

World Journal of *Clinical Cases*

World J Clin Cases 2021 April 26; 9(12): 2696-2950



MINIREVIEWS

- 2696** Standardization of critical care management of non-critically ill patients with COVID-19
Wang CS, Gao Y, Kang K, Fei DS, Meng XL, Liu HT, Luo YP, Yang W, Dai QQ, Gao Y, Zhao MY, Yu KJ
- 2703** Mediastinal lymphadenopathy in COVID-19: A review of literature
Taweasedt PT, Surani S
- 2711** Polycystic ovary syndrome: Pathways and mechanisms for possible increased susceptibility to COVID-19
Ilias I, Goulas S, Zabuliene L

ORIGINAL ARTICLE**Clinical and Translational Research**

- 2721** Circulating tumor cells with epithelial-mesenchymal transition markers as potential biomarkers for the diagnosis of lung cancer
Jiang SS, Mao CG, Feng YG, Jiang B, Tao SL, Tan QY, Deng B

Retrospective Study

- 2731** Management and implementation strategies of pre-screening triage in children during coronavirus disease 2019 pandemic in Guangzhou, China
Shi X, Cai YT, Cai X, Wen XL, Wang JY, Ma WC, Shen J, Wu JX, Liu HY, Sun J, He PQ, Lin Y, Zhao DY, Li PQ
- 2739** Clinicopathological features of superficial CD34-positive fibroblastic tumor
Ding L, Xu WJ, Tao XY, Zhang L, Cai ZG
- 2751** Application of a rapid exchange extension catheter technique in type B2/C nonocclusive coronary intervention *via* a transradial approach
Wang HC, Lu W, Gao ZH, Xie YN, Hao J, Liu JM

SYSTEMATIC REVIEWS

- 2763** Paradoxical relationship between proton pump inhibitors and COVID-19: A systematic review and meta-analysis
Zippi M, Fiorino S, Budriesi R, Micucci M, Corazza I, Pica R, de Biase D, Gallo CG, Hong W

META-ANALYSIS

- 2778** Predictive risk factors for recollapse of cemented vertebrae after percutaneous vertebroplasty: A meta-analysis
Ma YH, Tian ZS, Liu HC, Zhang BY, Zhu YH, Meng CY, Liu XJ, Zhu QS

CASE REPORT

- 2791** Malignant pheochromocytoma with cerebral and skull metastasis: A case report and literature review
Chen JC, Zhuang DZ, Luo C, Chen WQ
- 2801** Unresectable esophageal cancer treated with multiple chemotherapies in combination with chemoradiotherapy: A case report
Yura M, Koyanagi K, Hara A, Hayashi K, Tajima Y, Kaneko Y, Fujisaki H, Hirata A, Takano K, Hongo K, Yo K, Yoneyama K, Tamai Y, Dehari R, Nakagawa M
- 2811** Role of positron emission tomography in primary carcinoma ex pleomorphic adenoma of the bronchus: A case report
Yang CH, Liu NT, Huang TW
- 2816** Positive reverse transcription-polymerase chain reaction assay results in patients recovered from COVID-19: Report of two cases
Huang KX, He C, Yang YL, Huang D, Jiang ZX, Li BG, Liu H
- 2823** Laryngeal myxoma: A case report
Yu TT, Yu H, Cui Y, Liu W, Cui XY, Wang X
- 2830** Prostate stromal tumor with prostatic cysts after transurethral resection of the prostate: A case report
Zhao LW, Sun J, Wang YY, Hua RM, Tai SC, Wang K, Fan Y
- 2838** Intramuscular hematoma in rhabdomyolysis patients treated with low-molecular-weight heparin: Report of two cases
Yuan SY, Xie KF, Yang J
- 2845** Partial response to Chinese patent medicine Kangliu pill for adult glioblastoma: A case report and review of the literature
Sun G, Zhuang W, Lin QT, Wang LM, Zhen YH, Xi SY, Lin XL
- 2854** Behcet's disease manifesting as esophageal variceal bleeding: A case report
Xie WX, Jiang HT, Shi GQ, Yang LN, Wang H
- 2862** Successful endoscopic surgery for emphysematous pyelonephritis in a non-diabetic patient with autosomal dominant polycystic kidney disease: A case report
Jiang Y, Lo R, Lu ZQ, Cheng XB, Xiong L, Luo BF
- 2868** Robotically assisted removal of pelvic splenosis fifty-six years after splenectomy: A case report
Tognarelli A, Faggioni L, Erba AP, Faviana P, Durante J, Manassero F, Selli C
- 2874** Pulmonary alveolar proteinosis complicated with nocardiosis: A case report and review of the literature
Wu XK, Lin Q
- 2884** Detection of EGFR-SEPT14 fusion in cell-free DNA of a patient with advanced gastric cancer: A case report
Kim B, Kim Y, Park I, Cho JY, Lee KA

- 2890** Timing of convalescent plasma therapy-tips from curing a 100-year-old COVID-19 patient using convalescent plasma treatment: A case report
Liu B, Ren KK, Wang N, Xu XP, Wu J
- 2899** Torsades de pointes episode in a woman with high-grade fever and inflammatory activation: A case report
Qiu H, Li HW, Zhang SH, Zhou XG, Li WP
- 2908** Salivary duct carcinoma of the submandibular gland presenting a diagnostic challenge: A case report
Uchihashi T, Kodama S, Sugauchi A, Hiraoka S, Hirose K, Usami Y, Tanaka S, Kogo M
- 2916** Allogeneic hematopoietic stem cell transplantation in a 3-year-old boy with congenital pyruvate kinase deficiency: A case report
Ma ZY, Yang X
- 2923** Congenital bilateral cryptorchidism in an infant conceived after maternal breast cancer treatment: A case report
Hu WK, Liu J, Liu RX, Liu XW, Yin CH
- 2930** Sclerosing polycystic adenosis of the submandibular gland: Two case reports
Wu L, Wang Y, Hu CY, Huang CM
- 2937** Budd-Chiari syndrome associated with liver cirrhosis: A case report
Ye QB, Huang QF, Luo YC, Wen YL, Chen ZK, Wei AL
- 2944** Separated root tip formation associated with a fractured tubercle of dens evaginatus: A case report
Wu ZF, Lu LJ, Zheng HY, Tu Y, Shi Y, Zhou ZH, Fang LX, Fu BP

ABOUT COVER

Editorial Board Member of *World Journal of Clinical Cases*, Jing Liu, MD, PhD, Chief Doctor, Professor, Department of Neonatology and NICU, Beijing Chaoyang District Maternal and Child Healthcare Hospital, Beijing 100021, China. liujingbj@live.cn

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 indexed in Science Citation Index Expanded (also known as SciSearch®), Journal Citation Reports/Science Edition, Scopus, PubMed, and PubMed Central. The 2020 Edition of Journal Citation Reports® cites the 2019 impact factor (IF) for WJCC as 1.013; IF without journal self cites: 0.991; Ranking: 120 among 165 journals in medicine, general and internal; and Quartile category: Q3. The WJCC's CiteScore for 2019 is 0.3 and Scopus CiteScore rank 2019: General Medicine is 394/529.

RESPONSIBLE EDITORS FOR THIS ISSUE

Production Editor: Ji-Hong Lin; Production Department Director: Xiang Li; Editorial Office Director: Jin-Lai 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

Dennis A Bloomfield, Sandro Vento, Bao-Gan Peng

EDITORIAL BOARD MEMBERS

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

PUBLICATION DATE

April 26, 2021

COPYRIGHT

© 2021 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>

Partial response to Chinese patent medicine Kangliu pill for adult glioblastoma: A case report and review of the literature

Ge Sun, Wei Zhuang, Qing-Tang Lin, Lei-Ming Wang, Yu-Hang Zhen, Sheng-Yan Xi, Xiao-Lan Lin

ORCID number: Ge Sun 0000-0002-2243-1683; Wei Zhuang 0000-0003-3846-6351; Qing-Tang Lin 0000-0002-0661-2951; Lei-Ming Wang 0000-0002-8257-0175; Yu-Hang Zhen 0000-0002-9348-1581; Sheng-Yan Xi 0000-0002-8315-6742; Xiao-Lan Lin 0000-0001-7033-2981.

Author contributions: Sun G, Zhuang W and Lin QT were responsible for the study design, data collection, data analysis and interpretation; Sun G was responsible for composing the manuscript; Wang LM was responsible for pathological data collection, analysis, and interpretation; Zhen YH analyzed and interpreted the neuroimaging findings; Xi SY was responsible for English and grammar corrections, critical revisions, and approved the final version; Xi SY and Lin XL were responsible for acquisition, analysis, or interpretation of data, revision for important intellectual content, final approval of the version for publication, and agreed to be accountable for all aspects of the work related to its accuracy and integrity. All authors contributed to the article and approved the submitted version.

Supported by the Foundation for Beijing Science and Technology Development of TCM, No. JJ2016-10; and the National Traditional

Ge Sun, Wei Zhuang, Lei-Ming Wang, Xiao-Lan Lin, Department of Pharmacy, Xuanwu Hospital of Capital Medical University, Beijing 100053, China

Qing-Tang Lin, Yu-Hang Zhen, Department of Neurosurgery, Xuanwu Hospital of Capital Medical University, Beijing 100053, China

Sheng-Yan Xi, Department of Traditional Chinese Medicine, School of Medicine and Cancer Research Center, Xiamen University, Xiamen 361102, Fujian Province, China

Corresponding author: Xiao-Lan Lin, Chief Pharmacist, Reader (Associate Professor), Department of Pharmacy, Xuanwu Hospital of Capital Medical University, No. 45 Changchun Street, Beijing 100053, China. xlilin83@163.com

Abstract

BACKGROUND

Glioblastoma is the most common type of brain tumor and is invariably fatal, with a mean survival time of 8-15 mo for recently diagnosed tumors, and a 5-year survival rate of only 7.2%. The standard treatment for newly diagnosed glioblastoma includes surgery followed by concurrent chemoradiotherapy and further adjuvant temozolomide. However, the prognosis remains poor and long-term survival is rare. This report aimed to demonstrate a new therapeutic strategy for the treatment of glioblastoma.

CASE SUMMARY

A patient was referred to the Department of Neurosurgery with an intracranial space-occupying lesion with a maximum diameter of approximately 5 cm. The tumor was compressing functional areas, and the patient accordingly underwent partial resection and concurrent chemoradiotherapy. The imaging and pathological findings were consistent with a diagnosis of glioblastoma with oligodendroglioma differentiation (World Health Organization IV). The patient was finally diagnosed with glioblastoma. However, the patient discontinued treatment due to intolerable side effects, and was prescribed Kangliu pill (KLP) 7.5 g three times/d, which he has continued to date. Significant shrinkage of the tumor (maximum diameter reduced from about 3.5 to about 2 cm) was found after 3 mo of KLP therapy, and the tumor was further reduced to about 1 cm after 3 years. The patient's symptoms of headache, limb weakness, and left hemiplegia were relieved, with no side effects.

CONCLUSION

Chinese Medicine Innovative Talents Training Project from Beijing Municipal Science and Technology Commission, No. Z171100001717006.

Informed consent statement:

Written informed consent was obtained from the patient for publication of this report.

Conflict-of-interest statement: The authors report no conflicts of interest. The authors are solely responsible for the content and writing of the paper.

CARE Checklist (2016) statement:

The authors have read the CARE Checklist (2016), and the manuscript was prepared and revised according to the CARE Checklist (2016).

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: <http://creativecommons.org/licenses/by-nc/4.0/>

Manuscript source: Unsolicited manuscript

Specialty type: Medicine, research and experimental

Country/Territory of origin: China

Peer-review report's scientific quality classification

Grade A (Excellent): 0
Grade B (Very good): 0
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

Received: November 16, 2020

Peer-review started: November 16, 2020

First decision: December 30, 2020

Revised: January 13, 2021

KLP has been a successful intervention for glioblastoma, and the current case indicates that traditional Chinese medicine may offer effective alternative therapies for glioblastoma.

Key Words: Glioblastoma; Kangliu pill; Traditional Chinese medicine; Therapeutic effect; Adjunct therapy; Chinese patent medicine; Case report

©The Author(s) 2021. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: Glioblastoma is the most common type of malignant primary brain cancer. The standard treatment for newly diagnosed glioblastoma includes surgery followed by concurrent chemoradiotherapy and further adjuvant temozolomide. However, patients usually have a poor prognosis and high recurrence rate, and may develop drug resistance and serious adverse reactions to chemotherapy. Some recent studies suggested that traditional Chinese medicine may have a good therapeutic effect in patients with glioblastoma, and it is generally used as an adjunct therapy for various stages of tumors in clinical practice. We report a patient with glioblastoma who abandoned chemoradiotherapy due to intolerance, and subsequently received the Chinese patent medicine Kangliu pill without any other treatment. Three months after the start of treatment, the patient had a partial response, which persisted for more than 3 years. This surprising discovery indicates that the Chinese patent medicine Kangliu pill may provide a new option for the treatment of glioblastoma.

Citation: Sun G, Zhuang W, Lin QT, Wang LM, Zhen YH, Xi SY, Lin XL. Partial response to Chinese patent medicine Kangliu pill for adult glioblastoma: A case report and review of the literature. *World J Clin Cases* 2021; 9(12): 2845-2853

URL: <https://www.wjgnet.com/2307-8960/full/v9/i12/2845.htm>

DOI: <https://dx.doi.org/10.12998/wjcc.v9.i12.2845>

INTRODUCTION

Glioblastoma (GBM) is the most common type of malignant primary brain cancer with the lowest survival rate, representing approximately 48% of all primary malignant central nervous system tumors^[1,2]. GBM is one of the most devastating brain tumors, and is highly heterogeneous and invasive, with a high incidence rate. The overall annual incidence rate of glioma is high, at 9.23 cases per 100000 individuals in the United States, with GBM accounting for about half of all these cases^[2]. Patients diagnosed with GBM usually have a dismal prognosis and poor quality of life. Currently, the best outcome is a modest 14.6-mo median survival following surgical resection, radiotherapy, and/or chemotherapy with temozolomide (TMZ)^[3]. However, the survival outcomes are generally very poor, with a mean survival rate of recurring GBM of just 3-9 mo^[4] and a 5-year survival rate of 7.2%^[5]. This poor prognosis is mostly due to the tumor's therapeutic resistance and to tumor relapse after surgical removal^[6]. Despite extensive efforts, little progress has been made in prolonging the survival of patients with GBM^[7]. Thus, there is an urgent need to explore effective treatment strategies and drugs to improve the prognosis of patients with GBM. Traditional Chinese medicine (TCM) has recently gained wide attention due to its therapeutic effects and few side effects in patients with GBM, with increasing numbers of TCMS demonstrating antitumor effects against GBM. For example, toosendanin inhibited GBM cell proliferation and induced apoptosis *in vitro* and *in vivo*^[8]. Celastrol sensitized glioma cells to the apoptosis-induced ligand TRAIL *via* the death receptor pathway, indicating a promising tumor-killing therapeutic strategy with high efficacy and low toxicity^[9]. The aqueous extract of Pingliu Keli strongly inhibited cell proliferation and induced apoptosis in SHG-44 cells^[10], and Jinlong capsules partly regulated the mTOR/S6 pathway to inhibit glioblastoma cell migration and invasion *in vitro*^[11]. Kangliu pill (KLP) is a Chinese patent medicine consisting of 18 types of traditional Chinese medicine: *Smilax glabra* Roxb. (Tufuling) (Voucher Number: 140105), *Panax notoginseng* (Burkill) F. H. Chen (Sanqi) (Voucher Number: 140815), *Scleromitrium diffusum* (Willd.) R. J. Wang (Baihuasheshecao) (Voucher Number:

Accepted: February 22, 2021**Article in press:** February 22, 2021**Published online:** April 26, 2021**P-Reviewer:** Li H**S-Editor:** Zhang L**L-Editor:** Webster JR**P-Editor:** Li JH

140702), *Scutellaria barbata* D. Don (Banzhilian) (Voucher Number: 140912), calcined Alumen (Kufan) (Voucher Number: 140201), *Reynoutria multiflora* (Thunb.) Moldenke (Zhiheshouwu) (Voucher Number: 140705), *Aquilaria sinensis* (Lour.) Spreng. (Baimuxiang) (Voucher Number: 140615), *Monetaria annulus* (Linnaeus) (Baibeichi) (Voucher Number: 140216), *Solanum lyratum* Thunb. (Baiying) (Voucher Number: 140708), *Fritillaria cirrhosa* D. Don (Chuanbeimu) (Voucher Number: 140207), *Stemona japonica* (Blume) Miq. (Baibu) (Voucher Number: 140211), *Eriobotrya japonica* (Thunb.) Lindl. (Pipaye) (Voucher Number: 140416), *Aster tataricus* L.f. (Ziwan) (Voucher Number: 140409), stir-baked *Crataegus pinnatifida* Bunge (Jiaoshanzha) (Voucher Number: 140809), stir-baked *Hordeum vulgare* L. (Jiaomaiya) (Voucher Number: 140512), stir-baked *Massa Medicata Fermentata* (Jiaoshenqu) (Voucher Number: 140608), *Platycodon grandiflorus* (Jacq.) A. DC. (Jiegeng) (Voucher Number: 140713), and *Succinum* (Hupo) (Voucher Number: 140914). KLP has been used for 40 years and has been shown to reduce temperature and achieve detoxification, as well as promote blood circulation and resolve blood stasis^[12-15]. Preclinical studies showed that KLP promoted GBM cell apoptosis by adjusting the ratio of Bcl-2/Bax, suggesting that its inhibitory effect could be related to the induction of glioma cell apoptosis^[12,13]. In addition, researchers have identified the main components of KLP and determined quality standards^[14,15].

A clinical study also found that KLP exerted antitumor effects against malignant gliomas^[16]. Here we report a patient with GBM who experienced a remarkable response to KLP.

CASE PRESENTATION

Chief complaints

The protocols in this case were conducted in strict accordance with the clinical trial guidelines of the Ministry of Science and Technology of the People's Republic of China and the study was approved by the Ethics Committee of Xuanwu Hospital of Capital Medical University. The specimens of Chinese herbal medicine have been stored in the Pharmacy Department of Xuanwu Hospital of Capital Medical University for future reference, and were identified and independently verified by Professor Jing-Xia Wang from the Chinese Medicine Department of Beijing University of Chinese Medicine.

A 27-year-old man was referred to the Department of Neurosurgery with an intracranial space-occupying lesion on February 21, 2016.

History of present illness

Eight months before the current referral, the patient had experienced left upper limb convulsions, urinary incontinence, nausea, vomiting, and loss of consciousness with no apparent cause, which were relieved after a few minutes. He did not receive any treatment at that time. However, his headache, limb weakness, and left hemiplegia returned 4 mo later. The symptoms were partially relieved by symptomatic supportive treatment, including carbamazepine 400 mg twice/d orally; however, the patient stopped carbamazepine of his own accord due to aggravated limb weakness.

History of past illness

The patient had no previous medical history.

Personal and family history

The patient had no personal and family history.

Physical examination

The patient's temperature was 36.7°C, his heart rate was 70 bpm, his respiratory rate was 18 breaths/min, and his blood pressure was 110/70 mmHg. Clinical neurological examination revealed normal right limb muscle strength, but his left limbs were slightly weaker than his right limbs. His mental functions were normal, with no other pathological signs.

Imaging examinations

Computed tomography examination in a local hospital showed no obvious abnormalities, but magnetic resonance imaging indicated a space-occupying lesion in the right frontal lobe. The patient did not receive any treatment at that time. However, headache, limb weakness, and left hemiplegia returned 4 mo later, and repeat

computed tomography suggested a right frontal parietal lobe cerebral hemorrhage. He presented to the hospital for re-examination on February 18, 2016. Cranial magnetic resonance imaging showed that the right frontal-parietal lobe was occupied by a mass, with a maximum diameter of about 5 cm, irregular enhancement of the parenchyma ring, and the necrotic center was not enhanced, indicating a possible high-grade glioma (Figure 1A).

MULTIDISCIPLINARY EXPERT CONSULTATION

Qing-Tang Lin, MD, PhD, Associate Professor and Deputy Chief, Department of Neurosurgery, Xuanwu Hospital of Capital Medical University

The patient should undergo surgical treatment with right frontal craniotomy and resection of the brain tumor.

Lei-Ming Wang, MD, PhD, Attending Physician, Department of Pathology, Xuanwu Hospital of Capital Medical University

Under the microscope, the specimens submitted for examination showed diffuse growth of tumor cells, with short spindle-shaped nuclei in some areas and round-shaped nuclei in some areas. The cytoplasm was empty and bright, with vascular endothelial proliferation and palisade necrosis (Figure 2). Combined with the immunohistochemical results, these findings were consistent with the diagnosis of glioblastoma with oligodendroglioma differentiation (World Health Organization IV).

Xiao-Lan Lin, Associate Professor and Deputy Chief, Department of Pharmacy, Xuanwu Hospital of Capital Medical University; Qing-Tang Lin, MD, PhD, Associate Professor and Deputy Chief, Department of Neurosurgery, Xuanwu Hospital of Capital Medical University

The patient discontinued concurrent chemoradiation due to intolerable side effects, and he should therefore be prescribed KLP 7.5 g three times/d.

FINAL DIAGNOSIS

The final diagnosis of the presented case was glioblastoma.

TREATMENT

There was a clear indication for surgery, with no contraindications in the preoperative examination, and the patient underwent partial resection on February 23, 2016. The postoperative pathological report confirmed GBM. After surgery, the patient started concurrent chemoradiation therapy until April 2016, with 75 mg/m² TMZ once daily for 45 d combined with focal radiotherapy of 60 Gy administered in 30 fractions. However, he opted to discontinue the chemoradiotherapy due to intolerable adverse reactions, including nausea, vomiting, and loss of appetite. Two months later, the patient attended the hospital for postoperative review (Figure 1B) and was prescribed KLP 7.5 g three times/d.

OUTCOME AND FOLLOW-UP

After taking KLP for nearly 3 mo, the tumor had shrunk significantly (from about 3.5 to about 2 cm) (Figure 1C), and he therefore continued to take KLP as prescribed for the next 3 years. A subsequent examination showed that the tumor had shrunk to about 1 cm after 3 years (Figure 1D). No adverse reactions were detected throughout the course of KLP treatment, and the patient's symptoms of headache, limb weakness, and left hemiplegia were relieved (Table 1).

Table 1 Timeline

Relevant past medical history and interventions			
No relevant past medical history			
Date	Summaries from Initial and follow-up visits	Diagnostic testing	Interventions
June 2015	Left upper limb convulsions, urinary incontinence, nausea, vomiting, and loss of consciousness with no apparent cause	CT examination in a local hospital showed no obvious abnormality, but MRI indicated a space-occupying lesion in the right frontal lobe	Without any treatment
October 2015	Headache, limb weakness, and left hemiplegia	Repeat CT suggested a right frontal parietal lobe cerebral hemorrhage	Symptomatic supportive treatment, including carbamazepine 400 mg twice/d orally. However, the patient stopped carbamazepine of his own accord due to aggravated limb weakness
February 2016	Final diagnosis: glioblastoma, maximum diameter about 5 cm	Cranial MRI showed that the right frontal parietal lobe was occupied by a mass, identified as a possible high-grade glioma. Hematoxylin-eosin staining showed that the tumor cells diffused and infiltrated. Cells were heteromorphic with mitotic figures, microvessel hyperplasia and palisade necrosis. Tumor cells were immunopositive for glial fibrillary acidic protein immunostaining, and about 70% of tumor cells were positive for Ki-67	Partial resection and concurrent chemoradiation therapy until April 2016, with 75 mg/m ² TMZ once daily for 45 d combined with focal radiotherapy of 60 Gy administered in 30 fractions
April 2016	Intolerable ADRs, including nausea, vomiting, and loss of appetite	None	Discontinued the chemoradiotherapy
June 2016	Postoperative review: maximum diameter about 3.5 cm	Enhanced right frontal parietal lobe space-occupying lesion, maximum diameter about 3.5 cm	Kangliu Pill 7.5 g three times/d
October 2016	Maximum diameter from about 3.5 to about 2 cm	Enhanced lesion at the junction of the right frontal and parietal lobes, maximum diameter about 2 cm	Continue Kangliu pill 7.5 g three times/d
April 2019	Maximum diameter about 1 cm	Enhanced lesion at the junction of the right frontal and parietal lobes, maximum diameter about 1 cm	Continue Kangliu pill 7.5 g three times/d
Final outcome			
The patient's symptoms of headache, limb weakness, and left hemiplegia were relieved, with no side effects			

CT: Computed tomography; MRI: Magnetic resonance imaging; ADRs: Adverse reactions.

DISCUSSION

GBM, which accounts for the majority of gliomas (57.7%)^[5], is characterized histologically by appreciable cellularity with mitotic activity, vascular proliferation, and necrosis. The standard treatment for newly diagnosed GBM includes surgery followed by concurrent chemoradiotherapy and further adjuvant TMZ. The benefits of TMZ may derive from O-6-methylguanine-deoxyribonucleic acid methyltransferase promoter methylation, which silences epigenetic genes^[17]. TMZ is associated with toxicities including myelosuppression and nausea, and especially thrombocytopenia and neutropenia, particularly during adjuvant therapy. GBM usually recurs within 6 mo after standard concurrent chemoradiotherapy^[18]. The humanized vascular endothelial growth factor monoclonal antibody bevacizumab has been shown to improve progression-free but not overall survival in patients with GBM^[19]. Tumor-treating fields, delivering low-intensity, is approved for adjuvant TMZ therapy based on the progression-free and overall survival benefits^[20]. However, despite Food and Drug Administration approval, the evidence for and use of tumor-treating fields remain controversial. Extensive research efforts have also been made in the fields of immunotherapy and targeted therapy, but few encouraging outcomes have been observed^[18]. Overall, despite advances in multimodality therapy, the prognosis of patients with GBM thus remains poor and long-term survival is rare. There is accordingly a need to identify more effective therapies for GBM.

In the current case, the tumor location and the intense side effects meant that total resection with chemoradiotherapy was impossible, and KLP was therefore prescribed. Surprisingly, the patient experienced a remarkable response to KLP therapy, with a

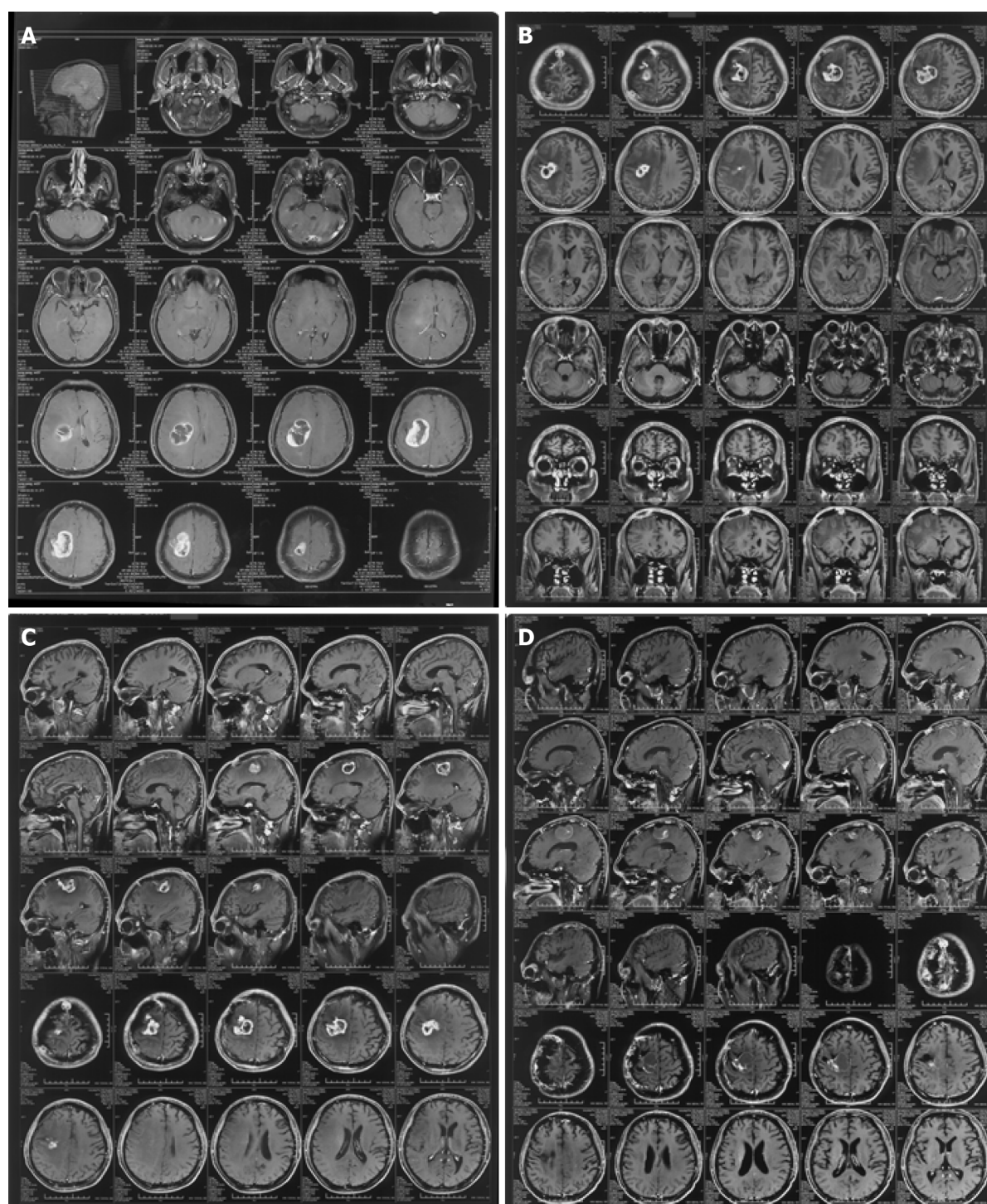


Figure 1 Neuroimaging findings. A: February 20, 2016 Preoperative image of enhanced right frontal parietal lobe space-occupying lesion, maximum diameter about 5 cm; B: June 3, 2016 End of chemoradiation. Enhanced right frontal parietal lobe space-occupying lesion, maximum diameter about 3.5 cm; C: September 14, 2016 Enhanced lesion at the junction of the right frontal and parietal lobes, maximum diameter about 2 cm, after taking Kangliu pill for 3 mo; and D: April 29, 2019 Enhanced lesion at the junction of the right frontal and parietal lobes, maximum diameter about 1 cm, after taking Kangliu pill for nearly 3 years.

reduction in tumor size from about 3.5 cm to about 1 cm. This therapeutic effect might have been related to the anti-tumor effects of the main components of KLP, such as *Smilax glabra* Roxb. (Tufuling), *Panax notoginseng* (Burkill) F. H. Chen (Sanqi), *Scleromitrion diffusum* (Willd.) R. J. Wang (Baihuasheshacao), and *Scutellaria barbata* D. Don (Banzhilian). *Smilax glabra* Roxb. (Tufuling) is a natural dietary supplement widely used in food-making and health care, based on its abilities to detoxify and reduce temperature^[21]. Previous studies revealed that it also had an anti-tumor function in counteracting the invasiveness of a subset of cancer cells by suppressing the transforming growth factor- β 1 pathway^[22]. *Panax notoginseng* (Burkill) F. H. Chen (Sanqi), which has been applied for medical uses for over four centuries, includes

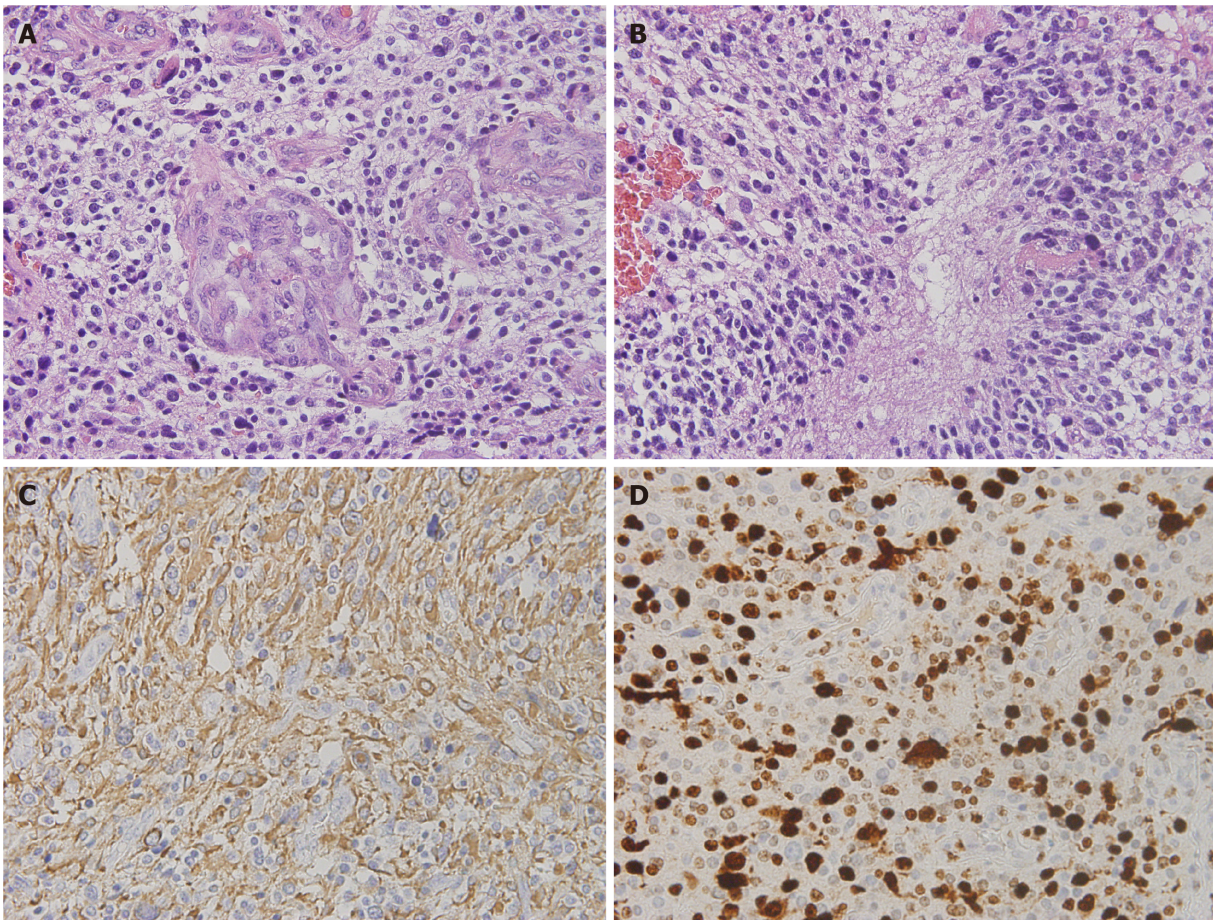


Figure 2 Pathological findings. A: Hematoxylin-eosin staining showed that the tumor cells diffused and infiltrated; B: Cells were heteromorphic with mitotic figures, microvessel hyperplasia, and palisade necrosis. Original magnification, $\times 40$; C: Tumor cells were immunopositive for glial fibrillary acidic protein immunostaining. Original magnification, $\times 40$; and D: About 70% of tumor cells were positive for Ki-67. Original magnification, $\times 40$.

saponins that can be effective in the treatment of cancer, partly by modulating the Met/miR-222 axis^[23]. *Scleromitron diffusum* (Willd.) R.J. Wang (Baihuasheshicao) was shown to suppress GBM growth *in vitro* by inducing mitochondria-mediated apoptosis via Akt/ERK signaling^[24]. *Scutellaria barbata* D. Don (Banzhilian) is used as an immunomodulatory and anti-tumor agent in TCM, and its extracts have exhibited growth-inhibitory effects in various cancers *in vitro* and/or *in vivo*^[25]. Recent studies have provided a preliminary understanding of the mechanism of traditional Chinese medicine in regulating the permeability of the blood-brain barrier. Some studies found that astilbin in *Smilax glabra* Roxb. (Tufuling) enters the brain tissue through the blood-brain barrier, at a low concentration, but with a long duration^[26]. *Notoginseng* saponins R1 and ginsenoside Rg1 in *Panax notoginseng* (Burkill) F. H. Chen (Sanqi) could penetrate the blood-brain barrier and enter the cerebrospinal fluid in rats^[27]. Few studies have investigated the ability of *Scleromitron diffusum* (Willd.) R. J. Wang and *Scutellaria barbata* D. Don to affect blood-brain barrier permeability, but we speculate that other components in KLP may also play a role in assisting the main components to enter the blood-brain barrier. TCMs act on the human body through multiple channels and targets; however, the mechanism of KLP is still unclear.

TCMs have demonstrated visible effects in relieving clinical symptoms, prolonging survival, and preventing recurrence of GBM, and even reducing the toxicity of chemotherapy^[28-31]. In addition, they have dual immunomodulatory effects of immune promotion and suppression, which can dramatically enhance the patient's immune function and improve their quality of life. TCMs are thus widely used as adjuvant therapy in all cancer stages, especially for the palliative treatment of advanced and refractory tumors. Progress in related technologies has allowed researchers to investigate the mechanisms of TCMs in relation to glioma treatment at the molecular level, and increasing evidence has confirmed their effectiveness and reliability^[31]. TCMs may thus offer new therapeutic strategies for the treatment of glioma.

CONCLUSION

Western medicine is usually considered to be the first choice of drug therapy for GBM in clinical practice. However, TMZ treatment was not suitable for the current patient and the TCM KLP was administered as an alternative. Compared with other therapies, KLP has the advantages of lower cost, comprehensive efficacy, and few side effects, and should thus be considered as a recommended option for the treatment of GBM. However, although this report demonstrated the potential suitability of TCM as an alternative therapy for GBM, the detailed mechanisms responsible for its effects remain complex and unknown. Extensive further research and more clinical trials are therefore required to confirm the efficacy and mechanisms of TCMs.

REFERENCES

- 1 **Poon CC**, Sarkar S, Yong VW, Kelly JJP. Glioblastoma-associated microglia and macrophages: targets for therapies to improve prognosis. *Brain* 2017; **140**: 1548-1560 [PMID: [28334886](#) DOI: [10.1093/brain/aww355](#)]
- 2 **Ostrom QT**, Gittleman H, Truitt G, Boscia A, Kruchko C, Barnholtz-Sloan JS. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2011-2015. *Neuro Oncol* 2018; **20**: iv1-iv86 [PMID: [30445539](#) DOI: [10.1093/neuonc/noy131](#)]
- 3 **Jacob F**, Salinas RD, Zhang DY, Nguyen PTT, Schnoll JG, Wong SZH, Thokala R, Sheikh S, Saxena D, Prokop S, Liu DA, Qian X, Petrov D, Lucas T, Chen HI, Dorsey JF, Christian KM, Binder ZA, Nasrallah M, Brem S, O'Rourke DM, Ming GL, Song H. A Patient-Derived Glioblastoma Organoid Model and Biobank Recapitulates Inter- and Intra-tumoral Heterogeneity. *Cell* 2020; **180**: 188-204. e22 [PMID: [31883794](#) DOI: [10.1016/j.cell.2019.11.036](#)]
- 4 **Anjum K**, Shagufta BI, Abbas SQ, Patel S, Khan I, Shah SAA, Akhter N, Hassan SSU. Current status and future therapeutic perspectives of glioblastoma multiforme (GBM) therapy: A review. *Biomed Pharmacother* 2017; **92**: 681-689 [PMID: [28582760](#) DOI: [10.1016/j.biopha.2017.05.125](#)]
- 5 **Ostrom QT**, Patil N, Cioffi G, Waite K, Kruchko C, Barnholtz-Sloan JS. CBTRUS Statistical Report: Primary Brain and Other Central Nervous System Tumors Diagnosed in the United States in 2013-2017. *Neuro Oncol* 2020; **22**: iv1-iv96 [PMID: [33123732](#) DOI: [10.1093/neuonc/noaa200](#)]
- 6 **Yi GZ**, Huang G, Guo M, Zhang X, Wang H, Deng S, Li Y, Xiang W, Chen Z, Pan J, Li Z, Yu L, Lei B, Liu Y, Qi S. Acquired temozolomide resistance in MGMT-deficient glioblastoma cells is associated with regulation of DNA repair by DHC2. *Brain* 2019; **142**: 2352-2366 [PMID: [31347685](#) DOI: [10.1093/brain/awz202](#)]
- 7 **Alexander BM**, Cloughesy TF. Adult Glioblastoma. *J Clin Oncol* 2017; **35**: 2402-2409 [PMID: [28640706](#) DOI: [10.1200/JCO.2017.73.0119](#)]
- 8 **Cao L**, Qu D, Wang H, Zhang S, Jia C, Shi Z, Wang Z, Zhang J, Ma J. Toosendanin Exerts an Anti-Cancer Effect in Glioblastoma by Inducing Estrogen Receptor β - and p53-Mediated Apoptosis. *Int J Mol Sci* 2016; **17** [PMID: [27869737](#) DOI: [10.3390](#)]
- 9 **Cha Z**, Cheng J, Xiang H, Qin J, He Y, Peng Z, Jia J, Yu H. Celastrol enhances TRAIL-induced apoptosis in human glioblastoma via the death receptor pathway. *Cancer Chemother Pharmacol* 2019; **84**: 719-728 [PMID: [31281953](#) DOI: [10.1007/s00280-019-03900-8](#)]
- 10 **Cao P**, Cai X, Lu W, Zhou F, Huo J. Growth Inhibition and Induction of Apoptosis in SHG-44 Glioma Cells by Chinese Medicine Formula "Pingliu Keli". *Evid Based Complement Alternat Med* 2011; **2011** [PMID: [20953401](#) DOI: [10.1155/2011/958243](#)]
- 11 **Shi J**, Zhang W, He L, Kong F, Pan M, Guo J, Xu X, Wang H, Wang Y. Jinlong capsule inhibits migration and invasion in human glioblastoma cells via the modulation of mTOR/S6 signaling pathway. *Drug Des Devel Ther* 2019; **13**: 1023-1032 [PMID: [31114156](#) DOI: [10.2147/DDDT.S195409](#)]
- 12 **Feng Y**, Zhang P, Chen F, Zhuang W, Lin X. Research on mechanism of action of Chinese medicine compound optimization Kangliuwan on BALB/c nude mice transplantation tumor model of U87. *Huanqiu Zhongyiyao* 2018; **10**: 1515-1519 [DOI: [10.3969/j.issn.1674-1749.2018.10.004](#)]
- 13 **Wang H**, Feng Y, Chen F, Zhang P, Lin X. Influence of KangLiu pills on the expressions of apoptosis factors of nude mice with glioma. *Xibu Zhongyiyao* 2019; **4**: 8-11 [DOI: [10.3969/j.issn.1004-6852.2019.04.003](#)]
- 14 **Feng YN**, Chen F, Zhang P, Zhuang W, Lin XL. Quality standard for KangLiuWan. *Huanqiu Zhongyiyao Zazhi* 2017; **5**: 527-531 [DOI: [10.3969/j.issn.1674-1749.2017.05.004](#)]
- 15 **Chen F**, Lin XL, Xi HW, Zhuang W, Li XL. Simultaneous determination of notoginsenoside R1, ginsenoside Rg1 and ginsenoside Rb1 in Chinese formula KLW by UPLC-MS-MS. *Zhongguo Shiyang Fangjixue* 2013; **16**: 156-159 [DOI: [10.11653/syfy2013160156](#)]
- 16 **Zhuang W**, Lin XL, Jiang DC, Lin QT, Wang YQ, Guo JX, Zhang P, Chen F, Xu G, Wu XG. Efficacy of KLW-1 in treatment of patients with malignant gliomas. *Zhongguo Xinyao Zazhi* 2011; **19**: 1894-1897
- 17 **Schreck KC**, Grossman SA. Role of Temozolomide in the Treatment of Cancers Involving the Central Nervous System. *Oncology (Williston Park)* 2018; **32**: 555-560, 569 [PMID: [30474103](#)]

- 18 **Tan AC**, Ashley DM, López GY, Malinzak M, Friedman HS, Khasraw M. Management of glioblastoma: State of the art and future directions. *CA Cancer J Clin* 2020; **70**: 299-312 [PMID: 32478924 DOI: 10.3322/caac.21613]
- 19 **Gerstner ER**, Emblem KE, Chang K, Vakulenko-Lagun B, Yen YF, Beers AL, Dietrich J, Plotkin SR, Catana C, Hooker JM, Duda DG, Rosen B, Kalpathy-Cramer J, Jain RK, Batchelor T. Bevacizumab Reduces Permeability and Concurrent Temozolomide Delivery in a Subset of Patients with Recurrent Glioblastoma. *Clin Cancer Res* 2020; **26**: 206-212 [PMID: 31558474 DOI: 10.1158/1078-0432.CCR-19-1739]
- 20 **Stupp R**, Taillibert S, Kanner A, Read W, Steinberg D, Lhermitte B, Toms S, Idhah A, Ahluwalia MS, Fink K, Di Meco F, Lieberman F, Zhu JJ, Stragliotto G, Tran D, Brem S, Hottinger A, Kirson ED, Lavy-Shahaf G, Weinberg U, Kim CY, Paek SH, Nicholas G, Bruna J, Hirte H, Weller M, Palti Y, Hegi ME, Ram Z. Effect of Tumor-Treating Fields Plus Maintenance Temozolomide vs Maintenance Temozolomide Alone on Survival in Patients With Glioblastoma: A Randomized Clinical Trial. *JAMA* 2017; **318**: 2306-2316 [PMID: 29260225 DOI: 10.1001/jama.2017.18718]
- 21 **Hua S**, Zhang Y, Liu J, Dong L, Huang J, Lin D, Fu X. Ethnomedicine, Phytochemistry and Pharmacology of *Smilax glabra*: An Important Traditional Chinese Medicine. *Am J Chin Med* 2018; **46**: 261-297 [PMID: 29433390 DOI: 10.1142/S0192415X18500143]
- 22 **She T**, Zhao C, Feng J, Wang L, Qu L, Fang K, Cai S, Shou C. Sarsaparilla (*Smilax Glabra* Rhizome) extract inhibits migration and invasion of cancer cells by suppressing TGF- β 1 pathway. *PLoS One* 2015; **10**: e0118287 [PMID: 25742000 DOI: 10.1371/journal.pone.0118287]
- 23 **Yang Q**, Wang P, Cui J, Wang W, Chen Y, Zhang T. Panax notoginseng saponins attenuate lung cancer growth in part through modulating the level of Met/miR-222 axis. *J Ethnopharmacol* 2016; **193**: 255-265 [PMID: 27566197 DOI: 10.1016/j.jep.2016.08.040]
- 24 **Zhang Y**, Xie RF, Xiao QG, Li R, Shen XL, Zhu XG. Hedyotis diffusa Willd extract inhibits the growth of human glioblastoma cells by inducing mitochondrial apoptosis via AKT/ERK pathways. *J Ethnopharmacol* 2014; **158** Pt A: 404-411 [PMID: 25456437 DOI: 10.1016/j.jep.2014.10.017]
- 25 **Li L**, Xu X, Wu L, Zhu H, He Z, Zhang B, Chi Y, Song G. Scutellaria barbata polysaccharides inhibit tumor growth and affect the serum proteomic profiling of hepatoma H22bearing mice. *Mol Med Rep* 2019; **19**: 2254-2262 [PMID: 30664217 DOI: 10.3892/mmr.2019.9862]
- 26 **Li YQ**, Gu J, Huan Z, Qiu J, Li YL, Deng CG. Tissue distribution of astilbin in mice. *Yaoxue Shijian Zazhi* 2013; **03**: 201-203 [DOI: 10.3969/j.issn.1006-0111.2013.03.011]
- 27 **Zhao C**, Guo H, Xu YY, Wang SX, Chai LJ, Yuan Q, Hu LM. Study of Xueshuantong injection on permeability of the blood brain barrier. *Zhongguo Linchuang Yaolixue Zazhi* 2017; **03**: 235-238 [DOI: 10.13699/j.cnki.1001-6821.2017.03.013]
- 28 **Chen ZZ**, Lu Y, Du SY, Shang KX, Cai CB. Influence of borneol and muscone on geniposide transport through MDCK and MDCK-MDR1 cells as blood-brain barrier *in vitro* model. *Int J Pharm* 2013; **456**: 73-79 [PMID: 23973509 DOI: 10.1016/j.ijpharm.2013.08.017]
- 29 **Guo Y**, Wang P. Chemo-sensitization effect of borneol combined with paclitaxel on brain glioma cell lines. *Yatai Chuantong Yiyao* 2018; **9**: 9-11 [DOI: 10.11954/ytctyy.201809004]
- 30 **Wang H**, Guo X, Wu G, Chen L. Combination of tetrandrine and paclitaxel overcomes multidrug resistance on C6/MDR glioma cells. *Zhongcaoyao Zazhi* 2018; **11**: 2584-2590 [DOI: 10.7501/j.issn.0253-2670.2018.11.015]
- 31 **Wang J**, Qi F, Wang Z, Zhang Z, Pan N, Huai L, Qu S, Zhao L. A review of traditional Chinese medicine for treatment of glioblastoma. *Biosci Trends* 2020; **13**: 476-487 [PMID: 31866614 DOI: 10.5582/bst.2019.01323]



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>

