Mucoepidermoid Carcinoma of the Larynx: a Case which Responded Completely to Radiotherapy and a Review of the Literature

Takaharu Shonai¹, Masato Hareyama¹, Koh-ichi Sakata¹, Atsushi Ouchi¹, Hisayasu Nagakura¹, Kazumitsu Koito¹, Kazuo Morita¹, Masaaki Satoh², Kohji Asakura³, Akikatsu Kataura³ and Yuji Hinoda⁴

Departments of ¹Radiology, ²Clinical Pathology, ³Otolaryngology and ⁴First Internal Medicine, Sapporo Medical University, School of Medicine, Sapporo, Japan

INTRODUCTION

Most laryngeal cancers are squamous cell carcinomas, and adenocarcinomas account for <1% of cancers of the larynx. Among them, mucoepidermoid carcinoma is extremely rare. According to our review of the literature, only 13 cases have been reported in Japan. We encountered laryngeal mucoepidermoid carcinoma (T¹bN⁰M⁰, Stage ¹) that had developed on the bilateral vocal cords. Surgery is the treatment of choice in most instances, but we successfully eliminated the laryngeal tumor with radiotherapy alone and the patient has been alive and well for more than six years. We present, here, a report on this case, together with a discussion on other relevant reports in the literature, with special reference to the cases occurring in Japan.

CASE REPORT

In November 1991, an 81-year-old man visited the Department of Otolaryngology at Sapporo University Hospital complaining of persistent hoarseness in spite of not having smoked since 1985. Tumors were noted on the bilateral vocal cords. A biopsy specimen revealed sheet arrangements of epidermoid cells intermingled with glandular components containing goblet cells (Fig. 1). Alcian blue and PAS revealed the presence of mucin in the acini and microcystic spaces (not shown). These findings suggested a typical feature of mucoepidermoid carcinoma. This case was classified as a low grade type, because the extent of nuclear atypia was less. Thus, the patient was referred to our department. In a flexible laryngeal endoscopic examination (Fig. 2), the entire larynx appeared erythematous due to a laryngomicrosurgical procedure that had been conducted earlier. In addition, an irregular swelling, suggesting malignant tumor, was seen extending from the anterior two-thirds of the left vocal cord, traversing the anterior and extending to the anterior quarter of the right vocal cord with normal mobility. The cervical lymph nodes were not swollen. In view of his old age, the early stage, and low grade of histopathology, radiotherapy was chosen. This patient was treated with bilateral laryngeal opposed wedged 6 x 6 cm fields (Fig. 3). Radiotherapy was delivered by accelerated hyperfractionation. A total dose of 55 Gy of ⁶⁰Co, over a three-week period, was delivered twice daily at 1.7 Gy per fraction, with a minimum interfraction interval of six hours, Monday–Friday. At the completion of radiotherapy, a laryngeal endoscopic examination showed a reddish reaction on the mucosa of the larynx. The bilateral vocal cords were marked with confluent mucositis, but no tumors were found. He has been alive and well for more than 6 years (Fig. 4).
DISCUSSION

Mucoepidermoid carcinoma was first reported by Stewart et al. (1). It occurs at various sites, such as the uterus, bladder, ovary, salivary glands, pharynx, nasal cavity and esophagus. Among them, the parotid gland is the site where the tumor is most likely to develop. An incidence involving the larynx is rare: this was first reported by Arcidiacono and Romeo in 1963 (2).

Because the laryngeal mucosa at the vocal cord is composed of squamous epithelium, squamous cell carcinoma is the most common carcinoma. On the other hand, the supra- and subglottis are composed mainly of ciliated columnar epithelium, which contributes to the development of adenocarcinoma. However, it has been reported that the incidence of adenocarcinomas is <1% of all the cancers that involve the larynx. The incidence of mucoepidermoid carcinoma is even lower. Cady et al. (3) reported two cases of mucoepidermoid carcinoma (0.08%) among 2500 cases of laryngeal cancers.

Cumberworth et al. (4) analyzed 41 cases of mucoepidermoid carcinoma of the larynx and found that the mean age of onset was 61 years for men and 52 years for women. In the same study, they noted that the incidence was 86% for men and 14% for women, with the incidence among women higher in comparison with that of squamous cell carcinoma. The most likely site to be affected is the supraglottis (61%), followed by the glottis (26%) and subglottis (13%). This tendency differs from that of squamous cell carcinoma of the larynx, which most frequently affects the glottis. Ho et al. (5) argued that this was due to an abundance of laryngeal glands histologically identical to the minor salivary glands in the submucosal region of the larynx. Mucoepidermoid carcinoma of the larynx originates from the intercalated cells which are one part of the laryngeal gland; therefore mucoepidermoid carcinoma is likely to develop at the supraglottis where the laryngeal glands are most frequently distributed.
Table 3. Cases of laryngeal mucoepidermoid carcinoma in Japan

<table>
<thead>
<tr>
<th>Case</th>
<th>Author</th>
<th>Year</th>
<th>Sex</th>
<th>Age</th>
<th>Complaint</th>
<th>Anatomical sites</th>
<th>Pathology</th>
<th>TMN</th>
<th>Therapy</th>
<th>Prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Koike et al. (6)</td>
<td>1978</td>
<td>M</td>
<td>64</td>
<td>Hoarseness</td>
<td>Epiglottis</td>
<td>Radiotherapy</td>
<td>Dead</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>Koike et al. (6)</td>
<td>1978</td>
<td>M</td>
<td>45</td>
<td>Hoarseness</td>
<td>Vocal cords</td>
<td>Radiotherapy</td>
<td></td>
<td></td>
<td>Unknown</td>
</tr>
<tr>
<td>3</td>
<td>Okinaka et al. (7)</td>
<td>1984</td>
<td>M</td>
<td>51</td>
<td>Hoarseness</td>
<td>Vocal cords</td>
<td>Unknown</td>
<td></td>
<td>Ope.</td>
<td>Unknown</td>
</tr>
<tr>
<td>4</td>
<td>Tanigawa et al. (8)</td>
<td>1988</td>
<td>M</td>
<td>78</td>
<td>Hoarseness</td>
<td>T1N2OM0</td>
<td>Ope.</td>
<td>Follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>5</td>
<td>Oki et al. (9)</td>
<td>1987</td>
<td>M</td>
<td>53</td>
<td>Hoarseness</td>
<td>T2N0M0</td>
<td>Ope.</td>
<td>Follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6</td>
<td>Yoshimura et al. (10)</td>
<td>1990</td>
<td>F</td>
<td>56</td>
<td>Hemato. sputa</td>
<td>Subglottis</td>
<td>Radiotherapy</td>
<td>Follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7</td>
<td>Yoshida et al. (11)</td>
<td>1991</td>
<td>M</td>
<td>63</td>
<td>Pharyngeal pain</td>
<td>Epiglottis Azytneoid</td>
<td>Radiotherapy</td>
<td>Follow-up</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8</td>
<td>Kimura et al. (12)</td>
<td>1991</td>
<td>M</td>
<td>74</td>
<td>Hoarseness</td>
<td>VTentricular bands</td>
<td>Radiotherapy</td>
<td></td>
<td>Ope.</td>
<td></td>
</tr>
<tr>
<td>9</td>
<td>Kuriyama et al. (13)</td>
<td>1991</td>
<td>M</td>
<td>65</td>
<td>Hoarseness</td>
<td>VTentricular bands</td>
<td>Radiotherapy</td>
<td></td>
<td>Ope.</td>
<td></td>
</tr>
<tr>
<td>10</td>
<td>Kawai et al. (15)</td>
<td>1993</td>
<td>M</td>
<td>81</td>
<td>Hoarseness</td>
<td>Dyspnea</td>
<td>Radiotherapy</td>
<td></td>
<td>Chemo.</td>
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<tr>
<td>11</td>
<td>Kawabata et al. (16)</td>
<td>1993</td>
<td>M</td>
<td>69</td>
<td>Hoarseness</td>
<td>Subglottis</td>
<td>Radiotherapy</td>
<td></td>
<td>Chemo.</td>
<td></td>
</tr>
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<td>12</td>
<td>Present study</td>
<td>1996</td>
<td>M</td>
<td>81</td>
<td>Hoarseness</td>
<td>Vocal cords</td>
<td>Radiotherapy</td>
<td></td>
<td>Follow-up</td>
<td></td>
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</table>

In Japan, Koike et al. (6) reported two cases in 1978. According to our review of the literature, only 14 cases including this case have been reported (Table 3) (6–16). Masuda et al. (17) stated that they observed two cases of mucoepidermoid carcinoma among 377 cases of malignant laryngeal tumors over a period of 15 years, but we excluded them from Table 3 because the details are unknown. All but one of the 13 cases reported in Japan occurred in males whose age ranged from 45 to 81 years (mean 65). However, the most common site was the subglottis. Mucoepidermoid carcinoma develops at the submucosal region, which is located under the squamous epithelium, and it is associated with a strong tendency to infiltrate and proliferate even when the mucosal surface is smooth (18). Therefore, it is difficult to determine the extent of infiltration macroscopically.

According to Eversole (19), mucoepidermoid carcinoma consists of three types of cells which are squamous epithelium, mucus-secreting and intermediate cells. The well-differentiated (low-grade) tumor is composed mainly of mucus-secreting and squamous epithelial cells. In the poorly differentiated (high-grade) tumor, on the other hand, squamous epithelial and intermediate cells dominate the lesion with marked cellular atypia. The mucus-secreting cells are demonstrated by staining with PAS, mucicarmine or alcian blue. As regards the differential diagnosis of adenoid cystic carcinoma, its stroma is myxoid, mucinous or hyaline, whereas the stroma of a mucoepidermoid carcinoma consists of fibrous connective tissue.

Compared with the low-grade tumor, the high-grade tumor is more invasive, and shows stronger tendencies for distant or lymphatic metastases. Among the cases reported in Japan with known pathological grades and clinical courses, a fatal outcome is limited to the high-grade type.

Squamous cell carcinoma of the larynx is relatively radiosensitive, which suggests a high probability of cure with radiotherapy. Mucoepidermoid carcinoma, on the other hand, has limited radiosensitivity and is most frequently treated with surgical procedures. Cady et al. (3) recommend total laryngectomy and radical neck dissection, while Whicker et al. (20) prefer partial laryngectomy if the tumor is limited to the supraglottis. Frable and Elzay (21) stated that a low-grade tumor is often associated with a favorable prognosis; therefore, a partial laryngectomy is adequate for such cases, while the recurrent lesions should be treated with total laryngectomy. Agreement on the details of the surgical procedures is lacking in these reports. Thomas (22) reported that the early foci which are limited to the vocal cords can be satisfactorily treated by radiation. However, although radiotherapy is employed mainly as a pre- or post-operative therapy, most of the cases reported in Japan were treated exclusively with radiotherapy. Some were found to be radiosensitive and exhibited reductions or complete dissolution of the lesions following radiotherapy alone (6,10,15). The old patient in the present study was classified as a low-grade type with early stage. Therefore, we decided to treat him with radiotherapy delivered by accelerated hyperfractionation, which is a more effective strategy of treating radioresistant tumors than conventional irradiation. However, in hyperfractionated accelerated radiotherapy, there is a trend toward more pronounced acute...
mucosal reaction, but the trade-off is promising tumor response rates. Bourhis et al. (23) reported that severe acute mucosal toxicity was observed in all cases delivered 62 Gy in 20 days with two daily fractions of 1.75 Gy, which required intensive nutritional support. Therefore, we designed total doses of 55 Gy in three weeks with two daily fractions of 1.71 Gy.

Ho et al. (5) reported that the five-year survival rate for mucoepidermoid carcinoma is 80%; and the rates for the low- and high-grade tumors were 91–100 and 50%, respectively, indicating a much poorer prognosis for the latter. In Japan, only a few cases have been followed for a long time, but no mortality has been reported for the low-grade tumor, suggesting a favorable prognosis.

In planning therapeutic modalities for mucoepidermoid carcinoma of the larynx, it would be logical to make an evaluation of the extent of neoplastic differentiation based on the histopathological examination, the spread of the lesion, the presence of cervical lymph node metastasis and stage. The most effective therapeutic procedures should be selected according to the needs of each individual patient.

We reported a case of mucoepidermoid carcinoma of the glottic region of the larynx treated with accelerated hyperfractionated irradiation, together with a discussion on the studies reported in the literature.

References
