Clinical and pathological study of meningiomas of the first two decades of life

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The clinical features and pathological materials of 51 cases of histologically verified meningiomas in patients under 21 years of age were reviewed. The age range was 7 to 20 years, with the majority of cases being clustered in the second decade of life. There was virtually a 1:1 sex ratio, with 26 females and 25 males. Thirty-eight patients had intracranial meningiomas, three had intraorbital tumors, and 10 had intraspinal tumors. Twelve patients (24%) had neurofibromatosis. Twenty patients (39%) had tumor recurrence. The cases were subdivided into five histological categories: meningotheliomatous, fibrous, transitional, psammomatous, and papillary. In each case, the clinical course was correlated with histological subtype. The 15-year survival rate in patients with intracranial meningiomas of all types was 68%. Factors adversely affecting survival included infratentorial location, papillary histology, and evidence of brain invasion.

Key Words: childhood * intracranial tumor * intraspinal tumor * meningioma * survival

MENINGIOMAS are predominantly tumors of the fifth and sixth decades of life and, in large series, account for 13.4% to 19.2% of all primary intracranial tumors,\(^\text{4,7}\) and 25.5% of all intradural spinal tumors.\(^\text{20}\) In children and adolescents, however, meningiomas are distinctly less common. In a review of 15 major series of intracranial tumors in children, Mendiratta, \textit{et al.}\(^\text{16}\) found only 38 of 2620 tumors (1.5%) to be meningiomas. Cushing and Eisenhardt\(^\text{7}\) found only six patients under 21 years of age among 313 cases of meningioma (1.9%). Matson\(^\text{15}\) reported a series of 750 intracranial tumors from a pediatric neurosurgical clinic and found meningiomas in just three children under 14 years of age. In the present study, surgically verified meningiomas were reviewed in 51 patients under 21 years of age. Only meningothelial tumors were sought. Undifferentiated neoplasms and the spectrum of meningeal sarcomas have been omitted. Particular emphasis has been placed on correlating clinical course with histopathological findings, especially with regard to the papillary meningioma. Where appropriate, comparisons were made between this group of patients and their adult counterparts.

Clinical Material and Methods

Clinical Material

Fifty-one patients under 21 years of age with surgically verified meningiomas were found in a review of Mayo Clinic records from 1907 to 1980. Clinical information was obtained by review of the patient records, operative reports, and follow-up correspondence with the patients or family members. Histological verification of all tumors was made by one of us (B.W.S.). Forty-seven of the 51 patients underwent neurosurgical procedures at this institution. Two of the remaining four patients had intracranial surgery elsewhere and subsequently had clinical examinations here, but no further surgery. A third patient had two craniotomies elsewhere for a papillary meningioma, then underwent pneumonectomy here for a massive pulmonary metastasis. The remaining patient had surgery elsewhere with subsequent review of autopsy material at this institution. Survival curves were calculated using the Kaplan-Meier method.

Pathological Studies

Pathological materials were obtained from the files
of the Mayo Clinic Tissue Registry. Slides stained with hematoxylin and eosin and occasionally connective tissue stains, as well as wet tissue and paraffin blocks, when necessary, were examined. The tumors were evaluated with regard to basic pattern, mitotic activity, nuclear atypia, and pleomorphism and, when possible, for invasive characteristics. This study was limited to benign and malignant neoplasms of undisputed meningothelial origin. Meningeal fibrosarcomas, fibrous histiocytomas, a variety of other sarcomas, and meningeal melanomas were eliminated.

Summary of Cases

General Characteristics

Among the 51 patients studied, virtually a 1:1 sex ratio was obtained, with 26 females and 25 males. The mean age of these patients at the time of their initial neurosurgical procedure was 15.2 years, with a range of 7 to 20 years (Table 1). Eleven patients were 12 years of age or younger and 40 were between 13 and 20 years of age. No history of previous cranial irradiation or significant cranial trauma was obtainable in any of these 51 patients. Twelve patients (24%) had neurofibromatosis. Twenty patients (39%) had definite evidence of tumor recurrence, documented either by repeat surgery, postmortem examination, or by clear-cut radiographic data, such as computerized tomography (CT) scans. In these patients, the average time between initial surgery and tumor recurrence was 7.4 years. Twenty-one of the 51 patients (41%) have died, most of recurrent tumor, and the 30 patients still alive have follow-up periods ranging from 1 to 35 years.

Location of Tumor

There were 38 patients with intracranial meningiomas (31 supratentorial and seven infratentorial), three with intraorbital tumors, and 10 with intraspinal tumors (Table 2). There were no extradural spinal tumors in this series.

Presenting Symptoms

Presenting symptoms were appropriate to the tumor location. The most common chief complaint among patients with intracranial meningiomas was headache; while patients with intraspinal tumors presented most frequently with gait disturbances, with or without back pain (Table 3).

Radiological Findings

Among the 41 patients with intracranial and intraorbital meningiomas, the reports of skull radiographs were available in 36. Nineteen were positive and 17 were negative. Among the positive studies, 10 showed x-ray evidence of increased intracranial pressure (ICP): spreading of the cranial sutures, increased convolution impressions, or sellar erosion. Six showed localized findings of hyperostosis or destruction of adjacent bone, and three studies showed both localized findings suggestive of tumor and nonspecific findings of increased ICP. Eleven patients had pneumoencephalograms; seven of these were abnormal, with the most common findings being displacement of or impingement on ventricular structures by a mass lesion. One patient had a radioisotope brain scan, and this study was abnormal. In recent years, patients with intracranial meningiomas have invariably had CT scans. Of the 12 scans done on patients in this study, nine were positive. The three negative studies were encountered in two patients with small optic nerve sheath tumors and one patient with a meningioma of the foramen magnum. Twenty patients underwent cerebral angiography; 14 of these studies showed abnormal findings. The most common angiographic findings were vessel displacement by tumor mass and increased vascularity of the tumor itself.

Pathology

The tumors of our 51 patients were classified according to the World Health Organization (WHO) classification of brain tumors23 (Table 4).

Meningotheliomatous Tumors. These tumors were composed of irregular islands of varying size made up
Meningiomas in patients under 21 years of age

TABLE 3
Major presenting complaints in 51 cases of meningioma*

<table>
<thead>
<tr>
<th>Symptom</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>intracranial tumors</td>
<td></td>
</tr>
<tr>
<td>headache</td>
<td>15</td>
</tr>
<tr>
<td>deteriorating vision</td>
<td>11</td>
</tr>
<tr>
<td>seizure disorder</td>
<td>10</td>
</tr>
<tr>
<td>proptosis</td>
<td>5</td>
</tr>
<tr>
<td>episodic loss of consciousness</td>
<td>3</td>
</tr>
<tr>
<td>diplopia</td>
<td>3</td>
</tr>
<tr>
<td>hemiparesis</td>
<td>2</td>
</tr>
<tr>
<td>dysphagia</td>
<td>1</td>
</tr>
<tr>
<td>hearing loss</td>
<td>1</td>
</tr>
<tr>
<td>personality change</td>
<td>1</td>
</tr>
<tr>
<td>neck pain</td>
<td>1</td>
</tr>
<tr>
<td>intraspinal tumors</td>
<td></td>
</tr>
<tr>
<td>paraparesis</td>
<td>7</td>
</tr>
<tr>
<td>back pain</td>
<td>4</td>
</tr>
<tr>
<td>leg pain</td>
<td>2</td>
</tr>
<tr>
<td>neck pain</td>
<td>1</td>
</tr>
<tr>
<td>quadriparesis</td>
<td>1</td>
</tr>
</tbody>
</table>

* Note that some patients had more than one presenting symptom, such as headache and a seizure disorder.

TABLE 4
Subdivision of the tumors by histological type

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>No. of Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>meningotheliomatous</td>
<td>18</td>
</tr>
<tr>
<td>fibrous</td>
<td>4</td>
</tr>
<tr>
<td>transitional</td>
<td>19</td>
</tr>
<tr>
<td>psammomatous</td>
<td>5</td>
</tr>
<tr>
<td>papillary</td>
<td>5</td>
</tr>
</tbody>
</table>

Neurofibromatosis

The patients with neurofibromatosis, most of whom had peripheral manifestations or a family history of the disease, were similar to the entire group with regard to age at the time of initial surgery (14.3 years), sex ratio (seven females to five males), and histological subtype (six transitional, four meningotheliomatous, one psammomatous, and one papillary tumor). Tumor location, however, was remarkable in that the neurofibromatosis group had an increased incidence of spinal (five of 12) and orbital or optic nerve sheath (three of 12) tumors. Nine patients (75%) had either tumor recurrence, development of a second or multiple meningiomas, or the development of a neuroectodermal tumor of variable histological type; that is, brain-stem glioma, ependymoma, or neurilemmoma. Thus, a broad range of central nervous system neoplasia was represented in this group of patients.

Survival Data

The two operative deaths in this series occurred in the 1920's. The 20-year survival rate of all patients with intracranial meningiomas having surgery since 1930 was 62% (Fig. 1). At that time interval, the survival difference between males (63%) and females (61%) was insignificant. Patients have done better in the 20-year periods of 1940 to 1959, and 1960 to 1979 than in the 20 years from 1920 to 1939 (Fig. 2). A posterior fossa location of the tumor correlated with...
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1.0

![Proportion surviving](image1)

**Fig. 2.** Twenty-year survival curves of patients with intracranial meningiomas by date of operation. n = number of patients.

a poor prognosis (21% 20-year survival rate), while a supratentorial location was associated with a much more favorable outcome (Fig. 3). Patients with neurofibromatosis had a 20-year survival rate of 58%. As might be expected, the patients with documented tumor recurrence did worse than those without recurrence (Fig. 4). It should be noted that some patients in the later group who poorly likely harbored recurrent tumors that were not documented, thus artificially lowering the survival curve of the “no recurrence” group. On the other hand, the survival rate of these patients was more common among tumors occurring at the skull base (76.9%) than over the convexity (32.2%), and the 20-year survivals in these two groups were 32% and 75%, respectively.

Correlating histology with survival, the transitional, meningotheliomatous, psammomatous, and fibrous tumors behaved in similar fashion, with a combined 20-year survival rate of 67%. It had been suggested by Cushing and Eisenhardt that the fibrous meningioma was more aggressive, but this was not borne out in the current series. By contrast, papillary tumors proved to be much more aggressive; the 5-year survival rate in this group was only 40% (Fig. 5). In addition, the clinical course of the five patients with papillary meningiomas has been marked by much morbidity. Two of the five patients had posterior fossa tumors and survived only 1 and 2 years after surgery, respectively. A third patient had a parietal convexity tumor and died 3 years after surgery with recurrent tumor. The patient initially had surgery for a right frontal tumor associated with brain invasion. A left parietal metastasis necessitated surgery 4 years later; and 2 years thereafter she was found to have a massive solitary metastasis in the left lung, which required pneumonectomy. This patient is alive 6 years after her initial surgery. The fifth patient, a girl with neurofibromatosis, initially had a large right frontotemporal lesion with gross brain invasion, and in the 3 years since her original operation, has undergone surgery for both a vaginal and a right acoustic neurilemoma.

**Discussion**

**Incidence of Meningioma**

Meningiomas are uncommon during childhood and adolescence. From 1976 to 1979, 240 intracranial tumors were seen in the 0- to 20-year-old age group at this institution; of these, only six (2.5%) were meningiomas. Looking at the incidence of childhood meningioma with regard to total number of meningiomas from all age groups, the 41 intracranial and intraoral tumors in our series represent 1.7% of the 2456 meningiomas of all ages seen over the same time span.

In contrast to the usual female preponderance seen in adults (2:1 female to male ratio in intracranial tumors and 4:1 in spinal tumors), we found a 1:1 sex ratio for both intracranial and intraspinal meningiomas. The recent finding of estrogen-receptor protein in meningiomas would suggest that there may be hormonal factors which place the female at greater risk for the development of meningioma later in life.

Congenital meningeal tumors are rare and are often sarcomas or hemangiopericytomas. True congenital meningiomas are curiosities, and none were encountered in the current series.

**Tumor Location**

It has been suggested that the lateral ventricle is a favored site for childhood meningiomas. In a review of 50 intraventricular meningiomas, Abbott and Courville found five (10%) in children and noted a predominance of tumors in the lateral ventricle, in particular the left side. Sunder-Plassman et al. reported three intraventricular meningiomas in children, and Lee et al. reported a third-ventricle meningioma in a 10-year-old boy. In our series, the two intraventricular meningiomas both occurred in the left lateral ventricle, and comprised 3.9% of the total group.
Meningiomas in patients under 21 years of age

Although Merten, et al.,17 found a 17% incidence of intraventricular tumors in a combined series of 48 cases of meningiomas in patients under 20 years of age, our figure of 3.9% more closely approximates the 3% incidence cited by Lee, et al.,12 and the 1.6% incidence reported by Earle and Richany in adults.9 Thus, we are not able to lend support to the suggestion that intraventricular meningiomas occur more frequently in children than in adults.

Although the incidence of posterior fossa location was reported to be 46% by Crouse and Berg,5 and 19% by Merten, et al.,17 in their reviews of meningiomas of childhood and adolescence, the 9.8% incidence (five of 51) in the current series equals the 9.8% incidence reported by MacCarty and Taylor in their review of a large series of meningiomas of all age groups.14 Cooper and Dohn4 stated that most childhood meningiomas are supratentorial; our data support this, and suggest that posterior fossa meningiomas are no more common in children than in adults. To highlight the rarity of childhood meningiomas, in particular in the posterior fossa, Matson15 reviewed 418 cases of posterior fossa tumors in children and found no meningiomas.

Up to 15% of spinal meningiomas have been reported to be extradural.30 This may be due in part to increased numbers of arachnoid villi at the root exit zone.10 None of the 10 spinal meningiomas in the current series were extradural; however, when faced with a child having an extradural spinal lesion, one should at least consider the possibility of extradural meningioma since there is a suggestion that this entity may be more common in children.2 In our group of spinal meningiomas, the thoracic level was favored. Although meningiomas in the lumbosacral region are uncommon, two such lesions were encountered in this series.

Histological Findings

In evaluating the biological potential of meningiomas, evidence of brain invasion and necrosis was considered to be the predominant gross feature associated with malignant behavior. Surprisingly, the presence of bone, dura, or soft-tissue invasion did not have an adverse effect on clinical outcome. Microscopic features associated with aggressive behavior included necrosis, brain invasion (as opposed to extension into the Virchow-Robin spaces), and mitotic activity. Although the small number of cases in our series make assessment difficult, there is a suggestion that tumors with more than two mitotic figures per 20 high-power fields are more apt to recur and be associated with aggressive tumor behavior. The presence of nuclear pleomorphism and cytological atypia was of no prognostic significance. "Sarcomatous transformation," that is, transformation of an initially histologically benign meningothelial tumor into a malignant spindle-cell tumor, was not observed.

Although, in our experience, less than 1% of adult meningiomas have been papillary tumors, 9.8% of the current series (five of 51) were papillary meningiomas. This is in agreement with the suggestion of Ludwin, et al.,13 that this variant is a tumor of the young. Our five patients with papillary meningiomas have done poorly, with clinical courses marked by local recurrence, and intracranial as well as distant metastasis. The 5-year survival rate in this small group of patients was only 40%. Four of these five patients have had documented tumor recurrence with a mean recurrence time of 2.0 years, compared with 9.4 years for all other histological types. This, too, supports the conclusion of Ludwin, et al.,13 that this is a particularly aggressive variant of meningioma and represents a distinct clinicopathological entity. In each of our five cases, the tumor had some papillary features from the start. Although we have observed such transition in adults, none of our current cases presented as a conventional meningioma only to manifest a papillary morphology at the time of a later resection. Since this variably malignant tumor is capable of metastasis, both intracranial and distant, the characteristic features of the papillary variant should be specifically sought.
Tumor Recurrence

Tumor recurrence was encountered in 39% of the current series, and appeared to be related to tumor location, histological type, and extent of removal. As would be expected, tumors situated at the base of the skull or in the posterior fossa were more likely to recur than tumors of the convexity; probably as a result of technical difficulties in attaining complete removal in the former group. A lower recurrence rate (20%) was found in the group of 10 spinal tumors; this likely reflects both the small size of such tumors and a location which favors complete removal. Regarding histology, four of the five patients (80%) with papillary meningiomas have had tumor recurrence, as compared with 35% for those with more benign histological subtypes.

References


Manuscript received August 4, 1981.
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