Intracranial meningiomas of the first two decades of life

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Meningiomas arising in the first two decades of life are uncommon and their characteristics are controversial. Some authors believe meningiomas in younger patients occur in different locations, have more malignant histological features, and have a worse prognosis than those in adults. To address this controversy, the authors retrospectively reviewed 23 cases of meningiomas in patients under 21 years of age at diagnosis who were operated on at the University of Turin (1948 to 1990) or at the University of California, San Francisco (1970 to 1989). These tumors represented 2.9% of all tumors in this age group and 1.8% of all meningiomas during the study period at the two institutions. There were 14 males and nine females. The mean age at surgery was 13.3 ± 5.6 years; nine cases occurred in the first decade and 14 in the second. The most common neurological symptoms were a focal neurological deficit (33%) and seizures (25%). Seventy percent of the tumors were supratentorial. A gross total resection was performed in 60% of the cases. Histologically, the majority (74%) of the tumors were meningothelial or mixed. An increased number of mitoses was observed in 33% of the tumors, focal necrosis in 29%, and invasion of adjacent brain in 14%; however, none of the tumors was classified as a Grade III (anaplastic) meningioma. All patients are alive without evidence of recurrent disease 3 to 22 years (mean ± standard deviation; 10 ± 7.3 years) after surgery. This study confirms the rarity of meningiomas of the first two decades of life and the absence of the female predominance associated with meningiomas in adults. The location and histological features of these tumors are similar to those in adults; they have a low recurrence rate, and the outcome and survival rate are excellent.

KEY WORDS • meningioma • brain neoplasm • histology • children

Meningiomas occur predominantly during the fifth decade of life and account for 13.4% to 27.3% of all primary intracranial tumors.5,9 Meningiomas of the first two decades of life are distinctly less common, with a corresponding incidence of 1% to 4%.2,4,9,11,13,14,16,21,25,26,29,39,36 and their characteristics relative to those of meningiomas in adults are controversial. Several authors believe that meningiomas in younger patients occur in different locations, have more malignant histological features, and have a worse clinical outcome.2,29,34 To help resolve this controversy, we reviewed retrospectively 23 cases of meningiomas arising in the first two decades of life and compared the findings with those of other studies in children and in adults. Particular emphasis was placed on the histopathological and immunohistochemical characterization of the tumors.

Clinical Material and Methods

The records of the University of Turin from July, 1948, to March, 1990, and of the University of California, San Francisco, from January, 1970, to December, 1989, were searched to identify patients with histologically proven intracranial meningiomas who were 20 years of age or younger at the time of diagnosis. The complete medical records documenting the presenting symptoms, preoperative radiological findings, extent of resection, and postoperative outcome were available for review in 10 cases.

The pathological specimens from each of the 23 patients were reviewed to ensure that all tumors met the criteria for classic meningioma as defined by the World Health Organization.8 Sarcomas, angioelastic meningal tumors, and other meningeal tumors were excluded. Each specimen was carefully analyzed for histological subtype and features of aggressive behavior.10,8,35 The following features were assessed: loss of architectural pattern, increased cellularity, nuclear pleomorphism, increased number of mitoses, focal necrosis, brain invasion, and papillary formations. The criteria of Jääskeläinen, et al.,23 were used to grade the tumors. In 21 of 23 cases, the tumor specimens were available for microsectioning and grading; the sections
were stained with hematoxylin and eosin, reticulin, and immunohistochemical stains for glial fibrillary acidic protein (GFAP) and vimentin.*7,37

A MEDLINE search of the literature in English from 1970 to the present was conducted to identify previously reported series of meningiomas of the first two decades of life. The information from these cases was pooled with the findings in our patients for comparison with data from adults with meningiomas.

Results

Incidence of Meningioma

During the study period, meningiomas accounted for 15 (2.4%) of 625 intracranial tumors of the first two decades of life diagnosed at the University of Turin and eight (4.5%) of 178 such tumors at the University of California, San Francisco. These tumors represent 1.5% of 1008 meningiomas diagnosed at the University of Turin and 3.3% of 246 meningiomas diagnosed at the University of California, San Francisco. Combined, the 23 cases represent 2.9% of all central nervous system tumors in this age group and 1.8% of all meningiomas diagnosed at the two institutions during the study period.

Clinical Characteristics

There were 14 males and nine females, with a mean age of 13.3 ± 5.6 years (± standard deviation) (range 6 to 21 years) at surgery. Nine (39%) of the 23 patients were in the first decade of life and 14 (61%) were in the second decade. The demographic data for our patients and previously reported patients with meningiomas of the first two decades of life are summarized in Table 1.

The most common presenting symptoms in our patients were focal neurological deficits (33%), seizures (25%), and symptoms of increased intracranial pressure (25%). The duration of symptoms varied from a few weeks to more than 10 years. A predisposing factor was identified in five cases: two patients had received radiation therapy for another central nervous system tumor, and three had neurofibromatosis.

Neuroimaging Findings

Preoperative magnetic resonance (MR) imaging suggested the diagnosis of meningioma in the three cases in which it was performed (Fig. 1). On T1-weighted MR
Pediatric intracranial meningiomas

**Fig. 2.** Photomicrographs of intracranial meningiomas that developed in the first two decades of life. A: Section showing a small area of focal necrosis. H & E, original magnification × 200. B: "Finger-like" cortical invasion by a meningioma is visualized. H & E, original magnification × 150. C: Section showing papillary formations in a meningothelial tumor. H & E, original magnification × 500. D: Intensely vimentin-positive cells (dark) are separated by collagen fibers in this fibroblastic meningioma. A few psammoma bodies are also seen (round). Immunohistochemical stain for vimentin, original magnification × 200.

images, the tumors were hypo- or isointense; on T2-weighted images, they were hyper- or isointense. Surrounding edema was best seen on T2-weighted images. Preoperative angiography was performed in four cases and computerized tomography in six; in no case did the radiological findings suggest the diagnosis of meningioma.

**Treatment**

A gross total resection was performed in 60% of the cases, and a subtotal resection was performed in 40%. Three patients received radiation therapy to the brain after subtotal resection. One patient received 5000 cGy of focal radiation, and one received 5400 cGy to the whole brain; in one patient, the dose and type of radiation therapy were unknown.

**Tumor Location**

More than two-thirds of the tumors were supratentorial, both in our patients (70%) and in the combined series of 278 tumors (67%) (Table 2). Only 13% of the tumors in our series and 9.4% in the combined series were intraventricular. Infratentorial tumors accounted for 13% of cases in our series and 14.4% in all series combined.

**Histological Findings**

The histological subtypes of tumors in our patients and other series of pediatric meningiomas are summarized in Table 2. In our series, 33% of the tumors had an increased number of mitoses, and 29% had small areas of circumscribed necrosis (Fig. 2A); 14% had invaded the adjacent brain (Fig. 2B). In one case, areas of papillary formations were seen, but most of the tumor had a well-preserved meningotheliomatous pattern (Fig. 2C). Reticulin staining showed preservation of the architectural pattern in all cases. Immunohistochemical stains were negative for GFAP and positive for vimentin in all cases (Fig. 2D). Of 21 tumor specimens available for resectioning and grading, 15 (71%)...
TABLE 2
Pathological data from 15 series of meningiomas of the first two decades of life

<table>
<thead>
<tr>
<th>Authors &amp; Year</th>
<th>No. of Cases</th>
<th>Location</th>
<th>Histology</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Supratentorial</td>
<td>Infratentorial</td>
<td>Intra-ventricular</td>
</tr>
<tr>
<td>Crouse &amp; Berg, 1972</td>
<td>13</td>
<td>7</td>
<td>6</td>
</tr>
<tr>
<td>Cooper &amp; Dohn, 1974</td>
<td>7</td>
<td>6</td>
<td>0</td>
</tr>
<tr>
<td>Merten, et al., 1974</td>
<td>48</td>
<td>24</td>
<td>9</td>
</tr>
<tr>
<td>Leibel, et al., 1986</td>
<td>13</td>
<td>8</td>
<td>4</td>
</tr>
<tr>
<td>Herz, et al., 1980</td>
<td>9</td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td>Sano, et al., 1981</td>
<td>18</td>
<td>13</td>
<td>2</td>
</tr>
<tr>
<td>Deen, et al., 1982</td>
<td>51†</td>
<td>29</td>
<td>7</td>
</tr>
<tr>
<td>Chan &amp; Thompson, 1984</td>
<td>4</td>
<td>4</td>
<td>0</td>
</tr>
<tr>
<td>Drake, et al., 1985-1986</td>
<td>13</td>
<td>12</td>
<td>0</td>
</tr>
<tr>
<td>Nakamura &amp; Becker, 1985</td>
<td>7</td>
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<td>Doty, et al., 1987</td>
<td>13</td>
<td>11</td>
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<td>Kolluri, et al., 1989</td>
<td>18</td>
<td>14</td>
<td>2</td>
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<tr>
<td>Ferrante, et al., 1989</td>
<td>19</td>
<td>17</td>
<td>2</td>
</tr>
<tr>
<td>Davidson &amp; Hope, 1989</td>
<td>22</td>
<td>13</td>
<td>5</td>
</tr>
<tr>
<td>Germano, et al., 1994</td>
<td>23</td>
<td>16</td>
<td>3</td>
</tr>
<tr>
<td>total cases</td>
<td>278</td>
<td>186</td>
<td>40</td>
</tr>
<tr>
<td>% of total</td>
<td>67</td>
<td>14.4</td>
<td>9.4</td>
</tr>
</tbody>
</table>

* Meningeal sarcoma.
† Melaemia, hemangiopericytoma.
‡ Merten, et al., and Deen, et al., include one and 10 spinal meningiomas, respectively.

were Grade I, six (29%) were Grade II, and none were Grade III (anaplastic).

Outcome
There was no perioperative mortality in the series reviewed in this study. All patients are alive without evidence of recurrent disease, 3 to 22 years (mean 12.9 ± 7.3 years) postoperatively. Data on recurrence and regrowth in cases with a long follow-up period are summarized in Table 3.

Discussion
Incidence and Demographics
Our findings confirm the low incidence of intracranial meningiomas of the first two decades of life, which ranges from less than 1% to 4.2%.2-4,9,11,13,14,18,21,25,26,28, 29,30 Three series13,25,36 have shown a higher incidence than others; this increase could reflect improvements in diagnostic modalities or differences in the cut-off point for defining pediatric patients, which varied considerably from study to study. To facilitate comparison of different studies, subdividing patients by decade of life could clarify differences obscured by variations in the definition of pediatric patients.

In adults, 60% to 80% of patients with meningiomas are women.8,32,34 In younger patients, however, there is no female predominance. Drake, et al.,14 reported a preponderance of males, and in several other series including ours there was a majority of male patients. The overall male-to-female ratio in our patients and other younger patients reported in the literature was about 1.2:1. This difference may reflect hormonal factors that favor the development of meningiomas in adult women.12

Clinical Presentation
Preoperative seizures do not appear to be less common in children than in adults. Seizures were present in 25% of our patients and in 31% of those in the large series of pediatric and adolescent meningiomas reported by Merten, et al.28 Ramamurthi, et al.,32 found a 29% incidence of seizures in adults.

Tumor Location
It has been suggested that the lateral ventricle is a favored site for childhood meningiomas. Intraventricular tumors constituted 17% of meningiomas in children and adolescents reported by Merten, et al.,28 and 44% of those reported by Herz, et al.,21 however, Crouse and Berg1 and Ferrante, et al.,31 found no meningiomas at this location. In our series, 13% of the tumors were intraventricular. In all pediatric series combined, 9.4% of meningiomas were intraventricular (Table 2). Recent studies have shown that 5% of adult meningiomas are intraventricular.33

There were no infratentorial meningiomas arising in the first two decades of life in several series2,13,14,28 and the percentage ranged from 19% to 46% in three others.4,5,28 Infratentorial meningiomas accounted for 13% of the tumors in our patients and 14.4% of tumors in all the pediatric series combined (Table 2). In adults, approximately 10% of meningiomas are infratentorial.33 Thus, although the great majority of meningio-
mas of the first two decades of life are supratentorial and extraventricular, they can occur more frequently in the ventricles and in infratentorial locations than meningiomas in adults.

**Neuroimaging Characteristics**

The MR imaging characteristics of meningiomas in adults have been well described. In many cases, there is a "dural tail," a small amount of contrast enhancement along the dura adjacent to the meningioma. Similar features were seen in our cases evaluated by MR imaging. Pathological studies have shown the absence of a dural attachment in meningiomas of the first two decades of life. Further studies are necessary to investigate whether this will correspond to the lack of a dural tail on MR images.

**Histological Considerations**

Meningiomas are difficult to diagnose and classify because their histological appearance is highly variable and they may mimic glial tumors. Many tumors classified as meningiomas prove to be misdiagnosed; in one series, only 48 of 75 meningiomas were classified as such after careful review. Immunochemical stains can help establish the diagnosis. In our series, all tumors were positive for vimentin and negative for GFAP, supporting the diagnosis of meningioma.

Meningiomas of the first two decades of life reportedly have a higher incidence of "malignant" changes than meningiomas in adults. The lack of universally accepted histological criteria to define aggressive behavior makes such comparisons difficult. In our series, necrosis was present in 29% of the tumors, an increased number of mitoses in 33%, and cortical invasion in 14%. However, 71% of the meningiomas in our patients were benign (Grade I), 29% were atypical (Grade II), and none was anaplastic (Grade III). In adults, 60% to 90% of meningiomas are benign, 5% to 20% are atypical, and approximately 10% are anaplastic. These findings suggest that meningiomas of the first two decades of life have histological features similar to those of adults and are not more malignant than their adult counterparts.

**Outcome**

The operative mortality rates in early series of pediatric meningiomas were high, probably because of the lack of modern medical support. Recent series, including ours, have shown no perioperative mortality. The determinants of long-term survival after surgery for intracranial meningiomas are still being debated. Meningeal tumors such as sarcomas, hemangiopericytomas, and angioelastic and melanocytic tumors are more aggressive than classic meningiomas and have a poor prognosis. In their review of the literature, Drake and Hoffman reported that the 5-year survival rate increased from 76% to 84% when meningeal sarcomas were excluded. We included only classic meningiomas in our series and we suggest that a similar criterion be used in other retrospective studies so as to facilitate comparison of data.

In adults with intracranial meningiomas, total excision seems to be the most important factor in decreasing the incidence of tumor recurrence. Barbaro et al. showed that 96% of patients who underwent gross total
Resection of an intracranial meningioma were recurrence-free during a follow-up period of 5 to 15 years. The recurrence of meningiomas in the first two decades of life is difficult to assess. In one study of pediatric meningiomas, recurrence was shown to decrease the 5-year survival rate from 94% to 64%. In most series, however, the authors stated that the patients were “doing well,” without specifying if the follow-up evaluation included radiological studies. Nevertheless, there have been no documented cases of recurrence after gross total resection of meningiomas developing in the first two decades of life.

Because the growth rate of meningiomas is slow and variable, the length of the follow-up period is important in assessing recurrence. After a maximum follow-up time of 20 years in 69 adults with intracranial meningiomas, Jääskeläinen reported a recurrence rate of 19%. The data available in the young population (Table 3) do not suggest such a high incidence after gross total surgical resection, even in cases with more than 20 years of follow-up review. Although further studies are necessary to corroborate this observation, meningiomas in the young population do not, as previously suggested, appear to be more aggressive than those in adults.

After incomplete resection, a tumor may continue to grow and become symptomatic. Regrowth after subtotal surgical resection in adults is thought to occur in 10% to 26% of cases. The available data on meningiomas of the first two decades of life (Table 3) do not allow us to establish a clear rate of regrowth after subtotal resection for meningiomas in this age group.

Several factors may influence regrowth. The histological subtype of meningioma does not correlate with the recurrence of subtotally resected meningiomas in adults. Although histological features such as necrosis, invasion of adjacent brain, and mitoses may portend a more aggressive behavior, meningiomas lacking these features have recurred after subtotal resection, and many of the histological features of malignant meningiomas can be observed to a lesser degree or as isolated characteristics in benign tumors. Moreover, benign meningiomas constitute the most frequent category of recurrence. Of 43 tumors that recurred in the series of Jääskeläinen, et al., 56% were benign. These contradictory data on the importance of histological features on regrowth after subtotal resection in adults make it very difficult to make useful comparisons with the findings in younger patients.

Radiation therapy after partial resection of meningiomas appears to be beneficial in adults. Owing to the paucity of cases, it is difficult to establish the role of radiation therapy in the treatment of meningiomas of the first two decades of life. In our series, all three patients who underwent radiation therapy after subtotal resection are recurrence-free, as is one patient who did not receive radiation therapy. Leibel, et al., reported three patients who received radiation therapy and were “well” at follow-up review (6 to 17 years). Nevertheless, the adverse effect of radiation on the developing brain cannot be ignored. With the widespread availability of MR imaging, frequent follow-up studies to document regrowth may be advocated before instituting radiation therapy.

**Conclusions**

Meningiomas of the first two decades of life are uncommon but not rare tumors. Unlike meningiomas in adults, which occur predominantly in women, meningiomas in younger patients appear to be slightly more common in males. As in adults, the great majority of meningiomas in younger patients are supratentorial. Histological types and features are similar to those observed in adults. Meningiomas developing in the first two decades of life have a low recurrence rate after gross total resection, and the outcome and survival rate are excellent.

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