

World Journal of *Clinical Cases*

World J Clin Cases 2023 May 16; 11(14): 3114-3368



OPINION REVIEW

- 3114 Modernising autism spectrum disorder model engineering and treatment *via* CRISPR-Cas9: A gene reprogramming approach
Sandhu A, Kumar A, Rawat K, Gautam V, Sharma A, Saha L

REVIEW

- 3128 Burden of disability in type 2 diabetes mellitus and the moderating effects of physical activity
Oyewole OO, Ale AO, Ogunlana MO, Gurayah T

MINIREVIEWS

- 3140 Postoperative hypoxemia for patients undergoing Stanford type A aortic dissection
Liu HY, Zhang SP, Zhang CX, Gao QY, Liu YY, Ge SL

ORIGINAL ARTICLE**Case Control Study**

- 3148 Impact of extended nursing model after multi-disciplinary treatment on young patient with post-stroke
Xu XY, Pang ZJ, Li MH, Wang K, Song J, Cao Y, Fang M
- 3158 Changes and significance of serum ubiquitin carboxyl-terminal hydrolase L1 and glial fibrillary acidic protein in patients with glioma
Zhu QH, Wu JK, Hou GL

Retrospective Study

- 3167 Multitrack and multianchor point screw technique combined with the Wiltse approach for lesion debridement for lumbar tuberculosis
Yuan YF, Ren ZX, Zhang C, Li GJ, Liu BZ, Li XD, Miao J, Li JF
- 3176 Clinical features and prognostic factors in 49 patients with follicular lymphoma at a single center: A retrospective analysis
Wu H, Sun HC, Ouyang GF
- 3187 Value of optical coherence tomography measurement of macular thickness and optic disc parameters for glaucoma screening in patients with high myopia
Mu H, Li RS, Yin Z, Feng ZL

Observational Study

- 3195 Comparative study of the clinical efficacy of all-inside and traditional techniques in anterior cruciate ligament reconstruction
An BJ, Wang YT, Zhao Z, Wang MX, Xing GY

- 3204** Positioning and design by computed tomography imaging in neuroendoscopic surgery of patients with chronic subdural hematoma

Wang XJ, Yin YH, Zhang LY, Wang ZF, Sun C, Cui ZM

- 3211** Evaluation of chronic idiopathic tinnitus and its psychosocial triggers

Hamed SA, Attiah FA, Fawzy M, Azzam M

- 3224** Intestinal complications in patients with Crohn's disease in the Brazilian public healthcare system between 2011 and 2020

Sasaki LY, Martins AL, Galhardi-Gasparini R, Saad-Hossne R, Ritter AMV, Barreto TB, Marcolino T, Balula B, Yang-Santos C

Randomized Controlled Trial

- 3238** Effect of non-pharmacological treatment on the full recovery of social functioning in patients with attention deficit hyperactivity disorder

Lv YB, Cheng W, Wang MH, Wang XM, Hu YL, Lv LQ

CASE REPORT

- 3248** Diagnosis of tuberculous uveitis by the macrogenome of intraocular fluid: A case report and review of the literature

Zhang YK, Guan Y, Zhao J, Wang LF

- 3256** Intragastric fish bones migrate into the liver: A case report

Dai MG, Zheng JJ, Yang J, Ye B

- 3261** Primary seminal vesicle adenocarcinoma with a history of seminal vesicle cyst: A case report and review of literature

Yao Y, Liu S, He YL, Luo L, Zhang GM

- 3267** Immune checkpoint inhibitor therapy-induced autoimmune polyendocrine syndrome type II and Crohn's disease: A case report

Gao MJ, Xu Y, Wang WB

- 3275** Late-onset mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes syndrome with mitochondrial DNA 3243A>G mutation masquerading as autoimmune encephalitis: A case report

Wang JW, Yuan XB, Chen HF

- 3282** Metastatic gastric cancer from breast carcinoma presenting with paraneoplastic rheumatic syndrome: A case report

Rech MB, da-Cruz ER, Salgado K, Balbinot RA, Balbinot SS, Soldera J

- 3288** Novel mutation of SPG4 gene in a Chinese family with hereditary spastic paraplegia: A case report

Wang J, Bu WT, Zhu MJ, Tang JY, Liu XM

- 3295** Chronic pulmonary mucormycosis caused by rhizopus microsporus mimics lung carcinoma in an immunocompetent adult: A case report

Guo XZ, Gong LH, Wang WX, Yang DS, Zhang BH, Zhou ZT, Yu XH

- 3304** Idiopathic sclerosing mesenteritis presenting with small bowel volvulus in a patient with antiphospholipid syndrome: A case report
Chennavasin P, Gururatsakul M
- 3311** *Neisseria mucosa* - A rare cause of peritoneal dialysis-related peritonitis: A case report
Ren JM, Zhang XY, Liu SY
- 3317** Rectal prolapse in a 30-year-old bladder stone male patient: A case report
Ding HX, Huang JG, Feng C, Tai SC
- 3323** Successful treatment of veno-arterial extracorporeal membrane oxygenation complicated with left ventricular thrombus by intravenous thrombolysis: A case report
Wang YD, Lin JF, Huang XY, Han XD
- 3330** Successful remimazolam sedation-epidural block in an older patient with severe chronic obstructive pulmonary disease: A case report
Yu JJ, Pei HS, Meng Y
- 3340** *De novo* mutation of NAXE (APOA1BP)-related early-onset progressive encephalopathy with brain edema and/or leukoencephalopathy-1: A case report
Ding L, Huang TT, Ying GH, Wang SY, Xu HF, Qian H, Rahman F, Lu XP, Guo H, Zheng G, Zhang G
- 3351** Iatrogenic atlantoaxial rotatory subluxation after thyroidectomy in a pediatric patient: A case report
Hong WJ, Lee JK, Hong JH, Han MS, Lee SS
- 3356** Bladder metastasis from epidermal growth factor receptor mutant lung cancer: A case report
Jin CB, Yang L
- 3362** Primary rectal mucosa-associated lymphoid tissue lymphoma treated with only endoscopic submucosal dissection: A case report
Lee WS, Noh MG, Joo YE

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Jaw-Yuan Wang, MD, PhD, Professor, Surgical Oncologist, Department of Surgery, Kaohsiung Medical University Hospital, Kaohsiung Medical University, Kaohsiung 807, Taiwan. jawyuanwang@gmail.com

AIMS AND SCOPE

The primary aim of *World Journal of Clinical Cases (WJCC, World J Clin Cases)* is to provide scholars and readers from various fields of clinical medicine with a platform to publish high-quality clinical research articles and communicate their research findings online.

WJCC mainly publishes articles reporting research results and findings obtained in the field of clinical medicine and covering a wide range of topics, including case control studies, retrospective cohort studies, retrospective studies, clinical trials studies, observational studies, prospective studies, randomized controlled trials, randomized clinical trials, systematic reviews, meta-analysis, and case reports.

INDEXING/ABSTRACTING

The *WJCC* is now abstracted and indexed in Science Citation Index Expanded (SCIE, also known as SciSearch®), Journal Citation Reports/Science Edition, Current Contents®/Clinical Medicine, PubMed, PubMed Central, Scopus, Reference Citation Analysis, China National Knowledge Infrastructure, China Science and Technology Journal Database, and Superstar Journals Database. The 2022 Edition of Journal Citation Reports® cites the 2021 impact factor (IF) for *WJCC* as 1.534; IF without journal self cites: 1.491; 5-year IF: 1.599; Journal Citation Indicator: 0.28; Ranking: 135 among 172 journals in medicine, general and internal; and Quartile category: Q4. The *WJCC*'s CiteScore for 2021 is 1.2 and Scopus CiteScore rank 2021: General Medicine is 443/826.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: *Hua-Ge Yu*; Production Department Director: *Xu Guo*; Editorial Office Director: *Jin-Lei Wang*.

NAME OF JOURNAL

World Journal of Clinical Cases

ISSN

ISSN 2307-8960 (online)

LAUNCH DATE

April 16, 2013

FREQUENCY

Thrice Monthly

EDITORS-IN-CHIEF

Bao-Gan Peng, Jerzy Tadeusz Chudek, George Kontogeorgos, Maurizio Serati, Ja Hyeon Ku

EDITORIAL BOARD MEMBERS

<https://www.wjgnet.com/2307-8960/editorialboard.htm>

PUBLICATION DATE

May 16, 2023

COPYRIGHT

© 2023 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS

<https://www.wjgnet.com/bpg/gerinfo/204>

GUIDELINES FOR ETHICS DOCUMENTS

<https://www.wjgnet.com/bpg/GerInfo/287>

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH

<https://www.wjgnet.com/bpg/gerinfo/240>

PUBLICATION ETHICS

<https://www.wjgnet.com/bpg/GerInfo/288>

PUBLICATION MISCONDUCT

<https://www.wjgnet.com/bpg/gerinfo/208>

ARTICLE PROCESSING CHARGE

<https://www.wjgnet.com/bpg/gerinfo/242>

STEPS FOR SUBMITTING MANUSCRIPTS

<https://www.wjgnet.com/bpg/GerInfo/239>

ONLINE SUBMISSION

<https://www.f6publishing.com>

Case Control Study

Changes and significance of serum ubiquitin carboxyl-terminal hydrolase L1 and glial fibrillary acidic protein in patients with glioma

Qing-Hua Zhu, Jing-Kun Wu, Gao-Lei Hou

Specialty type: Oncology**Provenance and peer review:**

Unsolicited article; Externally peer reviewed.

Peer-review model: Single blind**Peer-review report's scientific quality classification**Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0**P-Reviewer:** Pierro A, Canada;
Shah PS, Canada**Received:** February 19, 2023**Peer-review started:** February 19, 2023**First decision:** February 28, 2023**Revised:** March 17, 2023**Accepted:** April 6, 2023**Article in press:** April 6, 2023**Published online:** May 16, 2023**Qing-Hua Zhu, Jing-Kun Wu, Gao-Lei Hou**, Department of Neurosurgery, Affiliated Hospital of Hebei Engineering University, Handan 056002, Hebei Province, China**Corresponding author:** Jing-Kun Wu, MM, Associate Chief Physician, Department of Neurosurgery, Affiliated Hospital of Hebei Engineering University, No. 81 Congtai Street, Congtai District, Handan 056002, Hebei Province, China. wujingkunwjk@163.com

Abstract

BACKGROUND

Brain gliomas are malignant tumors with high postoperative recurrence rates. Early prediction of prognosis using specific indicators is of great significance.

AIM

To assess changes in ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) and glial fibrillary acidic protein (GFAP) levels in patients with glioma pre-and postoperatively.

METHODS

Between June 2018 and June 2021, 91 patients with gliomas who underwent surgery at our hospital were enrolled in the glioma group. Sixty healthy volunteers were included in the control group. Serum UCH-L1 and GFAP levels were measured in peripheral blood collected from patients with glioma before and 3 d after surgery. UCH-L1 and GFAP levels in patients with glioma with different clinicopathological characteristics were compared before and after surgery. The patients were followed-up until February 2022. Postoperative glioma recurrence was recorded to determine the serum UCH-L1 and GFAP levels, which could assist in predicting postoperative glioma recurrence.

RESULTS

UCH-L1 and GFAP levels in patients with glioma decreased significantly 3 d after surgery compared to those before therapy ($P < 0.05$). However, UCH-L1 and GFAP levels in the glioma group were significantly higher than those in the control group before and after surgery ($P < 0.05$). There were no statistically significant differences in preoperative serum UCH-L1 and GFAP levels among patients with glioma according to sex, age, pathological type, tumor location, or number of lesions ($P > 0.05$). Serum UCH-L1 and GFAP levels were significantly lower in the patients with WHO grade I-II tumors than in those with grade III-IV tumors ($P < 0.05$). Serum UCH-L1 and GFAP levels were lower in the patients

with tumor diameter ≤ 5 cm than in those with diameter > 5 cm, in which the differences were statistically significant ($P < 0.05$). Glioma recurred in 22 patients. The preoperative and 3-d postoperative serum UCH-L1 and GFAP levels were significantly higher in the recurrence group than these in the non-recurrence group ($P < 0.05$). Receiver operating characteristic curves were plotted. The areas under the curves of preoperative serum UCH-L1 and GFAP levels for predicting postoperative glioma recurrence were 0.785 and 0.775, respectively. However, the efficacy of serum UCH-L1 and GFAP levels 3 d after surgery in predicting postoperative glioma recurrence was slightly lower compared with their preoperative levels.

CONCLUSION

UCH-L1 and GFAP efficiently reflected the development and recurrence of gliomas and could be used as potential indicators for the recurrence and prognosis of glioma.

Key Words: Glioma; Ubiquitin carboxy-terminal hydrolase L1; Glial fibrillary acidic protein; Surgery; Prognosis; Clinical significance

©The Author(s) 2023. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Since the recurrence rate of glioma is high, it is important to early predict its prognosis. Ubiquitin carboxy-terminal hydrolase-L1 (UCH-L1) and glial fibrillary acidic protein (GFAP) are important markers for nervous system damages and lesions. Therefore, we evaluated the changes in UCH-L1 and GFAP levels in patients with glioma during the perioperative period and compared them with those in healthy volunteers to analyze their relationship with clinicopathological and postoperative recurrence. These results revealed that UCH-L1 and GFAP might reflect the development and recurrence of glioma and could be used as potential indicators to estimate prognosis of glioma.

Citation: Zhu QH, Wu JK, Hou GL. Changes and significance of serum ubiquitin carboxyl-terminal hydrolase L1 and glial fibrillary acidic protein in patients with glioma. *World J Clin Cases* 2023; 11(14): 3158-3166

URL: <https://www.wjgnet.com/2307-8960/full/v11/i14/3158.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v11.i14.3158>

INTRODUCTION

Brain glioma is an extremely common type of intracranial malignant tumor that deteriorates, grows rapidly and causes severe neurological impairment. Due to the poor sensitivity of brain gliomas to radiotherapy, they are mainly managed by surgical resection. However, some gliomas are large in size or close to important neural tissues and are difficult to completely remove intraoperatively. Therefore, the recurrence rate of brain gliomas after surgery is high[1,2]. Early prediction of postoperative prognosis in patients with gliomas is of great importance in clinical practice. Ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) is a cysteine hydrolase that regulates the cell cycle, is involved in apoptosis and inflammatory responses, is present at high levels in the brain, and is regarded as a biomarker of brain injury[3]. Glial fibrillary acidic protein (GFAP) is a specific indicator of astrocytes and involved in neurological damage and lesions[4]. In this study, we evaluated changes in serum UCH-L1 and GFAP levels in patients with glioma before and after surgery. We also assessed the relationship between the two indicators and analyzed data of the patients' clinicopathological characteristics and postoperative recurrence. We also aimed to determine the values of UCH-L1 and GFAP for predicting glioma recurrence.

MATERIALS AND METHODS

Participants

A total of 91 patients with gliomas who underwent surgery in the hospital between June 2018 and June 2021 were enrolled in the glioma group. The control group included 60 healthy volunteers during the same period.

Patients with glioma

The inclusion criteria comprised patients: Who were treated surgically; with glioma that was clearly

detected by postoperative pathological examination; who underwent no radiotherapy before surgery; and with complete clinical case data. Patients with: acromegaly, hepatitis, and other diseases; severe defects in vital organ function; severe complications, and postoperative death; or other malignant tumors were excluded from the study.

The control group

The age and sex ratios in the control group were similar to those in the glioma group: Both groups underwent physical examination and had no previous history of tumors, intracranial lesions, or brain injury.

Methods

All patients with gliomas were surgically treated, and 5 mL of peripheral venous blood was collected from these patients with glioma before and 3 d after surgery. In the control group, venous blood was collected during fasting in the early morning on day two after enrollment.

Blood samples were immediately centrifuged at 3000 rpm for 15 min. The liquid supernatant was separated and stored at -80°C for later use. Serum GFAP and UCH-L1 Levels were detected by ABC-ELISA, and kits were purchased from Rapid Bio, USA. The experimental procedure was performed in strict accordance with the relevant kit standards.

Study aims

(1) To compare UCH-L1 and GFAP levels between the glioma and control groups; (2) To analyze data of preoperative serum UCH-L1 and GFAP levels in patients with gliomas with different clinicopathological features; and (3) The patients were followed up until February 2022 to record the preoperative recurrence of glioma and compare serum UCH-L1 and GFAP levels between the recurring and non-recurring patients. A receiver operating characteristic (ROC) curve was drawn. Furthermore, the values of preoperative and postoperative serum UCH-L1 and GFAP levels for predicting postoperative glioma recurrence were analyzed.

Statistical analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 19.0. The measurement data was presented as mean \pm SD. The independent samples *t* test was used for mean comparison between the two groups. The mean data before and after treatment were analyzed using the paired *t* test, and the count data were conveyed by case. The χ^2 test was used to compare the two groups. ROC curves were drawn (Figure 1). In addition, the best critical value was calculated by the Youden index formula to evaluate the efficacy of preoperative and postoperative serum UCH-L1 and GFAP levels in predicting postoperative glioma recurrence. *P* value < 0.05 was considered statistically significant.

RESULTS

Comparison of serum UCH-L1 and GFAP levels between the glioma and control groups

UCH-L1 and GFAP levels in the patients with glioma decreased significantly 3 d after surgery compared with their pre-therapy levels (*P* < 0.05). However, the UCH-L1 and GFAP levels in the glioma group were significantly higher than those in the control group before and after surgery (*P* < 0.05, Table 1).

Analysis of the relationship between preoperative serum UCH-L1 and GFAP levels and clinicopathological characteristics in patients with glioma

There were no significant differences in the preoperative serum UCH-L1 and GFAP levels in patients with brain glioma with respect to sex, age, pathological type, tumor location, or number of lesions (*P* > 0.05, Table 2). The UCH-L1 and GFAP levels in the patients with WHO grade I-II tumors were lower than those in the participants with grade III-IV tumors. Additionally, the UCH-L1 and GFAP levels in the patients with tumor diameters \leq 5 cm were lower than those in the participants with tumor diameters > 5 cm.

Comparison of UCH-L1 and GFAP levels in patients with glioma recurrence and those without recurrence before and after surgery

All patients were followed up until February 2022. A total of 22 patients with gliomas experienced recurrence. The preoperative and 3 d postoperative serum UCH-L1 and GFAP levels were significantly higher in the recurrence group compared with the non-recurrence group (*P* < 0.05, Table 3).

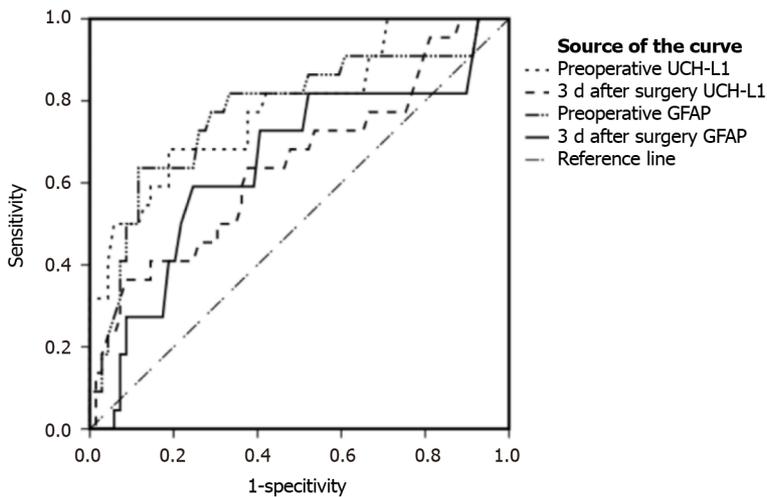
Table 1 Comparison of serum ubiquitin carboxy-terminal hydrolase L1 and glial fibrillary acidic protein levels between the glioma and control groups

Group	n	Time	UCH-L1 (pg/mL)	GFAP (ng/L)
Glioma group	91	Preoperative	96.89 ± 17.15 ^a	16.69 ± 2.16 ^a
		3 d after surgery	72.15 ± 12.33 ^{a,d}	7.53 ± 1.74 ^{a,d}
Control group	60		60.17 ± 10.78	1.16 ± 0.25

^a*P* < 0.05 vs the control group.

^d*P* < 0.05 vs the glioma group three days after surgery.

UCH-L1: Ubiquitin carboxy-terminal hydrolase L1; GFAP: Glial fibrillary acidic protein.



DOI: 10.12998/wjcc.v11.i14.3158 Copyright ©The Author(s) 2023.

Figure 1 Receiver operating characteristic curve of serum ubiquitin carboxy-terminal hydrolase L1 and glial fibrillary acidic protein levels for predicting postoperative recurrence of glioma. UCH-L1: Ubiquitin carboxy-terminal hydrolase L1; GFAP: Glial fibrillary acidic protein.

The value of UCH-L1 and GFAP levels for predicting postoperative recurrence of glioma

The AUC of the preoperative serum UCH-L1 and GFAP levels for predicting postoperative glioma recurrence were 0.785 and 0.775, respectively (Table 4). The efficacy of UCH-L1 and GFAP levels 3 d after surgery in predicting postoperative glioma recurrence was slightly lower than their preoperative levels.

DISCUSSION

Glioma is a tumor caused by glial cell lesions originating from the ectoderm of the nervous system with an incidence of approximately 5/100000. Owing to the lack of specific tumor markers related to gliomas, imaging examinations such as brain computed tomography or magnetic resonance imaging are the main methods for the clinical assessment of changes and treatment effects during the course of glioma. However, imaging examinations are particularly lagging behind clinical treatment and prognostic determination[5,6]. Therefore, finding more sensitive indicators that reflect treatment effect and prognosis in patients with glioma as soon as possible was one of the aims of the current study.

UCH-L1 is a member of the ubiquitin protease system family, which mainly consists of 223 amino acids, and is abundant in the brain. It is involved in cell proliferation, differentiation, apoptosis, and other physiological processes *via* the ubiquitin pathway. In addition, UCH-L1 has been shown to be relevant to brain nervous system development, brain tumors, and brain injury[7,8]. Studies have shown that[9] after acute cerebral infarction, a large amount of UCH-L1 could be released from damaged nerve cells and penetrate the blood-brain barrier into the blood circulation. Therefore, serum UCH-L1 levels were elevated in patients with cerebral infarction. Wang *et al*[10] found that serum UCH-L1 Levels had good clinical value for reflecting the degree of brain injury and prognosis in patients with severe cranio-cerebral injury. Elevated levels of UCH-L1 in the cerebrospinal fluid and peripheral blood have become effective indicators of the severity of central nervous cell damage.

Table 2 Analysis of the relationship between preoperative serum ubiquitin carboxy-terminal hydrolase L1 and glial fibrillary acidic protein levels and clinicopathological characteristics in the patients with glioma

Clinicopathological features	UCH-L1 (pg/mL)	GFAP (ng/L)
Gender		
Male (<i>n</i> = 49)	95.89 ± 16.79	16.58 ± 2.14
Female (<i>n</i> = 42)	98.05 ± 17.69	16.82 ± 2.20
<i>t</i> value	0.597	0.515
<i>P</i> value	0.552	0.608
Age (yr)		
< 40 (<i>n</i> = 44)	99.78 ± 18.42	17.03 ± 2.29
≥ 40 (<i>n</i> = 47)	94.19 ± 15.58	16.37 ± 2.01
<i>t</i> value	1.566	1.483
<i>P</i> value	0.121	0.141
Pathological type		
Glioblastoma (<i>n</i> = 76)	98.12 ± 17.14	16.84 ± 2.16
Medulloblastoma (<i>n</i> = 15)	90.65 ± 16.35	15.92 ± 2.04
<i>t</i> value	1.554	1.512
<i>P</i> value	0.124	0.134
Tumor location		
Frontal lobe (<i>n</i> = 41)	95.28 ± 16.24	16.50 ± 2.09
Temporal lobe (<i>n</i> = 39)	99.14 ± 17.59	16.97 ± 2.21
Other locations (<i>n</i> = 11)	94.93 ± 19.56	16.39 ± 2.29
<i>F</i> value	0.582	0.592
<i>P</i> value	0.561	0.555
Tumor grade		
WHO I-II grade (<i>n</i> = 33)	78.89 ± 5.05	14.39 ± 0.84
WHO III-IV grade (<i>n</i> = 58)	107.13 ± 12.48	18.01 ± 1.47
<i>t</i> value	12.402	12.900
<i>P</i> value	< 0.000	< 0.001
Tumor diameter		
≤ 5 cm (<i>n</i> = 19)	75.23 ± 3.04	13.80 ± 0.59
> 5 cm (<i>n</i> = 72)	102.61 ± 14.55	17.45 ± 1.73
<i>t</i> value	8.123	9.006
<i>P</i> value	< 0.001	< 0.001
Number of lesions		
Single (<i>n</i> = 70)	97.57 ± 17.70	16.77 ± 2.25
Multiple (<i>n</i> = 21)	94.63 ± 15.37	16.43 ± 1.84
<i>t</i> value	0.685	0.619
<i>P</i> value	0.495	0.537

WHO: World Health Organization; UCH-L1: Ubiquitin carboxy-terminal hydrolase L1; GFAP: Glial fibrillary acidic protein.

This study revealed that the preoperative serum UCH-L1 levels in patients with glioma were notably higher than those in the control group. Furthermore, UCH-L1 Levels in patients with gliomas significantly decreased after surgical treatment. However, the postoperative UCH-L1 level was also

Table 3 Comparison of ubiquitin carboxy-terminal hydrolase L1 and glial fibrillary acidic protein levels in patients with glioma recurrence and those without recurrence before and after surgery

Time	UCH-L1 (pg/mL)	GFAP (ng/L)
Recurrence group (<i>n</i> = 22)		
Preoperative	120.44 ± 6.41	19.59 ± 0.57
3 d after surgery	88.01 ± 2.44	10.00 ± 0.46
<i>t</i> value	37.398	289.806
<i>P</i> value	< 0.001	< 0.001
Non-recurrence group (<i>n</i> = 69)		
Preoperative	89.38 ± 11.83	15.76 ± 1.58
3 d after surgery	67.09 ± 9.60	6.74 ± 1.16
<i>t</i> value	78.571	172.100
<i>P</i> value	< 0.001	< 0.001
Preoperative comparison of the two groups		
<i>t</i> value	11.749	11.118
<i>P</i> value	< 0.001	< 0.001
Comparison of the two groups at 3 d after surgery		
<i>t</i> value	10.086	12.791
<i>P</i> value	< 0.001	< 0.001

UCH-L1: Ubiquitin carboxy-terminal hydrolase L1; GFAP: Glial fibrillary acidic protein.

Table 4 The value of ubiquitin carboxy-terminal hydrolase L1 and glial fibrillary acidic protein levels for predicting postoperative recurrence of glioma

Indicator	Critical value	AUC	95%CI	<i>P</i> value	Sensitivity (%)	Specificity (%)
Preoperative UCH-L1	103.85	0.785	0.670-0.901	< 0.001	68.2	81.2
3 d after surgery UCH-L1	85.61	0.646	0.507-0.785	0.040	63.6	62.3
Preoperative GFAP	18.70	0.775	0.651-0.898	< 0.001	63.6	88.4
3 d after surgery GFAP	8.58	0.648	0.508-0.787	0.038	59.1	75.4

AUC: Area under the curve; UCH-L1: Ubiquitin carboxy-terminal hydrolase L1; GFAP: Glial fibrillary acidic protein.

higher than that in healthy controls. This may be related to the fact that under compression by glioma, part of the brain nerve tissue could have been damaged, which in turn released a large amount of UCH-L1, leading to an increase in serum UCH-L1 Levels. Subsequently, the glioma was removed to relieve the compressed brain tissues and decrease the release of UCH-L1 from damaged nerve cells.

The WHO classifies gliomas into grades I-IV, with grades I-II as low-grade and those of III-IV as high-grade gliomas. This study demonstrated that UCH-L1 Levels in the patients with WHO grade III-IV-II tumors were higher than those in those with grade I-II tumors. Additionally, the UCH-L1 Level was greater in the patients with a tumor diameter > 5 cm than in those with diameter ≤ 5 cm. It has been suggested that serum UCH-L1 Levels reflected development of glioma.

GFAP is a cytoskeletal protein that maintains the morphological and structural stability of astrocytes and determines the degree of astrocyte response to injury[11]. Some studies have shown that after central nervous system damage, astrocytes were abnormally active, manifesting as rapid synthesis and secretion of GFAP, and the addition of GFAP-positive astrocytes could further promote astrocyte mitosis. Some studies have found[12] that positive GFAP expression in astrocytes adjacent to the cerebral cortex significantly increased after brain injury. Feng *et al*[13] found that an increase in GFAP levels in patients with severe craniocerebral injury after surgery was a risk factor for poor prognosis, which had a certain value in promoting postoperative survival. Wang *et al*[14] found that serum GFAP levels were elevated in asphyxiated preterm infants with brain injury and serum GFAP had some value

in the diagnosis of brain injury and could be used as a marker for central nervous system injury and prognosis.

We found that the preoperative serum GFAP levels in the patients with glioma were higher than those in the control group. After surgery, the serum GFAP levels in these patients with gliomas decreased. However, this level was higher than that observed in healthy controls. In addition, the serum GFAP levels in the patients with WHO grade III-IV-I-II tumors were dramatically higher than those in the participants with grade I-II tumors. The serum GFAP level in the patients with tumor diameter > 5 cm was higher than that in those with diameter ≤ 5 cm. It has been suggested that serum GFAP was valuable in predicting the occurrence and development of gliomas.

In the early stages of glioma, patients do not exhibit specific clinical manifestations. However, by the time the disease is diagnosed, glioma is mostly advanced, with a large tumor size involving important functional brain nerve areas[15-17]. In addition, distinguishing the boundary between the tumor and normal brain tissue becomes difficult, making complete removal of the tumor challenging and resulting in residual tumor tissue, which is considered the main reason for postoperative recurrence[18-20]. In this study, among the 91 patients with glioma, 22 experienced recurrence after surgery. In addition, the UCH-L1 and GFAP levels were higher in the recurrence group than that in the non-recurrence group before and 3 d after surgery. This indicated that serum UCH-L1 and GFAP levels had the potential to reflect postoperative glioma recurrence. By plotting ROC curves, we found that the efficacy of both preoperative UCH-L1 and GFAP levels in predicting postoperative glioma recurrence was slightly higher than that 3 d after surgery. However, limited by the study design, we did not discuss the optimal time points for serum UCH-L1 and GFAP levels to predict postoperative glioma recurrence. This study also did not consider the specific mechanisms of action of these two indicators of gliomas, which warrants further research.

CONCLUSION

The UCH-L1 and GFAP levels abnormally increased in patients with gliomas. Although the levels of these two indices decreased after the surgical treatment, they remained higher than those in the control group. Both serum UCH-L1 and GFAP levels may specifically reflect the development and postoperative recurrence of glioma. These two markers could be used as potential indicators of recurrence and prognosis in patients with postoperative glioma.

ARTICLE HIGHLIGHTS

Research background

Glioma is a very common intracranial malignant tumor with a high degree of malignancy, rapid growth, and high postoperative recurrence rate, which could cause severe damage to the nervous system. Early prediction of postoperative prognosis in patients with glioma is of great clinical significance.

Research motivation

Ubiquitin carboxyl terminal hydrolase L1 (UCH-L1) and glial fibrillary acidic protein (GFAP) reflect damage and lesions in the nervous system. Changes in serum UCH-L1 and GFAP levels in patients with glioma before and after surgery, and the relationship between them, have not been clarified.

Research objectives

This study aimed to assess the changes and correlation between pre-and postoperative serum UCH-L1 and GFAP levels in patients with glioma and predict the postoperative prognosis of patients with glioma after surgery.

Research methods

Total 91 patients with glioma were included in the experimental group and 60 healthy volunteers were selected as the control group. In the experimental group, 5 mL of peripheral venous blood was collected before and 3 d after surgery to detect UCH-L1 and GFAP levels in the peripheral blood serum. In the control group, venous blood was collected on an empty stomach morning on the second day after enrollment to monitor the levels of UCH-L1 and GFAP in the peripheral blood serum. At the same time, the postoperative recurrence of glioma was recorded to determine the value of serum UCH-L1 and GFAP for predicting glioma prognosis.

Research results

UCH-L1 and GFAP levels 3 d after surgery in the patients with gliomas were significantly lower than

those before surgery. Moreover, the UCH-L1 and GFAP levels in the glioma group were significantly higher than those in the control group before and after surgery. The levels of serum UCH-L1 and GFAP in 22 patients with glioma recurrence were higher compared with the non-recurrence group before and 3 d after surgery, and the difference was statistically significant.

Research conclusions

Although serum UCH-L1 and GFAP levels in the patients with glioma were abnormally increased, these levels decreased after surgery. Serum UCH-L1 and GFAP levels may be potential indicators for predicting the postoperative recurrence and prognosis of glioma.

Research perspectives

Future work and clinical research should be conducted to verify the accuracy of the experimental results through a more rigorous experimental design, expanded sample size, and multicenter studies and to provide favorable evidence for predicting the recurrence and prognosis of glioma.

FOOTNOTES

Author contributions: Zhu QH and Wu JK designed the study, and implemented and collected the data; Zhu QH analyzed the data, wrote and edited the manuscript; and Hou GL supervised and supported the research.

Supported by Hebei Medical Science Research Project, No. 20220648.

Institutional review board statement: This study was approved by the Ethics Committee of the Affiliated Hospital of Hebei Engineering University.

Informed consent statement: All study participants or their legal guardians provided written informed consent prior to study enrollment.

Conflict-of-interest statement: The authors have no conflict of interest to declare.

Data sharing statement: No additional data are available.

STROBE statement: The authors have read the STROBE Statement checklist of items, and the manuscript was prepared and revised according to the STROBE Statement checklist of items.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: <https://creativecommons.org/licenses/by-nc/4.0/>

Country/Territory of origin: China

ORCID number: Qing-Hua Zhu 0000-0003-0740-5126; Jing-Kun Wu 0000-0001-7381-6180; Gao-Lei Hou 0000-0002-2556-0261.

S-Editor: Wang JL

L-Editor: A

P-Editor: Yuan YY

REFERENCES

- 1 Ren CC, Zhang LT, Kang JS, Kang L, Wang QX, Zhao J. Expressions and Diagnostic Efficacies of Serum NSE, CA15-3, S100B and IGF-1 in Patients with Brain Glioma. *Jiefangjun Yiyao Zazhi* 2022; **34**: 25-28 [DOI: [10.3969/j.issn.2095-140X.2022.01.005](https://doi.org/10.3969/j.issn.2095-140X.2022.01.005)]
- 2 He LJ, Ren J, Zhao YB, Gao Q, Xu JC, Wang J. Scalp electroencephalogram characteristics of ganglioglioma and its correlation with post-operative prognosis. *Dianxian Yu Shenjingdianshenglixue Zazhi* 2022; **31**: 12-21 [DOI: [10.19984/j.cnki.1674-8972.2022.01.03](https://doi.org/10.19984/j.cnki.1674-8972.2022.01.03)]
- 3 Amoo M, Henry J, O'Halloran PJ, Brennan P, Husien MB, Campbell M, Caird J, Javadpour M, Curley GF. S100B, GFAP, UCH-L1 and NSE as predictors of abnormalities on CT imaging following mild traumatic brain injury: a systematic review and meta-analysis of diagnostic test accuracy. *Neurosurg Rev* 2022; **45**: 1171-1193 [PMID: [34709508](https://pubmed.ncbi.nlm.nih.gov/34709508/) DOI: [10.1007/s10143-021-01678-z](https://doi.org/10.1007/s10143-021-01678-z)]
- 4 Amalia L. Glial Fibrillary Acidic Protein (GFAP): Neuroinflammation Biomarker in Acute Ischemic Stroke. *J Inflamm Res* 2021; **14**: 7501-7506 [PMID: [35002283](https://pubmed.ncbi.nlm.nih.gov/35002283/) DOI: [10.2147/JIR.S342097](https://doi.org/10.2147/JIR.S342097)]

- 5 **Leibetseder A**, Leitner J, Mair MJ, Meckel S, Hainfellner JA, Aichholzer M, Widhalm G, Dieckmann K, Weis S, Furtner J, von Oertzen T, Preusser M, Pichler J, Berghoff AS. Prognostic factors in adult brainstem glioma: a tertiary care center analysis and review of the literature. *J Neurol* 2022; **269**: 1574-1590 [PMID: 34342680 DOI: 10.1007/s00415-021-10725-0]
- 6 **Nicholson JG**, Fine HA. Diffuse Glioma Heterogeneity and Its Therapeutic Implications. *Cancer Discov* 2021; **11**: 575-590 [PMID: 33558264 DOI: 10.1158/2159-8290.CD-20-1474]
- 7 **Richard M**, Lagares A, Bondanese V, de la Cruz J, Mejan O, Pavlov V, Payen JF; BRAINI investigators. Study protocol for investigating the performance of an automated blood test measuring GFAP and UCH-L1 in a prospective observational cohort of patients with mild traumatic brain injury: European BRAINI study. *BMJ Open* 2021; **11**: e043635 [PMID: 33632753 DOI: 10.1136/bmjopen-2020-043635]
- 8 **Papa L**, Ladde JG, O'Brien JF, Thundiyil JG, Tesar J, Leech S, Cassidy DD, Roa J, Hunter C, Miller S, Baker S, Parrish GA, Davison J, Van Dillen C, Ralls GA, Briscoe J, Falk JL, Weber K, Giordano PA. Evaluation of Glial and Neuronal Blood Biomarkers Compared With Clinical Decision Rules in Assessing the Need for Computed Tomography in Patients With Mild Traumatic Brain Injury. *JAMA Netw Open* 2022; **5**: e221302 [PMID: 35285924 DOI: 10.1001/jamanetworkopen.2022.1302]
- 9 **Shan HL**, Jiao GM, Cheng X, Ma Z, Gao YJ, Yang N, Dou ZJ. Changes and significance of serum UCH-L1 and Fibulin-5 levels in patients with acute cerebral infarction. *Shandong Yiyao* 2021; **61**: 32-36 [DOI: 10.3969/j.issn.1002-266X.2021.07.008]
- 10 **Wang J**, Zhang HY, Du P, Wan J. The Predictive Value of the Serum Ubiquitin Carboxyl-terminal Hydrolase L1 and Neutrophil Gelatinase-associated Lipocalin to the Ill Condition and Prognosis in Patients with Severe Brain Injury. *Biaojimianyifexi Yu Linchuang* 2020; **27**: 195-199, 205
- 11 **Yuan W**, Lu L, Rao M, Huang Y, Liu CE, Liu S, Zhao Y, Liu H, Zhu J, Chao T, Wu C, Ren J, Lv L, Li W, Qi S, Liang Y, Yue S, Gao J, Zhang Z, Kong E. GFAP hyperpalmitoylation exacerbates astrogliosis and neurodegenerative pathology in PPT1-deficient mice. *Proc Natl Acad Sci U S A* 2021; **118** [PMID: 33753498 DOI: 10.1073/pnas.2022261118]
- 12 **Hausmann R**, Riess R, Fiegluth A, Betz P. Immunohistochemical investigations on the course of astroglial GFAP expression following human brain injury. *Int J Legal Med* 2000; **113**: 70-75 [PMID: 10741479 DOI: 10.1007/pl00007711]
- 13 **Feng AP**, Wang W, Du C. The relationship between the postoperative levels of serum copeptin and GFAP and the prognosis of patients with severe traumatic brain injury. *Shiyong Yiyuan Linchuang Zazhi* 2022; **19**: 132-135 [DOI: 10.3969/j.issn.1672-6170.2022.01.035]
- 14 **Wang T**, Li YF, Wang XS, Liu ZHJ. Diagnostic value of serum HMGB1, GFAP, and UCH-L1 for brain injury in asphyxia premature infants. *Guoji Jianyan Yixue Zazhi* 2021; **42**: 1549-1553 [DOI: 10.3969/j.issn.1673-4130.2021.13.004]
- 15 **Yang Y**. The factors related to postoperative recurrence in frontal low-grade gliomas after neurosurgeon determined gross-total resection. *Litidingxiang He Gongnengxing Shenjingwaike Zazhi* 2020; **33**: 280-284 [DOI: 10.19854/j.cnki.1008-2425.2020.05.0006]
- 16 **Zhang QH**, Duan WC, Liu XZ, Zhang ZHY. Clinical characteristics and postoperative survival of asymptomatic patients with WHO grade II gliomas. *Zhonghua Shenjingwaike Zazhi* 2020; **36**: 405-409 [DOI: 10.3760/cma.j.cn112050-20190822-00364]
- 17 **Ng S**, Lemaitre AL, Moritz-Gasser S, Herbet G, Duffau H. Recurrent Low-Grade Gliomas: Does Reoperation Affect Neurocognitive Functioning? *Neurosurgery* 2022; **90**: 221-232 [PMID: 34995251 DOI: 10.1227/NEU.0000000000001784]
- 18 **Rubin MC**, Sagberg LM, Jakola AS, Solheim O. Primary versus recurrent surgery for glioblastoma-a prospective cohort study. *Acta Neurochir (Wien)* 2022; **164**: 429-438 [PMID: 33052493 DOI: 10.1007/s00701-020-04605-1]
- 19 **Teyateeti A**, Geno CS, Stafford SS, Mahajan A, Yan ES, Merrell KW, Laack NN, Parney IF, Brown PD, Jethwa KR. Does the dural resection bed need to be irradiated? *Neurooncol Pract* 2021; **8**: 190-198 [PMID: 33898052 DOI: 10.1093/nop/npaa073]
- 20 **Strand PS**, Berntsen EM, Fyllingen EH, Sagberg LM, Reinertsen I, Gulati S, Bouget D, Solheim O. Brain infarctions after glioma surgery: prevalence, radiological characteristics and risk factors. *Acta Neurochir (Wien)* 2021; **163**: 3097-3108 [PMID: 34468884 DOI: 10.1007/s00701-021-04914-z]



Published by **Baishideng Publishing Group Inc**
7041 Koll Center Parkway, Suite 160, Pleasanton, CA 94566, USA
Telephone: +1-925-3991568
E-mail: bpgoffice@wjgnet.com
Help Desk: <https://www.f6publishing.com/helpdesk>
<https://www.wjgnet.com>

