Malignant Epithelial Tumors of the Lacrimal Gland

A Clinicopathologic Study of 21 Cases

Ramon L. Font, MD; Shannon L. Smith, MD; Richard G. Bryan, MD, PhD

Objective: To analyze 120 lacrimal gland masses collected during a 23-year period in the Ophthalmic Pathology Laboratory at the Cullen Eye Institute, Houston, Tex.

Methods: Of the 120 lacrimal gland tumors, we focused on a detailed clinicopathologic study of 21 malignant epithelial tumors. Follow-up was available in 19 (90%) of 21 cases.

Results: About two thirds of the masses (75 cases) were inflammatory, one third (41 cases) were of epithelial origin, and 3% (4 cases) were malignant lymphomas. Of the epithelial tumors, 17 (41%) were benign mixed tumors, 12 (29%) were adenoid cystic carcinomas arising de novo, 2 (5%) were adenocarcinoma arising de novo, 7 (17%) were malignant mixed tumors, and 3 (7%) were metastatic carcinoma. All of the patients with adenoid cystic carcinoma had local recurrences, and 60% of the patients died of their tumors (mean survival, 5 years); only 2 patients were alive 13 and 16 years after the initial surgery, both of whom had radical surgical procedures for recurrence following orbital exenteration.

Conclusion: The histopathologic classification and management of these tumors are discussed. This study supports the dismal prognosis of adenoid cystic carcinoma arising de novo.


Masses of the lacrimal gland are generally divided into 4 categories: inflammatory lesions, lymphomas, metastatic cancer, and primary epithelial tumors. Metastatic carcinoma to the lacrimal gland is uncommon but can be observed, particularly with breast and lung carcinoma. The most common epithelial tumors are, in order, benign mixed tumor (BMT) (pleomorphic adenoma), adenoid cystic carcinoma, and adenocarcinoma. Other rare variants of carcinoma are also seen, such as mucoepidermoid carcinoma. Some of the primary malignant epithelial tumors may arise from a preexisting BMT (pleomorphic adenoma) through a malignant transformation, but most arise de novo.

Because epithelial tumors of the lacrimal gland are uncommon (5% of biopsy specimens from expanding orbital masses), many of the published reports concerning the clinicopathologic correlations and follow-up of these tumors have contained few patients. This series of lacrimal gland masses represents the 23-year experience of the Ophthalmic Pathology Laboratory at the Cullen Eye Institute, Houston, Tex. We have also obtained clinical follow-up information for most of the patients with primary malignant epithelial tumors of the lacrimal gland.

RESULTS

INCIDENCE

We have collected 120 cases of lacrimal gland masses during a 23-year period (Table 1). Of these, 67% of the cases were nonepithelial in origin. These included 75 inflammatory masses and 4 primary lymphomas of the lacrimal gland. Most of the inflammatory masses were chronic dacryoadenitis, either of infectious or autoimmune cause.

Of the 41 epithelial tumors encountered, 17 (41%) were BMT, also known as pleomorphic adenoma, and 24 (59%) were malignant epithelial tumors, including 3 metastatic carcinomas. The metastatic malignant epithelial tumors included 2 breast carcinomas and one mucus-secreting carcinoma of unknown primary site.

The 21 primary malignant epithelial tumors consisted of 14 tumors arising de...
MATERIALS AND METHODS

We reviewed 120 cases of lacrimal gland tumors on file in the Ophthalmic Pathology Laboratory at the Cullen Eye Institute during a 23-year period. Twenty-one of these were primary malignant epithelial tumors, all of which were studied in detail. After careful review of the slides, each case was classified by histopathologic diagnosis, using the classification of the World Health Organization. Clinical and follow-up data were obtained in 19 of 21 patients with primary malignant epithelial tumors.

Inflammatory tumors, malignant lymphomas, metastatic tumors, and BMTs were included in the general classification of the 120 cases studied, but were excluded from the detailed analysis.

Twelve (63%) of 19 patients with primary malignant epithelial tumors with known follow-up had at least 1 recurrence at a mean interval of 1.6 years from the time of initial excision (Table 3). Most of these recurrences involved orbital bones, intraorbital structures, and direct intracranial extension. All 12 adenoid cystic carcinomas had local recurrences with a mean interval of 3.25 years, but 2 of the 5 patients with adenocarcinoma had no evidence of local recurrence. To further reinforce the poor prognosis of adenoid cystic carcinoma, 5 of 10 patients with known follow-up status had distant metastases, but only 1 of 4 patients with adenocarcinoma had distant metastases (Table 3). Both patients with MMT, one with mucoepidermoid carcinoma and the other with carcinosarcoma, had local recurrences and distant metastases of their tumors. Twenty-five percent of all patients with tumor recurrence had documented incomplete removal of the mass at the time of initial excision (data not shown).

Of the patients who underwent excision of a first recurrence, 46% had a second recurrence at a mean interval of 9.7 months from the time of excision of the first recurrence. All patients with more than 1 recurrence had adenoid cystic carcinoma arising de novo. One of these patients had a third recurrence (intracranial extension).

RECURRENCES

Of the 10 patients with adenoid cystic carcinoma arising de novo and with known follow-up (Table 4), 6 patients were known to have died of their tumors with a short mean survival time (4.5 years from time of initial surgery), and 1 patient who had brain metastases died of complications related to a fall. However, 2 patients with adenoid cystic carcinoma are alive and well 13 and 16 years after initial surgery. Both of these patients had early orbital exenteration followed by radical excisions of 1 and 2 recurrences, respectively. Of the 2 patients with adenocarcinoma arising de novo, 1 is alive and well 13 years after excision; the other died of his tumor with a survival of 4 years following initial surgery.

Of the 6 patients with MMT (adenoid cystic carcinoma or adenocarcinoma arising from a BMT) and known follow-up information (Table 4), 2 died of their tumors, 3 are alive and well, and 1 died of unknown causes. Two patients had rare variants of MMT (Table 4). The patient with mucoepidermoid carcinoma is known to be

Table 1. Histologic Classification of 120 Lacrimal Fossa Masses During a 23-Year Period

<table>
<thead>
<tr>
<th>Histopathologic Diagnosis</th>
<th>No. (%) of Cases*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inflammatory</td>
<td>75 (63)</td>
</tr>
<tr>
<td>Chronic dacryoadenitis</td>
<td>43 (37)</td>
</tr>
<tr>
<td>Reactive lymphoid hyperplasia</td>
<td>13 (11)</td>
</tr>
<tr>
<td>Sarcoïdosis</td>
<td>13 (11)</td>
</tr>
<tr>
<td>Lipogranuloma</td>
<td>2 (2)</td>
</tr>
<tr>
<td>Dacryops</td>
<td>4 (5)</td>
</tr>
<tr>
<td>Epithelial tumors</td>
<td>41 (34)</td>
</tr>
<tr>
<td>Benign mixed tumor†</td>
<td>7 (17)</td>
</tr>
<tr>
<td>De novo adenocarcinoma</td>
<td>2 (5)</td>
</tr>
<tr>
<td>Malignant mixed tumor†</td>
<td>7 (17)</td>
</tr>
<tr>
<td>Metastatic carcinoma</td>
<td>3 (7)</td>
</tr>
<tr>
<td>Malignant lymphoma</td>
<td>4 (3)</td>
</tr>
</tbody>
</table>

*Percentage either of total number of masses (for boldface diagnoses) or within each category (lightface diagnoses).
†Includes 1 adenoid cystic carcinoma, 4 adenocarcinomas, 1 carcinosarcoma, and 1 mucoepidermoid carcinoma.

Table 2. Epidemiologic Characteristics of Patients With Primary Malignant Epithelial Tumors of the Lacrimal Gland

<table>
<thead>
<tr>
<th>Classification</th>
<th>Origin</th>
<th>No. of Cases</th>
<th>Mean Age, y (Range)</th>
<th>Mean Duration of Symptoms (Range)</th>
</tr>
</thead>
<tbody>
<tr>
<td>All types</td>
<td>All</td>
<td>19</td>
<td>49 (14-80)</td>
<td>2 y (2 mo-10 y)</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>De novo</td>
<td>12</td>
<td>40 (14-78)</td>
<td>1.2 y (1 mo-3 y)</td>
</tr>
<tr>
<td>BMT*</td>
<td>1</td>
<td>80</td>
<td>Unknown</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>13</td>
<td>44 (14-80)</td>
<td>1.2 y (1 mo-3 y)</td>
<td></td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>De novo</td>
<td>2</td>
<td>56 (46-66)</td>
<td>3 mo</td>
</tr>
<tr>
<td>BMT*</td>
<td>4</td>
<td>62 (46-73)</td>
<td>5.8 y (5 mo-10 y)</td>
<td></td>
</tr>
<tr>
<td>All</td>
<td>6</td>
<td>60 (46-73)</td>
<td>4.4 y (3 mo-10 y)</td>
<td></td>
</tr>
</tbody>
</table>

*BMT indicates benign mixed tumor. Two rare variants of malignant mixed tumor are excluded from this group: mucoepidermoid carcinoma and carcinosarcoma (1 each).

LAST KNOWN STATUS OF PATIENTS

Of the 10 patients with adenoid cystic carcinoma arising de novo and with known follow-up (Table 4), 6 patients were known to have died of their tumors with a short mean survival time (4.5 years from time of initial surgery), and 1 patient who had brain metastases died of complications related to a fall. However, 2 patients with adenoid cystic carcinoma are alive and well 13 and 16 years after initial surgery. Both of these patients had early orbital exenteration followed by radical excisions of 1 and 2 recurrences, respectively. Of the 2 patients with adenocarcinoma arising de novo, 1 is alive and well 1.5 years after excision; the other died of his tumor with a survival of 4 years following initial surgery.

Of the 6 patients with MMT (adenoid cystic carcinoma or adenocarcinoma arising from a BMT) and known follow-up information (Table 4), 2 died of their tumors, 3 are alive and well, and 1 died of unknown causes. Two patients had rare variants of MMT (Table 4). The patient with mucoepidermoid carcinoma is known to be
dead of his tumor, with survival time of 15 months after
diagnosis of malignant transformation. His total clinical
course ran 19 years and included multiple excisions of
recurrent BMT prior to malignant transformation. The
patient with carcinosarcoma is presumed to have died
of her tumor because she developed lung metastases and
was subsequently lost to follow-up.

This series of 120 patients represents the 23-year
experience of the Ophthalmic Pathology Laboratory of
the Cullen Eye Institute at the Baylor College of Medi-
cine with masses involving the lacrimal gland. Our
data demonstrate that approximately two thirds of the
lacrimal gland masses were nonepithelial in origin,
mostly inflammatory in nature. These data contradict
the commonly taught theory that 50% of the masses
arising in the lacrimal fossa are epithelial and 50% are
nonepithelial, as was shown in the study by Reese2 of
504 patients with biopsy-proven expanding orbital
lesions. The results of our study are more consistent
with recent data from Shields and Shields,4 which also
showed that approximately two thirds of 142 biopsy
specimens from lacrimal gland masses were nonepi-
theelial in origin.

Malignant lacrimal gland tumors are quite rare, and
thus information about them in the literature is rela-
tively sparse. There have been several other reports of
epithelial tumors of the lacrimal gland from the 1930s
(before the modern classification system of lacrimal gland
tumors was proposed by Forrest5) up to the 1990s, but
many of these studies had limited follow-up informa-
tion. However, 2 larger studies from Zimmerman et al6
(116 cases) and the larger clinicopathologic and fol-
low-up study by Font and Gamel7 (265 cases) from the
Registry of Ophthalmic Pathology at the Armed Forces
Institute of Pathology has provided the most compre-
hesive database to date. In addition, there is a recent
review of 30 cases of malignant epithelial tumors of the
lacrimal gland8 at a referral clinic at Moorsfield
Eye Hospital in Great Britain. The data for all of these
studies, including ours, were collected at a tertiary re-
ferral center, thus indicating a possible bias toward more
difficult cases.

Our data on the epidemiology and follow-up are con-
sistent with those reported by Font and Gamel7 and
Wright et al8 within the limits of statistical analysis. These
similarities apply to incidence of tumor type, age, race,
incidence of recurrence, duration of symptoms, and clin-
ic outcome.

Despite the dismal prognosis of adenoid cystic carci-
noma and the high frequency of recurrent disease, there
were 2 long-term survivors in our study (13 and 16 years)
of the 11 patients with known follow-up, although both
these patients required a second surgical procedure for
recurrent disease. This percentage of long-term survival
is not statistically different than the 15-year actuarial sur-
vival curves reported by Font and Gamel,8 which showed
a 14% survival. Both of these patients were treated with
early primary exenteration with local irradiation, rais-
ing the possibility that this more aggressive treatment is
preferable for improving the chances of long-term sur-
vival. Aggressive treatment is also advocated by Wright
et al,8 who suggested in their study that long-term sur-
vivors were disproportionately treated with radical cranio-
orbital resections as opposed to more conservative
measures, even if the mean survival was not signifi-
cantly different. However, some studies have suggested

### Table 3. Incidence of Tumor Recurrence
After Initial Surgical Excision

<table>
<thead>
<tr>
<th>Type</th>
<th>Origin</th>
<th>No. of Cases With Recurrence*</th>
<th>Mean Interval (Range)</th>
<th>No. of Cases With Distant Metastases</th>
</tr>
</thead>
<tbody>
<tr>
<td>All</td>
<td>All</td>
<td>12/19</td>
<td>1.6 y (1 mo-9 y)</td>
<td>8/16</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>De novo</td>
<td>11/11‡</td>
<td>3.5 y (1 mo-9 y)</td>
<td>5/9</td>
</tr>
<tr>
<td>BMT*</td>
<td>All</td>
<td>1/1</td>
<td>4 y</td>
<td>0/1</td>
</tr>
<tr>
<td>All</td>
<td>All</td>
<td>12/12</td>
<td>3.5 y (1 mo-9 y)</td>
<td>5/10</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>De novo</td>
<td>2/2</td>
<td>2.1 y (2 mo-4 y)</td>
<td>1/2</td>
</tr>
<tr>
<td>BMT*</td>
<td>All</td>
<td>1/3</td>
<td>1 mo</td>
<td>1/2</td>
</tr>
<tr>
<td>All</td>
<td>All</td>
<td>3/5</td>
<td>1.4 y (1 mo-4 y)</td>
<td>1/4</td>
</tr>
<tr>
<td>De novo</td>
<td>13/13</td>
<td>3.4 y (1 mo-9 y)</td>
<td>6/11</td>
<td></td>
</tr>
<tr>
<td>All malignant mixed tumors§</td>
<td>2/4</td>
<td>1.9 y (1 mo-4 y)</td>
<td>0/3</td>
<td></td>
</tr>
</tbody>
</table>

* BMT indicates benign mixed tumor.
‡ In 4 of 11 recurrences listed (presumed to be recurrent adenoid cystic carcinoma), no histologic proof was available.
§ Includes 4 cases of malignant mixed tumor with adenoid cystic carcinoma and adenocarcinoma components only. Two cases (1 each) of mucoepidermoid carcinoma and carcinosarcoma were excluded.

### Table 4. Follow-up Information of 18 Patients With Primary Malignant Epithelial Tumors of the Lacrimal Gland

<table>
<thead>
<tr>
<th>Classification</th>
<th>Origin</th>
<th>No. of Cases</th>
<th>Length of Follow-up, y</th>
<th>Alive and Well, y</th>
<th>No. Alive With Tumor</th>
<th>No. Dead of Tumor</th>
<th>No. Dead of Other Causes</th>
</tr>
</thead>
<tbody>
<tr>
<td>All types</td>
<td>All</td>
<td>18</td>
<td>1-19</td>
<td>6</td>
<td>1</td>
<td>9</td>
<td>2</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>De novo</td>
<td>10</td>
<td>1-16</td>
<td>2</td>
<td>1</td>
<td>6</td>
<td>1</td>
</tr>
<tr>
<td>BMT*</td>
<td>All</td>
<td>11†</td>
<td>6</td>
<td>1</td>
<td>3</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>De novo</td>
<td>2</td>
<td>1.5-4.3</td>
<td>1</td>
<td>1</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>BMT*</td>
<td>All</td>
<td>3†</td>
<td>4-9</td>
<td>2</td>
<td>3</td>
<td>3</td>
<td>1</td>
</tr>
</tbody>
</table>

* BMT indicates benign mixed tumor; ellipses, not applicable.
† Two rare variants of malignant mixed tumor are excluded from this group: mucoepidermoid carcinoma and carcinosarcoma; both patients died of their tumors.
that the treatment modality makes the difference in the survival.\textsuperscript{7,9,10} The problem with arriving at a consensus for treatment is that the number of long-term survivors with adenoid cystic carcinoma is so low that all studies advocating any particular treatment modality are anecdotal.

Accepted for publication January 21, 1998.

This study was supported in part by grants from the Retina Research Foundation, Houston, Tex, and Research to Prevent Blindness Inc, New York, NY.

Reprints: Ramon L. Font, MD, Ophthalmic Pathology Laboratory, Cullen Eye Institute, Baylor College of Medicine, Houston, TX 77030.

REFERENCES


Notes From Our Ophthalmic Heritage

A look at the past . . .

The Choroid and Retina

The medieval attempt to convict criminals by the soiling of a mirror exposed to their guilty vision has been supplanted in this scientific age by the use of the ophthalmoscope to detect murderers. . . . From some obscure source the idea has developed that if the victim of homicide gets a glimpse of the murderer before death the image of the murderer will be indelibly imprinted on the retina . . . . When Police Constable George William Gutteridge halted Frederick Guy Browne and William Henry Kennedy in a stolen car on a quiet English country lane in 1927, the thieves promptly killed him. Browne, who already had a criminal record and was desperately anxious not to be caught again, shot out both eyes of the corpse to prevent anyone finding the images of the murderers in dead man’s eyes. The 2 thugs were caught and hanged nevertheless.