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Clinical Article

Radiological Characteristics of Peritumoral Edema in Meningiomas

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Objective : The purpose of this study is to evaluate the radiological charactersitics related to the formation of peritumoral edema in meningiomas.
Methods : Fifty patients with meningioma were examined by magnetic resonance images and cerebral angiography. The predictive factors associated peritumoral edema, such as, tumor size, peritumoral rim (cerebrospinal fluid cleft), shape of tumor margin, signal intensity of tumor in T2WI, and pial blood supply were evaluated.
Results : Tumor size, peritumoral rim and pial blood supply correlated with peritumoral edema on univariate analyses. But in multivariate analyses, pial blood supply was statistically significant as a factor for peritumoral edema in meningioma.
Conclusion : In our results, pial blood supply is significant contributing factor for peritumoral edema in meningioma.

KEY WORDS : Meningioma · Peritumoral edema · Magnetic resonance image · Pial blood supply.

Introduction

Meningioma possesses the ability to produce peritumoral brain edema(PTBE) despite the fact that it is extracerebral origin, and benign, slow-growing tumor[15]. Peritumoral edema is present in at least half of the cases of the meningiomas, and it may be present in varying degree and in unpredictable fashion[15]. Though tumor size, location of tumor, histologic types, blood supply to tumors, level of endothelial growth factor(EGF), sex hormone in the tumors have been reported to correlate with peritumoral edema[9,10,12,13,17]. The mechanisms by which meningioma produces peritumoral edema is not fully elucidated. In this study, we retrospectively examined the magnetic resonance (MR) images of 50 patients who were diagnosed to have meningioma operatively and assessed the radiological characteristics associated with peritumoral edema in meningioma.

Patients and Methods

Between January 2000 and December 2003, fifty patients with histologically proven intracranial meningiomas, were studied preoperatively by MR image and cerebral angiography. We examined tumor size, peritumoral rim, shape of tumor margin, pial blood supply, and signal intensity of tumor on T2-weighted (T2WI) MR images. The presence of peritumoral edema was defined as a high signal intensity adjacent to tumors on T2WI. Tumor volume and edema were measured from MR image, in a manner similar to that of other authors[1]; maximal perpendicular diameters (radii a and b) of the tumor and the edema in the axial MR image sections were measured. Coronal diameters of the tumor and the

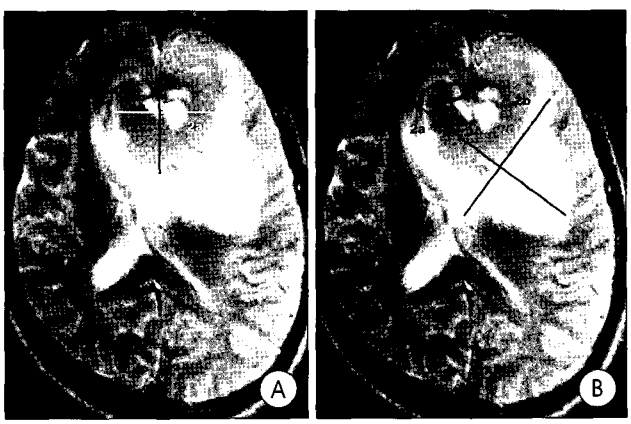

Fig. 1. A : Tumor volume (V_T) was measured from MR image, maximal perpendicular diameters (radii a and b) of the tumor. Coronal diameters of the tumor was approximated by coronal section images showing tumor tissue (radius c, not shown here). B : The resulting volume of tumor and edema (V_{T+E}) was then approximated using the formula for a spheroid : ($V = 4/3\ \pi \times abc$). Edema index(EI) = $(V_{T+E})/(V_T)$.

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edema were approximated by coronal section images showing tumor tissue and edema (radius c). The resulting volume of tumor and edema was then approximated using the formula for a spheroid : ($V = 4/3\pi \times abc$). The relation of peritumoral edema and tumor volume was defined as EI(edema index) = ($V_{Edema} + V_{Tumor}$)/V_{Tumor}, resulting in 1 when no edema was present[1,2] (Fig. 1). Tumor-brain interface was analyzed by two points of view, namely shape of tumor margin, and peritumoral rim (cerebrospinal fluid cleft). The signal intensity of meningioma was classified relative to that of the cortical gray matter on T2WI of MR images. We classified tumor margin as smooth and irregular group. The term "peritumoral rim" means a aperture that shows hypointensity on T1WI and hyperintensity on T2WI existing braintumor interface. The angiograms were evaluated to determine the presence of pial supply.

We examined the relationship between peritumoral edema and these factors by univariate and multivariate analyses. Statistical analysis was performed using commercially available computer software (SPSS 11 for window). Chi-square, Fisher, Mann-Whitney U tests, and Person's correlation coefficient were used for univariate analysis, and multivariate analyses were performed using the logistic regression method. Probability values of less than 0.05 were accepted as statistically significant.

Results

The patients studied included 11 men and 39 women whose age ranged between 29 and 73 years (average ± æ standard deviation, 53 ± 12years). Peritumoral edema was present in 18 cases, and absent in the other 32.

Tumor volume and PTBE

Tumor volume in the group with peritumoral edema (mean volume, 62.86cm^3) was significantly larger than in those without edema (mean volume, 36.42 cm^3: p=0.006, Mann-Whitney's U test) (Fig. 2). But tumor volume was not correlated with severity of PTBE (Pearson's correlation coefficient, co-rrelation coefficient(r)=0.191, p=0.183).

Peritumoral rim and PTBE

The incidence of brain edema was significantly higher in the non-peritumoral rim group than peritumoral rim group (p=0.018, Fisher's Exact Test). Peritumoral edema represents CSF space in the brain-tumor interface. There is a high possibility that tumor invades cortex in absence of rim (Table 1).

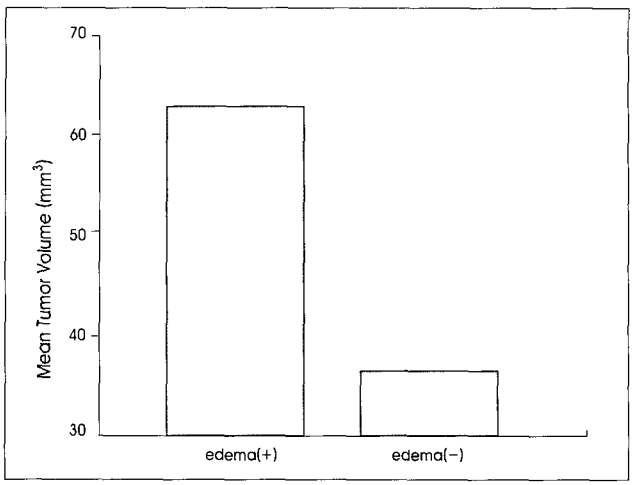

Fig. 2. Tumor volume correlated significantly with brain edema (p=0.006, Mann-Whitney U test).

Table 1. Peritumoral brain edema and peritumoral rim in brain magnetic resonance image

	Rim (+)	Rim (-)	Total
Edema (+)	5	13	18
Edema (-)	21	11	32
Total	26	24	50

p=0.018, (Fisher's Exact test)

Table 2. Peritumoral brain edema and shape of tumor margin in magnetic resonance image

	Regular margin	Irregular margin	Total
Edema (+)	9	9	18
Edema (-)	24	8	32
Total	33	17	50

p=0.119, (Fisher's Exact test)

Shape of tumor margin and PTBE

There was no significant correlation between irregularity of tumor margin and the presence of brain edema (p=0.119, Fisher's Exact Test). (Table 2).

Signal intensity of tumor on T2WI and PTBE

Of fourteen tumors whose signal intensity on T2WI was hypo- or isointense compared with gray matter, only one was accompanied by peritumoral edema. Of 36 tumors whose intensity was hyperintense compared with gray matter, 17 were accompanined by peritumoral edema. The incidence of peritumoral edema was significantly higher in the group with hyperintense tumor on T2WI than group with hypo or isointense tumor (p=0.009, Fisher's Exact Test) (Table 3).

Pial blood supply and PTBE

The incidence of peritumoral edema were higher in cases with a predominantly blood supply (p=0.001, Fisher's Exact

Table 3. Peritumoral brain edema and signal intensity of tumor on T2WI magnetic resonance image

	Low/iso signal	High signal	Total
Edema (+)	1	17	18
Edema (−)	13	19	32
Total	14	36	50

p=0.009, (Fisher Exact test)

Table 4. Peritumoral brain edema and pial blood supply

	Pial supply (−)	Pial supply (+)	Total
Edema (+)	8	10	18
Edema (−)	27	5	32
Total	35	15	50

p=0.001, (Fisher Exact test)

Table 5. Peritumoral edema and location of tumors

	Edema (+)	Edema (−)	Total
Convexity	3	8	11
Parasagittal, parafalcine	9	8	17
Frontal base	2	2	4
Parasellar	2	5	7
Posterior fossa	0	6	6
Temporal base	2	3	5
Total	18	32	50

Table 6. Peritumoral edema and histological types of tumors

	Edema (+)	Edema (−)	Total
Meningothelial	8	18	26
Fibroblastic	1	5	6
Transitional	2	5	7
Angioblastic	3	0	3
Atypical	4	0	4
Miscelleneous	0	4	4
Total	18	32	50

Table 7. Summary of univariate and multivariate statistical analyses

	Univariate[a]	Multivariate[b]
Tumor volume	0.006*	0.821
Peritumoral rim	0.018*	0.240
Shape of tumor	0.119	0.376
Signal intensity	0.009*	0.124
Pial blood supply	0.001*	0.031*

a : Chi-square, Fisher Exact test, Mann-Whitney U test b : Logistic regression method * : statistical significant, p<0.05

Test)(Table 4). Meningioma without pial blood supply had a small mean EI of 1.12. Pial supply correlated significantly with tumor size (p=0.011, Mann-Whitney U test).

Location of tumor and PTBE

Location of tumor were assessed from MR scan (Table 5). Although no significant correlation between location of tumor and peritumoral edema, peritumoral edema was not recognized in the posterior fossa meningioma. And parasagittal, parafalcine, frontal base, and temporal base meningioma frequently tended to develop peritumoral edema.

Histology and PTBE

Tumor histology associated with edema were evaulated (Table 6). Although no significant correlation was seen between benign histological type and edema, peritumoral edema frequently accompanied angioblastic and atypical types.

Multivariate analyses of predictive factors associated with PTBE

In mulitvariate logistic regression model, only vascular supply from pial-cortical arteries on angiographic studies significant correlated with peritumoral brain edema (p=0.031) (Table 7).

Discussion

Despite primarily extraaxial locations, slow progression rates, and usually benign histological characteristics, meningiomas frequently are associated with PTBE[3]. Peritumoral edema originates in the region of the tumor margin and travels by bulk flow through the relatively loosely interconnected fibers of white matter[6]. Peritumoral edema is found in approximately 50% of meningiomas[10]. But the exact pathogenesis of peritumoral brain edema in meningiomas is still unknown. Electron microscopic studies suggest that PTBE is of vasogenic origin, a type of brain edema that is attributed to dysfunctions of the blood-brain barrier[5,7]. However, the pathogenetic mechanisms that link primarily extracerebral meningiomas with blood-brain barrier disturbances remain obscure[1].

The results of author's studies suggest that meningiomas that are associated with peritumoral edema present large tumor, loss of peritumoral rim, high signal intensity of tumor on T2WI, and pial blood supply in univariate analyses. But in multivariate analyses, pial blood supply significantly correlated with PTBE. In our invastigation using MR images and cerebral angiography, loss of peritumoral rim and pial blood supply from intracerebral vessels were defined as the parameters to reveal cortical invasion of the tumor. The pial supply of meningiomas reflects the close spatial relationship between the tumor surface and the adjacent brain parenchyma. The ara-chnoid, which serves as a physiological barrier between the brain and extraaxial structures such as the meningioma, is either penetrated by the cerebral vessels or infiltrated by the tumor[2]. A recently published study demonstrated a strong

correlation between the adherence of the tumor to the surrounding brain tissue and the occurrence of edema[8].

Hyperintense signal on T2WI is considered a multifactorial process and is correlated with tumor consistency and vascularity indicating a higher water content[14]. We investigated the statistical correlation between intensity of tumor on T2WI and peritumoral edema (p=0.056). Hypointense tumors, by contrast, were accompanied by hardly any brain edema. This result seems to be due to the difference of water content in the tumors. The more water content tumors have, the more easily the edema fluid can diffuse to the surrounding brain tissue according to the water pressure gradient[14].

We found that atypical and angioblastic meningiomas tended to have more peritumoral edema and meningothelial meningiomas whose signal was relative high on T2WI, tended to develop peritumoral edema than fibrous meningiomas possibly due to difference of water content in the tumor. Smith et al[16] found that tumors with increased cellularity, vascularity, and mitotic activity had edema more frequently. Challa et al reported that more vascular tumors tend to have breakdown of capillary endothelial tight junctions, leading to increased permeability to water. And high vascularity may cause increased water content in the tumor[4].

In our results, although there was no correlation between tumor location and PTBE no PTBE was presented in the posterior fossa meningioma. This tendency may be due to the unique structure of cerebellum, such as the small white matter[9,12].

Conclusion

In our results, the cause of peritumoral edema associated with meningioma is most likely multifactorial. Although tumor volume, peritumoral rim, high signal intensity on T2WI, and pial vascular supply correlated with peritumoral brain edema in univariate analyses, multivariate analyses show hypervascular meningiomas , particularly, fed by the pial-cortical arteries, exhibited significantly more severe edema compared with those supplied only from meningial arteries.

References

1. Bitzer M, Topka H, Morgalla M, Friese S, Wockel L, Voigt K : Tumor-related venous obstruction and development of peritumoral brain edema in meningiomas. **Neurosurgery 42** : 730-737, 1998
2. Bitzer M, Wockel L, Luft AR, Wakhloo AK, Petersen D, Opitz H, et al : The importance of pial blood supply to the development of peritumoral brain edema in meningiomas. **J Neurosurg 87** : 368-373, 1997
3. Bradac GB, Ferszt R, Bender A, Schorner W : Peritumoral edema in meningiomas : A radiological and histological study. **Neuroradiology 28** : 304-312, 1986
4. Challa VR, Moody DM, Marshall RB, Kelly DL Jr : The vascular component in meningiomas associated with severe cerebral edema. **Neurosurgery 7** : 363-368, 1980
5. Gilbert JJ, Paulseth JE, Coates RK, Malott D : Cerebral edema associated with meningiomas. **Neurosurgery 12** : 599-605, 1983
6. Hossmann KA, Bloink M, Wilmes F, Wechsler W : Experimental peritumoral edema of the cat brain. **Adv Neurol 28** : 323-340, 1980
7. Hossmann KA, Wechsler W, Wilmes F : Experimental peritumorous edema : Morphological and pathophysiological observations. **Acta Neuropathol(Berl) 45** : 195-203, 1979
8. Ide M, Jimbo M, Kubo O, Yamamoto M, Takeyama E, Imanaga H : Peritumoral brain edema and cortical damage by meningioma. **Acta Neurochir Suppl 60** : 369-372, 1994
9. Inamura T, Nishio S, Takeshita I, Fujiwara S, Fukui M : Peritumoral brain edema in meningiomas-influence of vascular supply on its development. **Neurosurgery 31** : 179-185, 1992
10. Kalkanis SN, Carroll RS, Zhang J, Zamani AA, Black PM : Correlation of vascular endothelial growth factor messenger RNA expression with peritumoral vasogenic cerebral edema in meningiomas. **J Neurosurg 85** : 1095-1101, 1996
11. Kim IS, Kim HD, Kim KU, Shin HC, Choi HJ, Kim KH : Factors influencing the development of peritumoral brain edema in meningiomas. **J Korean Neurosurg Soc 26** : 940-945, 1997
12. Lobato RD, Alday R, Gomez PA, Rivas JJ, Dominguez J, Cabrera A, et al : Brain oedema in patients with intracranial meningioma. Correlation between clinical, radiological, and histological factors and the presence and intensity of oedema. **Acta Neurochir (Wien) 138** : 485-493, 1996
13. Maiuri F, Gangemi M, Cirillo S, Delehaye L, Gallicchio B, Carandente M, et al : Cerebral edema associated with meningiomas. **Surg Neurol 27** : 64-68, 1987
14. Nakano T, Asano K, Miura H, Itoh S, Suzuki S : Meningiomas with brain edema : radiological Characteristics on MRI and review of the literature. **Clin Imaging 26** : 243-249, 2002
15. Salpietro FM, Alafaci C, Lucerna S, Lacopino DG, Todaro C, Tomasello F : Peritumoral edema in meningiomas : Microsurgical observations of different brain tumor interfaces related to computed tomography. **Neurosurgery 35** : 638-641, 1994
16. Smith HP, Challa VR, Moody DM, Kelly DL Jr : Biological features of meningiomas that determine the production of cerebral edema. **Neurosurgery 8** : 428-433, 1981
17. Vries J, Wakhloo AK : Cerebral oedema associated with WHO-I, WHO-II, WHO-III meningiomas : correlation of clinical, computed tomography, operative and histological findings. **Acta Neurochir(Wien) 125** : 34-40, 1993
18. Yamaguchi N, Kawase T, Sagoh M, Ohira T, Shiga H, Toya S : Prediction of consistency of meningiomas with preoperative magnetic resonance imaging. **Surg Neurol 48** : 579-583, 1997

Commentary

Authors analyzed radiological(magnetic resonance image and angiography) findings of 50 patients of meningiomas about peritumoral brain edema(PTBE). Among the 50 meningioma patients 18 patients showed PTBE and 38 patients had not. They analyzed tumor volume, peritumoral rim, shape of tumor margin, Signal intersity of the tumor on T2WI, pial blood supply, location of the tumor, and histology which were usually suspected to relate with PTBE.

The results were positive correlation of the PTBE with tumor volume, peritumoral rim, signal intensity on T2WI, and pial blood supply on univariate analysis, but only the pial blood supply showed positive correlation with PTBE on

multivariate analysis. Shape of tumor margin, location of tumor, and histologic type were not shown to be correlated with the PTBE, partly because of small number of the positive PTBE patients(18 in number).

Pial blood supply from the intracerebral origin to the meningioma is an important factor for PTBE and consistent with the results of Yoshioka, et al.[2]. There are some different points in this article compared with the literatures. The first, tumor size is reported positively correlated with the severity of PTBE[1] but not in this article. There are a few articles with negative correlation in the tumor size too. The second, irregular shape of tumor margin and absence of peritumoral rim are considered as invasive pattern of the brain tumor interface, and positively correlated with the PTBE but not in this article. First of all the pial blood supply to the meningioma is an important factor in producing PTBE on radiologic point of view, and it was confirmed in this article. But the cause of PTBE in meningioma seemed to be multifactorial.

Lastly we have to think about the biochemical, molecular biologi aspects of the pathogenesis of the PTBE, and tumor plasminogen activator, macrophage infiltration, platelete-activity factor with leukocyte common antigen, and vascular endothelial growth factor expression in the meningioma have been studied so far.

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References

1. Go KG, Wilmink JT, Molenaar WM : Peritumoral brain edema associated with meningiomas. **Neurosurgery 23** : 175 - 179, 1988
2. Yoshioka H, Hama S, Taniguchi E, Sugiyama K, Arita K, Kurisu K : Peritumoral brain edema associated with meningoma : Influence of vascular endothelial growth factor expression and vascular blood supply. **Cancer 85** : 936 - 944, 1999