Uncommon malignant tumours of the larynx
A 35 year review

by


Abstract
Sixty-five primary malignant laryngeal tumours, other than simple squamous cell carcinomas, treated at the Royal Marsden Hospital between 1949 and 1984 are presented. Of the 11 histological types pseudosarcomas (24 cases), verrucous carcinomas (9 cases) and lymphoreticular tumours (9 cases) predominated. Determine three-year follow-up data were available in 50 cases. Sixteen patients (32 per cent) died of their neoplasms but survival was strongly related to histology. Only one death occurred among 24 determinate cases of pseudosarcoma and verrucous carcinoma. Radiotherapy was effective treatment for these two tumour types and for reticuloendothelial tumours. However, combined therapy yielded poor results with the other histological types.

Introduction
Malignant laryngeal neoplasms other than simple squamous cell carcinomas are rare, constituting about 5 per cent of all laryngeal malignancies (Batsakis, 1979; Batsakis and Fox, 1970; Cady et al., 1968). The group of tumours is mixed, being defined only by the exclusion of simple squamous carcinomas, and includes neoplasms of epidermoid (e.g. verrucous carcinoma) and non-epidermoid (e.g. adenocarcinoma and the sarcomas) origin. The inevitable problem with a rare and heterogeneous group of tumours lies in single centres gaining sufficient experience to formulate appropriate treatment policies. The aim of this paper is to report the experience of a large centre accumulated over a 35-year period.

Patients and methods
Ninety-five cases of malignant laryngeal tumours other than simple squamous carcinomas were treated at the Royal Marsden Hospital between 1949 and 1984. Twenty-seven cases with inadequate clinical or histological data and three cases of metastatic carcinoma affecting the supraglottic larynx have been excluded from the study, leaving 65 cases of primary laryngeal tumours for analysis. There were 54 males and 11 females, with ages ranging from 14 to 77 years (median 61 years). Pathology data were reviewed in 80 per cent of the determinate cases and no diagnosis was changed after review. Tumours usually found in other anatomical sites, like oat cell carcinoma, lymphoma and plasmacytoma, were included only if full clinical evaluation demonstrated absence of tumour in all sites other than the larynx. Tumours were staged according to the U.I.C.C. classification system (1978) although early cases had to be staged retrospectively.

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Initial treatment was radiotherapy in 50 cases, total laryngectomy in five, partial laryngectomy in three and combined radiotherapy and surgery in four. Chemotherapy was used alone in one case and was combined with the other modalities in two cases. Where radiotherapy was given as curative treatment, either radium or Cobalt 60 was used to deliver tumour doses between 60 and 70 Gy. over 38 to 51 days. Following persistence of recurrence of disease, salvage therapy was attempted in 13 cases (radiotherapy 7 and surgery 6). In 50 of the 65 cases there was either death from disease or a follow-up period of at least three years, making these determinate cases. Survival data refer to these cases only.

Results

Pathology

There were 11 different histological types represented and these are shown in Table I. The male:female ratio of patients with pseudosarcomas and verrucous carcinomas was 11:1, while for tumours of other histological types the ratio was 3.5:1. The gross appearance of tumours was variable. The pseudosarcomas were most often friable, fleshy pedunculated polyps, frequently with surface ulceration. The verrucous carcinomas were warty and exophytic. The various adenocarcinomas were either ulcers or fleshy polyps, while the reticuloendothelial tumours presented mainly as smooth swellings. The four sarcomas were two fibrosarcomas, one rhabdomyosarcoma and one chondrosarcoma.

Anatomical distribution and staging

The estimated site of the 65 primary tumours within the larynx is shown in Table II. Fifty-two per cent were glottic, 38 per cent supraglottic and 10 per cent subglottic; however, pseudosarcomas and verrucous carcinomas involved the vocal cord in 32 of 33 cases (94 per cent). If the 32 other tumours are considered separately, 70 per cent were supraglottic (22 cases), 20 per cent subglottic (7 cases) and 10 per cent glottic (3 cases). Table III shows the stage of the various tumours. There were inadequate clinical data for staging in three cases. The majority of tumours (77 per cent) presented as T1 or T2 lesions. Regional lymph nodes were clinically involved in four cases—two mucoepidermoid carcinomas, one rhabdomyosarcoma and one mucous gland carcinoma. No patient had distant metastases at presentation.

Results of treatment

Following initial therapy, 15 of the 65 patients either died of intercurrent diseases or were lost to follow-up before three years, leaving 50 determinate cases. Twenty-nine of this group of 50 patients remained disease-free following initial therapy, with a median follow-up of 8 years (range 3–20 years). Of the 21 cases where initial treatment failed, 12 patients had persistent disease and nine had tumour recurrence after a median disease-free interval of 11 months (range 3–24 months). Salvage therapy was attempted in 13 cases and the remaining 8 patients died of untreatable disease at a median of 6 months after initial therapy (range 2–12 months). Salvage treatment was radiotherapy in 7 cases.
TABLE II
DISTRIBUTION OF 65 PRIMARY MALIGNANT TUMOURS WITHIN THE LARYNX

<table>
<thead>
<tr>
<th>Tumour type</th>
<th>Supraglottic</th>
<th>Glottic</th>
<th>Subglottic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudosarcoma</td>
<td>2</td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Verrucous carcinoma</td>
<td>0</td>
<td>9</td>
<td>0</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>5</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Plasmacytoma</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Adenoid cystic</td>
<td>3</td>
<td>2</td>
<td>0</td>
</tr>
<tr>
<td>Mucoepidermoid</td>
<td>3</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>2</td>
<td>0</td>
<td>1</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>2</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Oat cell carcinoma</td>
<td>1</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Mucous gland carcinoma</td>
<td>2</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Carcinoma in mixed salivary</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>tumour</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>24</strong></td>
<td><strong>34</strong></td>
<td><strong>7</strong></td>
</tr>
</tbody>
</table>

and total laryngectomy in 6, and this treatment was successful in 5 patients, while 8 patients who failed salvage treatment died at a median of 20 months later (range 5 months–4 years). Therefore, a total of 16 of the 50 determinate patients (32 per cent) died of their disease, while 34 were free of disease following either primary or salvage treatment.

Mortality was strongly related to tumour type. Radical radiotherapy was the primary treatment in all 18 determinate cases of pseudosarcoma. This treatment failed in one case (a T4 tumour) and the patient died after 2 months. Four of the 6 determinate cases of verrucous carcinoma were treated by radiotherapy and the remaining 2 by surgery (one total laryngectomy and one local excision). The patient treated by local excision and one treated by radiotherapy failed but both were salvaged, the former by radiotherapy and the latter by radical surgery. Therefore, only one death from disease occurred in 24 cases of pseudosarcoma and verrucous carcinoma. Anaplastic change did not occur in any of the five determinate or three indeterminate cases treated by radiotherapy.

Determinant data were available in the six cases of lymphoma and two of the three cases

TABLE III
TUMOUR STAGE AT INITIAL PRESENTATION (N=62)*

<table>
<thead>
<tr>
<th>Tumour type</th>
<th>T1</th>
<th>T2</th>
<th>T3</th>
<th>T4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudosarcoma</td>
<td>19</td>
<td>1</td>
<td>2</td>
<td>1</td>
</tr>
<tr>
<td>Verrucous carcinoma</td>
<td>5</td>
<td>2</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td>Lymphoma</td>
<td>3</td>
<td>-</td>
<td>3</td>
<td>-</td>
</tr>
<tr>
<td>Plasmacytoma</td>
<td>2</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Adenoid cystic carcinoma</td>
<td>3</td>
<td>1</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Mucoepidermoid carcinoma</td>
<td>3</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Adenocarcinoma</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Sarcoma</td>
<td>1</td>
<td>-</td>
<td>1</td>
<td>1</td>
</tr>
<tr>
<td>Oat cell carcinoma</td>
<td>2</td>
<td>-</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td>Mucous gland carcinoma</td>
<td>2</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Carcinoma in mixed salivary</td>
<td>1</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>tumour</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Total</strong></td>
<td><strong>43</strong></td>
<td><strong>5</strong></td>
<td><strong>11</strong></td>
<td><strong>3</strong></td>
</tr>
</tbody>
</table>

*Adequate clinical information for staging was not available in 3 cases.
of plasmacytoma. The lymphomas were treated by radiotherapy and one death occurred due to dissemination of a T3 supraglottic lesion. One patient with plasmacytoma had recurrence of tumour after local excision but was disease-free after salvage radiotherapy. The other had persistent disease following radiotherapy and, although salvage laryngectomy was performed, the patient died with disseminated disease after two years. Therefore, two deaths occurred among eight patients with tumours of lymphoreticular origin.

The remaining 18 determinate cases were of seven histological types. Six patients were free of disease following initial treatment (three with adenoid cystic carcinoma, two with adenocarcinoma and one with mucous gland carcinoma). The remaining 12 patients had a median survival of 14 months (range 4–30 months), giving a mortality in this group of 50 per cent for glandular carcinomas and 100 per cent for the sarcomas and oat cell carcinomas despite combined therapy.

Discussion

Squamous cell carcinoma is the commonest laryngeal malignancy but about 5 per cent of malignant tumours of the larynx will be of other histological types. These are derived from epithelial, glandular and supporting cells but the origin of some tumours is unclear. Pseudosarcoma, for example, is regarded by most authors as a variant of squamous carcinoma (Lane, 1957; Friedel et al., 1976; Battifora, 1975; Spencer et al., 1983) but Batsakis (1981) points out that no single theory for its origin should be adopted because of the variable morphology of these tumours. Oat cell carcinoma of the larynx is thought to arise from the same precursor cell as oat cell carcinoma of the lung—the Kulchitsky cell (Batsakis, 1979; Gnep et al., 1983). This cell originates in the neural crest and is also the likely precursor of carcinoid tumours of the upper aerodigestive tract. Certain clinical aspects are also controversial, like the effectiveness and safety of radiotherapy for verrucous carcinoma. In this retrospective study we have not attempted to define the histogenesis of the 65 primary laryngeal malignancies under review but have concentrated on their clinical behaviour and response to treatment. We do not suggest that radiotherapy is the optimal therapy for all these tumours. However, since radiotherapy has been the principal method of treatment employed for laryngeal malignancies at the Royal Marsden Hospital, this review allows critical assessment of this method in many of these cases.

Pseudosarcoma, an uncommon but well-recognised tumour of the upper aerodigestive tract, made up the largest single group of tumours (24 cases). In a review of previously treated cases Batsakis (1981) found one-third of 65 patients with laryngeal pseudosarcoma were dead of their disease in less than 2 years and advised that treatment be dictated by clinical stage rather than histological composition of the tumour. Spencer et al. (1983) have recommended conservation surgery for early pedunculated lesions, preferring radiotherapy for larger tumours to avoid mutilating surgery. In the present series all 18 determinate patients were treated by radiotherapy and only one died. These results are encouraging but may reflect the fact that nearly all cases were early glottic lesions. The management of verrucous carcinoma has also provoked debate since its description by Ackerman in 1948. Poor response to radiotherapy and early lethal anaplastic change possibly induced by radiotherapy have been reported (Ryan et al., 1977; Perez et al., 1966; Kraus and Perez-Mesa, 1966; Burns and Nostrand, 1976). Surgery has been recommended as the treatment of choice (Myers et al., 1980; Maw et al., 1982) and Batsakis (1979) has stated that radiotherapy for this tumour appears to be contraindicated. Seven of nine cases of laryngeal verrucous carcinoma in this series were treated with radiotherapy with no anaplastic change. All six determinate patients were alive and free of disease at three years although two needed salvage laryngectomy. We agree with the recommendation of Schwade et al. (1979) that these tumours should be treated like other squamous carcinomas of this region of similar site and stage. The fear of anaplastic change...
appears to be based on limited and inconclusive evidence.

Primary lymphoma and plasmacytoma of the larynx have been previously reported (Shaw, 1972; Maniglia and Xue, 1983; De Santo and Weiland, 1970; Medini, 1980; Anderson et al., 1976) and both surgery and radiotherapy have been used to treat these rare tumours. Radiotherapy alone was effective therapy in six of eight determinate patients but two rapidly developed disseminated disease and died. Surgery would appear to have little place in the management of these tumours since early lesions are sensitive to radiotherapy and large lesions are unlikely to remain confined to the larynx.

Our overall experience with the 16 glandular tumours in this series has been less favourable than with the other tumours mentioned. No firm conclusions can be drawn from their response to therapy because of the small number of each histological type. These tumours are known to present late, with a high rate of nodal metastases (Spiro et al., 1976; Whicker et al., 1974). Of a total of 39 patients reported by Spiro et al. (1976) and by Whicker et al. (1974), only six were alive and free of disease at three years. In the present series three of 16 patients presented with nodal metastases and three developed them subsequently. Six of 11 determinate patients were alive and free of disease at three years and five of these were treated with radiotherapy alone. Oat cell carcinomas of the larynx, though very rare, readily metastasise to the neck and Gnepp et al. (1983) reported that mortality is high, irrespective of the stage at presentation and type of treatment. These findings correlate with our own limited experience. Similarly, the sarcomas in the present series failed to respond to combined therapy and were rapidly fatal. The poor prognosis of laryngeal sarcoma has been reported by other authors (Finn et al., 1984; Diehn et al., 1984; Hacihanefioglu and Oztürk, 1983), although chondrosarcoma is said to have a slightly better outcome than other types (Hyams and Rabuzzi, 1970).

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References


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