Chondrosarcoma of the Larynx and Review of the Literature

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Abstract. Chondrosarcoma (CS) of the larynx was first described in 1935. Cartilaginous tumours of the larynx are largely rare and there is little literature concerning them. Laryngeal CS manifest with a different pathological behaviour to other malignancies of the larynx and as such the treatment of these neoplasias are different. The purpose of this review is to present a detailed report of the laryngeal CS in recent literature. We present a case of laryngeal CS of the cricoid cartilage and a case of a sarcomatous neoplasm of the vocal cord as a potential differential diagnosis. Although representing a rare malignancy, the last decade has brought new insights in surgical treatment of laryngeal CS and subsequent reduction in recurrence rates, whereas progress in tumour biology and etiological agents is still scarce. We concentrate on new insights in classification, radiologic and pathologic features, and treatment modalities in the last two decades. Based on the literary evidence the authors recommend a conservative laryngeal function-preserving surgery. Total laryngectomy should be reserved to recurrent CS and rare cases of voluminous high-grade CS of the larynx.

Chondrosarcomas (CSs) are uncommon malignant neoplasms of the cartilage that occur anywhere in the body but are mostly commonly seen in the long bones and pelvis. Laryngeal CS account for less than 0.2% of all head and neck tumours and up to 1% of all laryngeal malignancies (1-3, 4). In 1816, Travers (5) reported the first case of a laryngeal chondroma as "a case of bony growth of the cartilage of the larynx" to the Medico-Surgical Society of London. The term chondrosarcoma of the larynx was introduced in literature by New in 1935 (6). In the previous century, the term chondroma was used to describe all cartilaginous tumours. Chondroma and CS are closely related, either synchronously or metachronously. As a result several cases of low-grade CS have been misinterpreted as low grade laryngeal chondromas (7). Although a number of broader studies of laryngeal CS have been published, a recent review showed that many cases have been reported several times or are rare single case reports (3). In fact the actual number of CS of the larynx might indeed be smaller than suggested. Although CSs of the larynx are rare, they are of great clinical relevance as their management is largely different from other malignancies of the larynx. We report two cases of histopathologically confirmed CS of the larynx and provide a comprehensive analysis of current advances in basic research and clinical management of laryngeal CS.

Case Reports

Case 1. A 93-year-old male patient presented with a two-year history of increasing stridor and dyspnoea. A left-sided large bulging of the intact subglottic mucosa, occluding 95% of the tracheal lumen, was visible with a flexible nasopharyngoscope. In a first step, tracheostomy was performed. Computed tomography (CT) of the neck showed a 3 x 3.5 cm tumour of the posterolateral lamina of the cricoid just inferior to the left vocal cord (Figure 1). The CT scan excluded enlarged lymph nodes of the neck. The patient underwent a flexible endoscopy and tumour resection with a CO₂ laser under general anaesthesia. The majority of the tumour was removed, which on biopsy was consistent with a low-grade chondrosarcoma (Figure 2 a and b). Immunohistochemical staining showed expression of S100 protein. Antibody staining against p53 revealed that there was no staining of the nucleus of the tumour cells, this indicating a low Ki-67 proliferation rate and therefore a low chance of malignancy. In view of the patient’s age and the histopathological results, a laryngectomy was declined and the patient scheduled for an endoscopy three months later. The patient was discharged with tracheotomy and a speech valve. The patient presented one month later with...
granulations and a progressive growth of the residual tumour. The residual tumour obstructed 50% of the subglottic tracheal lumen. The CS was resected again using a CO₂ laser. The patient was discharged and followed up in an outpatient setting. Three months on from the operation, the patient is doing well and the tracheostoma was closed without any evidence of further regional or distant disease.

Case 2. A 66-year-old male patient presented with increasing hoarseness over several months. The patient denied symptoms of dyspnoea or stridor. On rigid endoscopy, it was noted that the mobility of the right vocal cord was reduced and a 1 cm tumour at the posterior portion of the right vocal fold was visible (Figure 3 a). Histopathology revealed an undifferentiated chondrosarcoma, which was diagnosed as non-classified sarcomatous neoplasm. Two weeks after the histological diagnosis, the patient underwent chordectomy with CO₂ laser. The patient was discharged and followed up in an outpatient setting. Three months on from the operation, the patient is doing well and the tracheostoma was closed without any evidence of further regional or distant disease.

Epidemiology

Approximately 400 to 600 cases of laryngeal chondroma and CS have been reported in the literature. Worldwide, laryngeal chondromas are extremely rare and some authors consider all laryngeal chondromas as misdiagnosed low-grade CS (7, 8). The mean age at diagnosis is between 64 and 66 years, and the tumor affects three times more men than women (3). However CS accounts for up to 1% of all head and neck benign and malignant tumors in a review of a pediatric population (9). CS of the larynx is seven times more common in whites than in blacks (10). Approximately 80% of the cases of laryngeal CS are situated in the cricoid cartilage (3). The posterior lamina of the cricoid cartilage accounts for most of the malignancies arising in the midline (3). The thyroid cartilage, especially the inferolateral wall, is affected in about 20% of cases (11), followed by the arytenoid cartilage, which accounts for about 3% of CS malignancies (3). Vocal cords and the epiglottis are less frequently affected (7).

Pathology

Diagnosis of CS is based on the criteria described for malignant cartilaginous tumours of extralaryngeal bone origin first described by Lichtenstein and Jaffé in 1943 (15). Their definition depends upon the finding of any of the following in a cartilaginous tumour: (i) pronounced irregularity in the size of the cells and their nuclei; (ii) presence of numerous cells and their nuclei; (iii) pronounced hyperchromatism of the nuclei; and (iv) any large or giant cartilage cells with single or multiple nuclei or with clumps of chromatin. As these criteria refer to extralaryngeal bones, some authors question if the criteria of Lichtenstein and Jaffé is still appropriate for laryngeal CS (16). In 1977, Evans et al. (17) grouped CS of the long bones according to mitotic rate, cellularity and nuclear size into grades I, II and III, a higher histological grading being associated with a poorer prognosis. The criteria according to Evans et al. is still the most widely accepted classification for laryngeal CS. However, in the case of phalangeal CS some authors raise the question if this classification is still appropriate; this is because both laryngeal CS and phalangeal CS seldom metastasize, unlike malignant...
cartilaginous tumours of most extralaryngeal origin which do. (18). In CS localised to the larynx and phalanx, there are very few tumour related deaths described. In our case of laryngeal CS, the low expression of Ki-67 accurately indicated a low proliferation rate of the malignant cells (18). This result could describe the improved clinical outcome of laryngeal and phalangeal CS compared to CS of the long bones.

There are two other variants of laryngeal CS described in the literature. In 1971, the histological diagnosis of an undifferentiated CS was first described (19). In undifferentiated CS, high-grade spindle cell sarcomatous tissue is associated with low (I) to intermediate (II) grade CS. Undifferentiated CS have a poorer clinical prognosis. The second variant of laryngeal CS is clear cell CS. Clear cell CS is mainly characterized by rounded cells having conspicuous, clear cytoplasm with sparse intervening matrix, and by additional criteria such as osteoclast-like cells, bone trabeculae, aneurysmal bone cyst-like giant cells, and also

Figure 2. Low-grade chondrosarcoma arising in the cricoid cartilage of a 93-year-old man. (a) The tumour has a multilobular growth pattern and cords of eosinophilic cells are deposited within the abundant myxoid matrix. HE stain and x150. (b) Partially, aggregates of tumour cells with fibroblastic features are evident within the epitheloid strands. HE stain and x250.

Figure 3. Non-classified sarcomatous neoplasm in the right vocal fold of a 66-year-old man. (a) Endoscopy revealed a 1 cm tumour of the posterior portion of the right vocal fold. (b) Endoscopic control three months after prior surgery.
foci of conventional CS (20). To our knowledge no reports of metastases have been described in the literature. In CS, regional metastasis is a poor prognostic sign (3). Distant metastases are rare but have been observed more than regional neck metastases (7). Metastatic disease has only been reported in cases of poorly differentiated and undifferentiated tumours. Metastases can occur as long as 20 years after initial diagnosis (7).

**Radiographic Features**

CT scanning is a reliable method of evaluating CS of the larynx, especially in preoperative planning of partial laryngeal resection (1). A calcified mass involving one or more cartilages of the larynx or trachea that moderately enhances after the application of contrast medium is a typical CT finding for a cartilaginous tumour (7). A mass lesion demonstrating a fine, punctate stippled to coarse "popcorn-like" calcification within the tumour is a typical radiological feature in laryngeal CS. CT scans can determine the size and extent of the laryngeal tumour. They may also show invasion of surrounding structures and metastasis of lymph nodes. In the majority of cases, focal expansion and displacement of adjacent tissue will be demonstrated. MRI may improve preoperative evaluation of the extent of the lesion by depicting the tumour-soft tissue more clearly than can a CT scan. The common lateral soft tissue radiographs and anteroposterior tomography study of the larynx used in the past to define the location and extent of the tumour have been replaced today by CT and MRI scanning.

**Treatment Modalities**

Laryngeal CS can be considered as a relatively low-grade tumour, both histologically and by clinical aggressiveness. As a result, conservative surgery is the treatment of choice. The majority of the cases in the literature received a conservative laryngeal function-preserving surgical treatment. The choice of conservative surgical options is determined by the localization of the primary neoplasm. While radical removal is the aim, the margin of safe excision is difficult to determine, especially in function-preserving resections. Endoscopic removal, laryngofissure, thyrotomy or partial laryngectomy have been described in order to achieve an excision with a sufficient margin of normal, uninvolved cartilage. Most laryngeal CS affect the cricoid cartilage, which is considered crucial to normal laryngeal function. The thyrotoamy approach permits precise excision and preserves the cricoarytenoid, as well as the posterior cricothyroid muscle and the recurrent laryngeal nerves. The external approach permits excision with preservation of the internal perichondrium (21) which is crucial in order to prevent granulations and cartilage affections. Extensive resection beyond the midline may lead to significant airway narrowing. Hemicricoidectomy followed by implantation of a modified Montgomery stent in 8 patients achieved the best voice function following surgery (22). Cohen et al. (22) also emphasize the surgical preservation of the inner perichondrium and subglottic mucosa. The inability to reconstruct laryngeal defects often leads to the recommendation of total laryngectomy. Laryngeal reconstruction using local flaps or autogenic transplants can be used for neoplasms that involve large parts of the cricoid in order to permit laryngeal function-preserving surgery (16). In order to preserve the laryngeal framework and function, extensive excision of laryngeal tumours are followed by thyrotachal anastomosis with rib grafts. Endoscopic CO₂ laser resections have been used in our cases and have recently been reported as treatment for primary lesions and recurrences (14, 16). Cricoid involvement is the critical feature, especially concerning recurrences, and is the key to the extent of resection. Primary lesions located in thyroid cartilage or epiglottis are technically easier to remove by CO₂ laser. In Case 1 we excised the tumour from the cricoid cartilage by CO₂ laser. Although we had to remove granulation tissue after the first excision, the wound healing was not impaired after revision surgery. When recurrences develop, a further excision can again be used. A total laryngectomy might then be necessary, depending on the extent of the recurrent lesion or inability to reconstruct a sufficient airway. The partial resections offer patients a better quality of life with extra years of laryngeal function. This benefit is of further importance when considering that the majority of the cases are diagnosed at a high age. A larger study showed that the approach of partial resection laryngeal surgery did not impact on the long-term survival of patients (3). Adjuvant radiotherapy or chemotherapy seems to be ineffective in the management of laryngeal CS, similar to the results in CS in other anatomic sites (2, 7, 23).

Primary radiotherapy is not recommended as surgery is undoubtedly the best-studied form of laryngeal CS treatment. A study involving 12 cases showed long-term remission following irradiation in only two of the patients (24) laryngeal CSs do not respond to chemotherapeutic agents, therefore chemotherapy is not a recommended therapeutic option (3). Larger studies report an overall recurrence rate of 16% to 18% (2, 3). The recurrence may develop if the primary neoplasm was incompletely excised, especially in patients whose initial treatment included partial or local excision. The recurrence rate also depends on the grade of the tumour. High-grade tumours are associated with a significantly higher recurrence rate (3). A literature review showed that recurrent laryngeal CS does not affect the overall patient outcome. The curative rate of total laryngectomy after recurrent laryngeal CS is comparable to that of initial total laryngectomy (25). Thus there is no added survival advantage with total instead of partial laryngectomy (2). Our 93-year-old patient with CS
of the cricoid (case 1) developed recurrence despite conservative surgery in order to maintain laryngeal function due to the high age of the patient. However, although conservative surgical treatment failed to eradicate the neoplasm, we did not perform a total laryngectomy, instead the patient underwent further laryngeal function-preserving surgery. The fact that the patient could be decanulated after the second procedure argues in favour of larynx preserving procedures. Based on the good prognosis of these laryngeal tumours, regardless of partial or total laryngectomy, quality of life must be taken into account. Metastatic disease is described in about 2% to 10% of the reported cases of laryngeal CS (2, 3, 7). The development of metastases in the lung, bone and liver have been reported. In contrast to the good prognosis of laryngeal CS, a rapid clinical course with tumour-related death within two years was reported in the literature (2). Tumour-related death is nevertheless uncommon and occurs in rare cases with uncontrollable growth, recurrences, involvement of vital adjacent structures and persistent aggressive tumour (2, 11). Thompson and Gannon (3) observed that in laryngeal CS, only 4.5% of the patients died as a direct result of the disease.

Conclusion

CSs of the larynx are rare. In most cases, CS is being detected in older men complaining of stridor and hoarseness. This cartilaginous neoplasm is staged into three grades depending on histological analysis. Most tumours are low to intermediate grade, with a poorer prognosis of higher grade CS. The majority of CSs are located in the cricoid cartilage. Conservative surgical excision is recommended due to the good prognosis of laryngeal CS and the generally high age of the patients. Recurrence should be treated with salvage laryngectomy. Nevertheless, another conservative surgical option might be preferred because of the high age of the patient or concomitant serious disease.

References

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