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RESEARCH ARTICLE

Magnetic resonance imaging evaluation of brain glioma before postoperative radiotherapy

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Abstract

Purpose To investigate the magnetic resonance imaging (MRI) images of brain glioma before postoperative radiotherapy, and to provide reference for the delineation of postoperative radiotherapy target area.

Methods Retrospective analysis was performed on 106 cases of brain glioma confirmed by surgery and pathology in our hospital, including 70 cases of high-grade glioma (HGG) and 36 cases of low-grade glioma (LGG). The MRI images of the lesions within 1 month before and after surgery were analyzed, the apparent diffusion coefficient (ADC) values in the near and far tumor areas were measured, respectively, and the corresponding rADC values were calculated.

Results The incidence of residual tumors of postoperative HGG and LGG was 0, 15.7% (0/36, 11/70), respectively. The incidence of postoperative reactive enhancement was 11.0% and 52.9% (4/36 and 37/70), respectively. About 30.6% and 81.4% (11/36 and 57/70) of patients with adjacent meningeal enhancement were found in the operative area.

Conclusions The MRI images of HGG and LGG before postoperative radiotherapy had certain characteristics, providing a favorable guidance for the delineation of the target area of radiotherapy and the formulation of treatment plan.

Keywords High-grade glioma · Low-grade glioma · Magnetic resonance imaging · Postoperative radiotherapy · Apparent diffusion coefficient

Introduction

Brain glioma is the most common primary intracranial tumor, accounting for about 35%–61% of intracranial tumors, among which high-grade glioma (HGG) accounts for about 76% of brain gliomas, and the incidence is increasing year by year [1, 2]. Surgical resection is the main treatment, but because of its biological characteristics of invasive growth, complete resection is difficult and easy to recur, so postoperative radiotherapy is often used. Low-grade glioma (LGG) usually can be eradicated by surgical resection, and the prognosis is good. The magnetic resonance imaging (MRI) manifestations of HGG and LGG before postoperative radiotherapy have certain characteristics, which help us to define the position, size and morphology of residual tumors, accurately delineate the target area of radiotherapy, so as to achieve accurate treatment, reduce normal tissue damage, reduce recurrence rate and improve survival rate of patients.

Materials and methods

Clinical data

A retrospective analysis was performed on 106 cases of brain gliomas confirmed by surgery and pathology from June 2013 to June 2014 in our hospital, including 36 LGG (WHOI, WHOII), all of which were astrocytomas; 70 cases of HGG (WHO III, WHO IV), including 31 cases of anaplastic astrocytoma, 7 cases of anaplastic oligodendroglioma, 22 cases of glioblastoma, and 10 cases of mixed glioma. Among the 36 patients with LGG, 20 were males and 16 were females, aged 12–33 years, with an average age of (22.3 ± 4.1) years. Among the 70 patients with HGG, 41 were males and 29 were females, aged 17–72 years, with an average age of (42.6 ± 3.4) years. All 36 cases of

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LGG underwent complete resection, while among 70 cases of HGG, 59 cases underwent complete resection, and the remaining 11 cases were partially resected, because 5 cases involved the thalamus, 3 cases involved the basal ganglia, 1 case involved the internal capsule, and 2 cases involved the insula. The unresected but reserved lesion area was not included in this study. All patients underwent MRI plain scan and enhanced scan within 1 month before surgery, and MRI plain scan and enhanced scan after surgery and before radiotherapy were performed. The peritumor edema area was divided into a near tumor area and a far tumor area with 1 cm as the boundary, and the apparent diffusion coefficient (ADC) values were measured and the corresponding rADC values were calculated. This study complies with the provisions of the declaration of Helsinki and has been approved by the ethics committee of the First Affiliated Hospital of Zhengzhou University. All participants have signed the informed consent.

Examination method

A 3.0 T (Verio, Siemens) superconducting magnetic resonance machine was used, and a standard skull coil was used. The patient was asked to take supine position, and a vein channel was established in the elbow vein. Commonly used sequences and parameters: axial FL2DT1WI and sagittal T1WI, TR 7500 ms, TE 114 ms, FOV 229 mm × 229 mm, layer thickness 5 mm, matrix 288 × 288 or 512 × 512; axial T2WI, TR 6000 ms, TE 125 ms, FOV 240 mm × 240 mm, layer thickness 5 mm, matrix 384 × 384 or 512 × 512; axial T2FLAIR, TR 6000 ms, TE 85 ms, FOV 240 mm × 240 mm, layer thickness 5 mm. After the completion of the plain scan, dynamic contrast-enhanced MRI was performed. The contrast agent was Gd-diethylenetriamine pentaacetic acid, the dose was 0.2 mmol/kg, and the injection rate was 1.5 mL/s. After intravenous injection, T1WI scan was performed in cross section, sagittal and coronal planes, and the scanning parameters were the same as that of plain scan. Diffusion weighted imaging (DWI): SE plane echo imaging (SEEPI) sequence was used, TR 8000 ms, TE 102 ms, two b values (0 s/mm^2, 1000 s/mm^2) were adopted. Axial scanning FOV 240 mm × 240 mm, layer thickness 6 mm, interval 1 mm, matrix 128 × 128, imaging time 48 s.

All patients underwent MRI plain scan and enhanced scan within 1 month before surgery, and all patients had complete preoperative MRI data. The patients who need to receive radiotherapy also had at least one MRI examination within 1 month after surgery and before radiotherapy. The earliest postoperative MRI examination was within 24 h after surgery, and the latest was the 30th day after surgery. Among the 106 patients, 6 patients underwent MRI examination within 24 h after surgery, 51 patients were 24 h to 3d after surgery, 19 patients were 3 d to 7 d after surgery, 11 patients were 7 d to 14 d after surgery, and 19 patients were 14 d to 30 d after surgery. All the data included in this study were the first postoperative MRI examination data.

MRI diagnostic criteria

All subjects received radiotherapy about 1 month after surgery. This study focused on the MRI images before postoperative radiotherapy. According to the case tracking, only 1 case showed postoperative tumor recurrence after surgery and before radiotherapy.

Postoperative residual tumor: compared with the preoperative MRI data, if the MRI data met the following two points at the same time, it was considered as the enhancement of postoperative residual tumor. (1) Enhancement occurred at the first postoperative examination; (2) there was no trend of decreasing or disappearing of tumor until the enhanced part increased; (3) DWI diffusion was limited.

Postoperative reactive enhancement: the main judgment basis were: (1) Compared with the preoperative MRI data, there was no enhancement in LGG patients before surgery, and a new enhancement ring appeared around the tumor after surgery; (2) the above enhancement ring had no signs of diffusion restriction on DWI; (3) after follow-up observation, the enhancement ring gradually weakened or disappeared until the formation of softening focus at this site.

Peritumor edema: there was no enhancement in enhanced scan, no signs of diffusion restriction on DWI, FLAIR showed high signal, and some of them were contrast with preoperative edema.

Image analysis and data measurement of peritumoral edema area

Near tumor area and far tumor area: the area less than 1 cm outside the edge of tumor cavity was near tumor area, and the area more than 1 cm outside the edge of tumor cavity was far tumor area.

The Functool 3 analysis software was used to select the DWI horizontal axis with the largest tumor diameter and the most obvious placeoccupying effect according to the ADC image and the conventional MR image, and 2-6 regions of interest were selected from the near tumor area, the far tumor area and the corresponding normal white matter area on the opposite side, respectively. According to the measured ADC value, the corresponding rADC value (rADC value = ADC value of the lesion area/ADC value of the corresponding normal white matter area of the contralateral brain) was calculated, and the obtained results were averaged.

Statistical analysis

Three chief physicians analyzed the image data. The signal characteristics of tumor location, shape, size and surrounding edema were observed. SPSS17.0 statistical software was used to analyze the indicators.

Results

Postoperative residual tumor enhancement and postoperative reactive enhancement

The incidence of postoperative residual tumors in LGG and HGG was 0, 15.7% (0, 11/70), respectively, and the incidence of postoperative reactive enhancement was 11.0%, 52.9% (4/36, 37/70), respectively. The earliest occurrence time of reactive enhancement was 18 h after surgery, with varying durations, and the most significant enhancement was 6 d–30 d after surgery, see Table 1.

Postoperative meningeal enhancement

In LGG and HGG, the incidence of meningeal enhancement was 30.6% and 81.4% (11/36, 57/70), respectively, presenting obvious arc-like enhancement. The MRI features of meningeal enhancement are shown in Table 2.

Postoperative tumor recurrence

Due to the narrow time window of this study, which was only about 1 month after glioma surgery and before radiotherapy, there were no obvious signs of recurrence in most cases. Among the cases in this study, only one case had recurrence before radiotherapy, and the pathology was glioblastoma multiforme. The recurrence was characterized by obvious expansion of residual foci and obvious peripheral edema, see Fig. 1.

Postoperative peritumor edema

In the early postoperative period, edema of different degrees could be seen in LGG and HGG, the incidence was 55.6% and 87.1%, respectively. The rADC value of HGG in the near tumor area was significantly lower than that in the far tumor area, ($P=0.00$). The rADC value in the near tumor area of LGG was slightly lower than that in the far tumor area ($P=0.13$). The rADC value of LGG near tumor area was higher than that of HGG near tumor area ($P=0.02$). rADC value in the far tumor area of LGG was slightly higher than that in the far tumor area of HGG ($P=0.16$), see Table 3.

Discussion

The proportion of HGG in brain glioma is 77.5%, and the incidence rate is increasing year by year. The 5-year mortality rate of HGG is third in the whole body tumors, only second to pancreatic cancer and lung cancer [1, 2]. HGG is easy

Table 1 MRI features of postoperative residual tumor enhancement and postoperative reactive enhancement

Item	Enhancement type	Number	Thickness (mm)		Node		Boundary	
			<3	≥3	Yes	No	Clear	Vague
HGG	Residual tumor enhancement	11	4	7	8	3	2	9
	Reactive enhancement	37	32	5	9	28	30	7
LGG	Residual tumor enhancement	0	–	–	–	–	–	–
	Reactive enhancement	4	3	1	0	0	4	0

MRI magnetic resonance imaging; *HGG* high-grade glioma; *LGG* low-grade glioma

Table 2 MRI features of postoperative meningeal enhancement

Item	Meningeal enhancement location	Number	Thickness (mm)		Node		Existence time (year)	
			<2	≥2	Yes	No	<1	≥1
HGG	Near the operation area	48	10	38	9	39	11	37
	Remote area	9	6	3	1	8	8	1
LGG	Near the operation area	8	6	2	0	0	7	1
	Remote area	3	3	0	0	0	3	0

MRI magnetic resonance imaging; *HGG* high-grade glioma; *LGG* low-grade glioma

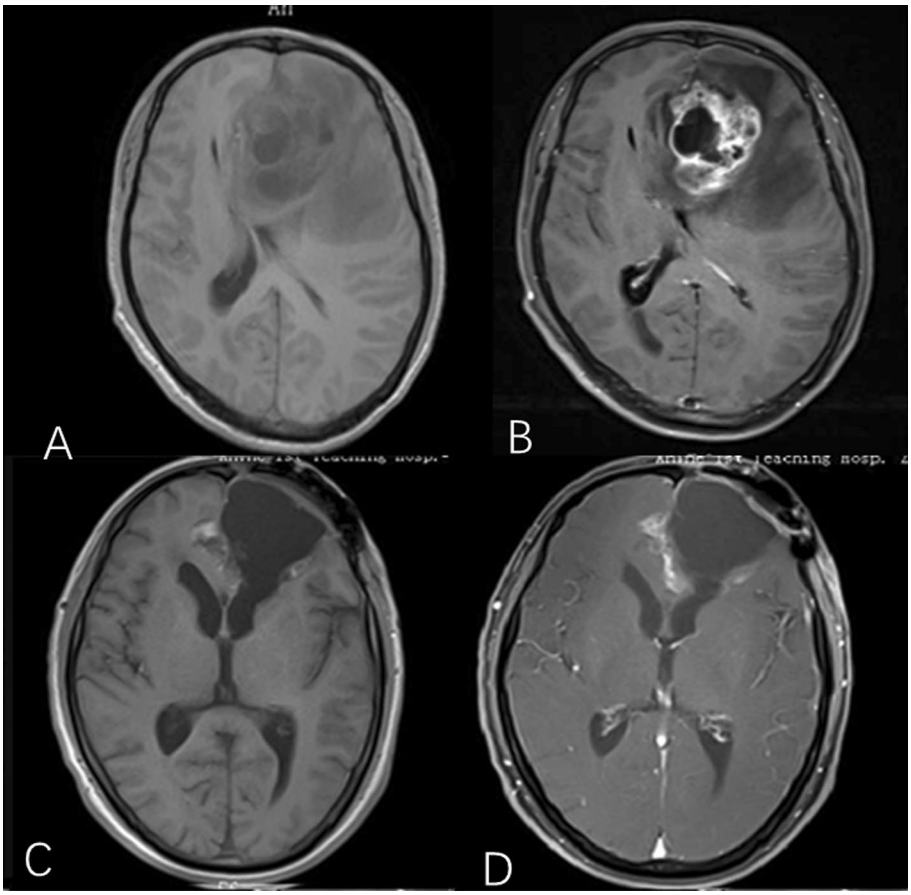

Fig. 1 A 43-year-old male patient with pleomorphic glioblastoma in the left frontal lobe. **a** Preoperative axial T1WI showed an inhomogeneous long T1 signal shadow, with large edema shadow around, accompanied by a hernia under the falcium cerebrum; **b** preoperative axial contrast-enhanced scan showed uneven enhancement of the lesion in the annular shape, and no obvious enhancement was found in the surrounding edema area; **c** postoperative axial T1WI showed that the lesion occupying effect and peritumoral edema were significantly reduced; **d** after surgery, the axial enhanced scan showed that the tumor margin showed patchy enhancement, the focus boundary was unclear, the thickest part was about 4 cm, and the meninges showed strip enhancement

Table 3 rADC values of benign and malignant glioma near tumor area and far tumor area

Item	rADC value of near tumor area	rADC value of far tumor area	*t*	*P*
HGG	1.62 ± 0.39	1.93 ± 0.56	1.41	0.00
LGG	1.93 ± 0.56	1.99 ± 0.22	3.25	0.13
t	2.67	3.57	–	–
P	0.02	0.16	–	–

ADC apparent diffusion coefficient; *HGG* high-grade glioma; *LGG* low-grade glioma

to remain and recrudesce after surgery. Radiotherapy has been proved to be one of the most effective adjuvant treatment methods after surgery of glioma, which can reduce the local recurrence rate and improve the postoperative survival rate [3, 4]. Due to the traumatic nature of surgical resection, pathophysiological changes will occur in the surgical area and adjacent normal brain tissues, mainly including peritumoral edema, reactive enhancement, residual tumor enhancement, adjacent meninges and subdural enhancement. There are very similar MRI findings between the peripheral ring reactive enhancement and the residual tumor enhancement in the operative area, and sometimes it is difficult to distinguish them [5–9]. It is of great clinical significance to study the MRI findings before postoperative radiotherapy for the detection of residual tumors, the accurate evaluation of the surgical effect and the early diagnosis of postoperative recurrence.

Postoperative tumor residue

Gliomas are often invasive, and some of them are deep or in important functional anatomical areas, so it is difficult to remove them completely. After complete resection of about 30% of tumors, abnormal enhancement of residual tumors can still be seen on enhanced MRI images [10, 11]. Postoperative residual tumors were found mainly by means of MRI enhanced scan images, and the remaining tumors showed abnormal enhancement in different degrees and ranges. Early postoperative enhancement could occur, but the enhancement was often vague and difficult to be defined, and its enhancement mechanism was the same as that before surgery [12, 13]. It was mainly due to the destruction of blood–brain barrier, which caused the overflow of contrast agent; the tumor tissue was rich in blood supply, which caused the retention of contrast agent; the brain's self-regulation function was disordered, and the

local blood circulation was increased, resulting in over perfusion [14, 15]. The characteristics of postoperative enhancement are mainly irregular flower ring, nodular or lumpy medium or obvious abnormal enhancement. Most of the rings are incomplete, uneven in thickness and unclear in boundary. If there is no intervention, it will gradually increase [16]. DWI sequence showed high signal and ADC image signal decreased. There is a corresponding relationship between postoperative tumor residue and preoperative enhanced tumor [17], but in this study, the corresponding relationship is not clear, which may be because the tumor boundary shown by MRI is more accurate than that shown by the naked eye, and there are many interference factors in the operative area, although theoretically established, it is difficult to keep the two consistent in fact. Postoperative radiotherapy is mainly aimed at killing postoperative residual tumor and preventing tumor recurrence. The enhanced part of glioma residual tumor in enhanced scan must be included in the delineation of radiotherapy target area.

Postoperative reactive enhancement

Postoperative reactive enhancement refers to the reactive ring enhancement around the tumor cavity during the early postoperative enhanced MRI, also known as benign enhancement, it is non-neoplastic, and non-infective. There was no contrast with the preoperative enhanced MR images, and the incidence was approximately 54%–100%. There are similarities between postoperative reactive enhancement and tumor residual enhancement, which is difficult to distinguish. Postoperative reactive enhancement mostly occurred in HGG, while its performance in LGG was not obvious. In this study, only 11% of the patients with LGG showed significant reactive enhancement after surgery, which was basically consistent with the literature reports [14–17]. The characteristics of postoperative reactive enhancement are ring enhancement around the tumor cavity, clear and sharp boundary, uniform thickness, generally no more than 3 mm, no nodular enhancement in local area, no correspondence with the preoperative enhancement image, no intervention will also disappear, and the occupying effect is not obvious. DWI showed no obvious signs of limited diffusion.

In this study, the incidence of postoperative reactive enhancement of HGG was 52.9%. Since most of the cases were reexamined about 1 week after surgery, the postoperative reactive enhancement was obvious and typical. Although there were similarities with the enhancement of residual tumors, it was not difficult to distinguish them through careful analysis. It is not necessary to consider postoperative reactive enhancement in the target area of postoperative radiotherapy.

Peritumoral edema

There are two main formation factors of postoperative peritumoral edema of HGG: preoperative peritumoral edema and postoperative edema caused by trauma. The incidence of edema caused by surgery is high, which can appear in early stage, mostly subside about 1 month after surgery, without obvious occupying effect, and the degree of edema is usually light. The peritumoral edema before and after surgery has a certain degree of contrast, generally in the form of fingers, with a certain occupying effect. Peritumoral edema is a common complication of gliomas. Its incidence and degree are often closely related to the grade of gliomas. The incidence of peritumoral edema in HGG is more than 80%, and the incidence of LGG is about 40%–60% [18].

Peritumoral edema showed long T1 and long T2 signals on MRI, and there was no enhancement in enhanced scan, and no obvious signs of limited diffusion in DWI scan. Burger et al. [19] found tumor cell infiltration in peritumoral edema area in glioma cadaver specimens. According to the study of Garden et al. [20], 75% of postoperative recurrent glioma lesions were located within 2 cm of the tumor. Thus, the recurrence of most gliomas may be caused by residual tumor cells in the peritumoral edema area.

At present, ADC value, as the only parameter that can quantitatively evaluate the diffusion of the tested tissue in vivo, can reflect the histological characteristics of the tumor. Due to the infiltration of tumor cells in the peritumoral edema area of malignant glioma, the diffusion of water molecules is limited, but its arrangement density is less than that in the tumor, so there is no obvious abnormal high signal in DWI image, but it can cause the ADC value to decrease, and the rADC value will also decrease [21, 22]. Zhang et al. [23] found that the rADC value of HGG peritumoral edema is lower than that of LGG, and the higher the grade, the more serious the infiltration of glioma. The infiltrative growth around HGG is from near to far, that is, the tumor cells near the tumor are more than those far from the tumor. Zhuang et al. [24] suggested that the number of tumor cells scattered in the peritumoral edema area was negatively correlated with the distance of tumor body.

To retain the function of brain to the maximum extent, during the surgery of glioma, the tumor body is usually removed and the peritumoral edema is not completely removed. Tumor cells infiltrated in peritumoral edema are the serious hidden danger of glioma recurrence in the future. Postoperative radiotherapy usually does not include peritumoral edema in the scope of target area delineation, mainly due to the lack of imaging basis for quantitative evaluation. In this study, according to the reduction of rADC value, appropriately including the edema area of 2–3 cm around the tumor in the target area can help reduce the recurrence of tumor in the future.

Postoperative meningeal enhancement

Under normal circumstances, the dural membrane can be thin and linear in thickness, often less than 1 mm, due to the lack of blood–brain barrier and the spread of contrast agents from the blood vessels to the extracellular space. After the surgery of HGG, the integrity of meninges is destroyed, and the local dura appears diffuse and nodular enhancement. The incidence of postoperative dura enhancement was high, and the results of this study showed that the incidence was 75%, which was slightly thicker. The possible mechanism of the enhancement was as follows: 1. Due to the stimulation of subarachnoid hemorrhage, the dura mater produced diffuse or localized chemical inflammatory reaction; 2. the blood flow velocity was slowed down due to the mechanical pressure of postoperative effusion on the meninges. The pathological basis of postoperative meningeal enhancement was complex, mainly granulation tissue and collagen fiber formation. The enhancement characteristics of the meninges after surgery of malignant gliomas are as follows: first, the occurrence rate is relatively high, about 90.9%; second, most of them are relatively thick, more than 2 mm. In this study, the thickest one is 5 mm, with irregular shape and locally visible nodules; third, the early postoperative can be strengthened, lasting for a long time, lasting from 1 year to more than 10 years, but if more than 1 year, the possibility of postoperative infection should be excluded; fourth, the distant meninges can also be strengthened.

In conclusion, tumor cells infiltrated within the 2–3 cm edema zone around the tumor, and about 15.7% of the tumors recurred within 1 month before the postoperative radiotherapy of HGG. Therefore, when delineating the radiotherapy target area on the MR image, the edema area within at least 2–3 cm of the tumor should be included, so as to reduce the recurrence of the tumor in the peritumoral edema area after surgery.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethics approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the First Affiliated Hospital of Zhengzhou University and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent Informed consent was obtained from all individual participants included in the study.

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