

Stroke Mimics and Chameleons from the Radiological Viewpoint of Glioma Diagnosis

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Abstract

Gliomas are sometimes difficult to differentiate from strokes and are often misdiagnosed on magnetic resonance imaging (MRI); thus, the terms “stroke mimics” and “stroke chameleons” have been introduced. In this study, we analyzed stroke mimics and stroke chameleons in glioma and discussed the diagnostic perplexity. We retrospectively reviewed cases that were removed from lesions that were considered to be brain tumors. This study enrolled 214 patients who underwent tumor resection for suspected glioma. Clinical characteristics and radiological findings of the patients were compared between the masquerade findings group, which was further divided into two groups: the stroke chameleons and stroke mimics according to their final diagnosis, and the intelligible findings group. Stroke chameleons and stroke mimics were significantly higher in age and smaller in lesion size than the intelligible findings group. In the multivariate analysis, the predictive factor of the masquerade finding group was higher age and smaller size. Stroke mimics group has a tendency to be higher rate of hyperintensity lesion on diffusion-weighted imaging (DWI) compared with stroke chameleons group. The average period from initial diagnosis to pathological diagnosis was 13.50 days in the stroke chameleons and 61.50 days in the stroke mimics, which proved significantly different. Proper diagnosis of glioma and stroke affects a patient’s prognosis, and should be diagnosed as soon as possible. However, stroke mimics and stroke chameleons caused by glioma can occur. Thus, the diagnosis of a stroke should take into consideration the possibility of a glioma in real clinical situations.

Keywords: glioma, stroke, stroke mimics, stroke chameleons

Introduction

Stroke is a medical emergency for patients because it may lead to severe disability or, in worse-case scenarios, death.^{1,2} Most strokes present with sudden onset focal neurologic disorder.³ However, fair clinical outcomes can be achieved by some ischemic stroke patients through intravenous thrombolysis and mechanical thrombectomy,^{4–6} or by controlling blood

pressure, treating coagulation disorders, and performing surgical evacuation of hematoma for hemorrhagic stroke patients.⁷ Thus, patients should receive immediate treatment with an accurate diagnosis as soon as possible from pre-hospital clinical information and appropriate clinical examination.⁸ The typical clinical sign of a stroke is the sudden onset of a focal neurological disorder with maximum intensity at onset. Other disorders that may be associated with a similar clinical sign include false-positive conditions called “stroke mimics.”⁹ Conversely, strokes may also show atypical clinical signs, such as when the clinical onset is not sudden or when the clinical sign is not explained by the lesion. These false-negative conditions are called “stroke chameleons”

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because the clinical sign suggests another disorder.¹⁰⁾ However, the terms “stroke mimics” and “stroke chameleons” are typically focused on the physical examination and little attention has been paid to the radiological viewpoint.¹¹⁾

Gliomas are a type of primary brain neoplasm mainly based on their morphological resemblance to glial cells. Malignant gliomas, especially glioblastomas, remain lethal even today with an approximate 9.8% 5-year survival rate.¹²⁾ There is no doubt that histopathological diagnosis is necessary for the final diagnosis of glioma. However, gliomas are sometimes difficult to differentiate from stroke and are often misdiagnosed on magnetic resonance imaging (MRI)¹³⁾; thus, the terms “stroke mimics” and “stroke chameleons” have also been included in gliomas. In this study, we analyzed patients with masquerade findings including stroke mimics and stroke chameleons in glioma and investigated the clinical characteristics of these patients and the appropriate timing for the invasive treatment.

Materials and Methods

Study population

We retrospectively reviewed pathological records for lesions that were considered to be a brain tumor. In total, 557 patients received brain tumor removal at Sapporo Medical University between January 2011 and September 2019. Of these, patients who were diagnosed with glioma and/or were suspected of having glioma were analyzed. Initial diagnosis was defined as the diagnosis made by the first physician for patients that were referred from other hospitals. In this study, stroke mimics and stroke chameleons were defined as follows: stroke mimic is a condition resembling a stroke (a false-positive stroke diagnosis) and stroke chameleon is a condition that appears to be different from a stroke but is actually a stroke (a false-negative stroke diagnosis). Pathological diagnosis was based on the WHO guidelines. As revised in 2016, the description of final pathological diagnosis was defined as the time of obtaining specimens. All diagnoses were performed by pathologists at Sapporo Medical University. In this study, stroke mimic and stroke chameleon cases were categorized as the masquerade findings group. On the other hand, patients diagnosed intelligibly as glioma were categorized into the intelligible glioma group, which were diagnosed radiologically from the outset. Characteristics of the patients, including age, sex, image findings, and stroke type, were compared between stroke mimics, stroke chameleons, and glioma. Stroke mimics and stroke chameleons were analyzed in glioma, and the clinical characteristics and appropriate

time of changing for the invasive treatment were investigated.

Radiological examination

MRI examinations were performed using Signa HDxt 3.0T ver16.1 (GE Healthcare, Arlington Heights, IL, USA) and Ingenia 3.0T R5.4.1 (Philips Healthcare, Amsterdam, Netherlands) using an 8-channel head coil. For the diagnosis of brain tumors, T1-weighted imaging, gadolinium (Gd)-enhanced T1-weighted imaging, T2-weighted imaging, fluid-attenuated inversion recovery (FLAIR) imaging, T2*-weighted imaging, three-dimensional arterial spin labeling (3D-ASL) imaging, diffusion-weighted imaging (DWI), and proton magnetic resonance spectroscopy (¹H-MRS) were used. The parameters of T1-weighted imaging were as follows: 3D-spoiled gradient echo, Repetition time (TR) 20 ms, Echo time (TE) 3.2 ms, Flip angle 20°, Field of view (FOV) 200 mm, Voxel size 0.62 × 0.89 × 2 mm, gap 0 mm, Slice 54, NEX 1, and scan time 2:50 seconds. The parameters of Gd-enhanced T1-weighted imaging were as follows: 3D-spoiled gradient echo, TR 20 ms, TE 3.2 ms, Flip angle 20°, FOV 200 mm, Voxel size 0.62 × 0.89 × 2 mm, gap 0 mm, Slice 54, NEX 1, and scan time 2:50 seconds. The parameters of T2-weighted imaging were as follows: Fast Spin echo, TR 4500 ms, TE 100 ms, Flip angle 90°, ETL 19, FOV 200 mm, Voxel size 0.52 × 0.78 × 3 mm, gap 1 mm, NEX 1, Slice 36, and scan time 1:08 minutes. The parameters of FLAIR imaging were as follows: Fast Spin echo, TR 10000 ms, TE 140 ms, Flip angle 90°, ETL 44, Inversion time 2600 ms, FOV 200 mm, Voxel size 0.62 × 1.04 × 3 mm, gap 1 mm, NEX 1, Slice 36, and scan time 3:20 minutes. The parameters of T2*-weighted imaging were as follows: gradient echo, TR 500 ms, TE 25 ms, Flip angle 20°, FOV 200 mm, Voxel size 0.62 × 1.04 × 3 mm, gap 1 mm, Slice 36, NEX 1, and scan time 3:32 minutes. The parameters of 3D-ASL imaging were as follows: TR 4500 ms, TE 9.4 ms, FOV 240 mm, Voxel size 3.75 × 3.75 × 5 mm, gap 0 mm, PLD 1525 ms, Slice 30, NEX 2, and scan time 3:09 minutes. The parameters of ¹H-MRS were as follows: Single voxel press, TR 3000 ms, TE 35 ms, Voxel size 15 × 15 × 15 mm, NEX 64, and scan time 4:12 minutes.

Computed tomography (CT) examination was performed using a multidetector-row CT scanner with 80 rows (Aquilion Prime; Canon Medical Systems, Tokyo, Japan). The following 3D CT scanning parameters were used: tube voltage = 120 kV, collimation = 0.5 mm × 80, 0.75 second per rotation, slice thickness = 0.5 mm, and slice interval = 0.25 mm. A total of 0.7–1.1 mL/Kg iopamidol (Iopamiron 370; Bayer Healthcare, Leverkusen, Germany), a low-osmolar, iodinated contrast material, was administered

intravenously using a bolus tracking method. The protocol for the contrast material injection has been previously described.¹⁴⁾

Statistical analysis

Data are presented as median (interquartile range) values. The Mann–Whitney U test and Fisher's exact probability test were used to compare the clinical and radiological characteristics between the masquerade findings group and the intelligible findings group. Subsequently, stroke chameleons and stroke mimics cases were compared similarly. For test results with p values of <0.25 in diagnostic difficulty, a simple logistic regression was used in the univariate analyses. Odds ratios (ORs) were obtained through these models with 95% confidence intervals (CIs). Each item was then selected according to stepwise methods (model selection criterion, 0.10), and a multivariate analysis of all potential predictive factors for a masquerade finding was performed. All statistical analyses were conducted using the SPSS software (version 22; IBM Corp., Armonk, New York, USA), and $p < 0.05$ was considered to be indicative of statistical significance.

Results

Patient data

This study enrolled 214 patients who underwent tumor resection or preoperative biopsy for suspected glioma. The median age was 55.0 years (interquartile range: 35.0–66.0). The lesion locations were mainly in the cortical and subcortical regions (175 cases), while some were in the deep-seated, cerebellum, and brainstem areas (39 cases). The clinical symptoms of the patients during the follow-up periods until final diagnosis were as follows: neurological symptoms due to mass effect in 137 cases, seizure in 52 cases, and 14 cases were asymptomatic. A patient had overlapping neurological symptoms due to mass effect and seizure. The breakdown of WHO grade of gliomas in total 210 cases (the intelligible findings group and stroke mimic group) was as follows: grade I in 15 cases, grade II in 68 cases, grade III in 68 cases, and grade IV in 90 cases.

A total 12 cases (5.6%) were included in the masquerade findings group, and of these, 4 cases were stroke chameleons and 8 cases were stroke mimics. The baseline characteristics of patients are shown in Table 1. The median age was 65.0 years (interquartile range: 63.0–68.0) in the masquerade findings group and 53.0 years (interquartile range: 34.0–63.0) in the intelligible findings group, indicating that younger patients were more intelligibly diagnosed with glioma ($p = 0.004$). In addition, motor weakness was significantly higher in the masquerade findings

group ($p = 0.040$), and maximum diameter of the lesions was significantly larger in the intelligible findings group ($p < 0.001$). There were no significant differences in sex, other symptoms (sensory disturbance, aphasia, seizure, headache, and cognitive dysfunction), Karnofsky Performance Status (KPS) score, presence of multiple lesions, location, and radiological variations such as Gd enhancement, DWI, 3D-ASL, or T2*-weighted imaging between the two groups. ¹H-MRS data were smaller than other modalities, and the number of patients who received ¹H-MRS is 5 cases in the masquerade findings group and 112 cases in the intelligible findings group. N-acetyl aspartate (NAA) decreased pattern of ¹H-MRS was higher in the intelligible findings group, although normal pattern, lactate (Lac) increased pattern, and choline-containing compounds (Cho)/creatine and phosphocreatine (Cr) ratio increased pattern were not different between the two groups. Each data item was also compared among three groups (stroke chameleons, stroke mimics, and intelligible findings group) and there was not much of a difference in trends between two and three comparisons. The risk factors associated with diagnostic difficulty in patients with suspicious gliomas are presented in Table 2 as identified by univariate and multivariate analyses. Each item of ¹H-MRS was excluded from these analyses due to certain level of lack of data. In the univariate analysis, the diagnostic difficulty was associated with age (OR, 1.053; 95% CI, 1.010–1.097; $p = 0.015$), motor weakness (OR, 3.467; 95% CI, 1.066–1.273; $p = 0.039$), and size (OR, 0.944; 95% CI, 0.911–0.979; $p = 0.002$). In the multivariate analysis, only two items were selected according to stepwise methods and a significant difference was noted in the age (OR, 1.060; 95% CI, 1.015–1.107; $p = 0.008$) and size (OR, 0.936; 95% CI, 0.898–0.976; $p = 0.002$).

The masquerade findings cases were classified into two subtypes according to the diagnostic difficulty: stroke chameleons and stroke mimics. Table 3 shows the clinical and radiological characteristics in the stroke chameleons group and the stroke mimics group. The stroke chameleons group included four cases, while the stroke mimics group included eight cases. The median age was 65.0 years (range: 58.3–78.5) in the stroke chameleons group, and 65.0 years (range: 63.0–68.5) in the stroke mimics group revealing a lack of statistical difference between these two groups ($p = 0.933$). The period from initial diagnosis to final pathological diagnosis was 13.5 days (range: 7.8–20.0) in the stroke chameleons group and 61.5 days (range: 50.0–111.5) in the stroke mimics group. In this case, there was a significant difference ($p = 0.004$), indicating that the stroke chameleons group required a longer time to receive the correct diagnosis.

Table 1 Clinical characteristics of patients in the masquerade findings group and intelligible findings group

		Total	Masquerade findings group	Stroke chameleons	Stroke mimics	Intelligible findings group	p value*
N		214	12	4	8	202	
Age		55.0 (35.0–66.0)	65.0 (63.0–68.0)	65.0 (58.3–78.5)	64.5 (63.0–68.5)	53.0 (34.0–63.0)	0.004 (0.015)
Sex (Male/Female)		115/99	5/7	2/2	3/5	110/92	0.388 (0.623)
Symptom onset	Motor weakness	51	6	2	4	45	0.040 (0.141)
	Aphasia	20	0	0	0	20	0.609 (0.488)
	Sensory disturbance	13	1	0	1	12	0.538 (0.300)
	Seizure	56	2	1	1	54	0.736 (0.630)
	Headache	41	0	0	0	41	0.129 (0.194)
	Cognitive dysfunction	8	0	0	0	8	1.000 (0.764)
KPS			90 (80–90)	85 (80–97.5)	90 (67.5–90)	90 (80–90)	0.906 (0.931)
Location	Cortical/subcortical	175	9	2	7	166	0.461 (0.411)
	Deepbrain/cerebellum/brainstem	39	3	2	1	36	
Multiple lesion		13	1	1	0	12	0.538 (0.329)
Size (maximum diameter of lesion) (mm)		55.64 (35.81–72.75)	28.02 (19.85–44.69)	19.12 (12.60–49.17)	31.12 (21.63–44.82)	57.01 (38.05–75.41)	0.000 (0.002)
Gd enhancement (+)		151/212	10/11	3/4	7/7	141/201	0.184 (0.203)
DWI hyperintensity (+)		112/212	7/12	0/4	6/8	105/200	0.694 (0.380)
3D-ASL hyperintensity (+)		103/190	4/10	0/3	4/7	99/180	0.273 (0.089)
T2* hypointensity (+)		54/172	4/10	2/3	2/7	50/162	0.386 (0.411)
¹ H-MRS	Normal pattern (NAA peak)	10/118	1/5	1/1	0/4	9/112	0.360 (0.087)
	NAA decreased pattern	59/118	0/5	0/1	0/4	59/112	0.030 (0.131)
	Lac increased pattern	51/118	0/5	0/1	0/4	51/112	0.057 (0.094)
	Cho/Cr ratio increased pattern	47/118	4/5	0/1	4/4	43/112	0.079 (0.023)

P value is a comparison between masquerade findings group and intelligible findings group, and () is p value of comparison among stroke chameleons, stroke mimics, and intelligible findings group. ASL: arterial spin labeling, Cho: choline-containing compounds, Cr: creatine and phosphocreatine, DWI: diffusion-weighted imaging, Gd: gadolinium, ¹H-MRS: proton magnetic resonance spectroscopy, KPS: Karnofsky Performance Status, Lac: lactate, NAA: N-acetyl aspartate, T2: T2*-weighted imaging.

From a radiological viewpoint, no cases showed hyperintensity on DWI in four cases in the stroke chameleons group. On the other hand, six cases revealed hyperintensity on DWI in the stroke mimics group. Although there was no significant difference

between the two groups ($p = 0.061$), indicating that the stroke mimics group is likely to show hyperintensity on DWI upon initial presentation. There was no significant difference in sex, symptoms, KPS score, presence of multiple lesions, location of tumors,

Table 2 Univariate and multivariate analyses of background characteristics of patients with masquerade findings who underwent lesionectomy

	Univariate analysis		Multivariate analysis	
	Odds ratio (95% CI)	p value	Odds ratio (95% CI)	p value
Age	1.053 (1.010–1.097)	0.015	1.060 (1.015–1.107)	0.008
Motor weakness	3.467 (1.066–1.273)	0.039		
Headache	0.000 (0.000)	0.998		
Gd enhancement	4.255 (0.533–33.984)	0.172		
Size	0.944 (0.911–0.979)	0.002	0.936 (0.898–0.976)	0.002

Gd: gadolinium.

Table 3 Clinical characteristics of patients in the stroke chameleons and stroke mimics

		Stroke chameleons	Stroke mimics	p value
n		4	8	
Age		65.0 (58.3–78.5)	64.5 (63.0–68.5)	0.933
Sex (male/female)		2/2	3/5	
Symptom onset	Motor weakness	2	4	1.000
	Aphasia	0	0	
	Sensory disturbance	0	1	1.000
	Seizure	1	1	1.000
	Headache	0	0	
	Cognitive dysfunction	0	0	
KPS		85 (80–97.5)	90 (67.5–90)	0.933
Location	Cortical/subcortical	2	7	0.236
	Deepbrain/cerebellum/brainstem	2	1	
Multiple lesion		1	0	0.333
Gd enhancement (+)		3	7	0.364
DWI hyperintensity (+)		0	6	0.061
3D-ASL hyperintensity (+)		0	4	0.167
T2* hypointensity (+)		2	2	0.333
¹ H-MRS	Normal pattern (NAA peak)	1/1	0/4	0.200
	NAA decreased pattern	0/1	0/4	
	Lac increased pattern	0/1	0/4	
	Cho/Cr ratio increased pattern	0/1	4/4	0.200
Size (maximum diameter of lesion) (mm)		19.12 (12.60–49.17)	31.12 (21.63–44.82)	0.368
Period from initial diagnosis to pathological diagnosis (days)		13.50 (7.75–20.00)	61.50 (50.00–111.50)	0.004

ASL: arterial spin labeling, Cho: choline-containing compounds, Cr: creatine and phosphocreatine, DWI: diffusion-weighted imaging, Gd: gadolinium, ¹H-MRS: proton magnetic resonance spectroscopy, KPS: Karnofsky Performance Status, Lac: lactate, NAA: N-acetyl aspartate, T2*: T2*-weighted imaging.

radiological variations such as Gd enhancement, DWI, 3D-ASL, T2*-weighted imaging, or ¹H-MRS, and maximum diameter of the lesion between the two groups. The breakdown of WHO grade in stroke mimics was as follows: grade I in 3 cases, grade II in 5 cases, and no cases in grades III and IV.

Representative cases

Figures 1 and 2 show two representative cases. A 65-year-old male suffered dizziness and gait disturbance from the day prior and received medical examinations from our affiliated hospital. MRI showed hyperintensity in the right cerebellar

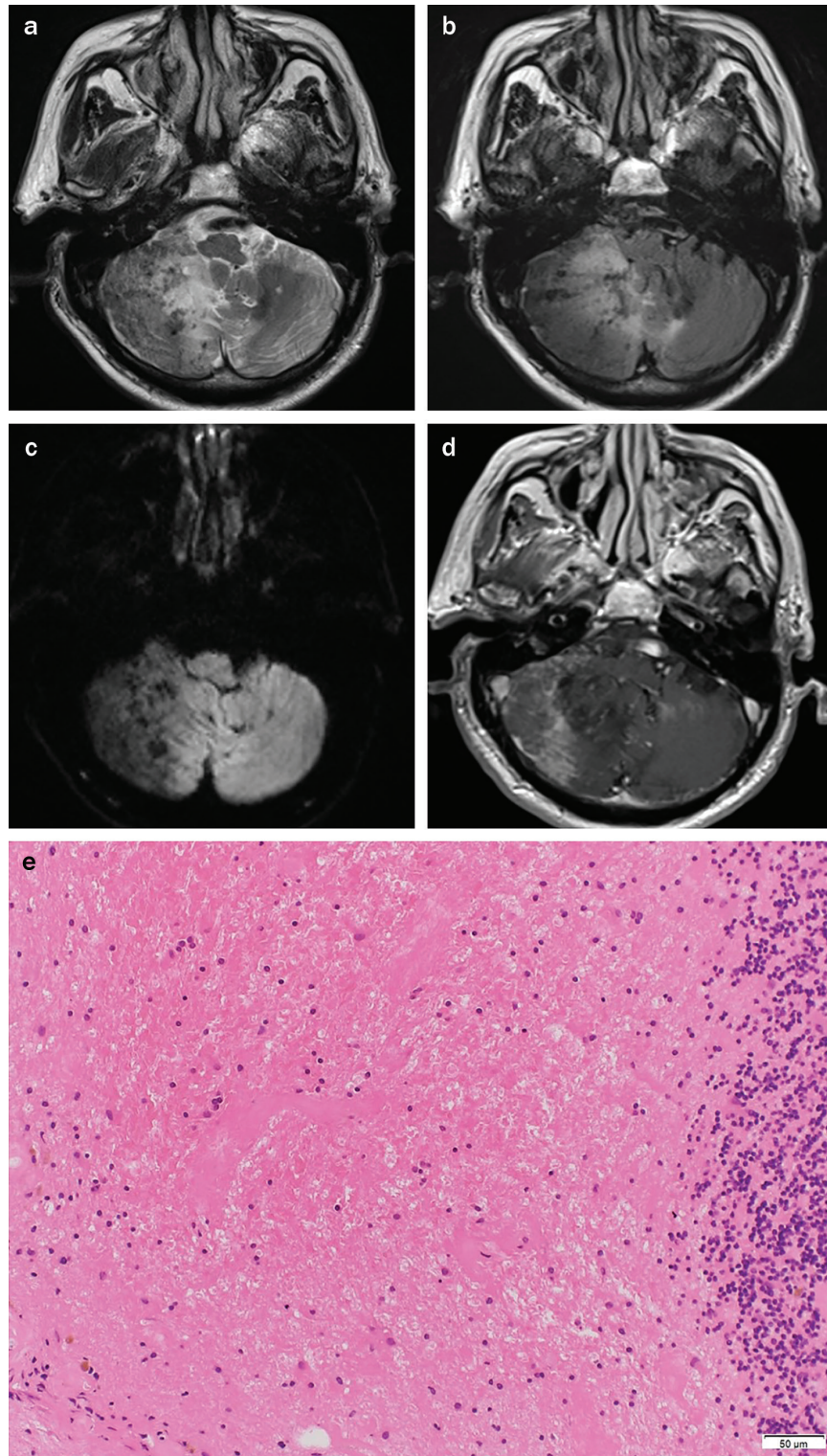


Fig. 1 MRI showed hypersignal intensity in the right cerebellar hemisphere including the cerebellar peduncle on T2-weighted imaging (a) and FLAIR imaging (b). DWI showed hyposignal intensity (c) and speckled enhancement with Gd on T1-weighted imaging (d). Histopathological specimen showed normal cerebellar tissue, including necrosis, lymphocytic infiltration, and hemosiderin deposition (e). No malignant tumor cells were found in the preparation. FLAIR: fluid-attenuated inversion recovery, DWI: diffusion-weighted imaging, MRI: magnetic resonance imaging.

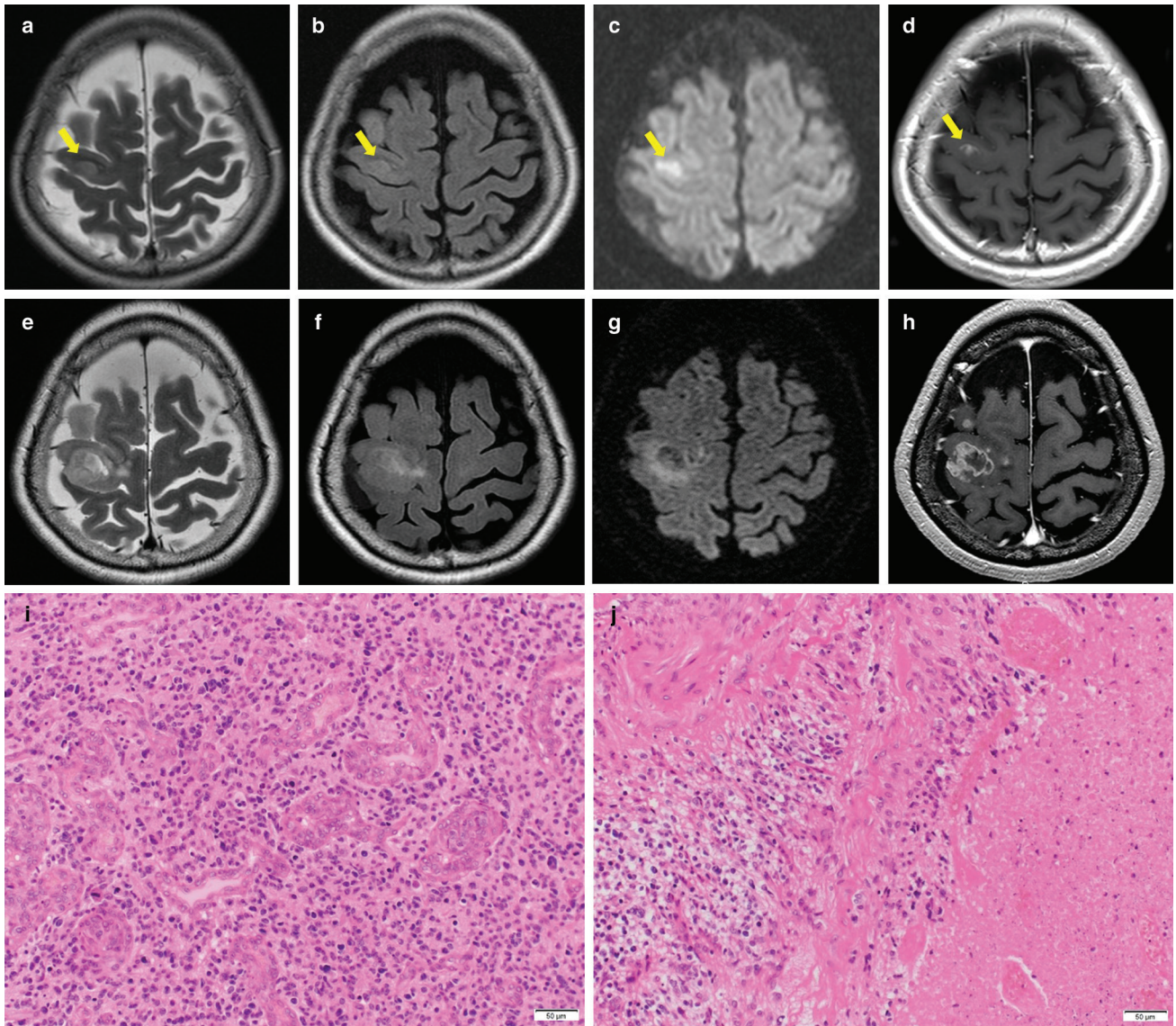


Fig. 2 MRI upon initial diagnosis showed hypersignal lesion at the right motor cortex on T2-weighted imaging (a), FLAIR imaging (b), and DWI (c). Gd enhancement on T1-weighted imaging was slightly (d). MRI at 71 days after initial diagnosis showed enlargement on T2-weighted imaging (e), FLAIR imaging (f), and DWI (g). The lesion revealed ring-like enhancement (h). Histopathological specimen showed the microvascular hyperplasia (i) and necrotic foci surrounded pseudopalisading cells (j). FLAIR: fluid-attenuated inversion recovery, DWI: diffusion-weighted imaging, MRI: magnetic resonance imaging.

hemisphere including the cerebellar peduncle on T2-weighted imaging and FLAIR imaging. DWI showed hypointensity and speckled enhancement with Gd on T1-weighted imaging. From the results, the patient was considered as having suspicious glioma, and swelling of cerebellar hemisphere and compression of brainstem were considered getting worse. After all, he was transferred to our hospital, where biopsy and decompressive craniotomy were performed urgently. Frozen section diagnosis revealed normal cerebellar tissue, including necrosis,

lymphocytic infiltration, and hemosiderin deposition. No malignant tumor cells were found in the permanent preparation. The final pathological diagnosis was a hemorrhagic infarction and was thus considered a stroke chameleon. The patient was treated with antiplatelet medicine with neurological symptoms recovering after rehabilitation.

Another case is that of a 57-year-old female. The patient experienced a sudden impairment of elaborate movement in her left upper limb and received medical examinations from our affiliated hospital.

MRI showed hyperintensity in the right motor cortex on DWI, T2-weighted imaging, and FLAIR imaging. Gd enhancement on T1-weighted imaging was slightly. The patient was thought to have suffered an ischemic stroke of subacute phase and was treated conservatively. After leaving the hospital, she suffered a seizure. The lesion was enlarged with ring-like Gd enhancement 71 days after initial diagnosis. The lesion was removed in our hospital, and the final pathological diagnosis was a glioblastoma. After tumor removal, chemotherapy (temozolomide) and radiotherapy were performed with chemotherapy continuing for 9 months.

Discussion

Our hospital and our affiliated hospital have introduced the use of MRI in the early evaluation of suspected stroke patients. Nevertheless, 5.6% of all suspicious glioma patients were still initially misdiagnosed at the onset. The annual incidence of ischemic stroke is 120–151.6 cases per 100000 population in Japan,¹⁵⁾ and the annual incidence of glioma in Japan is 2.67 cases per 100000 population.¹⁶⁾ From these numbers, MRI is presumed to be performed in about 9000–11000 cases of stroke diagnoses in our hospital and our affiliated hospital. Based on this, the incidence of misdiagnosis in acute stroke diagnosis is approximately 0.1%. This might be the current limitation of stroke diagnosis based on DWI. In recent advancements of acute stroke therapy, the role of MRI is to select patients eligible for thrombolytic therapy and mechanical thrombectomy. Of course, this is a fundamental principle in ischemic stroke therapy. However, the majority of patients in the frontline stroke center has ischemic stroke, and it is difficult to screen for patients with brain tumors. Thus, it should be considered a serious problem that requires further improvement. On the other hand, prognosis of malignant glioma is still extremely poor. The median survival of patients with glioblastoma is 14.6 months with the current standard of treatment involving radiotherapy and temozolomide.¹⁷⁾ The diagnostic delay of 2 months is regretful for patients with malignant glioma. However, prognosis may change if the patient is diagnosed before malignant transformation even in low-grade glioma. When a patient is misdiagnosed with ischemic stroke, we need more than 2 months so that we are freed from the spellbinding of the misdiagnosis. Conversely, MRI follow-up before pathological diagnosis should be performed within 2 months in patients with suspected stroke mimics caused by glioma.

Based on this study, diagnostic perplexity is associated with in cases with higher age and smaller

lesion in real clinical practice. These clinical characteristics are typical in stroke, and an inevitable result. In these cases, close attention should be required for differential diagnosis of stroke and glioma. From the view point of the radiological findings, signal intensity of DWI and Gd enhancement can cause misleading of the correct diagnosis. In this series, the stroke mimics group showed relative hyperintensity signal on DWI, while the stroke chameleons group showed hypointensity signal. Conversely, stroke chameleons included cases without Gd enhancement, while most of the stroke mimics cases were with Gd enhancement. Many strokologists consider hypointensity signal on DWI as a unique finding of ischemic stroke and Gd enhancement is revealed in the chronic stage of ischemic stroke. Although the ADC value of glioblastoma is higher than that of lymphoma,¹⁸⁾ diffusion restriction was present in 25%–30% of glioblastoma.^{19,20)} Moreover, the ADC value of high-grade glioma is lower than that of low-grade glioma.²¹⁾ Kolakshyapati et al. have reported that the presence of non-enhancing peritumoral DWI hyperintensity signal lesion is a specific finding of glioblastoma and indicates poor prognosis.²⁰⁾ Tumor ischemia due to insufficient vascular proliferation and neovascularization causes peritumoral DWI hyperintensity signal, which precedes abnormal enhancement and BBB disruption.^{22,23)} In the stroke mimics group of this study, six of eight cases (75.0%) with hyperintensity signal lesion on DWI were high-grade glioma included three cases of glioblastoma. In acute stroke diagnosis, strokologists are in the shackles of DWI findings. It should be recognized that glioblastoma is rarely misdiagnosed as ischemic stroke in subacute studies. In addition, the results of this study indicate that ¹H-MRS might be useful to diagnosis just like exactly the same well known from past studies, even though it was small data. This point must be careful that it does not bring a definitive diagnosis, but is just a supplementary modality. Therefore, patients who have not diagnosed either glioma or stroke should be received ¹H-MRS study as possible because it might be useful for auxiliary diagnosis.

University hospitals and cancer centers included our hospital have more kinds of diagnostic modality than affiliated municipal hospitals. And the distribution of treated diseases between university hospitals and municipal hospitals is completely different. Thus, medical disparity in diagnostic experiences is present. In this report, we advocated the diagnostic problem of glioma and stroke in real clinical practice.

Our study has several limitations. In this article, we examined the differences between stroke and glioma. Patients who were diagnosed with gliomas and/or were suspected of gliomas were included. Other pathologies, including multiple sclerosis and

lymphoma, which appear similar to these lesions radiologically, were excluded. In the real clinical world, strokes should be screened in a short time. Second, we did not register whole stroke patients. As a result, there is a possibility that this study did not capture the entire overview of the misdiagnosis of ischemic stroke. Third, we could not obtain other radiological data completely such as T2*-weighted imaging, 3D-ASL, or ¹H-MRS due to lack of data. Because the possible MRI scans in each affiliated hospital is different, and there was lack of time due to emergency surgery in cases with neurological deterioration has been progressed. Furthermore, ¹¹C-methionine positron emission tomography (PET) is not approved by the medical insurance in Japan. Then, we could not examine ¹¹C-methionine PET, although it is widely known as the validity of glioma diagnosis.

Conclusion

Diagnosis of glioma and stroke affects a patient's prognosis and should be assessed as soon as possible. However, misdiagnoses, such as stroke mimics and stroke chameleons caused or characterized by glioma, can occur. It is particularly important in cases of stroke mimic patients as treatment may be delayed, and the patient might be beyond cure. The diagnosis of a stroke should take into consideration the possibility of a glioma in clinical situations.

Statement of Ethics

This study was approved by the Ethics Committee of Sapporo Medical University Hospital (IRB number 292-128) and was performed in accordance with the ethical standards of the 1964 Declaration of Helsinki and its later amendments. This study was a prospective and observational study. As this study had a retrospective design, patient consent was obtained with an opt-out policy using a website.

Conflict of Interest Disclosure

The authors have no conflicts of interest to declare.

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