EXPRESSION OF SERUM GFAP AND IGF-1 IN GLIOMA AND ITS RELATIONSHIP WITH CLINICOPATHOLOGICAL PROGNOSIS

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ABSTRACT

Objective: *To investigate the expression of serum glial fibrillary acidic protein (GFAP) and insulin-like growth factor-1 (IGF-1) in brain glioma and its correlation with clinicopathological prognosis.*

Methods: *A retrospective analysis was performed on 74 patients with glioma admitted to our hospital from April 2014 to May 2015. These patients were selected as the observation group, and 67 healthy patients in our hospital were selected as the control group. All patients in the observation group were treated with surgery combined with chemoradiotherapy. The levels of GFAP and IGF-1 in the control group were compared on the day of physical examination and in the observation group before and after 1w as well as after chemoradiotherapy. According to the survival time of glioma patients, the patients were divided into 27 patients with good prognosis and 47 patients with poor prognosis. GFAP and IGF-1 levels were compared between the two groups. Patients were divided into a complete remission group, a partial remission group, a stable group and a progressive group according to the efficacy evaluation criteria of solid tumours. GFAP and IGF-1 levels were compared in each group. An ROC curve was drawn to analyse the diagnostic value of GFAP and IGF-1 in the prognosis of glioma.*

Results: *In comparison with the control group, GFAP and IGF-1 levels were significantly higher in the observation group at all time periods (P<0.05). Compared with the preoperative level, the GFAP and IGF-1 levels in the observation group were significantly decreased 1w after surgery and after chemoradiotherapy (P<0.05). Compared with 1w after surgery, GFAP and IGF-1 levels in the observation group after radiotherapy and chemotherapy were significantly reduced (P<0.05). Compared with the group having a good prognosis, GFAP and IGF-1 in the group with poor prognosis were significantly increased (P<0.05). Compared with the complete remission group, the GFAP and IGF-1 levels of patients in the partial remission group, stable group and progressive group were significantly increased. GFAP and IGF-1 levels were significantly higher than those in the stable group and the progressive group (P<0.05). The area under the GFAP and IGF-1 curves were 0.842 and 0.955, the specificity was 87.70% and 92.30%, and the sensitivity was 82.50% and 90.00%, respectively.*

Conclusion: *The expression levels of GFAP and IGF-1 in the serum of glioma patients were significantly increased, and both can be used as reference indexes for evaluating the prognosis of glioma patients, which is conducive to improving diagnostic efficiency and accuracy.*

Keywords: *GFAP, IGF-1, glioma, prognosis.*

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Introduction

Gliomas are extremely common in intracranial tumours, accounting for 40% to 50% of all primary intracranial tumours, among which glioblastoma is one of the most malignant types[(1)]. Gliomas can be diagnosed at all ages, especially in the middle-aged and elderly, and the 3-year survival rate for this type of patient is only 7.54% after diagnosis[(2)]. At present, surgery is the most important treatment, but it is difficult to remove the lesion completely, and the recurrence rate is very high. In addition, glioma cells exhibit high resistance to antitumor drugs, and radiotherapy can to a certain extent lead to the aggravation of the patient's condition. Without timely and effective intervention and treatment, malignant gli-

oma can cause a rapid increase in intracranial pressure as well as serious damage to intracranial nerve function, then cause central nervous dysfunction and even endanger the patient's life.

Therefore, current clinical research is focusing on exploring new treatment methods that can hinder glioma's invasiveness. The related literature reports that glial fibrillary acidic protein (GFAP) is a marker protein for glioblastoma, showing an abnormally high expression status in malignant glioma[3]. Clinical studies have shown that serum levels of GFAP in glioblastoma patients are significantly higher than in the normal population[4].

Insulin-like growth factor-1 (IGF-1) acts as a cellular regulator to promote growth and development in the body and plays an important role as tumour autocrine growth factor in tumorigenesis and development[5]. However, the exact relationship between serum GFAP, IGF-1 level changes and glioma patients is not clear. Therefore, this study further analysed the relationship between the two levels and the clinicopathological and prognostic characteristics of glioma patients by detecting serum GFAP and IGF-1 levels in glioma patients.

Materials and methods

General information

A retrospective analysis was performed on 74 cases of brain glioma admitted to our hospital from April 2014 to May 2015, among which 49 were males and 25 were females, with an average age of 57.41±3.62 years.

Inclusion criteria were as follows:

• Space-occupying lesions were clearly diagnosed by MRI and other imaging examinations;

• Postoperative pathological examination clearly diagnosed glioma grade III~IV;

• Patient had no previous systematic chemoradiotherapy;

• The patient and family members were informed and signed informed consent;

• Inclusion was approved by the hospital ethics council.

Exclusion criteria comprised the following:

• Participants who quit midway due to intolerance;

• Patients with malignant tumours or chronic diseases in other locations;

• Patients with postoperative recurrence of glioma. In our hospital, 67 healthy subjects were selected as the control group, including 37 males and 30 females, with an average age of 57.07±3.28 years.

No significant difference in general data was observed between the two groups, (P>0.05).

Methods

All patients in the observation group were treated with surgery combined with chemoradiotherapy, and the patients were treated with chemoradiotherapy at 3w after surgery according to their condition. The electron linear accelerator XHA600C (produced by Shandong Xinhua Medical Instrument Co., Ltd) was used to irradiate the 95% dose curve 60 Gy/30 F, 2 Gy each time, once a day, 5 days a week, and the treatment lasted for 6 weeks. After 2 weeks of radiotherapy, all patients were given temozolomide (specification: 20mg national drug approval: H20420153 Beijing SL Pharmaceutical Co., Ltd) orally 150~200mg/m^2, once a day, 5 days a week, 4 weeks for 1 course, a total of 6 courses.

Observation indicators

• Fasting venous blood of patients in the observation group was collected before surgery, 1w after surgery, and after chemoradiotherapy. After centrifugation, the levels of IGF-1 and GFAP were detected by a double-antibody sandwich method. Fasting venous blood was extracted from the control group on the day of physical examination, and the other steps were the same as those for the observation group.

• Efficacy evaluation: patients were divided into a complete remission group, a partial remission group, a stable group and a progressive group according to the efficacy evaluation criteria for solid tumours formulated by the World Health Organization. For a complete response, the lesion was completely cleared and no new lesion was found, lasting >for 4 weeks. In the partial remission group, the lesion was reduced by >50% and no new lesion was found. The duration of >was 4 weeks. In the stable group, lesion reduction <50% or enlargement <25%, no new lesion was found, while the progression group was characterized as lesion enlargement of >25% or discovery of new lesion.

• All patients in the observation group will receive follow-up for a period of 3 years. Patients with a survival time of more than 3 years will be considered in the group with a good prognosis, while those with a survival time of less than 3 years will be in the group with a poor prognosis.

In all, 27 cases were in the good group, and 47 cases were in the bad (poor) group.

• An ROC curve was drawn to analyse the diagnostic value of GFAP and IGF-1 in the prognosis of glioma.

Statistical methods

The levels of GFAP and IGF-1 in each group were expressed by ($\bar{x}\pm s$) and tested by t-test. The ROC curve was drawn to analyse the diagnostic value of GFAP and IGF-1 in the prognosis of glioma. P<0.05 was considered significant.

Results

Comparison of GFAP and IGF-1 levels between the two groups

In comparison with the control group, GFAP and IGF-1 levels were significantly increased in the observation group at all time periods (P<0.05). Compared with the preoperative level, the GFAP and IGF-1 levels in the observation group were significantly decreased 1w after surgery and after chemoradiotherapy (P<0.05). Compared with 1w after surgery, GFAP and IGF-1 levels in the observation group after radiotherapy and chemotherapy were significantly reduced (P<0.05). See Table 1.

Group	n	Time	GFAP (ng/L)	IGF-1 (ng/mL)
Observation group	74	Before surgery	84.06±1.15[a]	798.60±206.73[a]
		After surgery 1w	54.84±0.46[ab]	388.88±92.04[ab]
		After radiotherapy	6.39±0.78[abc]	123.56±36.55[abc]
Control group	67		6.14±0.66	98.28±28.36

Table 1: Comparison of GFAP and IGF-1 levels between the two groups ($\bar{x}\pm s$).
Note: Compared with the control group, [a]P<0.05; Compared with that before surgery, [b]P<0.05. Compared with 1w after surgery, [c]P<0.05.

Comparison of GFAP and IGF-1 levels in glioma patients in different prognostic groups

Compared with the group having a good prognosis, GFAP and IGF-1 in the group with a poor prognosis were significantly increased (P<0.05). See Table 2.

Group	n	GFAP (ng/L)	IGF-1 (ng/mL)
Good prognosis	27	49.46±5.75	397.45±94.56
Poor prognosis	47	98.63±6.19	845.26±214.89
t		25.581	10.250
P		<0.001	<0.001

Table 2: Comparison of GFAP and IGF-1 levels in different prognostic groups ($\bar{x}\pm s$).

Comparison of GFAP and IGF-1 levels in glioma patients in different therapeutic groups

Compared with the complete remission group, the GFAP and IGF-1 levels of patients in the partial remission group, stable group and progressive group significantly increased. Moreover, in comparison to the partial remission group, GFAP and IGF-1 levels significantly increased in the stable group and the progressive group (P<0.05). See Table 3.

Group	n	GFAP (ng/L)	IGF-1 (ng/mL)
Complete remission group	31	42.75±20.65	135.69±35.74
Partial remission group	16	53.25±35.78[d]	382.21±58.62[d]
Stable group	15	67.69±50.46[de]	476.34±78.25[de]
Progressive group	12	95.74±61.54[de]	804.56±198.26[de]

Table 3: Comparison of GFAP and IGF-1 levels in glioma patients in different therapeutic groups ($\bar{x}\pm s$).
Note: Compared with the complete remission group, [d]P<0.05; Compared with the partial remission group, [e]P<0.05.

Analysis of the diagnostic value of GFAP and IGF-1 in the prognosis of glioma

The areas under the GFAP and IGF-1 curves were 0.842 and 0.955, respectively, the specificity was 87.70% and 92.30%, and the sensitivity was 82.50% and 90.00%, respectively. See Table 4 and Figure 1.

Serum index	ROC	Sensitivity	Specificity	Standard error	*P*	95%CI
GFAP	0.842	82.50%	87.70%	0.042	0.045	0.886~1.011
IGF-1	0.955	90.00%	92.30%	0.055	0.039	0.756~0.928

Table 4: Analysis of the diagnostic value of GFAP and IGF-1 in the prognosis of glioma.

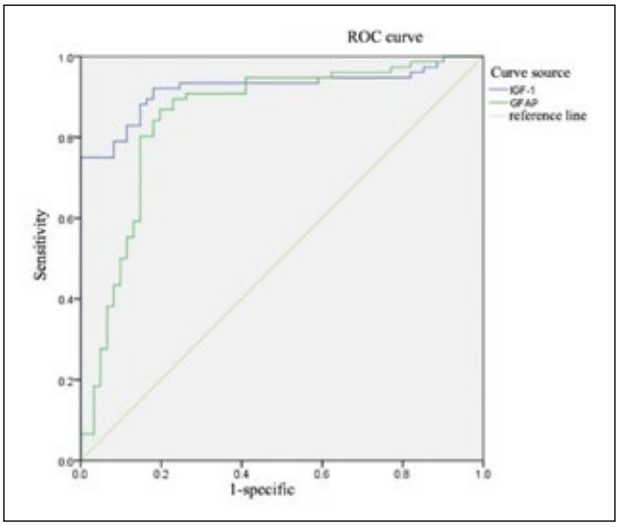

Figure 1: Diagnostic value analysis of GFAP and IGF-1 in the prognosis of glioma

Discussion

Malignant glioma is characterized by invasive growth, and it is difficult to separate from normal brain tissue. Meanwhile, cancer tissue is not limited to a single lobe, and surgical resection is extremely difficult, leading to a high risk of postoperative recurrence[6]. It has been reported in the literature that the median survival time of patients with malignant glioma is less than 18 months, and the 2-year survival rate is only 5%[7]. Surgical resection combined with chemoradiotherapy is the main means to relieve pain and prolong the survival time of glioma patients. However, the clinical effect is often difficult to achieve in terms of the desired goal, and the survival status of patients is not optimistic. Therefore, it is critical to find biological indexes that can effectively evaluate the clinical efficacy and prognosis of glioma patients. Since postoperative pathological tissues of glioma patients are difficult to obtain, the determination provided by serum protein markers offers high value in evaluating the prognosis of patients with glioma.

GFAP is a factor composed of aspartic acid and glutamic acid, which has the function of supporting and nourishing neurons. It was originally isolated from astrocytes and used to identify glia-originated tumours in intracranial tumours[8]. A number of reports have shown that the serum GFAP level in patients with cerebral ischemic injury is significantly higher than that in normal individuals, suggesting that this may be closely related to the damage to astrocytes after injury[9]. In these studies, astrocytes were destroyed under pathological conditions, and increased GFAP secretion resulted in increased GFAP content in cerebrospinal fluid, which further entered the blood through the blood-brain barrier and ultimately increased GFAP content in serum[10]. Clinical studies have confirmed that the level of astrocytes in patients with malignant glioma significantly increases, along with the content of GFAP, suggesting that GFAP can be used as an important reference indicator for the diagnosis of malignant glioma[11]. The occurrence and development of brain glioma can be controlled by a variety of cytokines such as IGF-1. Relevant literatures have shown that excessive IGF-1 content can lead to changes in normal cell activity, and further excessive proliferation and inhibition of apoptosis can lead to tumour formation[12]. Clinical studies have shown that IGF-1 is abnormally expressed in glioblastoma, which plays an important role in malignant proliferation and inhibition of apoptosis of cancer cells[13]. Several studies have conducted in-depth studies on the correlation between serum IGF-1 and tumour diagnosis and prognosis. Gramotnev[14] found that the serum IGF-1 level could be used as an important marker protein for the diagnosis of Parkinson's disease. In addition, Botusan[15] found that serum IGF-1 level was closely associated with tumour development and prognosis evaluation.

In this study, the serum IGF-1 level of 74 included glioma patients was detected before surgery, 1w after surgery and after chemoradiotherapy. The results showed that the levels of GFAP and IGF-1 in the observation group were significantly higher than for those in the control group ($P<0.05$). We followed up 74 patients with glioma for 3 years and analysed the prognosis according to the survival time of the patients. The results showed that compared with the group with a good prognosis, the GFAP and IGF-1 in the group with a poor prognosis were significantly increased ($P<0.05$). These results indicated that GFAP and IGF-1 levels were closely related to the prognosis of glioma patients. Next, we analysed the serum GFAP and IGF-1 levels of the patients according to the clinical efficacy, finding that with progression of the disease, the patients' serum GFAP and IGF-1 levels gradually increased. In addition, this study also established the curves of GFAP and IGF-1roc in the serum of the patients and analysed their value in the diagnosis and prognosis of glioma. The results showed that both displayed high sensitivity and specificity in glioma, allowing them to be used as reference indexes for evaluating glioma patients' prognosis.

In conclusion, the expression levels of GFAP and IGF-1 in the serum of glioma patients were found to be significantly higher than those for healthy individuals, meaning that these can serve as reference indicators when evaluating the prognosis of glioma patients, which is conducive to improving the diagnostic efficiency and accuracy.

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