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Original Article

Changes in CA15-3, S100B, and IGF-1 in glioma and their predictive value for treatment efficacy

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Abstract: Objective: To analyze the changes of carbohydrate antigen 153 (CA15-3), S-100 calcium-binding protein B (S100B) and insulin-like growth factor-1 (IGF-1) in the treatment of patients with high-grade glioma and their predictive value for efficacy. Methods: In this retrospective the PG and CG study, 74 patients with glioma who were treated in the Affiliated Hospital of Yan'an University from January 2015 to January 2017 were labeled as the patient group (PG); the other 70 patients who underwent craniocerebral trauma surgery during the same period were selected as the control group (CG). The expressions of CA15-3, S100B and IGF-1 in the PG and CG were compared. The relationship between CA15-3, S100B, IGF-1, and the pathologic data of patients was analyzed. The expression differences of CA15-3, S100B, and IGF-1 were compared between low-grade glioma patients and high-grade glioma patients and their diagnostic value was analyzed. The values of CA15-3, S100B, and IGF-1 expression for predicting treatment efficacy were analyzed. Results: Expressions of CA15-3, S100B, and IGF-1 in glioma patients were markedly higher than those in the CG ($P<0.0001$). The proportion of grade III+IV patients with high expression of CA15-3, S100B, and IGF-1 was higher than in grade II patients ($P<0.05$), and the expressions of CA15-3, S100B and IGF-1 in low-grade glioma patients were lower than in high-grade glioma ($P<0.01$). The AUCs of CA15-3, S100B, and IGF-1 in differentiating different grades of glioma were 0.822, 0.722, and 0.768, respectively. Serum CA15-3, S100B and IGF-1 levels of the patients after treatment were significantly lower than those before treatment ($P<0.0001$). With the deterioration of clinical efficacy, serum levels of CA15-3, S100B, and IGF-1 gradually increased ($P<0.05$), and CA15-3, S100B and IGF-1 were positively correlated with therapeutic efficacy ($P<0.05$). AUCs of CA15-3, S100B, and IGF-1 for predicting the clinical efficacy in glioma patients were 0.824, 0.741, and 0.800, respectively. Conclusion: CA15-3, S100B, and IGF-1 are highly expressed in patients with glioma. They are diagnostic indicators to distinguish patients with high-grade glioma, and have predictive value for treatment efficacy.

Keywords: CA15-3, S100B, IGF-1, high-grade glioma, efficacy prediction

Introduction

Gliomas are the most common tumors of the nervous system and one of the leading causes of death in patients with intracranial tumor [1]. According to the latest statistics, the incidence of glioma has risen from 5.9 per 100,000 in 1973 to 6.61 per 100,000 in 2016, and its mortality rate is second only to pancreatic cancer and lung cancer, ranking third among all lethal tumors in the world [2]. Because of its high incidence, tumor malignancy and recurrence rate, as well as the complex treatment process and poor prognosis, it is a serious threat to human health [3]. The World Health Organization (WHO) classification of gliomas is divided into four grades, I-IV (higher grade means more severe malignant degree) [4], among which, grades I-II glioma are collectively referred to as low-grade glioma, and III-IV grades are as high-grade glioma [5]. In the past few decades, great progress has been made in the treatment of glioma by neurosurgery, radiation therapy, chemotherapy and targeted therapy. However, its clinical prognosis evaluation mostly relies on imaging examinations such as computed tomography (CT) and magnetic resonance imaging (MRI), which may inevitably cause a negative impact on patients [6]. Therefore, it is of great value and significance to find a simple, non-invasive, accurate and repeatable detection method.

In recent years, serum tumor markers have been widely applied in solid tumor screening, clinical diagnosis, pathological grading, and prognosis assessment [7]. Carbohydrate antigen 153 (CA15-3) belongs to tumor-associated antigens, which are mostly located in the surface layer of tumor cells. Its expression increases when normal cells are transformed into tumor cells [8]. S100 calcium-binding protein B (S100B), an acidic calcium-binding protein with a small molecular weight, has significant biologic effects. It can regulate the synthesis of protein kinase C and calmodulin in the human body, affect cellular energy metabolism, and exert neurotrophic effects [9]. Previous study found that the expression of S100B in patients with glioma decreased after surgery [10]. Insulin-like growth factor-1 (IGF-1) is a mitogen that can promote cell proliferation and differentiation, and is one of the important factors for promoting tumor growth [11]. Previous studies have shown that IGF-1 was highly expressed in the serum of glioma patients, and could be used as a diagnostic indicator for glioma [12]. However, there is no relevant study focusing on whether the above indicators have clinical value in distinguishing high-grade gliomas from low-grade gliomas, nor whether they have significance for evaluating the prognosis of patients.

In this study, therefore, we aimed to analyze the expression of CA15-3, S100B, and IGF-1 in patients with different grades of glioma, and the changes in CA15-3, S100B, and IGF-1 before and after treatment in patients, to evaluate their possible use for clinical prognosis.

Materials and methods

Clinical information

In this retrospective study, 74 patients with glioma treated in Affiliated Hospital of Yan'an University from January 2015 to January 2017 were designated the patient group (PG). Another 70 patients who underwent craniocerebral trauma surgery during the same period were selected as the control group (CG). This study was approved by the Medical Ethics Committee of Affiliated Hospital of Yan'an University (LLSH2020 (037)).

Inclusion and exclusion criteria

Inclusion criteria: Patients in line with the relevant diagnostic criteria of "Guidelines for Diagnosis and Treatment of Brain Glioma (2018 Edition)" [13] and confirmed by pathologic diagnosis; Patients with first onset; Patients with no previous treatment such as radiotherapy and chemotherapy; Patients with complete clinical data. The patients in this study signed an informed consent.

Exclusion criteria: Patients with incomplete clinical data; Patients with presence of multiple brain tumors; Patients with other tumors; Patients with primary malignant tumors of other organs; Patients with an abnormal blood system, liver function, kidney function, and bone marrow function; Patients unwilling to receive treatment.

Therapeutic plans

The location and size of the lesion were determined according to the results of preoperative imaging examination, and the surgical incision and approach were designed. After general anesthesia, the sulcus or fissure approach nearest to the glioma was selected for routine cranio-cranial neurography. Decompression was performed on the bone flap, and a coronal and peritonal expansion approach was adopted. After the dura mater was opened, the glioma center and its surrounding infiltrated areas were fully exposed, and the boundary of diseased tissue and normal tissue was distinguished. The lesions were resected and sent for pathologic identification. The patients were designated to receive a CT examination within 72 h after surgery to determine whether there was residual tumor tissue. All patients who underwent radiotherapy received intensity-modulated radiation therapy 2 to 6 weeks after surgery. By referring to the preoperative and postoperative brain MRI to delineate the irradiation target area, we performed the following treatments for patients with low-grade glioma. GTV: T1-weighted enhancement of MRI, abnormal signal area of FLAIR/T2 images, CTV was GTV expansion 1~1.5 cm; PTV: CTV was evenly expanded by 0.5 cm, and the PTV dose was 50.4-54 Gy/1.8 Gy/28-30 Fx. As for high-grade glioma: GTV1: T1-weighted enhancement showed postoperative residual tumor and an operative cavity, abnormal signal area on T2-weighted/FLAIR images, CTV1 was GTV1 expanded by 1.5-2 cm. PTV1: CTV1 was evenly expanded by 0.3-0.5 cm. GTV2 was the residual tumor and surgical cavity after T1-weighted enhancement. CTV2: GTV2 expanded to 1-1.5 cm. PTV2: CTV2 expanded evenly by 0.3-0.5

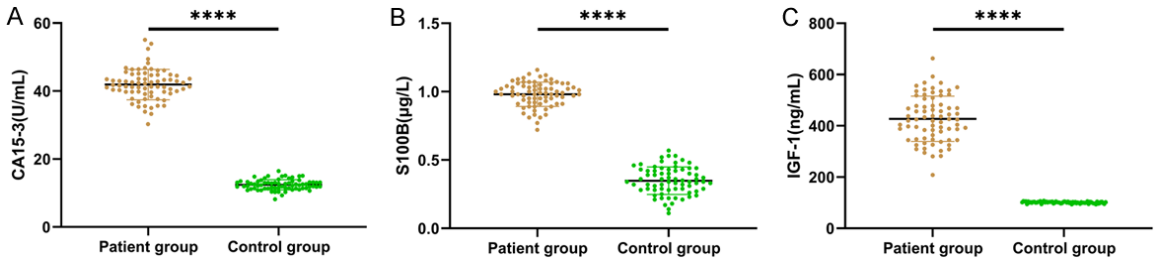

Figure 1. Expression of CA15-3, S100B, and IGF-1 in glioma patients. A. Comparison of serum CA15-3 expression between glioma patients and Controls. B. Comparison of serum S100B expression between glioma patients and Controls. C. Comparison of serum IGF-1 expression between glioma patients and Controls. Note: ****P<0.0001, carbohydrate antigen 153 (CA15-3), S-100 calcium binding protein B (S100B), insulin-like growth factor-1 (IGF-1).

cm. GTVp: Postoperative residual swelling on T1-weighted enhancement. PTV1 dose was 54 Gy/1.8 Gy/30 Fx, PTV2 dose was 60 Gy/2.0 Gy/30 Fx, GTVp dose was 64.2-66 Gy/2.14-2.2 Gy/30 Fx.

Serological testing

Fasting venous blood (5 ml) was drawn from patients before and after the treatments to obtain the supernatant, which was stored for further testing. Expression of CA15-3 was detected by the fully automatic chemiluminescence immunoassay analyzer TESMI i100 with the instrument kit (CP011010). ELISA was used to detect the expression of S100B (Shanghai, China, Beyotime, PS842) and IGF-1 (Shanghai, China, ELISA, mI022803), and the operation was carried out in strict accordance with kit instructions.

Observation indicator

Main outcome measures: Expressions of CA15-3, S100B, and IGF-1 in CG and PG were observed. The relationship between clinical efficacy and CA15-3, S100B, and IGF-1 level after treatment was analyzed, and the efficacy was divided into the following 4 categories: complete remission (CR) refers to the disappearance of all lesions which is maintained for at least 4 weeks; partial remission (PR) refers to more than 30% reduction of the tumor volume which is maintained for 4 weeks. Stable disease (SD) means that the increase and reduction of the tumor volume is between that of PR and disease progression (PD). PD means more than a 20% increase in tumor volume or occurrence of new lesions. CR and PR patients were designated the effective group, and SD and PD patients were designated the ineffective group. Then, the expression and diagnostic value of CA15-3, S100B, and IGF-1 were analyzed.

Secondary observation indicators: According to the median value of CA15-3, S100B, and IGF-1, patients were divided into high expression and low expression groups, and the relationship between CA15-3, S100B, IGF-1 and the pathologic data of the patients was compared. In addition, the differences and diagnostic values of CA15-3, S100B, and IGF-1 expression between patients with low-grade glioma and those with high-grade glioma were compared respectively.

Statistical analysis

SPSS20.0 software and GraphPad Prism 8 software were used to process, analyze, and visualize the data collected. Student t test was used for the inter-group comparison, and paired t test was for intra-group comparison. Rank-sum test was for the ranked data, chi-square test was for the counted data. Receiver operating curve (ROC) was to analyze the value of CA15-3, S100B, and IGF-1 in differentiating high and low grade of gliomas and observing the curative effect on patients. Spearman test was applied to analyze the correlation between the expressions of CA15-3, S100B, and IGF-1 in serum of patients and the clinical efficacy in patients. One-way ANOVA was for comparison among multiple groups, and LSD-t test was for post-hoc test. P<0.05 was used as the significance level.

Results

Expression of CA15-3, S100B, and IGF-1 in glioma patients

The expressions of CA15-3, S100B, and IGF-1 in the serum of glioma patients were determined, revealing that these three indicators in the PG were all higher than those in the CG (all P<0.0001, **Figure 1**).

Table 1. Relationship between CA15-3 and pathologic data of patients

Factor	CA15-3 (U/mL)		P
	High expression (n=37)	Low expression (n=37)	
Gender			0.051
Male (n=48)	20	28	
Female (n=26)	17	9	
Age			0.244
≥55 years old (n=34)	15	20	
<55 years old (n=40)	22	17	
WHO Classification			0.003
Grade II (n=30)	9	21	
Grade III+IV (n=44)	28	15	
Preoperative KPS score			0.235
≥80 points (n=60)	32	28	
<80 points (n=14)	5	9	
Tumor Diameter			0.242
≥5 cm (n=41)	23	18	
<5 cm (n=33)	14	19	
Pathologic type			0.991
Astrocytoma (n=28)	13	15	
Oligodendroglioma (n=22)	10	12	
Oligoastrocytoma (n=24)	14	10	

Note: World Health Organization (WHO), Karnofsky (KPS).

Table 2. Relationship between S100B and pathologic data of patients

Factor	S100B (U/mL)		P
	High expression (n=37)	Low expression (n=37)	
Gender			0.525
Male (n=48)	23	25	
Female (n=26)	15	12	
Age			0.161
≥55 years old (n=34)	20	14	
<55 years old (n=40)	17	23	
WHO Classification			0.017
Grade II (n=30)	10	20	
Grade III+IV (n=44)	27	17	
Preoperative KPS score			0.552
≥80 points (n=60)	31	29	
<80 points (n=14)	6	8	
Tumor Diameter			0.101
≥5 cm (n=41)	24	17	
<5 cm (n=33)	13	20	
Pathologic type			0.324
Astrocytoma (n=28)	12	16	
Oligodendroglioma (n=22)	10	12	
Oligoastrocytoma (n=24)	15	9	

Note: World Health Organization (WHO), Karnofsky (KPS).

Relationship between CA15-3, S100B, IGF-1 and pathologic data of patients

Our analysis showed that the proportion of III+IV patients with high expression of CA15-3, S100B, and IGF-1 was markedly higher than that of Grade II patients (**Tables 1**-**3**, P<0.05), but there was no statistical difference in other pathologic data (P>0.05).

Expression of CA15-3, S100B, and IGF-1 in high-grade and low-grade gliomas

In the above studies, we found that CA15-3, S100B, and IGF-1 were related to the WHO classifications of patients. In order to further determine the value of CA15-3, S100B, and IGF-1 in WHO classification, we divided patients into a low-grade glioma group (n=30) and a high-grade glioma group (n=44) according to WHO classification. It was found that CA15-3, S100B and IGF-1 in patients with low-grade glioma were significantly lower than those of patients with high-grade glioma (P<0.01, **Figure 2**).

Diagnostic value of CA15-3, S100B, and IGF-1 in high-grade and low-grade gliomas

To determine the value of CA15-3, S100B, and IGF-1 in the diagnosis of patients with different grades of glioma, we plotted an ROC curve (**Figure 3**) and found that the AUCs (areas under the curve) of CA15-3, S100B, and IGF-1 in differentiating different glioma grades were 0.822, 0.722, and 0.768, respectively, all of which have diagnostic value (**Table 4**). Notably, the area under the curve of CA15-3 was over 0.8, which was of high clinical diagnostic value.

Table 3. Relationship between IGF-1 and pathologic data of patients

Factor	IGF-1 (U/mL)		P
	High expression (n=37)	Low expression (n=37)	
Gender			0.626
Male (n=48)	25	23	
Female (n=26)	12	14	
Age			0.161
≥55 years old (n=34)	14	20	
<55 years old (n=40)	23	17	
WHO Classification			0.001
Grade II (n=30)	8	22	
Grade III+IV (n=44)	29	15	
Preoperative KPS score			0.074
≥80 points (n=60)	27	33	
<80 points (n=14)	10	4	
Tumor Diameter			0.815
≥5 cm (n=41)	21	20	
<5 cm (n=33)	16	17	
Pathologic type			0.137
Astrocytoma (n=28)	18	10	
Oligodendroglioma (n=22)	10	12	
Oligoastrocytoma (n=24)	9	15	

Note: World Health Organization (WHO), Karnofsky (KPS).

Changes in CA15-3, S100B, and IGF-1 before and after treatment

The serum CA15-3, S100B, and IGF-1 levels of patients after treatment were lower than those before treatment (P<0.0001, **Figure 4**).

Relationship between CA15-3, S100B, IGF-1, and clinical efficacy of patients

After treatment, we evaluated the efficacy of the markers in patients, including 28 patients with CR, 32 with PR, 11 with SD, and 3 with PD. We then further analyzed the relationships between CA15-3, S100B, IGF-1, and their efficacy in patients, and found that serum levels of these three gradually increased with a deterioration of clinical efficacy (P<0.05, **Figure 5**). Among these, IGF-1 was positively correlated with the efficacy in patients (P<0.05, **Figure 6**).

Value of CA15-3, S100B, and IGF-1 in predicting the clinical efficacy in patients

In this study, CR and PR patients were considered effective groups according to the clinical efficacy after treatment, while SD and PD patients were considered ineffective groups. The predictive values of CA15-3, S100B, and IGF-1 on clinical efficacy before treatment were analyzed. Results showed that the AUCs of CA15-3, S100B, and IGF-1 before treatment were 0.824, 0.741, and 0.800, respectively, all of which had diagnostic value (**Table 5**; **Figure 7**). Notably, the areas under the curve of CA15-3 and IGF-1 were both greater than 0.8, giving them high clinical diagnostic value.

Discussion

Glioma is a deadly disease [14]. In the early stage of brain glioma, there are usually no typical clinical symptoms and signs, which predisposes to missing the best time for treatment by clinical diagnosis merely based on brain CT and MRI [15]. Moreover, the therapeutic effect of glioma treatment programs such as targeted therapy, surgery, chemotherapy, and radiotherapy, and the prognosis of glioma patients are easily affected by various factors such as tumor location, degree of malignancy, and body state [16]. Therefore, despite significant progress in the diagnosis and treatment of glioma in recent years, the overall survival rate of patients remains unsatisfactory, so it is of great significance to evaluate the prognosis of patients.

CA15-3 is a glycoprotein of high molecular weight that is mainly located on the surface of tumor cells. When the cells become cancerous, it falls off the cells and enters the serum, resulting in an increase in serum CA15-3 levels [17]. IGF-1 is a growth regulator with similar effects on insulin and growth hormone, which can promote cell proliferation and differentiation. Its expression level is high in a variety of solid tumors, and plays a key role in promoting the occurrence and development of cancer [18]. Previous studies by Sinha et al. [19] found that IGF-1 could regulate the inflammatory response of glioma by inducing the HIF-1α/

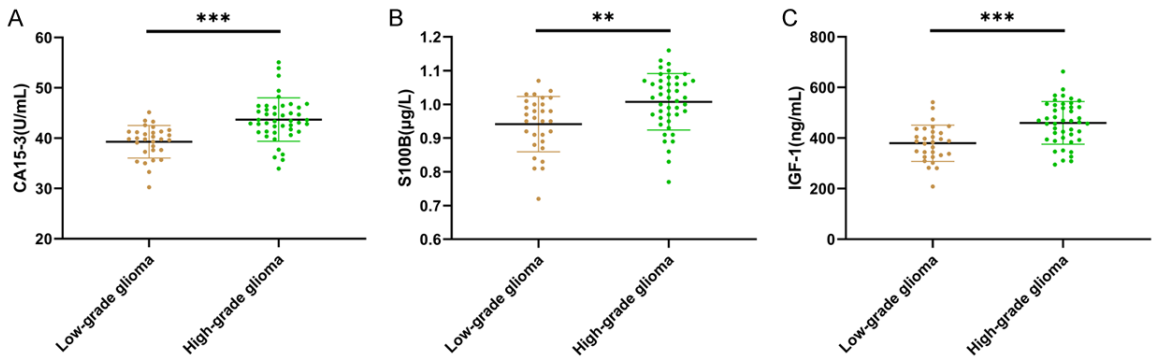

Figure 2. Expression of CA15-3, S100B, and IGF-1 in patients with different grades of glioma. A. Expression of CA15-3 in high-grade and low-grade glioma patients. B. Expression of S100B in high-grade and low-grade glioma patients. C. Expression of IGF-1 in high-grade and low-grade glioma patients. Note: ** means P<0.01, *** means P<0.001; carbohydrate antigen 153 (CA15-3), S-100 calcium binding protein B (S100B), insulin-like growth factor-1 (IGF-1).

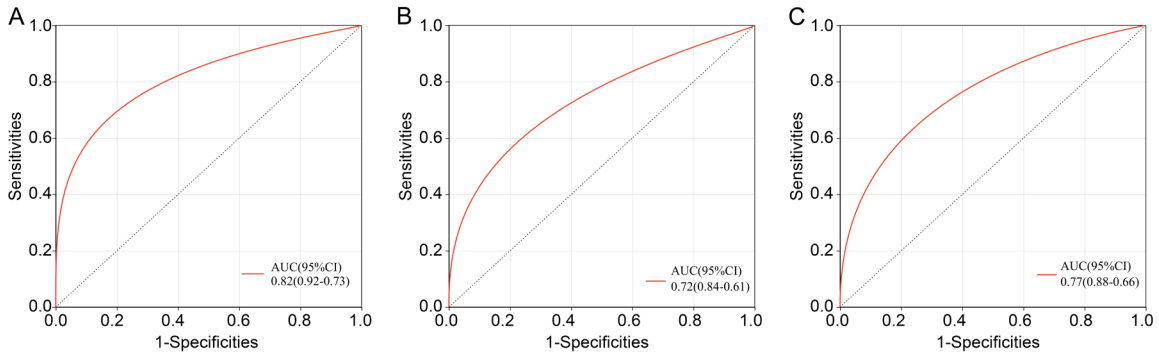

Figure 3. Diagnostic curves of CA15-3, S100B, and IGF-1 in patients with different grades of glioma. (A) ROC curve of CA15-3 for differentiating high-grade and low-grade gliomas. ROC curve of (B) S100B for differentiating high-grade and low-grade gliomas. ROC curve of (C) IGF-1 for differentiating high-grade and low-grade gliomas. Note: carbohydrate antigen 153 (CA15-3), S-100 calcium binding protein B (S100B), insulin-like growth factor-1 (IGF-1), receiver operating curve (ROC).

Table 4. ROC analysis of CA15-3, S100B, and IGF-1 to the diagnosis of high-grade and low-grade glioma

Predictor	AUC	95 CI%	Specificity	Sensitivity	Youden Index	Cut-off
CA15-3	0.822	0.726-0.918	86.70%	70.50%	57.10%	42.29
S100B	0.722	0.608-0.836	93.30%	43.20%	36.50%	1.03
IGF-1	0.768	0.660-0.876	90.00%	59.10%	49.10%	451.48

Note: receiver operating curve (ROC), Area under curve (AUC), carbohydrate antigen 153 (CA15-3), S100 calcium binding protein B (S100B), insulin-like growth factor-1 (IGF-1).

TLR9 axis. However, there was no relevant research on whether CA15-3 and IGF-1 are related to the prognosis of glioma patients. S100B protein is an acidic calcium-binding protein involved in neuronal cell metabolism, promoting the growth and differentiation of glial cells and other processes [20]. A study has found that S100B protein was specific to nerve tissue. Specifically, when brain tissue was damaged, it was released into the cerebrospinal fluid and entered the blood circulation through the damaged blood-brain barrier, resulting in elevated serum levels [21]. This suggests that changes in S100B are helpful for the diagnostic and prognostic evaluation of nervous system injury. In this study, we found that the proportions of CA15-3, S100B, and IGF-1 in patients with high-grade glioma were higher than in

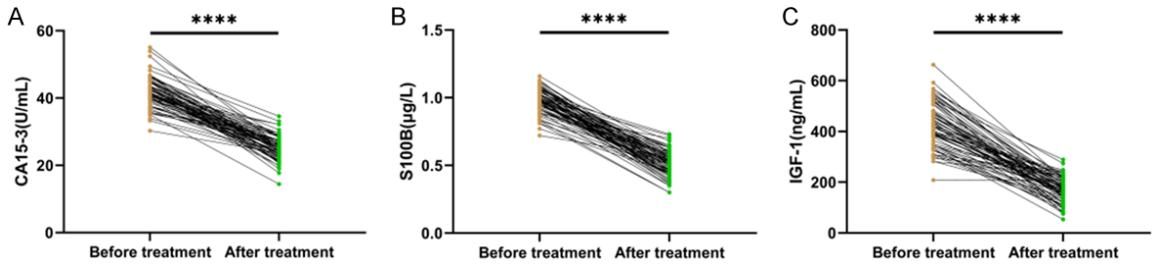

Figure 4. Changes in CA15-3, S100B, and IGF-1 in patients before and after treatment. A. Comparison of CA15-3 expression in patients before and after treatment. B. Comparison of S-100B expression in patients before and after treatment. C. Comparison of IGF-1 expression in patients before and after treatment. Note: ****P<0.0001, carbohydrate antigen 153 (CA15-3), S-100 calcium binding protein B (S100B), insulin-like growth factor-1 (IGF-1).

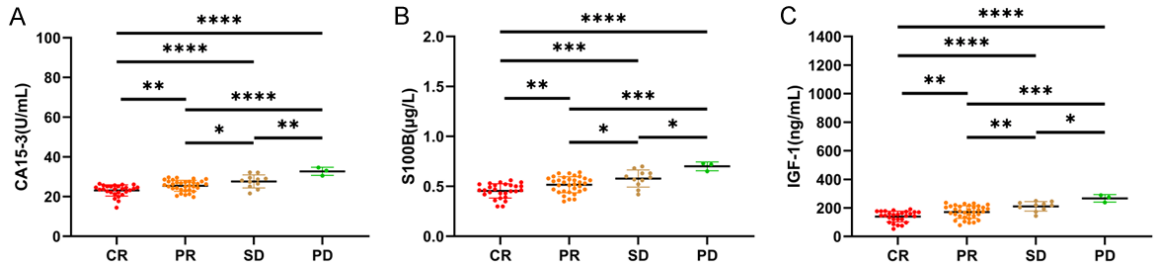

Figure 5. Expression of CA15-3, S100B, and IGF-1 in patients with different treatment efficacy. A. CA15-3 in serum of patients with different clinical efficacy after treatment. B. S100B in serum of patients with different clinical efficacy after treatment. C. IGF-1 in serum of patients with different clinical efficacy after treatment. Note: *P<0.05, **P<0.01, ***P<0.001, ****P<0.0001, carbohydrate antigen 153 (CA15-3), S-100 calcium binding protein B (S100B), insulin-like growth Factor-Factor 1 (IGF-1).

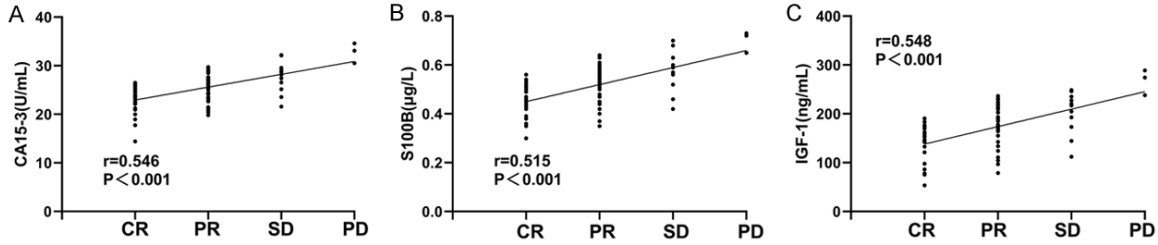

Figure 6. Correlation of CA15-3, S100B, IGF-1 and treatment efficacy. A. Analysis of the correlation between CA15-3 and treatment efficacy in patients. B. Analysis of the correlation between S100B and treatment efficacy in patients. C. Analysis of the correlation between IGF-1 and treatment efficacy in patients. Note: Carbohydrate antigen 153 (CA15-3), S-100 calcium binding protein B (S100B), insulin-like growth factor-1 (IGF-1).

patients with low-grade glioma, and the serum CA15-3, S100B and IGF-1 levels of patients after treatment were significantly lower than those before treatment. This indicates that CA15-3, S100B, and IGF-1 may become diagnostic indicators for patients with different grades of glioma, and are related to prognosis. In order to further determine the diagnostic value of CA15-3, S100B, and IGF-1 in patients with different grades of glioma, we plotted ROC curves and found that the AUCs of CA15-3, S100B, and IGF-1 in diagnosing patients with different grades of glioma were all greater than 0.7, and that of CA15-3 was 0.822, indicating that CA15-3, S100B, and IGF-1 could be used as indicators for the diagnosis of different grades of glioma. In the previous study by Zhang et al. [22], it was found that the AUC of serum miRNA-145-5p for diagnosing patients with different grades of glioma was 0.825, and the sensitivity and specificity were 76.1% and 76.9%, respectively. This is consistent with our

Table 5. ROC analysis of CA15-3, S100B, and IGF-1 in predicting the clinical efficacy in patients after treatment

Predictor	AUC	95 CI%	Specificity	Sensitivity	Youden Index	Cut-off
CA15-3	0.824	0.680-0.967	78.30%	78.60%	56.90%	43.39
S100B	0.741	0.573-0.909	91.70%	50.00%	41.70%	1.065
IGF-1	0.800	0.663-0.937	76.70%	78.60%	55.20%	465.02

Note: receiver operating curve (ROC), Area under curve (AUC), carbohydrate antigen 153 (CA15-3), S100 calcium binding protein B (S100B), insulin-like growth factor-1 (IGF-1).

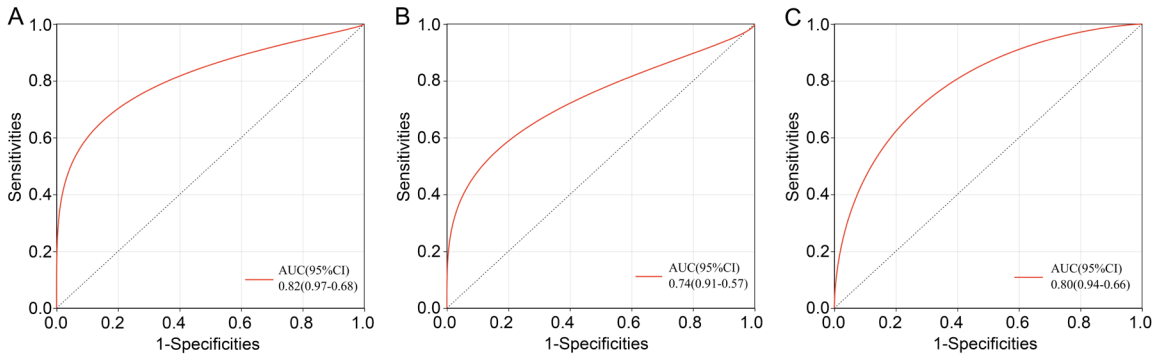

Figure 7. Diagnostic curves of CA15-3, S100B, and IGF-1 for predicting the clinical efficacy in patients after treatment. A. ROC curve of CA15-3 in distinguishing the effective group from the ineffective group. B. ROC curve of S100B in distinguishing the effective group from the ineffective group. C. ROC curve of IGF-1 in distinguishing the effective group from the ineffective group. Note: carbohydrate antigen 153 (CA15-3), S-100 calcium binding protein B (S100B), insulin-like growth factor-1 (IGF-1), receiver operating curve (ROC).

results on CA15-3. Compared to the detection of miRNA-145-5p, that of CA15-3 is economical and inexpensive, making it conducive to repeated tests.

The treatment efficacy evaluation for glioma has always been clinically detected by imaging methods [23] including CT and MRI, which are of relatively high resolution and accuracy. They can provide a basis for diagnosis of functional metabolism, or tissue anatomy, and can assist clinicians in later treatment [24]. However, CT testing introduces a certain amount of radiation to human body, and MRI testing may result in skin allergies, fever, nausea, or vomiting [25]. In recent years, serum tumor markers have been widely used in solid tumor screening, clinical diagnosis, pathologic grading, and prognosis assessment. In this study, we determined that CA15-3, S100B, and IGF-1 decreased in patients after treatment, suggesting that there may be a relationship between those three indicators and the efficacy in patients. To verify our hypothesis, we compared the expressions of CA15-3, S100B, and IGF-1 in patients with different curative effects after treatment, and found that all three indicators gradually increased with a deterioration in clinical efficacy, and were positively correlated with efficacy. The previous study of He et al. [26] found that MEK2 was highly expressed in glioma patients, while MEK2 expression was decreased in patients treated with temozolomide, and the increase in MEK2 was closely related to a progression in glioma grade. The results regarding CA15-3, S100B, and IGF-1 in our study showed a similar trend. However, it was noted that detecting CA15-3, S100B, and IGF-1 is are more convenient and less expensive, making them more suitable for clinical application. This suggested that CA15-3, S100B, and IGF-1 are involved in the occurrence of tumors, and can be used as effective observation indicators to evaluate the treatment efficacy in patients. However, the related mechanism remains unclear. We speculate that CA15-3 and IGF-1 are highly expressed in solid tumors, and the shrinkage or even disappearance of tumors would directly reduce the level of CA15-3 and IGF-1 in patients. This wouldfurther reduce S100B expression due to the improvement in brain injury. At the end of the study, we also

analyzed the value of CA15-3, S100B, and IGF-1 in predicting the clinical efficacy in patients. It was found that the AUCs of CA15-3, S100B, and IGF-1 were all greater than 0.7 for predicting treatment efficacy in glioma patients, which could be used as indicators to predict treatment efficacy.

Inevitably, this study has certain limitations. First, follow-up was not conducted, and it remains unclear whether CA15-3, S100B, or IGF-1 are related to patient survival. Second, as a retrospective study, we analyzed only the effect of a single treatment regimen on serum CA15-3, S100B, or IGF-1. More samples need to be collected for further verification on whether combination treatment with other drugs could affect serum CA15-3, S100B, or IGF-1 expression. Therefore, we hope to carry out prospective studies with a follow-up period to refine our findings.

Thus up, CA15-3, S100B, and IGF-1 are highly expressed in patients with glioma, and can be used as diagnostic indicators to distinguish patients with high or low grades. They also could predict the treatment efficacy in glioma patients.

Disclosure of conflict of interest

None.

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