Long-term Risk of Recurrence After Intact Excision of Pleomorphic Adenomas of the Lacrimal Gland

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Objective: To ascertain the need for follow-up after excision of pleomorphic adenoma of the lacrimal gland.

Methods: Medical records were reviewed for 133 patients and only those patients with 5 years or more of follow-up were classified into the following 5 subgroups: those with intact excision (group IA, n=46), those with surgically intact excision but areas of complete attenuation of the pseudocapsule at histologic analysis (group IB, n=7), those with previous inadvertent incisional biopsy (group IIA, n=9), those with breach of the pseudocapsule during attempted intact excision (group IIB, n=5), and those undergoing definitive surgery because of tumor recurrence after previous incomplete excision (group III, n=5).

Results: Seventy-two patients were followed up longer than 5 years; there were no known tumor recurrences among 61 patients excluded with shorter follow-up. Patients in groups IA and IB exhibited no tumor recurrences at 8.2 to 34.1 years of follow-up. A benign recurrence occurred along the superior orbital fissure in 1 patient in group IIA 12½ years after the initial surgery and was resected. There were no recurrences in patients in groups IIB or III.

Conclusions: Discharge would seem justified after intact excision of lacrimal gland pleomorphic adenoma, even when histologic examination shows extreme attenuation of the pseudocapsule. Long-term follow-up is, however, necessary when there has been tumor disruption, either inadvertently during previous biopsy or by capsular breach during definitive excision.

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Pleomorphic adenoma of the lacrimal gland has a tendency for pervasive recurrence after incomplete excision, and these recurrent tumors have substantial potential for late malignant transformation. Incomplete excision may arise from misguided or unintentional incisional biopsy before tumor recognition, from piecemeal excision of a large tumor, or as a result of a breach of the tumor's pseudocapsule during attempted intact excision. Preoperative recognition of these tumors is, therefore, imperative for correct management, and this has been aided by improvements in orbital imaging and better understanding of the signs and symptoms and the radiologic appearances of these tumors.

Intact excision of the tumor and biopsy track is recommended when there has been a previous inadvertent biopsy, and these cases have been kept under long-term follow-up for recurrence. Conjecturally, the possibility of recurrence is also greater when there has been disruption of the tumor pseudocapsule (the pseudocapsule being compressed remnants of the surrounding normal tissues) or when there has been intact excision but histologic examination reveals complete attenuation of the pseudocapsule.

The outcomes for 72 patients followed up longer than 5 years after treatment of lacrimal gland pleomorphic adenoma are reported; some of these patients have been included in previous reports. This study specifically addressed the long-term risk of recurrence and need for follow-up in these patients.

Methods

The medical records were reviewed for 133 patients (66 men) who, between January 1, 1969, and December 31, 1998, received treatment of lacrimal gland pleomorphic adenoma under the care of the Orbital Clinic at Moorfields Eye Hospital, London, England. At primary surgery, all underwent attempted intact excision of the tu-
When there had been default from clinical review, an attempt was made to contact both patients and their general practitioners for details, and only those patients with at least 5 years of verified follow-up were included in the final data analysis. For the analysis, patients were classified into the following 5 groups: those with intact excision (group IA, n = 46), those with surgically intact excision but areas of complete attenuation of the pseudocapsule at histologic analysis (group IB, n = 7), those with previous inadvertent incisional biopsy (group IIA, n = 9), those with breach of the pseudocapsule during attempted intact excision (group IIB, n = 5), and those undergoing definitive surgery because of tumor recurrence after previous incomplete excision (group III, n = 5).

REPORT OF CASES

A 66-year-old man was seen in 1989 with a 7-month history of left periorbital ache (worse on upgaze), proptosis, and diplopia. Lacrimal gland carcinoma was considered likely in view of the patient’s history, but findings at incisional biopsy revealed pleomorphic adenoma, and the patient underwent intact excision of the tumor via lateral orbitotomy, along with excision of the biopsy tract. Postoperatively, he experienced occasional paroxysms of retrobulbar pain but in 1999 was noted to have developed mild conjunctival chemosis and proptosis of the left eye (Figure, A). A computed tomographic scan showed a small, rounded, retrobulbar mass along the superior orbital fissure (Figure, B), and open biopsy demonstrated an amputation neuroma, which was thought to be possibly responsible for the patient’s periorbital pain. In 2002, he developed signs of left optic nerve disease, and worsening proptosis, and a computed tomographic scan showed further enlargement of the retrobulbar mass (Figure, C). An excision biopsy specimen showed pleomorphic adenoma with no evidence of malignant transformation.

RESULTS

Of the 133 patients with pleomorphic adenomas, 72 (54%) were followed up longer than 5 years (Table 1).

Surgically intact excision was achieved in 106 patients (80%), but there was histologic evidence of extreme attenuation of the pseudocapsule in 10 patients and tumor at the excision line in 1 patient. In patients followed up longer than 5 years with surgical and histologic clearance (group IA, n = 46), there were no recurrences after excision of either orbital (n = 38) or palpebral lobe (n = 8) tumors. Follow-up in this group ranged from 6 to 32 years (Table 1). Of the 11 patients having borderline histologic clearance (group IB; Table 1), 7 patients followed up more than 5 years have remained tumor free at 10.2 to 20.6 years (mean, 13.0 years). Two of the 7 patients defaulted follow-up after 12.9 and 18.6 years.

In 7 patients, there was some intraoperative doubt about the integrity of the pseudocapsule (group IIB; Table 1). In 5 of these patients, there was a definite or highly probable breach, with spillage of tumor cells; in 1, there was suspicion of tumor adherence to bone, which
was removed at surgery; and in 1, further tissue was excised along an area of extreme “capsular” attenuation. Of 5 patients with adequate follow-up, 1 tumor-free patient died of other causes and the other 4 were disease-free at 6 to 16 years of follow-up.

In recent years, the rate of inadvertent biopsy of pleomorphic adenomas has markedly decreased as a result of improved radiologic evaluation and better understanding of these tumors.6 Early in the study, however, 11 patients experienced inadvertent biopsy because the symptoms and radiologic findings suggested carcinoma, and 1 recent patient had an unrecognized palpebral lobe tumor after previous biopsy-proved chronic dacryoadenitis. Because these patients (group IIA) were treated earlier in the series, there is potential for longer follow-up than in the other groups (Table 2). Long-term follow-up data were available for 9 of 12 patients in group IIA (Table 1). Two of the 9 patients died without tumor recurrence, 2 failed to attend regular follow-up, and 5 are still being followed up. One has received treatment of recurrent tumor (Table 1).

Eight patients were referred with recurrent tumor after incomplete excision 3 to 44 years (mean, 16 years) before. Three of these patients required exenteration and 5 underwent local intact resection of the recurrent tumor. Two patients had palpebral lobe adenomas that developed at 3 and 12 years after the first surgery, and 6 were originally orbital lobe tumors, 1 in a patient who had already undergone surgery because of a previous recurrence and 1 in a patient with malignant transformation that developed 44 years after the initial surgery. Five patients had adequate follow-up for this study (group III; Table 1). Four of these patients are disease free at 7 to 13 years after treatment, and the patient with malignant transformation died of metastatic disease 11 years after surgery.

### Table 1. Clinical and Follow-up Characteristics in 133 Patients Having Surgery Because of Lacrimal Gland Pleomorphic Adenoma

<table>
<thead>
<tr>
<th>Definitive Surgery</th>
<th>No. of Patients</th>
<th>Subgroup With &gt; 5 Years of Follow-up</th>
<th>Male Patients</th>
<th>Definitive Surgery</th>
<th>Follow-up After Definitive Surgery</th>
<th>Tumor Recurrence/Time After Definitive Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgically and histologically clear (group IA)</td>
<td>95</td>
<td>46 (48)</td>
<td>24/46 (52)</td>
<td>46.8 Mean</td>
<td>17.2 Mean</td>
<td>None</td>
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<tr>
<td>Surgically clear but attenuated pseudocapsule (group IB)</td>
<td>11</td>
<td>7 (64)</td>
<td>4/7 (57)</td>
<td>45.7 Mean</td>
<td>15.0 Mean</td>
<td>None</td>
</tr>
<tr>
<td>Inadvertent biopsy before definitive procedure (group IIA)</td>
<td>12</td>
<td>9 (75)</td>
<td>4/9 (44)</td>
<td>43.0 Mean</td>
<td>16.6 Mean</td>
<td>1/9 (11)/12 y</td>
</tr>
<tr>
<td>Probable spillage of cells at definitive surgery (group IIB)</td>
<td>7</td>
<td>5 (71)</td>
<td>2/5 (40)</td>
<td>47.0 Mean</td>
<td>14.2 Mean</td>
<td>None</td>
</tr>
<tr>
<td>Recurrence after previous partial tumor excision (group III)</td>
<td>8</td>
<td>5 (63)</td>
<td>2/5 (40)</td>
<td>49.2 Mean</td>
<td>10.1 Mean</td>
<td>None</td>
</tr>
<tr>
<td>All patients</td>
<td>133</td>
<td>72 (54)</td>
<td>36/72 (50)</td>
<td>45.7 Mean</td>
<td>16.2 Mean</td>
<td>1/72</td>
</tr>
</tbody>
</table>

*Values are given as number of patients (percentage) unless otherwise indicated.

### Table 2. Potential Maximum Follow-up Intervals in 133 Patients, Calculated From an Arbitrary Datum

<table>
<thead>
<tr>
<th>Definitive Surgery</th>
<th>No. of Patients With Follow-up &gt; 5 Years</th>
<th>Potential Follow-up Interval (to Datum December 31, 2004), y</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surgically and histologically clear (group IA)</td>
<td>46</td>
<td>21.2 Mean</td>
<td>.01</td>
</tr>
<tr>
<td>Surgically clear but attenuated pseudocapsule (group IB)</td>
<td>7</td>
<td>20.3 Mean</td>
<td>.08</td>
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<tr>
<td>Inadvertent biopsy before definitive procedure (group IIA)</td>
<td>9</td>
<td>23.0 Mean</td>
<td>.005</td>
</tr>
<tr>
<td>Probable spillage of cells at definitive surgery (group IIB)</td>
<td>5</td>
<td>19.3 Mean</td>
<td>.11</td>
</tr>
<tr>
<td>Recurrence after previous partial tumor excision (group III)</td>
<td>5</td>
<td>12.6 Mean</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Values are given as number of patients (percentage) unless otherwise indicated.

Abbreviation: NA, not applicable.
*Probability of difference compared with group III mean.
Incomplete excision of lacrimal gland pleomorphic adenoma predisposes to tumor recurrence, and such recurrence often infiltrates normal orbital structures, leaving orbital exenteration as the only therapeutic option in some cases. In addition, the recurrent tumors are prone to malignant transformation. Reviewing 265 lacrimal gland tumors (although treated with different methods at multiple centers), Font and Gamel showed a 5-year recurrence rate of 3% for intact excision compared with 32% after incomplete excision and also estimated an overall 15-year recurrence rate of approximately 30%. Another series reported 16 recurrent tumors among 90 cases, of which showed malignant transformation at 5, 10, and 15 years after primary surgery. The surgical technique in this series was, however, most unsatisfactory, with surgical breach of the capsule or piecemeal tumor resection in at least 72 cases. Henderson reported on 19 patients with disease-free survival at 4 to 36 years after surgery despite capsular rupture in 2 cases—incisional biopsy in 1 and piecemeal tumor excision in another. The better disease-free survival for these patients probably owes much to heightened awareness of the imperative for intact tumor excision with preservation of the pseudocapsule and to improved imaging and understanding of the initial characteristics of lacrimal gland tumors.

On average, time to recurrence of pleomorphic adenoma of the head and neck is almost 15 years, that, together with reports in the ophthalmic literature and the characteristics of our group III patients, suggests that manifest recurrence is unlikely within 5 years of primary excision of such lacrimal gland lesions. To improve the reliability of the present investigation, therefore, only patients with more than 5 years of follow-up are included, although there were no recurrent tumors within the (excluded) group of patients with less than 5 years of follow-up.

The present series seems to be unique, with no tumor recurrence in 53 patients (groups IA and IB) at 8 to 34 years after surgically intact excision of the tumor, despite histologic evidence of severely attenuated pseudocapsule in 7 patients (group IB). Of 9 patients after resection of a previously biopsied tumor (group IIA), I had deep orbital recurrence at 12 years after primary surgery, and these patients would, therefore, seem to be at long-term risk of recurrent disease. Likewise, patients with surgical breach of the pseudocapsule are likely to be at risk of recurrence, although we noted no recurrences in 5 such patients (group IB) in this series.

We suggest that, although all patients should be apprised of the limited possibility of late recurrence, the long-term risk of recurrence after surgically intact excision is negligible and that occasional follow-up, rather than regular review, might be a preferred option in these patients. Repeated clinical review should probably be reserved for patients in whom there has been previous incisional biopsy or known breach of the capsule at surgery, or after surgery for recurrent disease.

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REFERENCES