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Expression of TIM-1 in patients with glioma and its correlation with clinicopathological features

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ABSTRACT

The objective of this research was to investigate the expression of TIM-1 in patients with glioma and its correlation with clinicopathological features. The clinical data of 79 patients with gliomas in our hospital from February 2016 to February 2020 were selected as the research objects of this experiment. TIM-1 detection kit, ELISA and eliysion kit were used to detect TIM-1. The expression of TIM-1 was detected by an automatic immunohistochemical analyzer. Results revealed that the expression of TIM-1 in glioma tissue was abnormal, and its level was significantly higher than that in normal tissue adjacent to the tumor. The high level of TIM-1 expression in gliomas was correlated with KPS grade and histological grade., The expression level of TIM-1 in glioma tissue can affect the survival rate of patients and become one of the independent risk factors of glioma. In conclusion, the histological grade and KPS grade of glioma are related to the high-level expression of TIM-1, which not only suggests that TIM-1 is involved in the occurrence and malignant progression of glioma but also suggests that the malignant change of glioma has a high risk.

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Introduction

Glioma is a tumor developed from glial cells of the neuroectoderm and is the most common malignant tumor in the brain. Its main characteristics are a high incidence rate, high mortality and low cure rate, which is mainly due to the aggressive growth of glioma, leading to a complete cure (1). Glioma cells can proliferate indefinitely in the cell and have strong invasiveness (2-4). It grows in an infiltrative growth environment, which makes other normal brain tissues invaded. Its growth speed is fast and it cannot be completely removed by surgery. After surgery, the patient will have a high probability of reoccurrence, and the recovery of patients after surgery is poor and the survival time after surgery is short (3,4). The main reason for tumor immune escape is tumor immunosuppression. In order to strengthen the immune response of tumors, and change the situation of immunosuppression, finding new targets has become the focus of research. T cell immunoglobulin mucin-1 (TIM-1), a newly discovered T cell immunoglobulin mucin-1, plays an important co-stimulatory role in Tim family. It is mainly expressed on the surface of T cells, which can promote cell activation and cell proliferation, and also plays an important role in tumor immune regulation. TIM-1 can also participate in the body's immune regulation. Tin-1 can regulate the patient's autoimmunity and autoimmunity and plays a key role in strengthening the immune function (5,6). It has been reported that TIM-1 can change the severity of the disease, and has an inseparable relationship with cancer, immune diseases and allergic reactions. It can be used for the treatment of tumors, autoimmune diseases and viral infections (7). TIM-1 is not obvious in healthy tissues, but it is upregulated in some tumor diseases, which has become the focus of medical workers and researchers (8,9). Studies have reported that TIM-1 has a strong stimulating effect, plays an important role in regulating autoimmune imbalance, and can play a key role in the anti-immunity of tumors. It has a suggestive role in the diagnosis of tumors. It may be a marker of some tumor diseases and may participate in some tumor-promoting mechanisms (10). There are few relevant reports on the phenomenon that TIM-1 can be upregulated in tumors. Therefore, this study used the glioma specimens and normal tissues adjacent to tumors from 79 patients with glioma in our hospital to explore the expression of TIM-1 in glioma patients and its correlation with clinicopathological characteristics.

Materials and Methods

General Materials

The clinical data of 79 patients with gliomas who were admitted to our hospital from February 2016 to February 2020 for surgical treatment and confirmed by pathological examination were retrospectively analyzed, including 45 males and 34 females; The age ranged from 25 to 70 (mean 55.24 ± 3.56) years; The glioma specimens of 79 patients and the normal tissue specimens besides the tumors of the same patients were collected. They were put into the preservation tube and immediately put into the liquid nitrogen

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environment at minus 80 degrees for preservation, so as to be separated and extracted.

Inclusion Criteria and Exclusion Criteria

Inclusion criteria: ①All patients were diagnosed with glioma by pathological examination; ②All the tumor organizers underwent surgical resection; ③The clinical data and tumor resection materials are well preserved; ④The patient and his / her family members shall sign the informed consent form and obtain the consent of the ethics committee of our hospital.

Exclusion criteria:①Patients who had received chemotherapy and tumor drugs before the operation were excluded;②Immune and blood diseases were excluded; ③Patients with distant metastasis before treatment were excluded; ④Patients with incomplete clinical data were excluded; ⑤Patients with other malignant tumors were excluded.

Instruments and Reagents

The full-automatic immunohistochemistry analyzer provided by Suzhou Hehui Biotechnology Co., Ltd. was used; the TIM-1 detection kit, ELISA ELISA and eliysion kit were used to determine TIM-1.

Test Method

The expression of TIM-1 was detected by an automatic immunohistochemical analyzer. The expression of TIM-1 in glioma and normal tissues adjacent to the tumor was detected by ELISA enzyme-linked immunosorbent assay. Eliysion kit was used. Operate in strict accordance with the instructions of the automatic immunohistochemical analyzer and kit.

Observation and Evaluation Index

Result judgment: two doctors judged that the brownish-yellow particles detected in the cells of glioma samples were positive. Six high-power fields were randomly selected from each slice. The number of cells in each field was 100, of which ≥ 0.1 was positive and < 0.1 was negative.

Postoperative follow-up: investigate the postoperative survival of all discharged patients by telephone, door-to-door and follow-up. The stop date of postoperative follow-up is May 2021 or the date of death. The mean follow-up time was (48.21 ± 2.34) months.

Statistical Method

SPSS15.0 statistical software was used for data analysis. The mean ± standard deviation (x ± s) method was used for the expression level of tin-1 in glioma tissues and normal tissues adjacent to tumors, and *t* expression was used for the difference between the two. The relationship between TIM-1 and the clinical and pathological characteristics of glioma patients was tested by χ^2. Kaplan Meier survival curve and Log-rank test were used to analyze the survival rate of patients. Univariate and multivariate Cox models were used to evaluate the relationship between different clinicopathological characteristics and survival rates. $P < 0.05$ indicates that the difference is statistically significant.

Results

Comparison of TIM-1 Expression in Glioma and Normal Tissue Adjacent to Tumor

The high expression level of TIM-1 in glioma (83.544%) was significantly higher than that in normal tissues (16.455%), $P<0.05$. It suggests that the level of TIM-1 is positively correlated with glioma. The denser the glioma cells are, the higher the level of TIM-1 will be.

The Relationship between the Expression of TIM-1 and the Clinicopathological Features of Glioma

The expression of TIM-1 was divided into a high-expression group and a low-expression group to further explore the relationship between the expression level of TIM-1 and the clinicopathological characteristics of glioma. The data showed that the expression of TIM-1 was related to histological grade and KPS grade, $P<0.05$, and the difference was significant; There was no significant difference in age, sex, tumor location and tumor diameter, $P>0.05$, see Table 1.

Table 1. Relationship between the Expression of TIM-1 and the Clinicopathological Features of Glioma.

Clinicopathological features		n	Tin-1 Positive Expression		χ^2 value	*P*-value
			High expression	Low expression		
Age	<50	36	30	6	0.0021	0.963
	≥50	43	36	7		
Gender	Male	45	31	14	2.853	0.091
	Female	34	29	5		
Histological grade	Grade I-II	30	21	9	14.342	0.001
	Grade III-IV	49	36	13		
Tumor location	Top	18	9	7	5.392	0.674
	Temporal part	17	10	7		
	Forehead	27	20	7		
	Other parts	17	9	8		
Tumor diameter	<4cm	29	21	8	0.998	0.317
	≥4cm	50	41	9		
KPS grading	≥80	41	36	5	5.631	0.017
	<80	38	30	8		

Table 2. Cox Multivariate Analysis of Survival Rate of Patients with Glioma.

Influencing factor	B	Wald	P value	HR value	95%CI
Tim-1 high expression	0.687	5.916	0.018	2.769	1.634~5.768
Histological grade	0.792	3.627	0.011	2.132	1.132~4,396
KPS grading	1.143	3.234	0.009	2.573	1.513~5.152

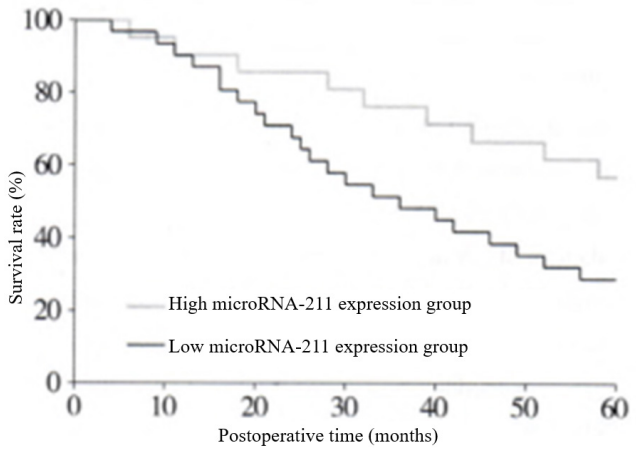

Figure 1. Survival Curve of Glioma Patients with High and Low Expression of TIM-1.

In this study, 79 patients with glioma were followed up. The follow-up rate was 100.00%, of which 56 survived and 23 died; the survival time of the patients was (30.14 ± 6.46) months. Kaplan Meier survival curve was used to express the expression level of TIM-1 in glioma tissues and normal tissues adjacent to tumors, as shown in Fig. 1.

Cox univariate regression model was used to analyze 79 patients. Data analysis showed that the high level of TIM-1, histological grade and KPS grade in glioma tissue were significantly related to the survival rate of glioma patients, $P<0.05$; Cox multivariate analysis showed that the high level of TIM-1, histological grade and KPS grade were independent prognostic factors affecting the survival rate of glioma patients, $P<0.05$, see Table 2.

Discussion

It is known from the relevant literature and data on brain glioma that about 15-23 of 100000 people in China suffer from brain glioma, which accounts for about 1.5% ~ 3% of the total malignant tumors. The incidence rate of brain tumors is 45% (11). Gliomas can occur at all ages. In the cases reported in the report on gliomas (12), the age of onset of the disease can range from newborn to 86 years old, and 35-65 years old is the age range with the highest prevalence of gliomas; the disease has no specific manifestation, and the main symptoms are mental disorder, personality change and hemiplegia. Due to the immunosuppressive environment caused by tumors, malignant tumors grow, reproduce and infiltrate rapidly. In the immunosuppressive environment, it plays an accelerating role in tumor cells' resistance to the immune system and suppression of the immune response of the body (13). Glioma is a rare tumor originating from special epithelial tissue and presenting diffuse infiltration. In severe cases, it can involve more than 3 cerebral hemispheres and lobes (14). Surgical resection of the tumor is the best method to treat glioma. However, due to its diffuse invasive growth, it is difficult to distinguish the tumor tissue from other normal tissues, which makes surgical treatment impossible to completely clear the tumor. Various research reports show that: (15) TIM-1 can be used as a marker of brain glioma to play a reference role in the discovery, diagnosis and treatment of tumors. It can be used in the research of brain glioma, reduce the mortality of patients, and play a significant role in early diagnosis, early treatment and early prevention of patients.

TIM-1 plays an important role in the tumor mechanism and can participate in the circulation of anti-tumor immunity in body fluids. It plays a key role in maintaining the positive and negative regulatory mechanisms of the body in immune regulation (16). Humoral immunity is dominated by B cells, and Breg is the main expression of TIM-1. TIM-1 can induce cell apoptosis through Breg induction, thus playing the role of TIM-1 in humoral immunity. TIM-1 can not only participate in the immune regulation of the body but also inhibit the immune response. It plays an inhibitory role on T cells and NK cells in the body. It can also cultivate tumor-related macrophages to achieve the inhibitory effect of anti-tumor immunity (17).

TIM-1 can be used to express epithelial cells and mast cells of the mucosa and can be used in autoimmune diseases and allergic reactions of the body. It is widely used. TIM-1 can also participate in the activation of the signal pathway, which is closely related to the occurrence of glioma, breast cancer and lung cancer (18). It may also be related to the prognosis of tumor patients after surgery and whether the tumor has metastasis. Under the overactivation of TIM-1, it can accelerate the cell cycle, resist cell apoptosis, promote the binding of intracellular proteins, and accelerate the development of tumors. TIM-1 accelerates the occurrence and development of tumors through a signaling pathway, thus activating anti-tumor immunity (19).

In this study, through the analysis and detection of the automatic immunohistochemical analyzer, TIM-1 expression was abnormal in brain glioma tissue, and its level was significantly higher than that in normal tissues adjacent to the tumor, and there was a statistical difference between the two, with statistical significance. The experimental study shows that the histological grade and KPS grade of brain glioma are related to the high-level expression of TIM-1, which not only suggests that TIM-1 is involved in the occurrence and malignant progression of brain glioma but also may indicate that the malignant change of this tumor has a high risk. According to this experiment, the expression level of TIM-1 in brain glioma tissue can affect the survival rate of patients and become one of the independent risk factors affecting brain glioma.

To sum up, the high expression level of TIM-1 in glioma tissue has a certain correlation with the KPS grade and histological grade of patients. At the same time, the difference in the expression of TIM-1 in glioma and adjacent normal tissues may have an impact on the survival rate and prognosis of patients. However, the occurrence, deterioration and prognosis of TIM-1 in glioma need further study

and analysis.

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