Chondrosarcoma of the Larynx

Inon Buda MD MHA, Roy Hod MD, Raphael Feinmesser MD and Jacob Shvero MD

Department of Otolaryngology–Head and Neck Surgery, Rabin Medical Center (Beilinson Campus), Petah Tikva, affiliated with Sackler Faculty of Medicine, Tel Aviv University, Ramat Aviv, Israel

ABSTRACT: Background: Chondrosarcoma of the larynx is a rare tumor. The most common symptom is hoarseness. Treatment is controversial. Objectives: To describe six patients with laryngeal chondrosarcoma from a single center. Methods: The medical records of a major tertiary hospital were reviewed for all patients with laryngeal chondrosarcoma diagnosed and treated from 1959 to 2010. Data on background, clinical treatment and outcome were collected. Results: Six patients, all males with a mean age of 53.3 years, were identified. Partial laryngectomy was performed in three patients, and total laryngectomy, local excision, and partial cricoidectomy in one patient each. Four patients had a permanent tracheostomy after surgery. One patient required postoperative chemotherapy and one radiotherapy. Follow-up time was 12–216 months (mean 102 months). Recurrence developed in two patients 2 and 8 years after initial treatment and was treated by salvage surgery in both patients. One patient died during the follow-up from an unrelated cause. The others are currently alive. Conclusions: This study supports earlier reports recommending initial treatment with partial or total laryngectomy for laryngeal chondrosarcoma. Long-term follow-up for recurrence is advised. We recommend preserving the larynx, if possible, even if a permanent tracheostomy is necessary.

KEY WORDS: chondrosarcoma, larynx, recurrence, treatment, resection

Chondrosarcoma of the larynx is an uncommon tumor, accounting for approximately 1% of all laryngeal neoplasms [1]. It is, however, the most common non-epithelial neoplasm of the larynx [2]. It was first described by Travers in 1816 [3], but the term chondrosarcoma at this site was introduced by New in 1935 [4]. Most of the reports on laryngeal chondrosarcoma to date have been limited in size [5-10]; the largest was published by Thompson and Gannon in 2002 [1] and included 111 patients. The literature contains a number of case series, but a review showed that many describe the same patients from the same database(s) [1,11,12].

The etiology of laryngeal chondrosarcoma is unknown, although it is usually assumed to derive from disordered ossification of the laryngeal cartilage [5,13]. No relationship to tobacco use or alcohol consumption has been proved [1]. The mean age at diagnosis is 60 to 64 years, with a male predominance [2,14]. Symptoms vary, depending on the location of the mass, and include hoarseness (most patients) caused by narrowing of the glottic plane and compression of the inferior laryngeal nerves; dyspnea and airway obstruction due to endolaryngeal and subglottic growth; dysphagia due to extralaryngeal growth, originating in the posterior cricoid; and painless neck mass due to tumor involvement of the thyroid cartilage (when present) [1,5,13].

The tumor arises from hyaline – and not elastic – cartilage: cricoid cartilage in 75% of patients, thyroid cartilage in 17%, arytenoid cartilage in 5%, and epiglottis and accessory cartilages in 3% [13]. Chondrosarcoma is a macroscopically smooth and lobular mass. Microscopically it has high nuclear-to-cytoplasmic ratio and hyperchromatic nuclei. Mitotic figures are not common [1].

Imaging studies have some diagnostic value, although it is
impossible to distinguish chondromas from chondrosarcomas. The imaging modality of choice is computed tomography [18]. Typical findings are a hypodense, well-circumscribed mass containing mottled calcifications, with displaced structures and destruction of the cartilage [Figure 2]. Magnetic resonance imaging has the added advantage of superior contrast resolution of the tumor and paralaryngeal tissues [19]. On X-ray the tumor appears as a popcorn-like calcification [1].

The initial treatment for chondrosarcoma of the larynx is surgery [16] in order to excise all tumor extensions with negative margins [20]. For low-grade tumors, options include CO2 laser resection, hemilaryngectomy, or hemilaryngectomy. For high-grade tumors and recurrences, the only choice is total laryngectomy. Attempts are made to spare the larynx for preservation of voice and normal swallow. When cricoideectomy is performed, laryngotracheal anastomosis or reconstruction by free flap is used to close the defect. The effectiveness of radiotherapy is still controversial. Chemotherapy is not considered an option [21].

Recurrence is common, with rates of 35-40%. Nevertheless, the long-term prognosis of laryngeal chondrosarcoma is good (95%, 10 year survival) and metastasis is rare (up to 10%) [1].

The aim of this study was to describe our experience with six patients diagnosed and treated for chondrosarcoma of the larynx at a major tertiary center in the last 51 years.

**RESULTS**

The results are shown in Table I. All six patients were male. The mean age at diagnosis was 53.3 years (range 24–66 years). Five patients presented with hoarseness and dyspnea; in the sixth patient, laryngeal chondrosarcoma was found incidentally on cervical CT performed for an unrelated reason. Histological study showed a well-differentiated tumor in one patient, well-to-moderately differentiated tumor in four, and a poorly differentiated tumor in one.

Surgery was performed in all patients as follows: partial laryngectomy in three, and total laryngectomy, endolaryngeal laser excision and cricoideectomy in one each. The patients treated with cricoideectomy and partial laryngectomy also had a permanent tracheostomy. Four patients were referred for additional therapy (radiotherapy/chemotherapy) because of recurrence, positive margins, or advanced-stage disease.

As of the end of 2011 the mean duration of follow-up was 102 months (range 12–216 months). The tumor recurred during follow-up in two patients, after 2 years and 8 years, and both underwent a second surgical procedure. No recurrence has been diagnosed in other patients or in those patients after the second surgical procedure. Five patients are currently alive. One patient died during follow-up from a cause unrelated to the chondrosarcoma.

**DISCUSSION**

This is our single-center experience. In the present series of six patients with chondrosarcoma of the larynx, the low-grade histologic findings in five cases prompted treatment with surgery with preservation of the larynx; only one
patient underwent initial total laryngectomy. Four of the five patients treated with partial surgery had positive margins. Two of them failed treatment, one in the larynx and one in the neck, and required postoperative chemo/radiotherapy. There was no evidence of a second failure during 1 to 4 years of follow-up. The four patients treated with cricoidectomy or partial laryngectomy remain dependent on tracheostomy for breathing; all have excellent speech. The patient after total laryngectomy is alive and well with no evidence of recurrence 10 years after treatment.

Our study confirms other observations in the literature that radical surgery is usually unnecessary for laryngeal chondrosarcoma because of the relatively benign course of the disease [1,16]. The role of postoperative radiotherapy is controversial. In our series, the disease recurred in the patient with positive margins treated with post-surgery radiation, placing the value of radiation in question. None of our patients had distant metastases, confirming the assumption that chemotherapy should not be part of the treatment regimen.

In conclusion, the good prognosis in our six patients with chondrosarcoma of the larynx is standardize the therapeutic approach to chondrosarcoma of the larynx.

Corresponding author:
Dr. I. Buda
Dept. of Otolaryngology–Head & Neck Surgery, Rabin Medical Center (Beilinson Campus), Petah Tikva 49108, Israel
Phone: (972-3) 937-6456
Fax: (972-3) 937-6467
email: inonb@clalit.org.il

References

Table 1. Clinical and treatment characteristics of six patients with chondrosarcoma of the larynx

<table>
<thead>
<tr>
<th>Patient</th>
<th>Year of diagnosis</th>
<th>Age (yrs)</th>
<th>Presenting symptom</th>
<th>Histopathology</th>
<th>Treatment</th>
<th>Additional therapy</th>
<th>Follow-up (yrs)</th>
<th>Recurrence</th>
<th>Treatment for recurrence</th>
<th>Additional therapy</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>1959</td>
<td>64 M</td>
<td>Hoarseness, dyspnea</td>
<td>Well to mod. diff. chondrosarcoma</td>
<td>Total laryngectomy</td>
<td>None</td>
<td>12</td>
<td>None</td>
<td>–</td>
<td>Chemo-radiotherapy</td>
</tr>
<tr>
<td>2</td>
<td>1993</td>
<td>56 M</td>
<td>Incidental finding of neck mass on CT</td>
<td>Well to mod. diff. chondrosarcoma</td>
<td>Partial laryngectomy</td>
<td>None</td>
<td>18</td>
<td>None</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>3</td>
<td>1997</td>
<td>24 M</td>
<td>Hoarseness, dyspnea</td>
<td>Poorly diff. chondrosarcoma</td>
<td>Laser endolaryngeal subtotal laryngectomy</td>
<td>None</td>
<td>14</td>
<td>None</td>
<td>Open resection of cervical mass</td>
<td>–</td>
</tr>
<tr>
<td>4</td>
<td>2007</td>
<td>57 M</td>
<td>Neck mass, dyspnea</td>
<td>Well to mod. diff. chondrosarcoma + papillary ca. of thyroid, 0.4 cm</td>
<td>Lt. hemi-thyroidectomy + resection of cricoidal mass + permanent tracheostomy</td>
<td>Radiotherapy</td>
<td>4</td>
<td>At 8 yrs</td>
<td>Partial laryngectomy + completion thyroideectomy + lt. lateral neck dissection</td>
<td>–</td>
</tr>
<tr>
<td>5</td>
<td>2008</td>
<td>66 M</td>
<td>Hoarseness, dyspnea</td>
<td>Well to mod. diff. chondrosarcoma</td>
<td>Cricoideotomy + permanent tracheostomy</td>
<td>Radiotherapy</td>
<td>2</td>
<td>At 2 yrs</td>
<td>–</td>
<td>–</td>
</tr>
<tr>
<td>6</td>
<td>2010</td>
<td>53 M</td>
<td>Hoarseness, sensation of foreign body</td>
<td>Well-diff. chondrosarcoma</td>
<td>Partial laryngectomy + tracheostomy + reconstruction with buccal mucosa</td>
<td>Radiotherapy</td>
<td>1</td>
<td>None</td>
<td>–</td>
<td>–</td>
</tr>
</tbody>
</table>

Table 1. Clinical and treatment characteristics of six patients with chondrosarcoma of the larynx

- Additional therapy – Chemo-radiotherapy
- Recurrence – None
- Treatment for recurrence – Open resection of cervical mass
- Additional therapy – Chemo-radiotherapy
- Follow-up (yrs) – 12, 18, 14, 4, 2, 1
- Age (yrs) – 64 M, 56 M, 24 M, 57 M, 66 M, 53 M
- Presenting symptom – Hoarseness, dyspnea, Incidental finding of neck mass on CT, Hoarseness, dyspnea, Neck mass, dyspnea, Hoarseness, dyspnea, Hoarseness, sensation of foreign body
- Histopathology – Well to mod. diff. chondrosarcoma, Well to mod. diff. chondrosarcoma, Poorly diff. chondrosarcoma, Well to mod. diff. chondrosarcoma + papillary ca. of thyroid, 0.4 cm, Well to mod. diff. chondrosarcoma, Well-diff. chondrosarcoma
- Treatment – Total laryngectomy + lt. hemi-thyroidectomy, Partial laryngectomy + permanent tracheostomy, Laser endolaryngeal subtotal laryngectomy, Lt. hemi-thyroidectomy + resection of cricoidal mass + permanent tracheostomy, Cricoideotomy + permanent tracheostomy, Partial laryngectomy + tracheostomy + reconstruction with buccal mucosa
- Additional therapy – Chemo-radiotherapy, None, None, None, Radiotherapy, Radiotherapy
- Follow-up (yrs) – 12, 18, 14, 4, 2, 1
- Recurrence – None, None, None, At 8 yrs, At 2 yrs, None
- Treatment for recurrence – Open resection of cervical mass, Partial laryngectomy + completion thyroideectomy + lt. lateral neck dissection, –, –

**Capsule**

**A metagenome-wide association study of gut microbiota in type 2 diabetes**

Assessment and characterization of gut microbiota has become a major research area in human disease, including type 2 diabetes, the most prevalent endocrine disease worldwide. To carry out analysis on gut microbial content in patients with type 2 diabetes, Qin et al. developed a protocol for a metagenome-wide association study (MGWAS) and undertook a two-stage MGWAS based on deep shotgun sequencing of the gut microbial DNA from 345 Chinese individuals. The authors identified and validated approximately 60,000 type 2 diabetes-associated markers and established the concept of a metagenomic linkage group, enabling taxonomic species-level analyses. MGWAS analysis showed that patients with type 2 diabetes were characterized by a moderate degree of gut microbial dysbiosis, a decrease in the abundance of some universal butyrate-producing bacteria, and an increase in various opportunistic pathogens, as well as an enrichment of other microbial functions conferring sulphate reduction and oxidative stress resistance. An analysis of 23 additional individuals demonstrated that these gut microbial markers might be useful for classifying type 2 diabetes.

*Nature* 2012; 490: 55

Eitan Israeli

**Capsule**

**An atlas of Epstein-Barr virus**

Epstein-Barr virus (EBV), which has been associated with B cell lymphomas, gastric carcinomas, and nasopharyngeal carcinoma, may be responsible for 1% of all human cancers. Arvey and co-workers have pooled data from nucleosome positioning maps and viral protein-binding analyses with more than 700 publicly available high-throughput sequencing data sets from human lymphoblastoid cell lines to generate a large-scale functional genomics atlas of the virus. Although much of the data were already publicly available, it was scattered, and has now been integrated in a highly usable form. Their analysis revealed possible regulatory domains within the viral genome and combinatorial control of viral gene expression by human transcription factors. There were also indications of three-dimensional organization, including loop formation between the viral origin of latent replication and latent membrane proteins 1 and 2, linked by human transcriptional repressor CTCF and cohesin. B cell specificity factor Pax5 was shown to bind to EBV terminal repeats, and deletion experiments showed that Pax5 is involved in the regulation of EBV transcription during latent infection.

*Cell Host Microbe* 2012; 12: 233

Eitan Israeli

**Discovery consists of seeing what everybody has seen and thinking what nobody has thought**

Albert Szent-Györgyi (1893-1986), Hungarian physiologist who won the Nobel Prize in Physiology/Medicine in 1937. He is credited with discovering vitamin C and the components and reactions of the citric acid cycle. He was active in the Hungarian Resistance during World War