WT1 Expression in Reactive and Neoplastic Glial Cells as a New Diagnostic Tool

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ABSTRACT

Background: Glial tumors are the most common primary brain tumors. The majority of glial tumors are malignant**.** In small brain biopsies, morphological features of astrocytic neoplasms overlap with reactive astrogliosis occurring within or around brain lesions of various etiologies. So far no immunohistochemical marker allows a reliable distinction and this may result in a diagnostic dilemma. The Wilms' tumor suppressor gene (WT1) encodes for a zinc-finger transcription factor. The WT1 protein is involved in proliferation, differentiation and apoptosis. Interaction with other transcription factors like EGR-1 and p53 shows that WT1 has oncogenic properties.

Objective: To evaluate retrospectively the immunohistochemical expression of WT1 in reactive and neoplastic glial cells.

Material & methods: This retrospective study included 55 cases, 45 cases of which were previously diagnosed as glial tumors(astrocytomas, oligodendrogliomas and ependymomas) and 10 cases as reactive brain tissue (5 cases of reactive brain tissue adjacent to metastatic tumors and 5 cases of reactive gliosis). The cases were received at the Pathology Department of Ain Shams University Hospital and Ain Shams Specialized Hospital. Immunohistochemistry using Anti-WT1 a mouse monoclonal antibody, Clone 6F-H2 was performed to detect the expression of WT1 (cytoplasmic staining) which was in turn correlated with clinico-pathological factors.

Results: Immunohistochemical staining of WT1 expression was cytoplasmic within glial neoplastic cells and negative in reactive glial cells. There was a highly significant difference statistically between WT 1 expression in cases of gliosis and different WHO grades(**P <0.01).** Cases of glial tumors were positive with variable scores. WT1 immunostaining revealed significant positive relationship between grade and score, ($P < 0.001$).

Conclusion: WT1 can be used to differentiate normal astrocytes from neoplastic cells. WT1 not only plays a role in neoplastic transformation of astrocytic cells, but also may have a key role in progression and aggressive transformation of astrocytic tumors where it might be one of the switches for the emergence of GBM. Over-expression of WT1 in astrocytic brain tumors, especially high-grade types, suggests that WT1 could be a suitable target for cancer immunotherapy.

Keywords: Gliosis, Glial tumors, GBM (Glioblastoma Multiform), WT1 Immunohistochemistry.

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List of abbreviations

Abbreviation	Name
AA	Anaplastic astrocytoma
BTSC	Brain tumor stem cells
CNS	central nervous system
CSF	Cerebrospinal fluid
CT	Computed tomography
EGFR	Epidermal growth factor receptor
FLAIR	Fluid attenuation inversion recovery
GFAP	Glial fibrillary protein
IHC	immunohistochemistry
IARC	International agency for research on cancer
LOH	Loss of heterozygosity
MRI	Magnetic resonance imaging
NCI	National Cancer Institute
NF-1	Neurofibromatosis type 1
NF-2	Neurofibromatosis type 2
PTEN	Phosphatase and tensin homolog
PI3K	Phosphatidyl inositol 3 kinase
P53	Protein weighing 53 kildaltons
VEGF	Vascular endothelial growth factor
WT1	Wilm's tumor-1
WHO	World health organization

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