Malignant meningioma: clinical and pathological features

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The records of 15 patients with a diagnosis of malignant meningioma were reviewed. In one of these patients, in whom invasion of the brain and pituitary gland was the only unusual feature, the tumor was reclassified as benign. Seven tumors, four hemangiopericytomas and two transitional and one syncytial meningioma, were considered to be only borderline-malignant despite necrosis and invasion of the brain, because of few mitoses and regular architecture. Of this group of patients, four men and three women, two are alive and well, three died after incomplete resections, and two succumbed to recurrent tumor that had become inoperable. The other seven patients, six men and one woman, had lesions classified as histologically frankly malignant, on the basis of marked anaplasia and numerous mitoses. These comprised three hemangiopericytomas and three syncytial and one fibrous meningioma. One of these patients is alive and well and the others are dead, three as a result of metastases. The initial clinical course of malignant meningiomas tends to be short but is otherwise indistinguishable from that of benign meningiomas. The chances of recurrence and eventual death are high, and extracranial metastases are not rare. The tumors are most often hemangiopericytomas, but not exclusively so, and men are particularly at risk.

KEY WORDS meningioma • malignant tumor • hemangiopericytoma • metastasis

The line of demarcation between benign and malignant meningiomas is equivocal. Modern methods of diagnosis, such as ultrastructural and tissue culture studies, have not been helpful in differentiating between these two types. Cytogenetics may prove useful in the future, since malignant meningiomas display nonrandom karyotypic aberrations, particularly in chromosome 22. At present, however, one must still rely on clinical and pathologic criteria to establish the diagnosis. A history of rapid recurrence, even after apparently complete removal, overt histological anaplasia, and finally the appearance of metastases are usually cited as indications of malignancy. There is as yet no consensus whether the early clinical course is significant and whether histological criteria are reliable in foretelling the behavior of the neoplasm. We reviewed our cases of malignant meningiomas to assess these points, with a follow-up study to determine what eventually happened to the patients.

Clinical Material and Methods

The records of all cases diagnosed as malignant meningioma at biopsy or autopsy at Vancouver General Hospital between 1950 and 1977 were reviewed. Some cases were excluded since they had been labeled malignant solely because of invasion of the skull and dura, others because they were now considered to be gliomas. Fifteen cases remained and are included in this series. The salient features are summarized in Table 1.

Summary of Cases

Clinical Features

The series comprised 15 patients, 10 men and five women. Ages ranged from 32 to 69 years, with an average of 50 years. Symptoms before surgery were present for 1 year or less in all patients but one, who had suffered head pains for 4 years. Symptoms and signs were identical with those commonly seen in benign meningiomas: four patients had enlarging nontender lumps on the head, five had severe headache, and four of these had papilledema. Five patients had focal seizures, three presented with hemiparesis, and three with unsteadiness and dizziness. Fourteen tumors were situated in the cerebral hemispheres, six of
these in the frontal lobes, seven in the parietal lobe, and one on the sphenoid ridge; the 15th was in the cerebellopontine angle.

Pathological Features

Gross pathological examination revealed a few specimens that were firm and white, but many contained softer areas or were fleshy throughout. Cystic degeneration or foci of yellow necrosis were obvious in some tumors, and several had adherent portions of brain. Two tumors were hemorrhagic.

On microscopic examination, seven tumors were classified as hemangiopericytoma, two as transitional, one as fibrous, and five as syncytial meningioma. With increasing malignancy, the architectural characteristics became blurred. In the hemangiopericytomas, vessels were fewer, the perivascular arrangement became less obvious, and the cells looked more bizarre (Fig. 1). In the other meningiomas, organoid patterns such as whorls disappeared, and cells lay arranged in broad sheets or streamed in bands; the cells often had uniform oval nuclei with prominent nucleoli (Fig. 2 left). Two tumors eventually became so anaplastic that parts resembled a spindle-cell sarcoma (Fig. 2 right).

The specimens from 14 patients contained mitoses. These ranged from one in every 10 high-power fields to one to two per high-power field overall. Atypical mitoses could be identified in only four cases. Mitoses tended to be focally congregated, so that in the tumors with numerous mitoses, four or five mitoses were seen in many adjacent high-power fields, whereas in meningiomas with a low mitotic rate, large areas contained no mitoses. The specimens from 10 patients were partly necrotic. Six tumors contained foci of increased cellularity, sometimes as perinecrotic palisading cells (Fig. 3).

In eight patients, the meningioma infiltrated the brain, sending out finger-like projections or lying as islets in the heavily gliosed nerve parenchyma. Two malignant hemangiopericytomas had provoked a marked vascular proliferation adjacent to the advancing tumor. In the patient with the sphenoid ridge meningioma (Case 15), the tumor spread diffusely throughout the subarachnoid space and into the Virchow-Robin spaces of the hypothalamus; it also directly infiltrated the pituitary gland. Increasing dedifferentiation and malignancy was seen in recurrent tumors of five patients. In 10 others, successive specimens showed no change in histology.

Two hemangiopericytomas and one transitional meningioma were selected for ultrastructural examination. The basic structure of both types was that of their benign counterparts. Necrosis was present in the transitional meningioma. In the hemangiopericytomas, the reduction in the number of vessels was again noted. Definite leiomyoblastic differentiation, as described by Peña, was not encountered.

Follow-up Results

Three patients died postoperatively after resections that were incomplete because of technical difficulties. Of the remaining 12 patients, 10 required further surgery because of recurrences. Sixteen operations were performed after presumed complete removals. The interval between resections in 19 recurrences ranged from 3 months to 19 years; in nine instances it was 1 year or less, in five others between 1 and 2 years.

Of the 12 patients surviving the postoperative period, nine died as a result of their tumor. The duration of their illness varied from 2½ to 21 years, with an average of 7.8 years. Three patients are alive and well 5 years, 3 years, and 1 month after their last resection. All three had received radiation, as did seven others who succumbed. Two of the survivors had hemangiopericytomas, the third a transitional meningioma. According to Fukui, et al., hemangiopericytomas are much more sensitive to radiation than are other tumors.
Malignant meningioma

Three patients had metastatic disease. One patient (Case 3) had repeated operations for an increasingly dedifferentiated hemangiopericytoma. Finally, a metastasis appeared in the jaw which on biopsy resembled the intracranial tumor. The second patient (Case 7) with a highly malignant syncytial meningioma had x-ray evidence terminally of pulmonary metastases. The third patient with a syncytial meningioma (Case 6) presented 1 year later with cardiac symptoms due to metastatic spread to the heart, a very rare occurrence. He died with widely disseminated metastases.

Discussion

In the extensive literature on meningiomas, few articles deal specifically with the problem of malignancy. Some of the older literature is unreliable because of erroneous diagnoses. Features suspected as indicating malignancy are necrosis (particularly small foci), mitoses, increased cellularity, anaplasia, and cell type; the angioblastic meningioma is considered the tumor that most commonly becomes malignant.

FIG. 2. Photomicrographs of malignant syncytial meningioma specimens from two patients. Left: The tumor grows in uniform sheets. Arrows indicate mitoses. H & E, x 330. Right: Bizarre cells are prominent in this specimen from a patient with cardiac metastasis. H & E, x 440.

FIG. 3. Photomicrograph of a malignant hemangiopericytoma showing necrosis and palisading. H & E, x 220.
## TABLE 1
Clinical summary in 15 cases of malignant meningioma*

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Sex, Age (yrs)</th>
<th>Length of Preop Symptoms</th>
<th>Location of Tumor</th>
<th>Tumor Type</th>
<th>Increased Cellularity</th>
<th>Anaplasia†</th>
<th>Mitoses</th>
<th>Necrosis</th>
<th>Brain Invasion</th>
<th>Tumor Removal</th>
<th>Time to Recurrence</th>
<th>Irradiation</th>
<th>Follow-up Status</th>
<th>Total Duration of Illness</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M, 55</td>
<td>1 yr</td>
<td>lt parietal</td>
<td>H</td>
<td>++++</td>
<td>yes</td>
<td>1/hpf</td>
<td>yes</td>
<td>no</td>
<td>complete</td>
<td>6 mos</td>
<td>no</td>
<td>alive &amp; well 3 yrs after last op</td>
<td>4 yrs, 6 mos</td>
</tr>
<tr>
<td>2</td>
<td>F, 69</td>
<td>4 mos</td>
<td>rt parietal</td>
<td>H</td>
<td>++++</td>
<td>yes</td>
<td>1/hpf</td>
<td>yes</td>
<td>no</td>
<td>complete</td>
<td>1 yr, 10 mos</td>
<td>no</td>
<td>died of tumor 3 yrs after last op</td>
<td>5 yrs, 2 mos</td>
</tr>
<tr>
<td>3</td>
<td>M, 69</td>
<td>8 mos</td>
<td>rt parietal</td>
<td>H</td>
<td>+</td>
<td>yes</td>
<td>1/hpf</td>
<td>yes</td>
<td>no</td>
<td>complete</td>
<td>3 yrs, 8 mos</td>
<td>no</td>
<td>died of tumor 2 yrs after last admission; autopsy records destroyed</td>
<td>11 yrs</td>
</tr>
<tr>
<td>4</td>
<td>M, 32</td>
<td>3 wks</td>
<td>rt frontal</td>
<td>F</td>
<td>0</td>
<td>no</td>
<td>1/hpf</td>
<td>no</td>
<td>no</td>
<td>complete</td>
<td>6 mos</td>
<td>no</td>
<td>invasion of scalp at last admission; many metastases</td>
<td>2 yrs, 10 mos</td>
</tr>
<tr>
<td>5</td>
<td>M, 65</td>
<td>1 wk</td>
<td>lt parietal</td>
<td>S</td>
<td>+</td>
<td>yes</td>
<td>1/hpf</td>
<td>yes</td>
<td>no</td>
<td>complete</td>
<td>1 yr</td>
<td>yes</td>
<td>died 6½ yrs postop of tumor</td>
<td>6 yrs, 6 mos</td>
</tr>
<tr>
<td>6</td>
<td>M, 33</td>
<td>1 yr</td>
<td>lt parietal</td>
<td>S</td>
<td>+</td>
<td>yes</td>
<td>1/hpf</td>
<td>yes</td>
<td>no</td>
<td>complete</td>
<td>yes</td>
<td>died 1½ yrs after surgery; many metastases</td>
<td>2 yrs, 6 mos</td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>M, 42</td>
<td>1 yr</td>
<td>lt parietal</td>
<td>S</td>
<td>+</td>
<td>yes</td>
<td>1/hpf</td>
<td>yes</td>
<td>no</td>
<td>complete</td>
<td>1 yr, 3 mos</td>
<td>no</td>
<td>died of tumor 7 yrs after last surgery; metastases to lungs</td>
<td>7 yrs, 6 mos</td>
</tr>
<tr>
<td>8</td>
<td>F, 35</td>
<td>9 mos</td>
<td>rt parietal</td>
<td>T</td>
<td>0</td>
<td>no</td>
<td>0</td>
<td>no</td>
<td>0</td>
<td>incomplete</td>
<td>19 yrs</td>
<td>no</td>
<td>died of tumor 1 yr after last op</td>
<td>21 yrs, 4 mos</td>
</tr>
<tr>
<td>9</td>
<td>F, 53</td>
<td>1 mo</td>
<td>lt frontal</td>
<td>T</td>
<td>0</td>
<td>yes</td>
<td>1/20 hpf</td>
<td>yes</td>
<td>0</td>
<td>complete</td>
<td>3 yrs</td>
<td>yes</td>
<td>alive &amp; well 5 yrs after last operation</td>
<td>8 yrs, 1 mo</td>
</tr>
<tr>
<td>10</td>
<td>F, 48</td>
<td>5 mos</td>
<td>rt frontal</td>
<td>H</td>
<td>0</td>
<td>yes</td>
<td>1/5 hpf</td>
<td>no</td>
<td>+</td>
<td>incomplete</td>
<td>yes</td>
<td>alive &amp; well 1 mo postop</td>
<td>5 yrs, 5 mos</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>M, 46</td>
<td>3 mos</td>
<td>rt frontal</td>
<td>H</td>
<td>0</td>
<td>yes</td>
<td>1/5 hpf</td>
<td>yes</td>
<td>0</td>
<td>incomplete</td>
<td>5 yrs</td>
<td>no</td>
<td>died postop 3 mos</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>M, 34</td>
<td>1 yr</td>
<td>cerebello-pontine</td>
<td>H</td>
<td>0</td>
<td>yes</td>
<td>1/5 hpf</td>
<td>yes</td>
<td>0</td>
<td>autopsy</td>
<td>no</td>
<td>no</td>
<td>died postop 1 yr</td>
<td></td>
</tr>
<tr>
<td>13</td>
<td>M, 42</td>
<td>4 yrs</td>
<td>lt parietal</td>
<td>H</td>
<td>0</td>
<td>yes</td>
<td>1/10 hpf</td>
<td>yes</td>
<td>+</td>
<td>incomplete</td>
<td>no</td>
<td>died postop 4 yrs</td>
<td></td>
<td></td>
</tr>
<tr>
<td>14</td>
<td>M, 57</td>
<td>1 wk</td>
<td>lt frontal</td>
<td>S</td>
<td>0</td>
<td>yes</td>
<td>1/10 hpf</td>
<td>yes</td>
<td>0</td>
<td>complete</td>
<td>10 yrs</td>
<td>no</td>
<td>died 5 yrs after last op</td>
<td></td>
</tr>
<tr>
<td>15</td>
<td>F, 64</td>
<td>1 yr</td>
<td>sphenoid ridge</td>
<td>T</td>
<td>0</td>
<td>yes</td>
<td>1/10 hpf</td>
<td>yes</td>
<td>0</td>
<td>incomplete</td>
<td>6 yrs</td>
<td>no</td>
<td>died 1 yr after last op</td>
<td></td>
</tr>
</tbody>
</table>

* Tumor type: H = hemangiopericytoma, S = syncytial, T = transitional, F = fibrous; hpf = high-power field.
† Anaplasia is graded 0 (absent) to ++++ (severe).
‡ At autopsy: subarachnoid spread, invasion of hypothalamus and pituitary.
Malignant meningioma

Necrosis, both massive and minute, was a common feature in this series, but this occasionally also occurs in benign meningiomas. Foci of increased cellularity frequently show no evidence of anaplasia, and we think these are harmless. However, we believe that small foci of necrosis surrounded by dense palisades of cells with markedly increased mitotic activity (noted in three hemangiopericytomas) definitely indicate malignancy.

Anaplasia is evident both cytologically and ultrastructurally in malignant meningiomas. The loss of architecture may make it difficult to identify a subtype, and even to differentiate between hemangiopericytomas and other meningiomas. A stain for reticulum, which in the hemangiopericytoma encloses individual cells, is helpful in diagnosis. The undifferentiated growth of a dedifferentiated neoplasm in sheets of cells without any organoid patterns has led to the large number of reported malignant "syncytial" meningiomas. A papillary pattern indicates malignancy, but was not encountered in our series.

Although rare mitoses can be found in benign meningiomas, numerous mitoses predict active growth and recurrence. Atypical mitoses are always proof of malignancy. There is controversy whether invasion of the brain indicates malignancy. Although Simpson believed that the infiltrating "fingers" of a meningioma usually pull out with the main mass, there is undoubtedly a chance in these cases for fragments to be left behind, and incomplete removal is the most important cause for recurrence; indeed no recurrence is possible without it. Yet we see no reason to ascribe greater biological significance to invasion of the brain by the tumor than to its extension into mesenchymal tissues, which likewise makes complete extirpation difficult.

The hemangiopericytoma, also called "angioblastic" or "undifferentiated" meningioma, has gained increasing attention in recent years. Histological, ultrastructural, and behavioral characteristics indicate that it is a distinct entity, although this view has recently been challenged. These neoplasms are always at least potentially malignant. Goellner, et al., classified nine of 26 meningeal hemangiopericytomas as borderline-malignant and 17 as malignant; all the latter recurred. In our series, seven of 15 tumors were hemangiopericytomas, a percentage far exceeding previous reports of their incidence among meningiomas, which is 1.2% to 1.7%. Two of our patients with hemangiopericytomas are at present alive and without clinical evidence of disease.

Metastasis is incontrovertible proof of malignancy. It is more common in meningiomas than is generally realized. Although hemangiopericytomas undoubtedly contribute greatly to the incidence of metastatic disease, other types of meningioma also metastasize, as shown by two of our three cases. The tumor spreads most commonly to the lungs, but no area is immune. The heart is seldom affected. Only rarely is the metastatic disease rather than the primary tumor responsible for death.

Meningiomas have been classified according to their grade of malignancy. After analyzing the histological features in our tumors, we reclassified one tumor (in Case 15) as benign. The other 14 tumors formed two groups. The first we consider histologically as only borderline-malignant despite necrosis and brain invasion, since there was only minor anaplasia and few mitoses. This group comprised seven patients. Four had hemangiopericytomas (one woman and three men, aged 34 to 48 years old), and of these three died of postoperative complications and one has just undergone reoperation after a recurrence 5 years after initial resection followed by irradiation. Of the other three patients (two women and one man, with transitional and syncytial meningiomas, aged 35 to 57 years), one is alive and well after one recurrence and the others died as a result of their tumor, which was either inoperable initially or became so later. The second group of seven patients we classify as frankly malignant. Three patients had hemangiopericytomas (two men and one woman, aged 55 to 69 years), and only one is alive after one recurrence. The other four patients had meningiomas, three synctial and one fibrous. All were men, aged 32, 33, 42, and 69 years, and all died.

Conclusions

In our series, the preponderance of men affected by this tumor was striking, since other reports indicate a high incidence among women. The initial symptoms progress rapidly, the course is punctuated by recurrences, and the tumor often becomes inoperable. Hemangiopericytomas are especially prone to malignant degeneration. Histologically ominous features are anaplasia with numerous or atypical mitoses, with necrosis and brain invasion being less indicative of malignancy. There is no convincing difference in the number of survivors and length of survival between cases of obvious malignancy and of borderline malignancy, indicating that other factors besides histological evidence of anaplasia are important in determining the outcome. The large number of patients who died attests to the poor prognosis associated with these tumors. Radiation was not beneficial in our series, and we believe that improved surgical technique leading to total extirpation holds greater hope for patients with malignant meningiomas.

References


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