

Original Article

A comparison of the multimodal magnetic resonance imaging features of brain metastases vs. high-grade gliomas

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Abstract: Objective: We aimed to explore the multimodal magnetic resonance imaging (MRI) features of brain metastases and high-grade brain gliomas. Methods: Fifty patients with brain metastases and 28 patients with high-grade gliomas treated in the neurosurgery department of our hospital were selected for this study. All patients underwent routine MRI, diffusion tensor imaging, and perfusion-weighted magnetic resonance imaging. The average diffusion coefficient (ADC), fractional anisotropy (FA), regional cerebral blood flow (rCBF), and regional cerebral blood volume (rCBV) in the tumor parenchyma, peritumoral edema area, and the contralateral normal cerebral white matter were compared between the patients with brain metastases and the patients with high-grade brain gliomas. Results: There were differences in the degree of peritumoral edema between the two groups of patients ($P = 0.017$). Compared with the patients with high-grade gliomas, the patients with brain metastases had lower FA values in the tumor parenchyma area, higher ADC values in the peritumoral edema area, and lower rCBV and rCBF values in the peritumoral edema area (all $P < 0.001$). Conclusion: The measurement of the ADC, rCBV, and rCBF values in the peritumoral edema area and the FA values in the tumor parenchyma area using multimodal MRI can have essential clinical value in the differentiation between brain metastases and high-grade gliomas.

Keywords: Multimodal magnetic resonance imaging, brain metastases, high-grade gliomas, imaging features

Introduction

Brain metastases, as common intracranial tumors, have high mortality and disability rates [1]. The disease develops in 20-40% of patients with malignant tumors [2]. With the increasing incidence of malignant tumors worldwide, the incidence of brain metastases has been rising each year [3, 4]. Moreover, 2-14% of patients with malignant tumors are first diagnosed with brain metastases before being diagnosed with the primary tumors [5]. Therefore, the early and accurate diagnosis of brain metastases is not only conducive to the early intervention and treatment of brain metastases, it is also conducive to the early diagnosis of primary tumors.

Glioma is a primary brain tumor. The clinical manifestations of glioma, especially the clinical manifestations of high-grade glioma, are quite similar to those of brain metastases [6].

Magnetic resonance imaging (MRI) is a traditional method of detecting neurological diseases, but conventional MRI still has limitations in diagnosing brain metastases [7]. Diffusion tensor imaging (DTI) is a newly developed imaging technology. It can accurately reflect the microstructure of the tissues by visualizing the diffusion of water molecules in the tissues and has been applied in the glioma grading and the diagnosis of breast cancer and stroke [7]. Perfusion-weighted magnetic resonance imaging (PWI) is an imaging method with a high resolution and a high signal-to-noise ratio. PWI can measure the relative cerebral blood volume and relative cerebral blood flow, so it is helpful for the differential diagnosis of tumors and can reflect the degree of malignancy well [8]. Pathological examination is considered the gold standard for diagnosing high-grade gliomas and brain metastases, but its application

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is limited due to its invasive nature. Since it is unclear whether the use of multimodal MRI can help to distinguish brain metastases from high-grade gliomas, we aimed to investigate the multimodal MRI features of high-grade glioma and brain metastases in this study [9].

Materials and methods

Participants

One hundred and twenty-eight patients treated in the neurosurgery department of The Second People's Hospital of Jiaozuo (First Affiliated Hospital of He'nan Polytechnic University) between December 2016 and July 2020 were selected. Among them, 78 cases were included in this study based on their pathological results (brain metastases, 50 cases; high-grade gliomas, 28 cases). The patients were between 32 and 73 years old (51.6 ± 8.9 years). The study was approved by the Ethics Committee of The Second People's Hospital of Jiaozuo (First Affiliated Hospital of He'nan Polytechnic University), and the enrolled participants signed the informed consent.

Inclusion criteria: 1) patients whose tumor type (brain metastases or high-grade gliomas) was confirmed through a pathological examination; 2) patients who underwent an MRI, DTI, and PWI before the pathological examination; 3) patients whose MRI and DTI images were clear without artifacts; 4) patients who had complete clinical data.

Exclusion criteria: 1) patients whose MRI and DTI images were unclear; 2) patients with low-grade glioma; 3) patients with incomplete clinical data.

Methods

An MRI scanner (Skyra 3.0T, Siemens, Germany) was used to perform the routine scanning followed by DTI. The DTI parameters were set as follows: time of repetition = 3,700 ms, time of echo = 95 ms, field of view = 220 mm, slice thickness = 4 mm, slice interval = 1.2 mm, diffusion-sensitive gradient magnetic field in 20 directions, and b value = 0/1,000 s/mm². The PWI parameters were: time of repetition = 3,700 ms, time of echo = 93 ms, field of view = 280 mm, slice thickness = 6 mm, and slice interval = 1.2 mm; flip angle = 120°; 60 time

phases were collected for each slice. The contrast agent gadolinium-DTPA (Bayer Schering, Germany) was injected in the patients at a speed of 4 mL/s and a dose of 0.2 mmol/kg. After the image processing, the images were analyzed by two professionals. The tumor parenchymal area, the peritumoral edema area, and the contralateral normal cerebral white matter were selected to calculate the average diffusion coefficient (ADC), fractional anisotropy (FA), regional cerebral blood volume (rCBV), and regional cerebral blood flow (rCBF). The results were calculated three times to obtain the means. During the measuring of the FA and the ADC values, the regions of interest (about 10 mm²) in the tumor parenchymal area, the peritumoral edema area, and the contralateral normal cerebral parenchyma region were chosen to measure the FA and the ADC values. The tumor parenchymal area was the markedly enhanced tumor area, the peritumoral edema area was located at the midpoint of the horizontal line between the tumor edge and the edema edge, and the contralateral normal cerebral parenchyma area was the normal cerebral white matter area about 2 cm away from the edema margin. The relative ADC and FA values were the ratios of the ADC and the FA values to the ADC and the FA values in the contralateral normal white matter. Each value was measured three times, and three means were calculated.

The degree of edema around each tumor was classified as follows: 1) mild: the edema diameter was less than 1/2 of the maximal diameter of the tumor; 2) moderate: the edema diameter was between 1/2 of the maximal diameter and the maximal diameter of the tumor; 3) severe: the edema diameter exceeded the maximal diameter of the tumor [10].

Outcome measures

The degree of edema around the tumor and the ADC, FA, rCBV and rCBF values of the tumor parenchymal and the peritumoral edema area were analyzed and compared between the brain metastases and the high-grade brain gliomas.

Statistical methods

SPSS 17.0 was applied for the data analysis. Independent samples t-tests were performed if there was a normal distribution and homogene-

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Table 1. The two groups' baseline data

Baseline data	Brain metastases group (n = 50)	High-grade glioma group (n = 28)	χ^2/t	P
Age (years)	50.7±9.7	51.9±8.5	0.645	0.520
Gender (male-to-female ratio)	29:21	16:12	0.005	0.941
Neurological symptoms	25	16	0.367	0.544
Tumor site			0.003	0.953
Supratentorial	39	22		
Infratentorial	11	6		
Tumor morphology			39.798	<0.001
Regular	39	1		
Irregular	11	27		
Intratumoral bleeding			5.797	0.016
Yes	3	7		
No	47	21		

Table 2. The degree of peritumoral edema in the two groups

Degree of peritumoral edema	Brain metastases group (n = 50)	High-grade glioma group (n = 28)	χ^2	P
None	4	0	8.777	0.032
Mild	7	1		
Moderate	16	5		
Severe	23	22		

ity of variance. Groups were compared using the independent samples t-tests, and the comparisons between different regions within a group were conducted using paired samples t-tests. Continuous variables are expressed as the mean ± standard deviation. The count data were examined using Pearson's chi-square test. $P < 0.05$ indicated a statistically significant difference.

Results

Baseline data

No significant differences were found in terms of age, gender, or the occurrences of neurological symptoms between the brain metastases group and the high-grade gliomas group (all $P > 0.05$), but intergroup differences were observed in the tumor morphology and the incidences of intratumoral hemorrhage (both $P < 0.01$). See **Table 1**.

Degree of peritumoral edema

Differences were also observed in the degree of peritumoral edema between the brain

metastases group and the high-grade gliomas group ($P < 0.05$). See **Table 2**.

ADC and FA values at different regions in the two groups

In the tumor parenchymal area, the FA value in the brain metastases group was lower than it was in the high-grade glioma group ($P < 0.001$), but the ADC value did not differ between the two groups ($P > 0.05$). In the peritumoral edema area, the ADC value was higher in the brain metastases group than in the high-grade glioma group ($P < 0.001$), but the FA value did not differ between the two groups ($P > 0.05$). See **Table 3**.

rCBV and rCBF at different regions in the two groups

In the tumor parenchymal area, the rCBV and rCBF values in the brain metastases group were similar to those in the high-grade glioma group (both $P > 0.05$). In the peritumoral edema area, the rCBV and rCBF values in the brain metastases group were lower than they were in the high-grade glioma group (both $P < 0.001$). See **Table 4**.

Imaging of brain metastases and high-grade gliomas

The DTI results showed that, in the peritumoral edema area, the ADC value in the brain metastases group was higher than it was in the high-grade glioma group, and the rCBV and rCBF values in the brain metastases group were lower than they were in the high-grade glioma group. In the tumor parenchymal area, the FA value in the brain metastases group was lower than it was in the high-grade glioma group. See **Figures 1 and 2**.

Discussion

MRI plain scan is often applied in the differential diagnosis of high-grade gliomas and brain

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Table 3. The ADC and FA values in the different regions in the two groups

	ADC		FA	
	Tumor parenchyma area	Peritumoral edema area	Tumor parenchyma area	Peritumoral edema area
Brain metastases group (n = 50)	1.408±0.487	2.276±0.523	0.135±0.059	0.198±0.087
High-grade glioma group (n = 28)	1.395±0.512	1.927±0.438	0.247±0.103	0.224±0.095
t	0.131	3.525	7.319	1.451
P	0.896	<0.001	<0.001	0.150

Note: ADC: average diffusion coefficient; FA: fractional anisotropy.

Table 4. The rCBV and rCBF values in the different regions in the two groups

	rCBV		rCBF	
	Tumor parenchyma area	Peritumoral edema area	Tumor parenchyma area	Peritumoral edema area
Brain metastases group (n = 74)	5.61±1.33	1.24±0.35	5.04±0.61	0.92±0.27
High-grade glioma group (n = 38)	5.57±1.27	1.68±0.28	4.98±0.71	1.27±0.24
t	0.153	6.179	0.466	6.738
P	0.879	<0.001	0.642	<0.001

Note: rCBF: regional cerebral blood flow; rCBV: regional cerebral blood volume.

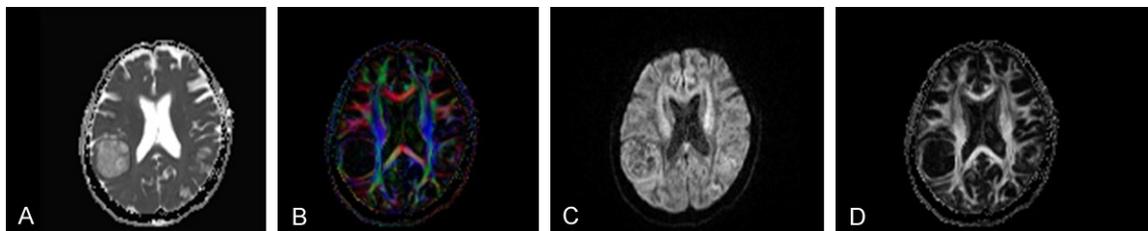


Figure 1. DTI of brain metastases from pancreatic cancer, patient: female, 55 years of age. A: ADC result; B: FA result; C: DWI result; D: FA result. DTI: diffusion tensor imaging; ADC: average diffusion coefficient; FA: fractional anisotropy; DWI: diffusion-weighted imaging.

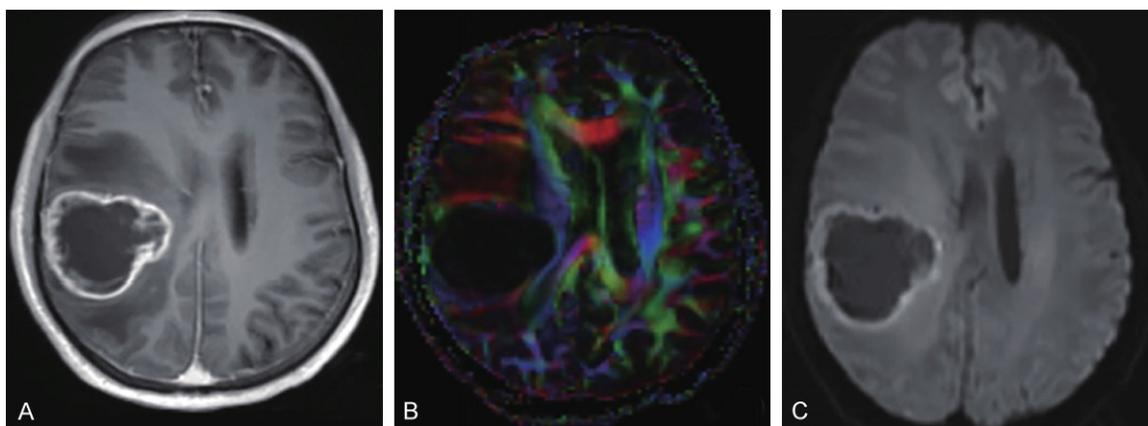


Figure 2. DTI of high-grade glioma, patient: male, 45 years of age. A: Enhanced visualization of DTI; B: DTI result; C: DWI result. DTI: diffusion tensor imaging. DWI: diffusion-weighted imaging.

metastases by observing the tumor morphology, boundary, bleeding, and cystic necrosis [10-

12]. However, this method often requires subjective judgment by doctors and lacks an objec-

tive basis. DTI is a method of assessing the white matter fiber bundles by mainly measuring FA and ADC. When a tumor develops in the brain tissues, the FA and ADC values are changed in the imaging due to the invasion of cancer cells in the surrounding tissues, the disorganized arrangement of the tumor structure, and the edema caused by the tumor compressing the surrounding tissues [13]. Therefore, assessing the changes in the FA and ADC values can help to identify the nature of the tumor. FA is a marker reflecting the degree of anisotropic water diffusion [14]. Both brain metastases and high-grade glioma can show a reduction in the FA value due to nerve fiber bundle damage. However, glioma can produce an extracellular matrix that causes tumor cell adsorption and migration, thereby slowing down the decrease of FA [15]. In the present study, we also found that the FA value in brain metastases was lower than it is in high-grade glioma.

Previous studies have reported that evaluating the ADC value can help to diagnose and differentiate brain tumors [16]. ADC is a marker reflecting the water molecular diffusion. In tumors, the ADC value is decreased due to the complexity and limitation of water molecular diffusion. The ADC values decrease in both brain metastases and high-grade gliomas in the tumor parenchymal area, and the magnitudes of reductions in both cases are similar [17]. Brain metastases occur when the cancer cells in another part of the body travel to the brain tissue. Metastatic brain tumors can compress the surrounding tissue and damage the blood-brain barrier, eventually causing vasogenic edema around the tumor. In glioma, since the peritumoral edema is caused by the tumor cell infiltration and the edema area is filled with a large number of tumor cells, the water molecular diffusion in the peritumoral edema is quite limited. Unlike glioma, the water molecular diffusion in the peritumoral edema in brain metastases is easier, which can explain why the ADC value in the peritumoral edema in the brain metastases are higher than they are in the glioma [18, 19]. Some studies suggested that ADC value can be an essential marker in the differentiation of brain tumors and can be used to monitor the early response of brain tumors to radiotherapy and chemotherapy [20, 21].

Some studies have revealed that the cerebral blood flow is also a key maker in identifying the

nature of a tumor [8]. Both rCBF and rCBV can reflect cerebral blood flow. The peritumoral brain edema induced by brain glioma is due to the infiltration of the tumor cells to the surrounding tissues, but in brain metastases, the edema is caused by the compression of the tumor parenchyma on the surrounding tissues. The compression of the brain metastases on the surrounding tissues can affect the blood-brain barrier and can cause thinning and narrowing of the blood vessels and low blood perfusion. Thus, the rCBF and rCBV values measured in the brain metastases were lower than those in the gliomas [21]. Some researchers even speculate that the determination of cerebral blood flow in patients with brain metastases may help to identify the location of the primary tumor [22].

In conclusion, compared with high-grade glioma, brain metastases have lower FA values in the tumor parenchyma area, higher ADC values in the peritumoral edema area, and lower rCBF and rCBV values in the peritumoral edema area. Multimodal MRI has a clinical value in the differential diagnosis of brain metastases and high-grade glioma. However, the study was a single-center study, and the sample size was small. Therefore, we need to carry out a multi-center study and increase the sample size in the future for verification.

Disclosure of conflict of interest

None.

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