

ORIGINAL ARTICLE

Sarcoma of the Larynx: Treatment Results and Literature Review

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Background: Sarcomas of the larynx are rare neoplasms that constitute less than 1% of laryngeal malignancies. A Medline search found no large series focusing on laryngeal sarcomas. We reviewed the cases of laryngeal sarcomas treated in our cancer center and compared our experiences and treatment results with those from other centers.

Methods: A retrospective review of 10 patients with laryngeal sarcoma treated in our institute between 1980 and 2000 was done to identify tumor characteristics, therapeutic modalities, and treatment outcomes.

Results: The patients showed a male predominance (9/10) and presented 8 types of pathology. Nine patients underwent surgery, including 2 total laryngectomy, 4 partial laryngectomy, and 3 endoscopic laser cordectomy. During a median follow-up of 92 months, the 5-year overall survival and disease-specific survival were 76% and 90%, respectively. Two patients developed recurrence, including 1 local recurrence and 1 distant metastasis.

Conclusion: Surgical intervention was the first choice in the treatment of laryngeal sarcomas. The prognosis is relatively good when compared with sarcoma originating from other anatomic sites. [*J Chin Med Assoc* 2006;69(3):120–124]

Key Words: carcinoma, larynx, sarcoma

Introduction

Sarcomas account for less than 1% of malignant neoplasms arising in the head and neck in adults.^{1,2} These tumors are derived from the mesodermal tissue with a diversity of clinical behaviors due to various types of pathologic classifications. The classification of sarcoma according to the anatomic location in the head and neck region has proven helpful because of the influence of location on decisions regarding disease management.¹ However, previous articles have rarely focused on sarcomas that originated in the larynx. The paucity of cases and variety of tumor characteristics make it difficult to analyze the treatment modalities and outcomes in a large series.

The purpose of this study was to review the patients with laryngeal sarcoma treated at our institute over a 20-year period. The clinical presentation, histopathologic features, treatment modalities, and outcome were analyzed. The literature was also reviewed.

Methods

Between 1980 and 2000, 1,389 patients with laryngeal malignancies were registered in the database of the Cancer Center, Taipei Veterans General Hospital. Ten of the patients were diagnosed as sarcoma and the main tumor was confirmed to originate from the larynx. All of the patients were histologically proven to be sarcoma. None of them had a history of irradiation.

The clinical records of the patients were reviewed for demographic data, presenting symptoms, risk factors, site of primary tumor, extension of local and regional disease, treatment modalities, site and date of recurrence, status, and date of last follow-up. As far as we know, no specific staging system for laryngeal sarcoma has been noted so far. The tumors were staged retrospectively according to the American Joint Committee on Cancer (AJCC) 2002 classification.³ All of the pathologic specimens were reviewed by a single pathologist to evaluate histologic type, grading

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of tumor cells, status of surgical margins, perineural invasion, lymphovascular invasion, and cartilage invasion.

Clinical and pathologic data were entered into a computer database (Microsoft Access 2000), and statistical analysis was performed with a commercially available software package (JMP 4.0; SAS Institute Inc, Cary, NC, USA). The follow-up interval was calculated in months from the date of initial diagnosis until death or the date of last follow-up. For overall survival (OS), patients were counted as being alive or dead, regardless of the cause. For disease-specific survival (DSS), patients who died of noncancer-related causes were censored at the date of death. OS and DSS were calculated by the Kaplan-Meier method.

Results

Table 1 outlines the epidemiologic characteristics, features of the tumors, treatment, posttreatment functional status, and the outcomes of these patients. There were 9 men and 1 woman, and the age at diagnosis ranged from 18 to 76 years of age with a median of 62. The site of the primary tumor was the glottic region in 6 patients (60%), and the supraglottic region in 4 patients (40%). Five patients were T1, 3 were T2, 1 was T3, and 1 was T4. One patient (10%) had cervical lymph node metastasis. No patient had distant metastasis at presentation. Five patients were stage I, 3 stage II, and 2 stage IV.

The initial presenting complaints varied, depending on the location of the tumor. Hoarseness was the most frequent complaint in our study. Five patients (50%) had a history of tobacco use and 4 patients (40%) had a history of alcoholic consumption.

The treatment modalities included surgery alone in 5 patients, surgery combined with postoperative radiotherapy (RT) in 4 patients, and RT alone in 1 patient. Conservation surgery with laryngeal preservation was performed in 7 patients, including endoscopic CO₂ laser cordectomy in 3, vertical partial laryngectomy in 2, and supraglottic laryngectomy in 2. Total laryngectomy was performed in 2 patients. Neck dissection was performed in 1 patient who had a palpable cervical mass at advanced T4 stage. Three patients received postoperative RT because of positive surgical margin in 1 and high tumor cell grading in 2. One patient had RT as the primary treatment.

There were 8 histologic types in these cases. There were 2 cases each of malignant fibrous histiocytoma and hemangiosarcoma. The other types had only 1 case each. Histologic grading was determined as low, intermediate, or high grade on the basis of differentiation, cellularity, vascularity, amount of stroma and necrosis, and the number of mitosis per 10 high-power microscopic fields. Four patients had intermediate-grade tumor, 4 high grade, 1 low grade, and 1 was unavailable. The surgical margins showed 6 negative margins, 1 close, and 2 positive. No case had perineural or lymphovascular invasion. There were 2 cases with thyroid cartilage invasion.

Table 1. Epidemiologic characteristics of patients, histology, details of treatment, and outcome

Case	Age	Sex	Primary site	Stage	Histology	Treatment	Type of surgery	Laryngeal preservation	Outcome
1	55	M	Glottic	T1N0M0	ChondroSa	S	TL	No	DNED at 239 months
2	65	M	Glottic	T1N0M0	CarcinoSa	RT		Yes	DNED at 120 months
3	18	M	Glottic	T1N0M0	MFH	S	VPL	Yes	ANED at 123 months
4	21	M	Supraglottic	T2N0M0	HemangioSa	S + RT	SGL + ND	Yes	ANED at 91 months
5	65	M	Supraglottic	T2N0M0	HemangioSa	S + RT	Endo Laser	Yes	ANED at 94 months
6	49	M	Supraglottic	T2N0M0	MFH	S	SGL	Yes	DNED at 31 months
7	68	M	Glottic	T1N0M0	LeiomyoSa	S	Endo Laser	Yes	Local recurrence at 8 months; ANED at 48 months
8	59	F	Glottic	T3N0M0	RhabdomyoSa	S+RT	VPL	Yes	ANED at 9 months
9	76	M	Glottic	T1N0M0	Mal giant cell tumor	S	Endo Laser	Yes	ANED at 122 months
10	70	M	Supraglottic	T4N2M0	FibroSa	S+RT	TL+ND	No	Died of distant metastasis at 22 months

ANED = alive with no evidence of disease; CarcinoSa = carcinosarcoma; ChondroSa = chondrosarcoma; DNED = dead with no evidence of disease; Endo Laser = endoscopic laser; F = female; FibroSa = fibrosarcoma; HemangioSa = hemangiosarcoma; LeiomyoSa = leiomyosarcoma; M = male; Mal giant cell tumor = malignant giant cell tumor; MFH = malignant fibrous histiocytoma; ND = neck dissection; RhabdomyoSa = rhabdomyosarcoma; RT = radiotherapy; S = surgery; SGL = supraglottic laryngectomy; TL = total laryngectomy; VPL = vertical partial laryngectomy.

With a median follow-up period of 92 months (range from 9 to 239 months), the 5-year OS and DSS were 76% and 90%, and 10-year OS and DSS were 57% and 90%, respectively. One patient had local recurrence and 1 had distant metastasis to the lung. The patient with local recurrence had a T1 glottic lesion, and underwent endoscopic laser cordectomy with undetermined margins. Tumor recurrence was noted 8 months after surgery. He received the second endoscopic laser excision and kept disease-free over a 38-month follow-up. The patient with distant metastasis had a T4N2bM0 supraglottic lesion. Tumor recurrence was found 20 months after surgery. A second primary tumor in the retroperitoneal region was found in 1 patient, and the pathology proved to be renal cell carcinoma.

Discussion

Sarcomas are malignancies derived from the mesodermal tissue of the body. They are uncommon neoplasms of the head and neck, accounting for less than 1% of malignant tumors in this region and less than 10% of all soft tissue sarcomas.^{1,2} According to the report of the Memorial Sloan-Kettering Cancer Center, less than 5% of soft tissue sarcomas in adults occur in the head and neck, with the neck, face, forehead, and sinuses as the common sites.⁴ Laryngeal sarcoma has come to be regarded as rare, comprising less than 1% of all laryngeal tumors.¹ These neoplasms display a diverse array of histologies and a wide spectrum of clinical activity ranging from relatively slow-growing lesions to aggressive locally and regionally destructive lesions with the potential for systemic metastasis. In addition, the anatomic and pathophysiologic heterogeneity demonstrated by this group of neoplasms demands that management considerations be broad and multifactorial if a treatment approach is to be effective.

Sarcoma of the head and neck commonly presents as a painless submucosal or subcutaneous mass of uncertain duration. Symptoms attributable to growth vary according to the location. Those involving the aerodigestive tract generally become symptomatic earlier in the course of disease as compared with tumors involving the neck. The early symptoms of laryngeal sarcoma are a result of mechanical interference with function, and depend on the size and situation of the tumor growth. They are, as a rule, insidious in onset and progression. Hoarseness is usually the first symptom noted. Stridor and even dyspnea follow in the course of time unless the tumor

is removed at its early stages. Dysphagia is not likely to be a prominent symptom, especially at the early stage, until it becomes large enough and protrudes into the hypopharynx.⁵

Laryngeal sarcomas are important in the differential diagnosis for laryngeal submucosal masses. Physically, the neoplasms are often pedunculated and they may be lobulated. Ulceration does not ordinarily develop, which is in contrast with the early ulceration commonly present in carcinoma of the larynx. Sarcomas may originate in any part of the larynx, but, like carcinoma of this organ, it is most often primarily situated in the vocal cords.^{4,5} It is usually more definitely localized and less likely to infiltrate. Clinically, crossing of the anterior commissure and involvement of the contralateral side is infrequently noted.

The etiology of laryngeal sarcoma is obscure so far. The probable relationship of various forms of chronic irritation has never been assumed. Sarcoma of the larynx is observed much more frequently among males than females. The elderly group predominates.⁶ In our cases, only 1 female was noted and the median age was 62 years. This is compatible with the demographic findings of previous studies for sarcomas.

Neither the symptoms nor the physical findings are sufficiently characteristic in cases of laryngeal sarcoma to permit a clinical diagnosis. An accurate diagnosis depends on careful biopsy under a laryngoscope. It is important to get the core of tissue and not only the superficial tumor. Complete study by an experienced pathologist and extensive immunohistochemistry tests to distinguish various types of soft tissue sarcomas are usually required.⁵

There is no standardized staging system for soft tissue sarcomas of the head and neck or for the larynx. The Task Force on Soft Tissue Sarcoma of the AJCC evolved in 1968^{2,7} and most authors (Table 2) consider 5 cm (< 5 cm is T1, and \geq 5 cm is T2) as the reference size for tumor staging according to the TNM system with a grade of tumor (G) added.^{2,7,15} For laryngeal sarcomas, due to their complex and unique anatomic sites, no specific staging system is valid. Therefore, in this study, we used the AJCC staging system for laryngeal tumors to stage our cases.

Treatment of sarcomas is dictated by tumor type, staging, location, size, and patient age.¹⁶ The treatment planning for sarcoma of the larynx depends on its size, situation, and biologic behavior. Because many of these tumors are pedunculated, show less tendency to infiltrate the surrounding structures, and metastasize later than laryngeal carcinomas, they may remain operable for a considerably longer period after diagnosis compared to squamous cell carcinoma.¹⁷

Table 2. Review of literature on sarcoma of the head and neck

Author	Site of primary tumor	Pathologic type	No. patients	5-year OS
Farr, 1981 ⁸	Head and neck region	Soft tissue sarcoma	285	32%
Littman et al, 1983 ⁹	Head and neck region	Soft tissue sarcoma	32	75%
Lavertu and Tucker, 1984 ¹⁰	Larynx	Chondrosarcoma	46	77%
Farhood et al, 1990 ¹	Head and neck region	Soft tissue sarcoma	176	55%
Kowalski and San, 1994 ¹¹	Head and neck region	Soft tissue sarcoma	128	48%
Eeles et al, 1993 ²	Head and neck region	Soft tissue sarcoma	103	50%
Tran and Parker, 1992 ¹²	Head and neck region	Soft tissue sarcoma	164	66%
Le et al, 1997 ¹³	Head and neck region	Soft tissue sarcoma	65	56%
Dudhat et al, 2000 ¹⁴	Head and neck region	Soft tissue sarcoma	72	60%
VGH in Taipei, 2001	Larynx	Sarcoma	10	76%

OS = overall survival rate.

Actually, many of them at the early stage may be removed readily just by means of a direct laryngoscope. If the tumor is too extensive to remove in this manner, laryngectomy may be necessary.¹⁷ In our study, 9 patients received surgery, including 2 total laryngectomy, 5 partial laryngectomy, and 3 who had removal of tumors by means of endoscopic laser. Only 1 patient received a full course of radiation therapy as the main treatment because of small lesions and old age at diagnosis, and which eventually resulted in a good prognosis. Surgery is the mainstay therapy in treatment planning for laryngeal sarcomas. Organ preservation is possible because most patients can be diagnosed early.

The literature shows that 10–12% of soft tissue sarcomas of the head and neck develop neck metastasis early;¹⁸ however, it is not common in laryngeal sarcomas, except at advanced stages. In the case of fibrosarcoma, which is found most frequently, even the poorly differentiated type metastasize in fewer than 25% of patients.¹⁹ Elective neck dissection is generally not required. In our series, only 1 patient with a palpable neck mass had neck dissection (10%), which proved to be a neck metastasis.

The role of RT in the treatment of sarcomas of the head and neck has evolved considerably over the past 30 years. Although, in many instances, sarcomas demonstrate considerable radio-resistance, RT remains an important adjunct in the treatment of soft tissue sarcoma to diminish the incidence of local recurrence.¹³ The major indications for postoperative RT are high-grade lesions, positive surgical margins, larger tumor (> 5 cm) and recurrent lesions.²⁰ In our cases, adjunctive postoperative RT was administered in 4 patients with high-grade tumors to achieve better local control. On the other hand, the effect of chemotherapy to various laryngeal sarcomas has not

been documented statistically. None of our patients received chemotherapy, although established nonsurgical protocols involving chemotherapy and RT have been standardized for rhabdomyosarcoma.^{21,22}

With these treatment modalities, treatment failure was noted in 2 patients: 1 patient had local recurrence (leiomyosarcoma, high grade) after endoscopic laser surgery; the other with a T4 lesion eventually had distant lung metastasis (fibrosarcoma, high grade). These 2 cases had the common feature of high-grade tumors, although the former case was categorized as early T stage when diagnosed.

In most series of head and neck soft tissue sarcomas,^{8,9,19,23,24} local control relative to grade and margin status, together with the development of distant metastasis, was the most influential determinant of survival in this heterogeneous group of tumors.⁸ Different pathologic classifications may also influence the prognosis. Certain pathologic kinds of soft tissue sarcomas are often associated with high histologic grading, such as malignant fibrous histiocytoma and rhabdomyosarcoma,^{8,19,23} and usually indicate poor prognosis clinically. In contrast, chondrosarcoma is usually well differentiated pathologically and brings better prognosis.⁹ As in head and neck malignancies, patients with recurrent local disease are at risk for developing disseminated sarcoma, and the most common site is in the lungs.¹⁹ This is particularly true in patients with high-grade lesions, even if evidence of primary local recurrence is not established. For this, high-grade tumors warrant adjunctive postoperative RT in the treatment planning.²⁰

In general, the survival rate of sarcomas in the head and neck is worse than if they are found in the extremities. In reviewing the literature, 5-year OS of patients with soft tissue sarcoma of the head and neck

ranged from 32% to 75% (Table 2).^{1,2,9-14,25} Because of the rarity of laryngeal sarcoma, no convincing data about survival have been available so far. One series that focused on laryngeal chondrosarcoma revealed similar survival to ours (77% vs 76%).⁹ The 5-year OS was about 50% for well-differentiated laryngeal fibrosarcoma in a previous series.¹⁹ It seems that the prognosis of laryngeal sarcoma is somewhat better than that of sarcoma in other sites of the head and neck.^{10,11,25}

To head and neck surgeons, sarcoma of the larynx is an uncommon neoplasm. Surgical intervention has been considered as the treatment of choice. Because most of the patients can be diagnosed early, conservation surgery with laryngeal preservation is usually possible. Postoperative adjuvant RT is only reserved for a high-grade tumor and positive surgical margins. The prognosis is relatively good when compared with a tumor originating from other anatomic sites.

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