Radiation therapy for incompletely resected meningiomas

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Twelve patients with incompletely resected meningiomas were treated with postoperative radiation therapy. Nine of these patients had previously undergone incomplete surgical resection, and three had suffered one or more postoperative recurrences. The median dose of irradiation was 5490 rads in 6 weeks (range 4800 to 6080 rads). All patients were followed with serial neurological examinations and computerized tomography (CT) scans. Median follow-up period was 54 months (range 20 to 120 months); 10 of the 12 patients were followed for longer than 42 months posttreatment. Nine patients had no clinical evidence of recurrent disease after radiation therapy, and CT scans confirmed lack of progression or a gradual decrease in tumor size. Three patients had tumor recurrences; two of these lesions appeared at 70 and 112 months after irradiation as extracranial extensions beyond the margin of the irradiation field, and one has exhibited recurrence within the field at 48 months. Three patients who were treated after prior recurrences have demonstrated prolonged progression-free intervals in comparison to the intervals between recurrences prior to irradiation. No significant complications attributable to treatment have been found in any of the patients. These results are discussed in relation to previous reports of the incidence of meningioma recurrence after incomplete resection.

KEY WORDS • meningioma • radiation therapy • incomplete resection •

MENINGIOMAS are benign intracranial neoplasms which constitute approximately 15% of all primary brain tumors. Surgical removal is the treatment of choice for these lesions; the role of radiation therapy, either as a primary or postoperative modality, remains to be established. Several investigators have been impressed with the relative insensitivity of meningiomas to irradiation and thus have concluded that radiation therapy has little value in the management of these tumors. In contrast, recent reports, including those of Bouchard, Wara, et al., Carella, et al., have found radiation therapy to be of benefit in patients with incompletely excised meningiomas. The latter studies show that postoperative radiation therapy is able to significantly reduce the rate of local recurrence in patients followed for 5 to 10 years posttreatment, implying clinically significant growth arrest or actual elimination of growth potential of these low-grade lesions.

The natural history of meningiomas is usually measured over many years, requiring long-term follow-up periods to clinically document tumor status. This review was undertaken to examine our experience with 12 patients treated with modern techniques of radiation therapy following incomplete resection of meningiomas. Our study differs from previous reports as we have routinely obtained detailed serial computerized tomography (CT) scans for all patients during the last 8 years, both as an aid to precise radiation therapy and to evaluate response to treatment. In addition, the patients in this series were treated with standard fractionation to similar doses in a relatively systematic manner.

Clinical Material and Methods

We reviewed the charts of all patients with a diagnosis of intracranial meningiomas who were seen at the Medical College of Wisconsin, Department of Radiation Oncology, from 1970 through 1981. A total of 15 such patients were treated during this time, of whom three were excluded because of concurrent second malignant neoplasms (one lung, one glioblastoma, and one intracranial angiosarcoma). The 12 remaining patients had undergone previous surgery and were known to have had gross residual meningioma as confirmed by the operating surgeon and/or as evidenced by postoperative CT scans. Histological confirmation of meningiothelial or transitional cell meningioma was obtained in all cases at the initial surgical resection.

This series included eight females and four males.
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TABLE 1
Location of tumor, radiation therapy (RT), and course in 12 patients

<table>
<thead>
<tr>
<th>Case No.</th>
<th>Location of Tumor</th>
<th>No. of Ops Prior to RT</th>
<th>RT Dose*</th>
<th>Progression-Free Period†</th>
<th>Time to Recurrence†</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>petrous</td>
<td>1</td>
<td>5800/24/78</td>
<td></td>
<td>9½</td>
<td>marginal recurrence in the neck; recurrent tumor histologically malignant; pt alive with disease at 10 yrs</td>
</tr>
<tr>
<td>2</td>
<td>parasagittal</td>
<td>1</td>
<td>5400/18/43</td>
<td>10+</td>
<td></td>
<td>1st recurrence 2 yrs after 1st surgery; 2nd recurrence 2 yrs after 2nd surgery; marginal recurrence in the maxilla 6 yrs after 3rd surgery + RT; pt alive with disease at 7 yrs</td>
</tr>
<tr>
<td>3</td>
<td>sphenoid</td>
<td>1</td>
<td>4800/16/35</td>
<td>6+</td>
<td></td>
<td>recurrence 1½ yrs after 1st surgery; clinical progression 7 mos after 2nd surgery; no recurrence at 4 yrs after RT</td>
</tr>
<tr>
<td>4</td>
<td>sphenoid</td>
<td>1</td>
<td>5400/30/44</td>
<td>5+</td>
<td>6</td>
<td>recurrence 1 yr after 1st surgery; no recurrence at 4½ yrs after 2nd surgery + RT; in-field recurrence at 4 yrs after surgery + RT; pt alive with disease after further surgery + 125I implants</td>
</tr>
<tr>
<td>5</td>
<td>sphenoid</td>
<td>3</td>
<td>5400/36/52</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>sphenoid</td>
<td>1</td>
<td>5800/29/42</td>
<td>4½+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
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<td>2</td>
<td>5400/30/42</td>
<td>4+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
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<td>5630/32/45</td>
<td>4½+</td>
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<tr>
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<td>4½+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>sphenoid</td>
<td>1</td>
<td>5580/31/44</td>
<td></td>
<td>4</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>sphenoid</td>
<td>1</td>
<td>6080/33/56</td>
<td>2½+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>sphenoid</td>
<td>1</td>
<td>5220/29/44</td>
<td>2+</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Radiation dose to tumor/number of fractions/days of course.
† Years after irradiation.

The median age at the time of treatment was 48 years; there was one 15-year-old child and the 11 adults ranged in age from 31 to 74 years. Eight tumors were located along the sphenoid bone, two at the base of the sphenoid bone in the midline and six along the lateral aspects of the greater sphenoid wing. In two of the latter tumors, extension into the orbit was noted. The remaining lesions were located as follows: one in the posterior parasagittal sinus, one in the orbit, and two along the petrous bone.

Primary treatment consisted of initial surgical resection. Nine of the 12 patients were referred for radiation therapy after initial subtotal resection, and gross residual tumor was identifiable in each instance. Three patients were referred following documented tumor recurrence. A second incomplete surgical resection was undertaken prior to referral for radiation therapy in two of these cases. In the third case, the patient was referred for irradiation after two recurrences and a third subtotal resection.

All patients were treated with megavoltage irradiation, using photons of 6, 18, or 25 MeV energy. Ten patients were treated with daily fractions of 180 to 200 rads five times per week, and two patients received 300 rads per fraction at three fractions per week. Total tumor doses ranged from 4800 to 6080 rads, with a median dose of 5490 rads.

All patients were followed jointly by the Departments of Radiation Oncology and Neurosurgery or Ophthalmology. Serial CT scans were obtained in 11 of the 12 patients. Deterioration of neurological status or an increase in tumor mass visualized on CT scans was taken as evidence of recurrent disease. The median follow-up period after irradiation is 54½ months, with a range of 20 to 120 months. Ten of the 12 patients have been followed for longer than 42 months posttreatment.

Results

A clinical summary including treatment and current status of the 12 patients studied is presented in Table 1. Nine patients remain free of clinical and radiographic signs of tumor progression. Serial CT scans in these nine cases have shown stability or gradual diminution in tumor size (Fig. 1), confirming a lack of tumor growth.

Tumor Recurrence

The tumor has recurred in three patients. Two patients developed recurrent tumors at the edge of the previously irradiated fields, thus representing "marginal" recurrences. In both instances, the marginal extensions occurred after treatment of sizable basal meningiomas, with extracranial extensions beyond the treatment fields in regions adjacent to the calvaria. One patient (Case 1) suffered a recurrence 112 months after completion of radiation therapy. This patient initially had a large tumor extending along the petrous ridge into the posterior fossa. Recurrence was in the upper portion of the neck, below the inferior margin of the treatment field. The lesion was considered to be histologically malignant at the time of recurrence, in contrast to the initial pathological diagnosis of a benign meningioma. The second patient (Case 5, reported below), with a marginal recurrence, developed tumor extension into the maxillary region, below and anterior to a large sphenoid wing meningioma which initially
FIG. 1. Computerized tomography scans in Case 6. Upper Left: Preoperative study demonstrating extensive tumor with marked proptosis, and bone involvement. Upper Right: Scan obtained postoperatively and prior to irradiation, showing significant residual tumor still present. Lower: Scans 6 months (left) and 42 months (right) postirradiation, showing decrease in size of the residual meningioma.

had massive orbital involvement. The third patient (Case 10) developed a true in-field recurrence following postoperative irradiation for a large lesion of the sphenoid bone. The lesion recurred 4 years after treatment at the medial resection margin adjacent to the cavernous sinus.

Complications

Postoperative complications were uncommon in this series despite the central location of these tumors. Radiation therapy at doses of 5000 to 5500 rads has been well tolerated. No serious complication has occurred secondary to irradiation. Immediate effects of irradiation were limited to the anticipated temporary alopecia; no significant debilitating effects, such as nausea or lassitude, required treatment during irradiation. Three patients developed acute conjunctival irritation during treatment when the orbit was intentionally irradiated; signs were transitory with no permanent clinical problem. In Case 5, a 15-year-old boy, there has been deterioration in endocrine status after irradiation. This patient had tumor extending to the pituitary gland; 6 months following the third operative intervention and course of irradiation, panhypopituitarism was documented. There has been no other long-term disability among the patients in this series.

Illustrative Case Reports

Three of the 12 patients had initially been treated with surgery alone, and subsequently developed recurrences 1 to 2 years postoperatively. The clinical courses clearly demonstrated biologically aggressive disease (Fig. 2). Postoperative irradiation substantially prolonged the progression-free interval in one patient (Case 5) and has apparently prevented recurrence or progression in two patients (Cases 7 and 9). Brief case reports of these three patients are presented.

Case 5

This 11-year-old boy was brought to the hospital in 1973 with a 1-year history of seizures manifested by vertigo and abnormal olfactory sensations. He was found to have a huge meningioma involving the sphenoid bone from the right supraorbital region to the foramen magnum, extending along the optic nerve into the orbit. A subtotal resection was performed, leaving gross residual tumor along the optic nerve (Fig. 3a).

The patient did well for 19 months. He then presented with progressive seizures and proptosis of the eye. He was found to have a recurrent retrobulbar mass and sphenoid bone tumor. Combined orbitocraniotomy was performed and the lesion was largely resected with minimal residual tumor in the medial orbit. He did well for 23 months, when he was readmitted for evaluation of further proptosis and seizure activity. A CT scan revealed a second recurrence along the sphenoid bone, extending to the midline and into the orbit. A third surgical procedure was performed, consisting of a frontal craniotomy which subtotally resected the tumor, leaving behind gross disease at the petrous apex and in the orbital region (Fig. 3b). The patient was referred for postoperative irradiation. He received 5400 rads in 36 fractions over 52 days to a large volume including the lower anterior and middle cranial fossae and the involved orbit. Stable disease was apparent on CT scanning 4 years postirradiation (Fig. 3c and d).

The patient did well until 70 months after irradiation when he returned with prominent right malar swelling.
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A CT scan confirmed recurrence of the tumor along the inferior orbit and into the maxillary region (Fig. 3e), with no significant change in the intracranial and orbital regions within the irradiated volume (Fig. 3f). Whereas the intervals between recurrences were approximately 2 years after each of two surgical procedures, the progression-free interval after irradiation was longer than 6 years, with apparent control of tumor within the volume of irradiation.

Case 7

This 47-year-old woman came to the hospital in June, 1976, with a 3-month history of decreased vision in the left eye and associated left-sided headaches. Angiographic and CT studies revealed a 5- to 6-cm tumor lying along the left sphenoid wing. At frontotemporal craniotomy the tumor was found to envelop the middle cerebral artery, optic nerve, and carotid artery, and to extend along the third cranial nerve. The tumor was subtotally resected. Postoperatively, the patient had a flaccid hemiparesis. She declined postoperative radiation therapy, and subsequently had gradual improvement in her neurological function, with only moderate residual right arm weakness.

In January, 1978, 16 months after surgery, the patient returned with progressive visual loss in the left eye and a dense right hemiparesis. A CT scan showed progression of the meningioma, which surrounded the carotid artery and its major branches (Fig. 4 left). At surgery, the tumor was found completely encasing the left carotid artery and optic nerve; subtotal resection was then effected and the left optic nerve was sectioned to relieve distortion of the chiasm. The patient had gradual improvement in her hemiparesis postoperatively until September, 1978, when she suffered further neurological deterioration. Residual tumor was identifiable on CT, and she now consented to irradiation. She received 5400 rads in 30 fractions over 42 days, and had mild improvement in her hemiparesis during irradiation. At follow-up examination 4 years after irradiation, she remained stable neurologically, with a slight decrease in tumor size on CT scans (Fig. 4 right).

Case 9

This 42-year-old man came to the hospital in July, 1977, with progressive diplopia and left ptosis of 5 years' duration. Examination revealed weakness of the left third, fifth, and sixth cranial nerves. Radiographic
studies were consistent with a meningioma of the para-
ellar petrous tip region. Gross total resection was
performed. One year later, the patient presented with
recurrent diplopia, ptosis, and exophthalmos. X-ray
films showed development of exostosis of the postero-
lateral aspect of the sella. Angiograms demonstrated
recurrent meningioma. A temporoparietal craniotomy
revealed tumor extending into the cavernous sinus and
wrapped around the fifth cranial nerve. Subtotal resec-
tion was accomplished, and postoperatively the patient
improved but exhibited intermittent diplopia and facial
paresthesias. He was referred for postoperative irra-
diation, receiving a total dose of 5400 rads in 30 fractions
over 41 days to the left sphenoid site. After irradiation,
he had moderate improvement in his diplopia and
paresthesias, and returned to full employment. At 4½
years, he has had no significant deterioration of neu-
rological status, and CT scans have shown no significant
change in the residual tumor mass.

Discussion

In this series, 12 patients with incompletely resected
meningiomas were treated in a similar fashion using
modern techniques of radiation therapy. The charac-
teristics of this patient population are similar to many
of those reported in the literature. The median age of
the patients at the time of treatment was 48 years; this
is consistent with most series, which have found menin-
giomas to be most common in the fourth, fifth, and
sixth decades of life. The female: male ratio in this series
was 2:1; this female predominance is in agreement with
most reported data. This series differs from most re-
ports, however, in regard to the location of the tumor.
In surgical series, parasagittal tumors are most com-
mon.3,10,11,13 The predominance of lesions in the sphen-
oid area (eight of 12 in this series) reflects the increased
difficulty of completely resecting meningiomas along
the medial sphenoid bone.

Several retrospective studies have shown that the
completeness of surgical excision is the major progno-
stic factor predicting freedom from recurrence and ulti-
mate survival. Wara, et al.,13 Luk, et al.,7 and Melamed,
et al.,9 each concluded that recurrence-free survival
after apparent complete resection was sufficiently high
(88% to 100%) that further adjuvant therapy was not
indicated. In contrast, patients who have undergone an
incomplete resection are at significant risk for a subse-
quent recurrence of their meningioma. Of 58 patients
reported by Wara, et al.,13 who had incomplete resec-
tion of their tumor without postoperative irradiation,
74% subsequently suffered recurrence. Melamed, et
al.,9 and Luk, et al.,7 each found a recurrence rate of
approximately 50% in their series of patients with
incomplete removal treated without postoperative ir-
radiation.

Despite the known natural history of meningiomas
suggesting the chronicity of these tumors, most recur-
rences are manifest within a short period of time.

Available data confirm that clinical signs of recurrence
appear with a peak incidence between the 2nd and 4th
postoperative years; the mean interval to clinical re-
currence is approximately 4 years.6,9 Recurrence has an
adverse effect on ultimate survival.3,7

Radiation therapy as the sole modality of treatment
for inoperable meningiomas has been used with some
success. Bloom6 reports 5-year progression-free survival
in 73% of 87 patients treated with irradiation alone.
Friedman7 has reported growth arrest in seven of 12
inoperable or recurrent meningiomas after irradiation
alone. Meningiomas of the optic nerve sheath have
been found by Smith, et al.,12 to respond favorably to
irradiation alone. These reports of the efficacy of radia-
tion therapy as primary treatment certainly justify its
consideration as an adjuvant to surgery in selected cases
with incomplete removal.

In view of the significant recurrence rate among
incompletely resected meningiomas, radiation therapy
has been added at many centers as a postoperative
measure in an attempt to delay or prevent such recur-
rences. Several reports now indicate encouraging re-
results. Wara, et al.,13 found an incidence of recurrence
of 29% (10 of 34 patients) between 5 and 20 years after
postoperative irradiation following incomplete resec-
tion. Bouchard3 found a recurrence rate of only 11% am-
ong 17 patients following irradiation. Carella, et al.,3
have found neurological stabilization in 41 of 43 pa-
tients who underwent subtotal resection and postoper-
ative radiation therapy.

In our series of 12 patients with incompletely resected
meningiomas and a median follow-up period of 54½
months, only three patients have had recurrences fol-
lowing irradiation. The recurrent lesions were found 4,
6, and 9 years after radiation therapy. In two of these
patients, the recurrent tumor was located beyond the
margins of the irradiation fields. Only one patient has
clearly had tumor recurrence within the previously
irradiated area. Nine of the 12 patients remain neuro-
logically free of tumor progression; eight of these pa-
tients show no evidence of tumor recurrence or pro-
gression on follow-up CT scans.

The efficacy of irradiation in preventing or delaying
 tumor progression is readily apparent in the three pa-
tients, who serve as their own “controls” following
clinically aggressive disease prior to irradiation. These
three patients had evidence of multiple recurrences
soon after surgery. Only one has suffered a recurrence
after radiation therapy, and in this patient the time
interval to extension beyond the irradiation field was
significantly longer than the previous intervals to recur-
rence. One cannot conclude that these patients are
“cured” of their disease; longer follow-up monitoring
is needed, as can be seen with the development of
recurrences at 112 months and 70 months after therapy
in Cases 1 and 5, respectively. However, it does appear
that irradiation has at least provided significant growth
arrest of these tumors, prolonging the interval to recur-
rence and perhaps preventing regrowth of the tumor.
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The documentation of disease extension beyond the cranium in sizeable basal meningiomas indicates the necessity to incorporate fairly wide margins below the base of the skull. The dose herein reported (approximately 5000 rads in 30 fractions over 6 weeks) is well within normal brain tolerance. No serious complications were noted among the patients in this series. In view of the efficacy and lack of morbidity associated with postoperative irradiation, we conclude that postoperative radiation therapy is indicated for incompletely resected meningiomas. The pattern of recurrence at the margin of previous treatment fields suggests that wide-field irradiation may be necessary for extensive meningiomas at the base of the skull to achieve disease control.

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References


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