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Mediobasal and lateral temporal gliomas exhibit different growth patterns, surgical outcomes and prognoses

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ABSTRACT

Objective: This study was aimed at investigating the differences between mediobasal temporal gliomas and lateral temporal gliomas.
Methods: One hundred and forty-seven patients with temporal gliomas who were admitted in the Department of Supratentorial Neoplasms at Beijing Tiantan Hospital between 2008 and 2011 were included in this prospective study. Temporal gliomas involving the limbic and paralimbic systems were classified as mediobasal temporal gliomas (MTGs), while those without the involvement of the limbic and paralimbic systems were defined as lateral temporal gliomas (LTGs). The clinical, radiological, histopathological, and molecular features were compared between MTG and LTG patients.
Results: Compared to LTGs, MTGs were significantly larger in size ($P = 0.013$) and displayed a more aggressive invasion of surrounding tissues ($P < 0.001$). Marginally significant differences of the IDH1/2 mutation rate were observed between MTG and LTG patients ($P = 0.058$). The postoperative disability rate of MTGs was significantly higher than that of LTGs ($P = 0.031$). Resection degree according to tumor grade between LTG and MTG showed no statistical significance, while it mixed all grades showed marginally significant difference ($P = 0.060$). Regardless of tumor grade, the PFS and OS of MTG was shorter than that of LTG, except for OS in grade II ($P = 0.189$).
Conclusions: Temporal gliomas can be classified into two types, MTG and LTG which have different growth patterns, surgical outcomes and prognoses. Due to the significantly worse prognosis of patients with MTGs, this classification is useful for the clinical prognostic prediction of temporal gliomas.

1. Introduction

Evolutionarily, mediobasal temporal and lateral temporal lobes originate from the paleocortex and neocortex, respectively [1,2]. Anatomically, the temporal lobe contains a large amount of subcortical white matter, including the anterior commissure, arcuate fasciculus, inferior longitudinal fasciculus and uncinate fasciculus, and the Meyer's loop of the geniculocalcarine tract [1]. When survival analysis investigated, temporal gliomas were studied as an entirety without consideration of the difference of evolution and anatomy in previous studies [3,4].

Based on our experience and previous study, however, both high-grade [5] and low-grade gliomas [6] in the limbic and paralimbic systems usually expand along the white matter track, rather than growing locally like gliomas in the lateral temporal lobes. Therefore, determination of the initiation of temporal gliomas is difficult in some cases. Molecular genetic alterations, especially the 1p19q codeletion and IDH1/2 mutations, have been proven to have a predictive value in patients with gliomas [7–9]. For example, temporal gliomas have a lower incidence of 1p/19q co-deletions [4], insular gliomas exhibit a higher rate of IDH1/IDH2 mutations compared with paralimbic gliomas [10], and seizure is linked with a higher incidence of IDH1/2 mutations [11]. Whether temporal gliomas in mediobasal and lateral temporal lobes have differences in terms of clinical, pathological, or radiological features, as well as molecular genetics, are largely unknown. The surgical outcomes of temporal gliomas in these two distinct locations are also unclear.

To better understand the clinical features of temporal gliomas and in order to identify potential prognostic factors, we classified temporal gliomas into lateral and mediobasal types based on radiology, according to the involvement of the limbic and paralimbic systems. Mediobasal temporal gliomas (MTGs) were defined as tumors involving the limbic and paralimbic systems including

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amygdale, hippocampus, and parahippocampus. Temporal gliomas without the involvement of the limbic and paralimbic systems were defined as lateral temporal gliomas (LTGs).

In this study, in order to identify the differences between these two types of gliomas, originating from the paleocortex and neocortex, clinical, radiological, pathological, and molecular pathological features were compared.

2. Materials and methods

2.1. Eligible patients

This clinical study was approved by the Medical Ethics Committee of Beijing Tiantan Hospital, affiliated with the Capital Medical University, Beijing, China. Informed consent was obtained from all patients included in this study.

One hundred and forty-seven patients pathologically diagnosed with temporal glioma in the Department of Neurosurgery, Beijing Tiantan Hospital, between 2008 and 2011 were included. The clinical data and surgery record were retrospectively reviewed. The removal degree was determined by comparing the pre- and post-operative MR images [12] by an independent neuroradiologist blinded to patient outcomes, within 72 h after surgical resection of tumors. Disability was determined according to the modified Barthel index (<75). Histological diagnoses of tumor specimens were reviewed and confirmed by a third neuropathologist, according to the 2007 World Health Organization (WHO) Classification of Tumors of the Central Nervous System [13].

2.2. Detection of 1p/19q co-deletion, polysomy, IDH1/2 mutation, and MGMT promoter methylation

The 1p/19q codeletion was identified using the 1p/19q fluorescent probe kit (Vysis, USA) based on the Fluorescence in situ hybridization (FISH) technique, as previously described [4]. The Assessment and interpretation of FISH results were performed according to guidelines defined by the SIOP Europe Neuroblastoma Pathology and Biology and Bone Marrow Group [14]. Tumors where >30% of nuclei had experienced DNA loss were defined as having chromosomal loss. The tumor was considered to have polysomy when >30% of nuclei showed more than two 1q and 19p signals [15]. IDH1/2 mutation was identified by direct DNA sequencing [4]. The DNA methylation pattern of the MGMT gene promoter was determined by methylation-specific polymerase chain reaction (MSP) [16].

2.3. Immunohistochemical analysis

The immunohistochemical staining results were assessed using a semi-quantitative scoring system. Negative staining was defined as positively stained cells totaling <30% of tumor cells and positive staining was defined as positively stained cells totaling ≥30% of tumor cells. However, for TOPO-II, negative staining was defined as positively stained cells totaling <10% of tumor cells and positive staining was defined as positively stained cells totaling ≥10% of tumor cells. The secondary antibodies used were as follows: P-gp (1:40, Invitrogen, CA, USA), MGMT (1:100, Invitrogen, CA, USA), GFAP (1:100, Zeta, CA, USA), EGFR (1:100, Invitrogen, CA, USA), GST-π (1:100, Leica, Bannockburn, USA), MDM-2 (1:100, Leica, Bannockburn, USA), VEGF (1:150, Zeta, CA, USA), MMP-9 (1:100, Spring Bioscience, CA, USA), P53 (1:50, Spring Bioscience, CA, USA), Ki-67 (1:150, Invitrogen, CA, USA), PTEN (1:150, Lab Vision, CA, USA), TPOP-II (1:50, Leica, Bannockburn, USA).

2.4. Statistical analyses

Progression-free survival (PFS) and overall survival (OS) was defined as initial surgery to tumor progression and death, respectively. SPSS 13.0 (SPSS Inc., Chicago, Illinois) was used for statistical analyses. Chi-square test and univariate analysis was used to analyze the difference between MTG and LTG patients. The forward stepwise multivariate analysis was used to identify independent donor risk factors for the survival of temporal glioma patients. The probability value was obtained from 2-sided tests, with statistical significance defined as $P < 0.05$.

3. Results

3.1. Radiological classification of temporal gliomas

As mentioned above, temporal gliomas were divided into mediobasal and lateral types, according to involvement of limbic and paralimbic systems, based on MR images. According to this classification, 74 (50.3%) and 73 (49.7%) cases were defined as MTGs and LTGs, respectively (Fig. 1a and b). Staff-Member Constitution

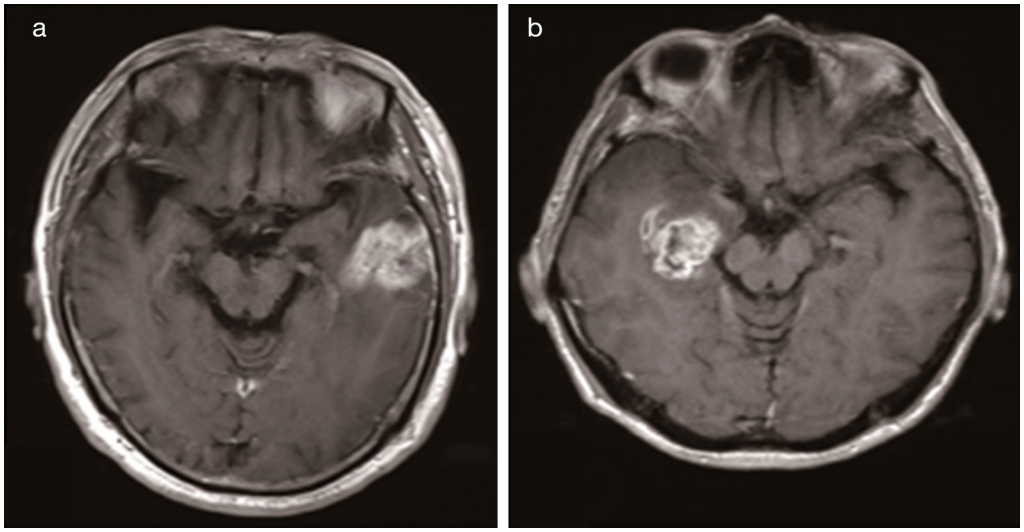

Fig. 1. Definition of temporal gliomas in this study. (a) Glioma restricted in lateral temporal lobe was defined as lateral temporal glioma (LTG). (b) Glioma involved limbic and paralimbic system was defined as mediobasal temporal glioma (MTG).