IJAE
Vol. 118, n. 2 (Supplement): 106, 2013
ITALIAN JOURNAL OF ANATOMY AND EMBRYOLOGY

# Relevance of tumour surrounding area in chemoresistance of glioblastoma (GBM)

Fortunata Iacopino, Filippo Biamonte, Gabriella Proietti, Silvia Sorrentino, Annunziato Mangiola, Giulio Maira and Gigliola Sica

[1] Istituto di Istologia ed Embriologia e [2]Istituto di Neurochirurgia; Università Cattolica del Sacro Cuore, 00168 Roma, Italia

The mechanisms responsible for resistance to damage in normal cells might determine chemoresistance in both tumor cells and cancer stem cells (CSC). Relapse due to chemoresistant residual disease is a major cause of death in GBM. Increasing body of evidence indicates that not only tumor area (TT), but also tissue surrounding the tumor border (pTT) of GBM contains tumor cells and CSC, which could contribute to the disease progression. Therefore, the need to have a deeper insight in this area through identification of the characteristics that confer chemoresistance.

In this study, the expression of molecules involved in chemoresistance was investigated in samples derived from TT and from pTT at <1 cm from the tumor border, in 40 patients with GBM. The expression of $O_6$-methylguanine-DNA methyltransferase (MGMT), a suicidal DNA repair protein; Breast Cancer Resistance Protein (BCRP1), a drug efflux transporter, and A2B5 (c-series gangliosides) has been determined by immunohistochemistry.

The percentage of MGMT positive cells was higher ($p<0.0001$, paired Student's t test) in pTT (median: 53.5, range: 0.6-92.4) with respect to TT (median: 3.3, range: 0.0-70.7). The same trend was observed in BCRP1 expression ($p<0.02$; pTT, median: 27.6, range: 1.0-95.6; TT, median: 10.1, range: 0.2-72.1). No difference was found between pTT and TT in A2B5 expression ($p=0.69$, pTT, median: 29.8, range: 0.0-98.4; TT, median: 26.0, range: 0.0-96.8). Patients were then divided into two groups according to presence (group A) or absence (group B) of tumor cells in pTT. The trend previous observed in MGMT expression was maintained in both groups, while only in group A a statistically significant difference in BCRP1 expression was observed.

Our results confirm that the tissue surrounding GBM is not a normal tissue, and that it represents a frontline of tumor invasion, particularly for the presence of some molecules involved in chemoresistance, which could explain the disease recurrence after the conventional treatment of GBM.

Experiments about the expression of above mentioned molecules in CSC from pTT and TT are in progress.

Supported by FIRB, ACCORDI DI PROGRAMMA 2010

Key words

MGMT, BCRP1, A2B5, chemoresistance, GBM, peritumor tissue, cancer stem cells.