazarların "Radyoterapiyle Kombine Edilen Temozolomid Duyarlı Pitüiter Atipik Adenom veya Karsinom: Erken Tanımlama ve Yönetimle İlgili Bir Olgu Sunumu" Makalesine Cevabı

Lorenzo CURTÒ, Francesco TRIMARCHI

University of Messina, Department of Clinical and Experimental Medicine - Section of Endocrinology, Messina, Italy

Corresponding Author: Lorenzo CURTÒ / E-mail: curto.loren@libero.it

KEYWORDS: Aggressive pituitary adenoma, Pituitary carcinoma, Temozolomide, O6-methylguanine DNA methyltransferase, Chemotherapy
ANAHTAR SÖZCÜKLER: Agresif pitüiter adenom, Pitüiter karsinom, Temozolomid, 06-metilguanin DNA metiltransferaz, Kemoterapi

Dear Editor,

I have read with interest the paper by Zhong et al. entitled "**Pituitary atypical adenoma or carcinoma sensitive to temozolomide combined with radiation therapy: a case report of early identification and management"** in which the authors described the case of a 30-year-old woman with highly suspect pituitary carcinoma without metastasis, sensitive to early radio-chemotherapy with temozolomide (TMZ) (4).

In a manuscript published in 2010, we reported the case of effective TMZ treatment in a 42-year-old man with ACTH-secreting pituitary carcinoma (1). The tumor grew over 4 years, from 2.2 to 31.1 cm^3, despite 3 surgical approaches and γ-knife treatment. Ki-67 progressively increased from 2 to 18%. In our patient, an intradural metastasis at the foramen magnum was detected by MRI after the third operation. Low O-6-methylguanine-DNA methyltransferase (MGMT) expression (<5% nuclear staining) was detected in specimens recovered from the second surgery.

TMZ, a second-generation alkylating cytostatic drug introduced for treatment of glioblastoma multiforme, but effective in other CNS neoplasms as well as in neuroendocrine tumors, has also been proposed for management of pituitary carcinomas and aggressive pituitary adenomas (3). This drug can alkylate and methylate specific guanine residues, damaging DNA and triggering the death of tumor cells. Effectiveness of TMZ is related to the down-expression of MGMT, an enzyme able to repair this type of DNA damage (2).

In our case, 4 cycles of 5-day TMZ administration (200 mg/m^2/day during the first, and 150 mg/m^2/day during the following cycles, for 5 days) induced a dramatic shrinkage of the tumor size (>90%) with stabilization of the intradural metastasis volume. Clinical conditions improved progressively and, after 17 months from the beginning of TMZ administration, the patient was still alive. The drug was well tolerated and a transient thrombocytopenia, requiring platelet transfusion, was the only side effect that occurred after the first cycle of treatment.

TMZ can be considered an effective and safe approach to carcinomas and aggressive pituitary adenomas. MGMT expression can predict the effectiveness of TMZ, but since this observation has not been definitively confirmed, MGMT status should be considered a poor predictor of treatment outcome and should not be used for the selection of patients candidate to TMZ therapy. Moreover, a short trial with TMZ could be useful to identify potential responder patients in comparison with the MGMT expression.

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