Malignant Minor Salivary Gland Tumors of the Larynx

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Objective: To report our experience in treating patients with malignant minor salivary gland tumors of the larynx.

Design: Thirty-three-year retrospective study.

Setting: Tertiary referral center specializing in head and neck surgery.

Patients: Twelve patients with malignant minor salivary gland tumors of the larynx were identified from a search of the institutional databases and pathology records at Memorial Sloan-Kettering Cancer Center, New York, NY, between the years 1970 and 2003. All slides were independently reviewed by 2 pathologists (R.G. and D.C.). Details on patient and tumor characteristics, as well as treatment and surgical outcome, were recorded.

Results: Ten patients (83%) had adenoid cystic carcinoma and 2 (17%) had myoepithelial carcinoma. Five (42%) were located in the supraglottis and 7 (58%) in the subglottis. Ten (83%) had surgery (6 with adjuvant radiotherapy) and 2 (17%) were treated with radiotherapy alone. Of the 10 patients who had surgery, total laryngectomy was required in 6 (60%), supraglottic horizontal laryngectomy in 2 (20%), and cricotracheal resection in 2 (20%). With a median follow-up of 55 months (range, 1-194 months), 10 patients are alive, 6 of whom have no evidence of disease. Seven patients (58%) developed recurrent disease, 2 of whom had local recurrence alone, 1 had regional recurrence alone, 3 had distant recurrence alone, and 1 had local and distant recurrence.

Conclusions: Up to 60% of patients with malignant minor salivary gland tumors of the larynx will develop recurrent disease locally, regionally, or at distant sites. In adenoid cystic carcinoma, regional recurrence is rare, but distant recurrence is common and may occur up to 10 years after the index therapy. For both adenoid cystic and myoepithelial carcinoma, partial surgery is possible in selected cases, but because of the high propensity for submucosal spread and perineural and lymphovascular invasion, total laryngectomy is usually recommended.
METHODS

Twelve patients who had malignant minor salivary gland tumors of the larynx were identified from a search of institutional databases and the pathology records at Memorial Sloan-Kettering Cancer Center, New York, NY, between the years 1970 and 2003. The study design was approved by the institutional review board. Details on patient characteristics, tumor characteristics, treatment, and outcome were recorded.

RESULTS

PATIENT AND TUMOR CHARACTERISTICS

Table 1 summarizes the patient and tumor characteristics. Seven patients (58%) were men and 5 (42%) were women. The tumors occurred over a wide age range: 40 to 76 years, with a median of 54 years. Ten patients (83%) had adenoid cystic carcinomas, 3 supraglottic and 7 subglottic in location. Two patients (17%) had myoepithelial carcinomas, both supraglottic in location. Seven patients presented with advanced stage III and IV disease.

PATHOLOGIC TYPE

The histopathologic features are given in Table 2. For adenoid cystic carcinoma, 4 (40%) were high-grade tumors using the M. D. Anderson grading system,8 4 tumors (40%) had lymphovascular invasion, and 9 (90%) had perineural invasion. Of 9 patients treated by surgery, resection margins were positive in 3 (33%). For myoepithelial carcinoma, the 1 patient treated with surgery had lymphovascular invasion, perineural invasion, and positive resection margins.

TREATMENT AND OUTCOME

Details of the treatment are given in Table 3. Ten patients (83%) had surgery (6 of whom also received adjuvant postoperative radiotherapy), and 2 (17%) had radiotherapy alone. Of the 10 patients who had surgery, total laryngectomy was required in 6 (60%), supraglottic horizontal laryngectomy in 2 (20%), and cricotracheal resection in 2 (20%). All 4 patients with positive resection margins received postoperative radiotherapy.
Of the 10 patients who had surgery, 4 had a neck dissection; 3 patients had adenoid cystic carcinoma (patients 1, 2, and 7) with clinical neck staging cN2b, cN0, and cN2c, respectively, of which only patient 7 had pathologically positive nodes (pN1). The other patient who had a neck dissection had myoepithelial carcinoma (patient 12) with clinical neck staging of cN1 and pathological staging of pN2b.

Of the 2 patients who underwent primary radiotherapy, 1 had a T1 false cord supraglottic myoepithelial carcinoma managed by external beam radiotherapy. The other patient had a T4a subglottic adenoid cystic carcinoma with extralaryngeal extension to the thyroid gland. This patient was treated by neutron beam therapy and intraluminal brachytherapy.

Follow-up ranged from 1 to 194 months, with a median of 55 months. Because of the limited numbers of patients, survival analysis by the Kaplan-Meier method was not attempted. Ten patients are alive, 6 of whom have no evidence of disease. Seven patients (58%) developed recurrent disease, 2 of whom had local recurrence alone, 1 had regional recurrence alone, 3 had distant recurrence alone, and 1 had local and distant recurrence. Both patients who were treated by primary radiotherapy had local recurrence; 1 had a T1 false cord myoepithelial carcinoma, which was successfully salvaged by total laryngectomy. The other patient with T4a subglottic adenoid cystic carcinoma had positive resection margins and local recurrence; this patient was managed conservatively by observation. The other patient who had local recurrence after treatment of a T2 subglottic adenoid cystic carcinoma required a total laryngectomy. The margins of surgical resection were negative, and therefore this patient did not receive postoperative radiotherapy. The patient went on to develop local recurrence, but salvage surgery was not carried out owing to the presence of lung metastases. An analysis of the pattern of recurrence by histologic type showed that distant recurrence occurred exclusively with adenoid cystic carcinoma. The lung was the site of distant failure in all 4 patients, with 1 patient also having bone metastases. The only patient with regional recurrence had a myoepithelial carcinoma; local recurrence occurred in patients with both histologic types.

### Table 3. Details on Treatment and Outcome

<table>
<thead>
<tr>
<th>Patient No.</th>
<th>Management</th>
<th>Resection Margins</th>
<th>Adjuvant Therapy</th>
<th>Recurrence</th>
<th>Salvage</th>
<th>Follow-up Months</th>
<th>Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Total laryngectomy and modified radical neck dissection</td>
<td>+ RT</td>
<td>None</td>
<td>Distant (lung)</td>
<td>None</td>
<td>103</td>
<td>DOD</td>
</tr>
<tr>
<td>2</td>
<td>Supraglottic horizontal laryngectomy and ipsilateral jugular neck dissection</td>
<td>− RT</td>
<td>None</td>
<td>Distant (lung and bone)</td>
<td>None</td>
<td>144</td>
<td>AWD</td>
</tr>
<tr>
<td>3</td>
<td>Supraglottic horizontal laryngectomy</td>
<td>− None</td>
<td>None</td>
<td>NA</td>
<td>80</td>
<td>ANED</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>Total laryngectomy</td>
<td>− None</td>
<td>None</td>
<td>NA</td>
<td>1</td>
<td>ANED</td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Primary radiotherapy (brachytherapy and neutron beam therapy)</td>
<td>NA None</td>
<td>Local</td>
<td>None</td>
<td>18</td>
<td>AWD</td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Cricotracheal resection</td>
<td>+ RT</td>
<td>None</td>
<td>Distant (lung)</td>
<td>None</td>
<td>52</td>
<td>AWD</td>
</tr>
<tr>
<td>7</td>
<td>Total laryngectomy and bilateral jugular neck dissection</td>
<td>− None</td>
<td>None</td>
<td>NA</td>
<td>21</td>
<td>ANED</td>
<td></td>
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<tr>
<td>8</td>
<td>Cricotracheal resection</td>
<td>+ RT</td>
<td>None</td>
<td>NA</td>
<td>69</td>
<td>ANED</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Total laryngectomy</td>
<td>− RT</td>
<td>None</td>
<td>NA</td>
<td>2</td>
<td>ANED</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Total laryngectomy</td>
<td>− None</td>
<td>Local and distant (lung)</td>
<td>None</td>
<td>58</td>
<td>AWD</td>
<td></td>
</tr>
<tr>
<td>11</td>
<td>Primary radiotherapy</td>
<td>NA None</td>
<td>Local</td>
<td>Total laryngectomy</td>
<td>33</td>
<td>ANED</td>
<td></td>
</tr>
<tr>
<td>12</td>
<td>Total laryngectomy and ipsilateral radical neck dissection</td>
<td>+ RT</td>
<td>Regional (contralateral)</td>
<td>Neck dissection</td>
<td>194</td>
<td>AWD</td>
<td></td>
</tr>
</tbody>
</table>

Abbreviations: ANED, alive with no evidence of disease; AWD, alive with disease; DOC, dead of other cause; DOD, dead of disease; NA, not applicable; RT, radiotherapy; +, positive; −, negative.

Minor salivary gland tumors of the larynx are rare and constitute less than 1% of laryngeal tumors. They are usually malignant and, as observed in our study, the most common type is adenoid cystic carcinoma. The histologic distribution in our study is different from that reported by other investigators in that there were no cases of mucoepidermoid carcinoma or adenocarcinoma. Mahlstedt et al reported on 15 cases and found that adenoid cystic carcinoma was also the most common tumor type (40%), with mucoepidermoid carcinoma (33%) and poorly differentiated adenocarcinoma (27%) accounting for the remainder. In contrast, Spiro et al reported on 20 cases from 1939 to 1968 and found the most common type was adenocarcinoma (63%), with adenoid cystic carcinoma accounting for only 15% of patients. However, Batsakis et al have investigated previously reported cases of adenocarcinoma and showed that these were in fact cases of neuroendocrine tumors, either large-cell carcinoma or small-cell neuroendocrine tumors. Therefore, our observation that adenoid cystic carcinoma is the predominant type of malignant minor salivary gland tumor of the larynx is an important point to make. These tumors are predominantly subglottic, in keeping with their origin from submucosal glands, which are more frequently found in the subglottic region of the larynx.

In our series, 7 patients (58%) presented with advanced stage III and IV disease. This observation is similar to other reported figures of 54% to 67%. This late stage of presentation may be explained by the submucosal growth
pattern of these tumors. In our study, both patients treated with primary radiotherapy had local recurrence, an observation in keeping with the known relative radioresistance of these tumors. Instead, surgical excision is recommended. Alavi et al reported that because of submucosal spread, partial laryngectomy is inappropriate for minor salivary gland tumors and that total laryngectomy should be carried out. This was based on their observation that positive margins were found in 2 of 3 patients treated by partial laryngectomy, both of whom died within 2 years of treatment. In our series, 2 supraglottic horizontal laryngectomies were carried out, both for T2 adenoid cystic tumors. In these patients, surgical margins were negative. To date, local recurrence has not occurred in these patients. This would suggest that partial laryngectomy is possible in select patients with small, well-defined tumors and negative surgical resection margins. However, close follow-up is recommended so that salvage total laryngectomy can be carried out for local recurrence.

Batsakis et al reported that 18% of patients with adenoid cystic carcinoma presented with cervical node metastases. Similarly, in our series, 2 (20%) of 10 patients with adenoid cystic carcinoma had clinically positive necks at presentation; however, only 1 patient had a pathologically positive single lymph node. An analysis of recurrence revealed that no patient with adenoid cystic carcinoma had regional recurrence. Therefore, our data suggest that neck dissection is not required in the clinically negative (cN0) neck, a finding also reported by Ferlito et al.

In our series, all patients who had distant recurrence had adenoid cystic carcinoma and all occurred in the lung (though 1 patient also had bone metastases). Distant metastases occurred up to 10 years from the index therapy. Cohen et al have also reported that adenoid cystic carcinoma recurs later with lung metastases, and such patients can survive for 3 to 4 years or longer. Indeed, in our study, 3 of 4 patients with distant disease are still alive. Thus, adenoid cystic carcinoma of the larynx appears to behave in a similar fashion to adenoid cystic carcinoma of other head and neck sites.

In conclusion, up to 60% of patients with malignant minor salivary gland tumors of the larynx will develop recurrent disease either locally or distant. Surgical excision is recommended owing to the relative radioresistance of these tumors. Partial surgery is possible in a few selected cases, but because of the propensity for submucosal spread and perineural and lymphovascular invasion, total laryngectomy is often required. In adenoid cystic carcinoma, regional recurrence is rare but distant recurrence common, may occur up to 10 years after the index therapy, and is often the cause of death in such patients.

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REFERENCES