Case Report

Chondrosarcoma of the Larynx and Possibility of Conservative Surgery

Augusto Cattaneo*, Stefano Zorzi, Valeria Navach and Mohssen Ansarin

Department ENT-Head and Neck Surgery, European Institute of Oncology, Italy

Abstract

Chondrosarcoma, a sub mucosal hard, slow growing and local aggressive tumor, is the most frequent mesenchymal neoplasm of the larynx. Diagnosis is supported both by clinical appearance and radiological evaluation, even because a biopsy is not always easy to obtain, due to its hardness. Laryngeal chondrosarcomas are histologically differentiated as low-, intermediate- and high-grade lesions and total laryngectomy was considered the common treatment, even if nowadays, conservative open neck or endoscopic surgery, especially for low-grade lesions, is reported in several studies published in the literature.

We discuss seven cases of laryngeal chondrosarcoma treated at our institution with different types of conservative surgery. The aim of this article is to assess the role of conservative treatments regarding the management of laryngeal chondrosarcomas, based upon personal experience and reviewing the literature data.

ABBREVIATIONS

TC: Computed Tomography; MRI: Magnetic Resonance Imaging; TLM: Trans oral Laser Microsurgery; FNAB: Fine Needle Aspiration Biopsy; PET: Positron Emission Tomography; CHEP: Crico-Hyoido-Epiglottoto-Pexy

INTRODUCTION

Laryngeal chondrosarcoma represents less than 0.2% of all head and neck cancers and up to 1% of all laryngeal malignancies. The mean age at diagnosis is 60 to 65 years and men are about three times more frequently affected than women. Low-grade chondrosarcoma has a torpid evolution and good prognosis, while high-grade chondrosarcoma may have a fast negative course. The overall recurrence rate after treatment varies from 16% to 18%. Metastatic disease is described in about 2% to 10% of the reported cases in literature [1-2].

Surgery, namely total laryngectomy, remains the gold standard treatment [3], even if conservative surgery has been increasingly applied in selected cases. Radiation therapy is reserved for non-resectable tumours, while chemotherapy does not yet have a clear role for these tumours [4]. Nowadays, surgical conservative open neck or endoscopic approaches with a wide margin, including the external perichondrium, are considered the most appropriate method and suggested, when feasible, for low-grade lesions [5-8].

CASES PRESENTATION

Seven patients (age range 39-82 years, mean age 62.4 years; male to female ratio M:F=3:4) were identified in a review of about 1500 patients with primary laryngeal malignances, in the registry files of the Otolaryngology Head & Neck Surgery Division at the European Institute of Oncology (IEO, Milan, Italy) from 2000 to 2012. The main characteristics of the patients are briefly reported in (Table 1).

The most common presenting symptoms in our group of patients were dyspnoea and dysphonia: two patients had a paresis of the vocal fold, two further cases showed a voice change without vocal fold paralysis. Every case was treated with different surgical techniques and after surgery, all patients had normal oral intake, one patient had a permanent tracheostomy and no patient had adjuvant treatment. There was no evidence of recurrences in clinical and radiological follow-up evaluations.

Case 1

A nodule of the superior pole of the thyroid gland was detected in a 66-year-old male. An MRI showed a “4.5 cm nodule in the superior pole of right thyroid lobe invading the thyroid cartilage” and a FNAB was positive for a suspicious papillary tumor (Figures 1,2). In October 2005 the patient underwent total thyroidectomy with recurrent central neck dissection: the histopathological examination showed low-grade chondrosarcoma, not completely...
Table 1: characteristics of the patients.

<table>
<thead>
<tr>
<th>Patient/case no.</th>
<th>Sex/Age</th>
<th>Symptoms</th>
<th>Primary site</th>
<th>Original Therapy</th>
<th>Histopathologic</th>
<th>Recurrence Metastasis</th>
<th>F-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>B.L./1</td>
<td>M/70</td>
<td>No symptoms</td>
<td>Superior pole right thyroid and thyroid cartilage</td>
<td>10/2005 Vertical partial hemilaryngectomy + reconstruction with submental flap</td>
<td>Chondrosarcoma grade I (invasive thyroid cartilage)</td>
<td>Chondrosarcoma grade I</td>
<td>No</td>
</tr>
<tr>
<td>A.F./2</td>
<td>F/50</td>
<td>Dysphonia, dyspnea</td>
<td>Cricoid</td>
<td>01/2006 Cricotracheal resection + anastomosis</td>
<td>Chondrosarcoma grade I</td>
<td>No</td>
<td>NED 09/2015</td>
</tr>
<tr>
<td>P.C./4</td>
<td>F/57</td>
<td>Dysphonia, dyspnea</td>
<td>Cricoid</td>
<td>05/2010 Cricotracheal resection + anastomosis</td>
<td>Chondrosarcoma grade I</td>
<td>No</td>
<td>NED 09/2015</td>
</tr>
<tr>
<td>C.M./5</td>
<td>F/82</td>
<td>Dyspnea and dysphagia</td>
<td>Cricoid</td>
<td>07/2011 Total Laryngectomy</td>
<td>Chondrosarcoma grade II</td>
<td>no</td>
<td>NED 09/2015</td>
</tr>
<tr>
<td>N.U./6</td>
<td>M/39</td>
<td>No symptoms</td>
<td>thyroid</td>
<td>02/2012 Open neck excision + costal cartilage reconstruction</td>
<td>Chondrosarcoma grade I</td>
<td>no</td>
<td>NED 09/2015</td>
</tr>
<tr>
<td>S.L./7</td>
<td>M/65</td>
<td>Dysphagia</td>
<td>Cricoid</td>
<td>09/2012 Total Laryngectomy</td>
<td>Chondrosarcoma grade I</td>
<td>no</td>
<td>NED 09/2015</td>
</tr>
</tbody>
</table>

Abbreviations: NED: No Evidence of Disease

removed at the superior segment of right thyroid ala, without nodal metastases. After two months a partial hemilaryngectomy plus temporary tracheotomy and reconstruction with local sub-mental flap was carried out. The histopathological analysis confirmed the diagnosis of chondrosarcoma extended to the superior resection margin of the cricoid: after multidisciplinary discussion with the medical oncologist we decided not to perform chemotherapy. He is clinically and radiologically followed-up in an outpatient setting with no evidence of recurrence or metastasis; at the last clinical assessment in September 2015 no signs of recurrence were seen and results were satisfactory even though the patient still had a tracheostomy.

**Case 2**

A 46-year-old female with a two-year history of progressive dysphonia and dyspnea, was referred to our clinic in November 2005. Laryngeal endoscopy showed a paresis of the left vocal cord and a CT scan revealed a glottic-subglottic lesion from the thyroid cartilage. A FNAB of the lesion under ultrasound scan demonstrated suspicious chondrosarcoma. In January 2006 the patient underwent a crico-tracheal resection-anastomosis (between the remnant part of the cricoid ring and trachea) and temporary tracheotomy. Histopathology confirmed a low-grade chondrosarcoma. The patient was last seen in September 2015: there was no evidence of local recurrence or regional or distant metastasis.

**Case 3**

A 74-year-old female presented increasing dysphonia, severe dyspnoea and hoarseness (Figures 3, 4). A clinical examination revealed a subglottic mass, right side deviation of trachea and normal mobility of vocal cords. A CT scan showed a left subglottic mass of 2x3 cm, invading the posterior wall and left side of cricoid cartilage, with sclerosis of the homolateral thyroid cartilage. Tumor excision, with a temporary tracheotomy, was carried out in October 2009 with CO2 laser, paying close attention to sparing the external cricoid perichondrium: histopathological diagnosis was low-grade chondrosarcoma. On September 2015 the patients was alive without disease.

**Case 4**

A 57-year-old female presented at our clinic with a four-year history of voice changing and one year of mild dyspnoea. Clinical examination showed a normal mobility of vocal cords and a subglottic reddish mass with intact mucosa (Figure 5). A CT scan
Case 5

An 82-years-old female was referred to our department after an urgent tracheotomy (Figure 6), due to ingravescent dyspnoea. Clinical examination showed a quite complete adduction of both vocal folds with minimal residual respiratory space. A CT scan showed a lesion of the entire cricoid that subtotally occluded the endolaryngo-subglottic lumen. She underwent a fine-needle trans-laryngeal biopsy, indicative of intermediate grade chondrosarcoma. Considering the age of the patient our exclusive proposal was a total laryngectomy, performed in July 2011. The histopathological definitive response confirmed a middle-grade chondrosarcoma extended to the soft pre-laryngeal tissue, completely removed. After four years the patient is clinically and radiologically negative and regularly followed up (the last clinical assessment in September 2015 was satisfactory).

Case 6

A 38-years-old male was referred to our Department for assessment of a cervical right nodular mass (Figure 7-9). Clinical examination showed normal vocal fold motility and minimal reduction of the respiratory space. On the right side of the neck a hard, nodular, swallowing-mobile lesion of about 4 cm was observed. A CT scan showed a 3.5 cm lesion of the right thyroid ala with minimal deviation of the laryngeal tract. He underwent a trans-laryngeal biopsy, indicative for well-differentiating chondrosarcoma. Considering the age of the patient and the location of the nodule, we proposed exeresis of the lesion shown a subglottic mass from the right side of the cricoid cartilage (2x1.9 cm); the biopsy confirmed a low-grade chondrosarcoma. In April 2010 she underwent a laryngotracheal resection with tracheo-thyroid anastomoses plus temporary tracheotomy; the definitive histopathological diagnosis confirmed a low-grade chondrosarcoma. Subsequent examination revealed normal vocal cord mobility, a resolution of dysphagia and satisfactory general conditions.

Figure 6 Case 5 specimen, after total laryngectomy.

Figure 7 Case 6 pre-operative.
complementary with the thyroid ala and reconstruction with autologus rib cartilage associated with temporary tracheotomy, in June 2012. The histopathological exam confirmed a low-grade chondrosarcoma completely removed. The patient’s postoperative course was uneventful with no evidence of recurrence or metastasis (September 2015).

Case 7

A 64-year-old male was referred to our Department for evaluation of a nodular retrocricoid mass with initial dysphagia (Figure 10). The patient had a history of previous ictus cerebri with residual left hemiplegia, diabetes and previous heart stroke. Clinical examination showed a retrocricoid nodule that completely closed the oesophageus inlet and reduced arytenoid motility. An MRI scan showed a 42mm lesion of the retrocricoid region with erosion of the posterior wall of the cricoid. A biopsy under general anaesthesia was indicative of well-differentiating chondrosarcoma.

Considering the age of the patients, his comorbidities, the location and dimension of the nodule, we performed a total laryngectomy in September 2012. The definitive histopathological response confirmed a low-grade chondrosarcoma completely removed. The postoperative course was regular. On September 2015 the patient has shown no evidence of disease.

DISCUSSION

A search for “laryngeal chondrosarcoma” in PubMed (US NIH: National Library of Medicine) retrieved about 300 items (in August 2014): 176 articles reported on 484 cases of this neoplasm. Only 26 papers reported experience with more than four cases, because the rarity of these tumors makes it difficult to collect many cases in a single centre.

The etiology of chondrosarcoma is unknown and still remains unclear. Several theories have been put forward, but three have gained the greatest acceptance: 1) abnormality of ossification of the laryngeal cartilages, 2) mechanical micro trauma and ischemia produced by contraction of laryngeal muscles and 3) chronic inflammation or ischemic changes in a pre-existing chondroma [9].

Ossification in cricoid and thyroid cartilages begins in the third decade: the observation that cartilaginous tumors most often originate in old age suggests a possible correlation between ossification process and chondrosarcoma development [10].

The progressive ossification of the larynx is also related to the influence of mechanical microtrauma and ischemia produced by contraction of the laryngeal muscles: this concept explains how most commonly chondrosarcoma occur on the postero-lateral wall of the cricoid and on the infero-lateral thyroid cartilage [11].

About 60% of chondrosarcomas were superimposed...
on a pre-existing benign chondroma: chronic inflammation or ischemic changes in a pre-existing chondroma may also contribute to the development of a chondrosarcoma. The differential diagnosis is with chondroma, chondrometaplasia and tracheopathtoosteoplastica. Chondrometaplasia consists in elastic-rich cartilage nodules and is generally located on the vocal cords. Tracheopathtoosteoplastica is very uncommon and affected the tracheal cartilage rings [12]. Histologically, chondrosarcomas had increased cellularity with nuclear atypia including bi- or multinucleation and when the hypercellularity, the mitotic activity and the atypical mitosis increased, the grading increases and permits to differentiate chondrosarcomas into low, intermediate or high grade [13-15] (Figure 11). About 75% of laryngeal chondrosarcomas are low grade and only higher grading tumors are associated with a poor prognosis.

Common presenting symptoms, generally depending upon the anatomic location and size of the lesion, are hoarseness, airway obstruction, dysphagia, dysphonia, dysphagia, voice changes and pain [16]. Clinical examination reveals a very hard, subglottic bulging mass covered by intact smooth mucosa without ulceration. The chondrosarcomas that arise from the cricoid plate grow into the lumen of the larynx and later invade the piriform sinus and the post-cricoid region; differently, chondrosarcomas arising from the thyroid lamina mainly grow in an external direction. Vocal cord paralysis can occur frequently in cricoid chondrosarcoma due to involvement or interference of the cricoarytenoid joint rather than the recurrent laryngeal nerve [17].

After clinical evaluation, a radiological evaluation is mandatory, even though chondromas and chondrosarcomas cannot be distinguished solely on the basis of radiological features. CT scan is more sensitive in demonstrating fine calcifications associated with chondrosarcomas; MRI is less specific, but it aids in delineating the extent of the lesion with the surrounding soft tissue [18,19].

A biopsy, to obtain an accurate identification of tumor type as well as of tumor grade, is generally performed under general anesthesia, with or without a temporary tracheotomy, because the lesions are very hard and not readily penetrable. In selected cases, a tru-cut ultrasound guided biopsy, in local anesthesia, is feasible [20].

Management of this lesion is by complete surgical excision, including the external perichondrium and a margin of normal tissue. Specific conservative modalities and surgical techniques performed, including those with reconstruction using tracheo-laryngeal anastomoses or rib replacement, are the subject of many reports: laryngofissure, thyrotomy, open partial laryngectomies and endoscopic removals have been described. Cantrell was the first to propose the conservative surgery for condrosarcoma of the larynx, describing a method of surgical excision and laryngotracheal reconstruction when the tumor involves the cricoid [6]. AliSaleh et al., [19], reported on five cases treated with open surgery: laryngofissure and partial laryngectomies; Tiwary discussed five cases treated with surgery by laryngo fissure [21]. Merrot described the advantages of Nd-YAG over CO2 laser in 13 cases of both chondroma and low grade chondrosarcomas [22].

All these reports underlined the importance of the preservation of the cricoid cartilage that is considered crucial for normal laryngeal functions. When this cartilage is involved, the structure of the larynx is weakened and also the integrity and normal function of the cricoarytenoid joint, the recurrent laryngeal nerve and the continuity of the tracheo-crico wall are undermined. Removal of a large part of the cricoid interrupts the laryngeal support and, when more than half of cricoid cartilage is involved, total laryngectomy is often necessary. Nowadays, considering both the site of the neoplasm and patients age, it is sometimes difficult to adequately remove the tumor and at the same time maintain laryngeal structural integrity and functions: despite attempts at laryngeal preservation, more than one third of patients may need to undergo a total laryngectomy [23].

We report a single-centre experience in the treatment of these rare slow-growing locally aggressive tumors that can be successfully treated with conservative surgery. Before choosing a tailored treatment modality, patient’s age, comorbidities and their general health conditions must always be considered. Generally we studied all our cases with a CT scan and we reserved the MRI only for selected cases.

We needed to obtain an adequate tumor sampling to define the tumor type as well as the tumor grade: a tru-cut ultrasound guided biopsy in local anesthesia was performed in two of our cases obtaining more tissue sampling and correct diagnosis. These aspects play a key role in the treatment decision process.

Conservative laryngeal endoscopic laser surgery permits (as clearly reported in the literature for squamous cell carcinomas) a complete and effective resection of tumors, in early and intermediate stages (T1-T3): we suggest that these results could be achieved even in chondrosarcomas, especially when the lesion is low-grade and of small size [24-26]. In our series we decided to use an endoscopic approach for low-grade lesions, in patients with no radiologic evidence of macroscopic involvement of the crico-arytenoid joint or without laryngeal nerve palsy.

When endoscopic surgery was not feasible, we preferred an open neck conservative approach: if the lesion involves the thyroid cartilage without invading mucosa we remove cartilage and reconstruct with autologous graft, to avoid laryngocele. If this approach is not feasible we perform classic CHEP. We reserved total laryngectomy only when more than half of cricoid cartilage is invaded by the lesion or when a reconstruction is quite not feasible.

Radiotherapy is reserved for recurrent and for high-grade lesions, although chondrosarcomas are generally considered radio-resistant tumors. None of our cases received adjuvant treatment.

Our results allow us to state that a complete removal is always mandatory for a correct treatment of these lesions, above all in cases in which partial laryngectomies can definitively resolve the problem and preserve laryngeal functions. On follow-up, none of our patients had regional or distant metastasis or tumor-related death, despite our follow-up period being short (last follow-up on September 2015).

Some authors [27] supported the idea that even a partial,
incomplete removal could obtain a good result, especially in low-grade chondrosarcomas, due to the possibility of multiple repeated resections, slow re-growth and low propensity for metastasis of these tumors. We support the idea that a total laryngectomy with radical excision of the lesion is better than a non-functional preserved larynx with permanent tracheostomy. It reduces the stress of a short clinical evaluation and it avoids the necessity of new repeated surgery under general anesthesia, even because patients are generally advanced in aging.

ACKNOWLEDGEMENTS

The authors thank Fausto Maffini, MD, for histopathological scan and images.

REFERENCES