Peritumoral Edema and Seizure in Patients with Cerebral Convexity and Parasagittal Meningiomas

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Abstract

Epileptogenic factors associated with cerebral convexity or parasagittal meningiomas were investigated by retrospective analysis of clinical symptoms and computed tomographic findings in 83 consecutive patients. The patients were divided into Group A consisting of 27 patients presenting with epilepsy as the first symptom, and Group B consisting of 56 patients presenting with other symptoms. Tumor location, tumor size, histological subtype, and the amount of peritumoral edema were compared between the groups. Tumor size, location, and histological subtype did not differ significantly between the two groups, but the area of peritumoral edema was significantly greater in Group A than in Group B. Similar results were found in subgroups of patients with frontal meningioma, central meningioma, and fibroblastic meningioma. Generalized seizures tended to occur in patients with frontal or fibroblastic meningioma, and partial seizures in those with central or parietal meningioma. Peritumoral edema is a significant epileptogenic factor associated with both cerebral convexity and parasagittal meningiomas, and may be especially related to the occurrence of secondarily generalized seizures in frontal and fibroblastic meningiomas.

Key words: computed tomography, epilepsy, meningioma, peritumoral edema

Introduction

Epilepsy is one of the most common symptoms of brain tumor. The incidence of epilepsy is generally related to tumor pathology and cortical location. In general, tumors with slow growth and those close to the cortex, especially the centroparietal areas, are more likely to cause seizures. Seizures occur in approximately 25–30% of patients with supratentorial tumors but rarely in those with infratentorial tumors. However, the mechanism of epileptogenesis associated with brain tumor is unknown. Meningioma commonly presents with epilepsy as the first symptom with own incidence of 20–50%. Meningiomas, like many other central nervous system tumors, can induce peritumoral edema, but the volume of edema varies greatly. The relationship between seizures and peritumoral edema has not been investigated.

This study examined epileptogenic factors associated with cerebral convexity and parasagittal meningiomas.

Subjects and Methods

Eighty-three patients with cerebral convexity or parasagittal meningiomas treated at the Niigata University Hospital between 1976 and 1994 were reviewed excluding patients with hemangiopericytoma and von Recklinghausen’s disease. The patients were aged from 23 to 85 years (mean 56.7 ± 13.7 years) and included 25 males and 58 females. The patients were divided into two groups. Group A consisted of 27 patients presenting with epilepsy as the first symptom. Group B consisted of 56 patients presenting with other symptoms.

Computed tomography (CT) was performed with five different scanners: EMI-1000, EMI-1010 (Toshiba Co., Tokyo), GE-8800CT/T (GE Medical Systems, Milwaukee, Wis., U.S.A.), SOMATOM-DR3 (Siemens, Erlangen, Germany), and Hitachi-W1000 (Hitachi Medical Co., Tokyo). The area of the tumor and the peritumoral edema were calculated from computer measurements of the maximum size on preoperative postcontrast CT scans. Peritumoral edema was defined as an area with densities from 7 to 25 Hounsfield units. The computer measurements
Fig. 1 Preoperative postcontrast CT scan demonstrating an enhanced meningioma with extensive peritumoral edema. The dotted lines were traced for measurement of the contrast enhanced area defined as the tumor size (T), and the peritumoral hypodensity area (approximately 7-25 Hounsfield units) defined as the peritumoral edema area (E).

used an image digitizer controlled by a personal computer (Fig. 1). The area is given in cm². The edema/tumor (E/T) ratio was calculated by dividing the size of the peritumoral edema by the tumor size. An E/T ratio > 1 indicates that the peritumoral edema was large for the tumor. The areas of the tumor and the peritumoral edema, and the E/T ratio were compared between the two groups and according to the location of the tumor and its histological subtype.

Statistical analysis was performed using Student's t test. A p value of <0.05 was considered significant.

Results

Clinical and histological features are shown in Table 1. There was no significant gender difference between the two groups. However, the mean age in Group A (52.3 ± 13.0 years) was significantly less than that in Group B (58.8 ± 13.5 years) (p = 0.01). Age was not correlated with tumor size or peritumoral edema area (p = 0.2/r = −0.04, p = 0.11/r = −0.17, respectively). The peritumoral edema area and the E/T ratio were significantly larger in Group A than in Group B (p < 0.02 and p < 0.005, respectively). Comparison of the 13 parasagittal tumors in Group A and 30 in Group B showed there was no significant difference in tumor size (p = 0.20). However, the peritumoral edema area and E/T ratio were significantly larger in Group A than in Group B (p < 0.03 and p < 0.001, respectively).

The location of each tumor was determined from CT or operative findings, and was classified as frontal, central, parietal, or others. Tumors in the proximity of the rolandic fissure were classified as central. Tumor size and peritumoral edema area were not significantly correlated with tumor location. Frontal tumors in Group A had significantly larger peritumoral edema area and E/T ratios than those in Group B (p < 0.01 and p < 0.001, respectively) (Fig. 3), and central tumors in Group A had significantly higher E/T ratios than those in Group B (p < 0.03) (Fig. 4). Parietal tumors showed no significant difference in tumor size, peritumoral edema area, or E/T ratio between the two groups.

Histological examination revealed 24 meningotheliomatous, 33 fibroblastic, four transitional, five angiomatous, and three anaplastic meningiomas. The remaining tumors were classified as "other" or were unidentified. The peritumoral edema area and E/T ratio were significantly higher for fibroblastic meningiomas in Group A than those in Group B (p < 0.002 and p < 0.001, respectively).
Fig. 2 Distributions of tumor size, peritumoral edema area, and E/T ratio for all patients in Groups A and B. Bars denote mean values.

Fig. 3 Distributions of tumor size, peritumoral edema area, and E/T ratio in patients with frontal meningiomas in Groups A and B. Bars denote mean values.
Fig. 4  Distributions of tumor size, peritumoral edema area, and E/T ratio in patients with central meningiomas in Groups A and B. Bars denote mean values.

Fig. 5  Distributions of tumor size, peritumoral edema area, and E/T ratio in patients with fibroblastic meningiomas in Groups A and B. Bars denote mean values.
Table 2 Presenting symptoms and tumor location

<table>
<thead>
<tr>
<th>Symptoms</th>
<th>Frontal</th>
<th>Parietal</th>
<th>Central</th>
<th>Others</th>
</tr>
</thead>
<tbody>
<tr>
<td>Group A</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Generalized seizure</td>
<td>8</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Partial seizure</td>
<td>5</td>
<td>5</td>
<td>5</td>
<td>2</td>
</tr>
<tr>
<td>Jacksonian seizure</td>
<td>3</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Group B</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Motor and sensory symptoms</td>
<td>9</td>
<td>7</td>
<td>1</td>
<td>2</td>
</tr>
<tr>
<td>Mental symptoms</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>0</td>
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<tr>
<td>Headaches</td>
<td>6</td>
<td>3</td>
<td>1</td>
<td>4</td>
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<tr>
<td>Speech disturbances</td>
<td>1</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Swelling of scalp</td>
<td>0</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Visual symptoms</td>
<td>0</td>
<td>1</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Others</td>
<td>4</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
</tbody>
</table>

Group A: patients with epilepsy as the first symptom, Group B: patients with other symptoms.

(Fig. 5). There was no difference between the two groups associated with the meningotheliomatous and angiomatous subtypes.

Generalized seizure occurred in 10 patients, eight of whom had frontal lobe meningiomas. Partial seizure occurred in 17 patients, nine of whom manifested Jacksonian seizures (Table 2). There was no correlation between tumor size or the peritumoral edema area and the seizure type.

Discussion

Previous studies of convexity and parasagittal meningiomas have shown that frontal meningiomas caused seizures in 20–40% of patients, including generalized seizure in 20–30% and partial seizure in 15–20%, and centroparietal meningiomas precipitated seizures in 60–70% of patients, including generalized seizure in 20–25% and partial seizure in 45–60%. Similarly, our study found central meningiomas had a high incidence of associated epilepsy (63%), almost all causing partial seizure (Table 2). In contrast, frontal meningiomas initially tended to cause generalized seizure (62%), and fibroblastic meningiomas had a high incidence of generalized seizure (69%). Therefore, there is a significant relationship between the seizure type and tumor location.

The pathogenesis of epileptic seizures associated with brain tumors remains unknown, but is likely to be multifactorial. Meningioma is extracerebral, generally benign, and usually relatively slow-growing. Impaired vascularization of the surrounding cerebral cortex may produce hypoxic-ischemic neuronal changes. Direct irritation of the cortex by a tumor may also result in seizures. Therefore, continuous direct stimulation and changes in the cortex adjacent to meningioma may both contribute to epileptogenesis. Brain tumors may produce "denervation hypersensitivity" related to the partial isolation and transection of a region of the cerebral cortex. In this study, all patients presenting with epilepsy demonstrated significantly larger peritumoral edema than those with other symptoms, although there was no significant difference in tumor size. This was also true of both frontal and central tumors. We suggest that peritumoral edema may be involved in "denervation hypersensitivity" and propagation of excitatory influences via the callosal connection. Peritumoral edema associated with meningiomas is most likely the vasogenic type, in which excessive concentrations of glutamate and aspartic acid are present. Therefore, edema fluid may expedite "denervation hypersensitivity" and excitatory neurotransmitter amino acids could be involved in increasing the threshold of seizure sensitivity. We suggest that peritumoral edema is one of the significant epileptogenic factors associated with both cerebral convexity and parasagittal meningiomas, and is especially important in secondarily generalized seizure in frontal and fibroblastic meningiomas.

References


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Commentary

This important manuscript addresses a very critical question, making a meticulous retrospective analysis in meningiomas presenting with epilepsy and peritumoral edema. The authors have clearly shown the importance of the peritumoral area of edema in generalized and/or partial seizures, depending on tumor location, size, histology and edematous reaction; implicating that peritumoral edema is a significant epileptogenic factor in meningiomas, a problem that has not been adequately investigated in the medical literature as yet.

LeBlanc and Rasmussen have already demonstrated, in 19746) that seizures occur approximately in 50% of patients with brain tumors. Penfield et al., in 19407) have also reported that among patients with meningiomas, about 1/3 continue to have seizures. Also, Flyger5) demonstrated that with parasagittal and convexity meningiomas up to 40% of patients not showing preoperative seizures develop seizures postoperatively. So many neurosurgeons are dismayed by this surprise after removal of a meningioma, a slow-growing glioma or a cavernous angioma to see their patients still showing the same preoperative seizures. Nowadays we know that critical normal tissue is usually left behind or “in situ” in the so-called epileptogenic zone after the epileptogenic lesion (tumoral or non-tumoral) has been removed, making “lesionectomy-only” responsible for lack of freedom from seizures. Infiltrating tumors are usually congruent with the epileptogenic lesion, while in non-infiltrating lesions the epileptogenic zone tends to include adjacent cortex and/or gliosis as in cavernous angiomias or meningiomas.

We presently have learned that, under these circumstances, tumor surgery in the presence of a surrounding epileptogenic or symptomatic zone must borrow and utilize the contributions of functional and epilepsy surgery. Several authors1–4) have emphasized that, but controversy still exists regarding the need for intraoperative electrocorticography to identify, and consequently resect, those adjacent areas of gliosis or edema responsible for seizure generation and whose removal will produce a definitive cure of the seizures, instead of removing tumor alone. Electrocorticography is presently advocated1,3,4) mainly in longstanding seizure disorders, in order to maximize seizure control, while minimizing or abolishing the need for a reoperation or high levels of anticonvulsant medication.

The Niigata Brain Institute members are to be congratulated on their further contribution to the definitive surgical treatment of symptomatic tumoral seizures.

References


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Although epilepsy is one of the most common symptoms in patients with convexity and parasagittal meningiomas, the mechanism of epileptogenesis remains unknown. Kawaguchi et al. have clinically reviewed consecutive 83 patients by comparing those with and without epilepsy. They found that patients with epilepsy consistently showed a significantly intense peritumoral edema compared to those without epilepsy. Interestingly, there were no significant differences in the tumor size, tumor location and histological subtypes. Edema size/tumor size ratio may be a critical factor.

Three possibilities emerge as a source of peritumoral edema associated with meningioma: compression of the surrounding cortical vein by the tumor, breakdown of leptomeninges at the tumor-brain interface causing disruption of blood-brain barrier, and the possibility that meningioma cells might secrete certain chemical factors inducing increased vascular permeability. The candidates include bradykinin, prostaglandin, interleukin, and vascular permeability factor/vascular endothelial growth factor (VEGPF). The comparative study between the small meningiomas with marked brain edema and the large meningiomas without edema should be done using appropriate biochemical and/or molecular approaches.

Reference


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