Case report

High-grade chondrosarcoma of the larynx: treatment and management

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SUMMARY

We present a case of an 88-year-old man with high-grade chondrosarcoma of the larynx. The patient presents with a history worsening dysphonia and dyspnoea treated with antibiotic and corticosteroid therapy as it was a bronchopneumonia. Thanks to fibrolaryngoscopy, radiological imaging and final biopsy with immunohistochemistry, we have done differential diagnosis with the others sarcomas of the larynx. The histological diagnosis and the correct grading are essential for treatment and management of the pathology. The best treatment is primary surgical resection with negative margins. Chemoradiotherapy may provide some benefit if there are margin positive resections or with palliative intent. In our case, we performed only surgery treatment and a close follow-up at 1-3-6 months and after every 6 months. After 18 months from surgery, there are no signs of recurrence of disease.

BACKGROUND

Chondrosarcoma of the larynx is a rare tumour that accounts around 0.1% of all head and neck neoplasms and represent <1% of all laryngeal neoplasm,^{1 2} usually it is located in the cricoid cartilage. However, it is the most common non-epithelial tumour of the larynx and most frequently occur between 50 and 80 years of age, more commonly in men (four men to one woman) and more prevalent among Caucasians.³ Most chondrosarcomas are low-to-intermediate grade, around 5%–10% are high-grade and are associated with a poor prognosis.⁴

The aetiology of laryngeal chondrosarcoma is multifactorial. It derives from the alteration of the normal ossification of the laryngeal cartilage. Laryngeal chondrosarcoma usually derives from the hyaline cartilage of cricoid, but it can also origin from the thyroid, accessory cartilages, epiglottis and arytenoid cartilages.

Microscopically, this pathology has hyperchromatic nuclei with rather poor cytoplasm. Macroscopically, it looks like a lobulated and smooth mass. Chondrosarcoma of the larynx has a good prognosis, with 5-year survival recurrence of 79.4% and 88.6%. However, this pathology is characterised by local recurrence, with rates up to 40% described in the literature. Low-grade, T1 and T2 glottic tumours can be successfully treated with CO₂ lasers techniques. High-grade, high-stage and relapsed tumours need more

aggressive therapeutic surgery such as partial or total laryngectomy.⁵

We describe a case of high-grade chondrosarcoma that occurs with dysphonia and dyspnoea in an 88-year-old man, without signs of recurrence after 18-month follow-up. The aim of our manuscript is to explain the correct treatment and management of this rare, often deadly, disease.

CASE PRESENTATION

We present a case of an 88-year-old Caucasian male with a history of dyslipidemia and chronic obstructive pulmonary disease. He was ex-smoker from 40 years with 10 cigarettes-day smoking history⁶. The patient came to our observation with 5-month history of worsening dysphonia treated with antibiotic and corticosteroid therapy as it was a bronchopneumonia. Physical examination revealed no evidence of disease within the oral cavity or cervical lymphadenopathy. Fibrolaryngoscopy revealed a large neoformation that occupies left hemilarynx and that infiltrates the anterior commissure and the false vocal cord. The pathology caused the reduction of respiratory glottic space. For this reason, the patient underwent an emergency tracheotomy. He performed a contrast-enhanced CT of the neck that revealed voluminous neoformation of the left hemilarynx which infiltrates the false vocal cord, the caudal part of the pyriform sinus, the ventricle of Morgagni and the true vocal cord. The caudal portion of the previously mentioned heteroplastic lesion infiltrates the anterior commissure and the anterior portion of the right vocal cord and presents a portion that invades the subglottic space (figure 1).

We performed a biopsy of the lesion under local anaesthetic with the operative fibrolaryngoscope. The pathologist informed us that it was a non-epithelial tumour and advised us to send the next surgical piece of the larynx to fresh (not stored in formalin) for immunohistochemistry studies.

The patient underwent surgical resection of the tumour with total laryngectomy extended to the hyoid bone (figure 2A). Histological evaluation revealed high-grade chondrosarcoma with free margins (figure 2B,C).

DIFFERENTIAL DIAGNOSIS

There are different kinds of sarcomas that involved the larynx that have been described in the literature. The most frequent kind is the chondrosarcoma. Other kinds of sarcoma are Kaposi sarcoma,

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Figure 1 Contrast-enhanced CT of the neck showing a neoplasm of the left hemilarynx, that invades the anterior commissure, the anterior portion of the right vocal cord and the subglottic space.

leiomyosarcoma, angiosarcoma, osteosarcoma, synovial sarcoma, rhabdomyosarcoma, fibrosarcoma, liposarcoma and pleomorphic sarcoma. CT and MRI are essential instruments for the diagnosis and the staging of these tumours, but for the final diagnosis is essential the histological biopsy.

Chondrosarcoma of the larynx has peculiar histological characteristics. This kind of lesion is characterised by myxoid-type chondrosarcoma, high-grade foci or dedifferentiation. Sometimes, there are components juxtaposed to a low-grade chondrosarcoma, such as marked anaplasia, tumour necrosis, presence of high-grade spindle cell and mitosis. The grading is given by their nuclear atypia (binucleation or multinucleation), increased cellularity and possibility to invade or destroy nearby tissues. This is essential for the prognosis and the treatment of the patients. Chondrosarcoma has to be differentiated from chondroblastic osteosarcoma. The presence of osteoid material and lobules of cellular chondroid of high-grade malignancy encircled by hypercellular spindle cells are typical of osteosarcoma. Low-grade chondrosarcomas should be misdiagnosed as condrometaplastic nodule or chondroma of the larynx. The hyperchromasia,

Figure 2 (A) Surgical resection 'en bloc' of the larynx, which presents a voluminous neoformation of the left hemilarynx with subglottic extension covered by normal appearance mucosa. (B) Fragmented pieces of cartilaginous nodules (H&E 20 $\times$). (C) The nodules show chondrocytes with mild to moderate atypia, hyperchromatic nuclei and occasional binucleated lacuna (H&E 200 $\times$).

increased cellularity, binucleation and nuclear atypia argue in favour of chondrosarcoma.

A further confirmation of the final diagnosis of chondrosarcoma was given by the immunohistochemical test positive for the S-100 protein and Vimentina. Ki67 was 3%.

OUTCOME AND FOLLOW-UP

Postoperative recovery was uneventful, only a benign paroxysmal positional vertigo released successfully.⁷ As the tumour from the CT scan would be classified as a T4, the possibility of postoperative radiotherapy was discussed with the patient. He was evaluated by our radiotherapists who did not subject the patient to radiation treatment but decided to follow him with close follow-up at 1-3-6 months and after every 6 months, following the most recent evidences described in the literature about chondrosarcoma of the larynx.^{5,8,9} He was discharged and currently there are no signs of relapse of disease. After 18 months from surgery, there are no signs of recurrence of disease at the CT study and in fibrolaryngoscopy.

DISCUSSION

Chondrosarcoma is in third place in the frequency of presentation, after squamous cell carcinoma and laryngeal adenocarcinoma.⁵ It is a mesenchymal tumour originating in bone and cartilage, it accounts for 1% of laryngeal cancers with 80% originating from cricoid cartilage,¹⁰ especially in its posterior lamina. The WHO considers chondrosarcoma as atypical cartilaginous tumours. Its aetiology is unknown, probably deriving from disorganised ossification, due to the tendency of hyaline cartilage to ossification. Patients most frequently present with a complaint of hoarseness. The smoking attitude, exposure to radiation and antecedent of concurrent malignancies are considered as risk factor. The grading system is on a scale 1–3 and looks at mitotic activity, nuclear size and degree of cellularity.¹¹ In Thompson's review, 60.4% of chondrosarcomas arose from pre-existing chondroma. Laryngeal chondrosarcoma predominates in males with an H:M ratio of 3:1, the age of diagnosis is 62.5 years old and it has slow growth even in high-grade lesions.

Biopsy is considered the gold standard procedure for the diagnosis but sometimes it is difficult to obtain because of the difficult intubation in some patient with large tumours or of the submucosal location of chondrosarcoma.

Management of laryngeal sarcomas is based on excision of the tumour with clear resection margins. Total laryngectomy continues to be the treatment of choice in up to 29.4% and is recommended for lesions involving more than half of the cricoid ring, the rest of patients were treated with conservative techniques reporting a cure rate >90%.¹² However, for those tumours considered more aggressive and higher grade, more radical procedures are recommended. In 1973, Jones¹³ gave the standards for total laryngectomy, that include

1. Extensive tumour with inability to preserve airway patency.
2. Recurrence.
3. Anaplastic histology.

Given the frequency of recurrence of chondrosarcoma on the cricoid, and mostly the posterior lamina of the cricoid, any lesion involvement >50% of this cartilage has been normally treated with a total laryngectomy.

The traditional radiotherapy is considered not very effective because chondrosarcoma has slow-growing behaviour. In a recent systematic review of 592 cases, adjuvant therapy was used in 18 cases. Radiotherapy was used in 16 cases, while chemotherapy was used in 2 cases.

Recurrences were treated with radiotherapy in four cases. Three patients underwent chemoradiation therapy following recurrence.⁵ Radiotherapy may be useful as adjuvant therapy in case of margin positive resection or when used with palliative aim. For Goda *et al*, adjuvant radiation therapy secured local control in 94% of positive margin resections, with a median follow-up 75 months. Anyway, this study population included especially tumours of grade 1 and 2 with only 14% being grade 3.^{8,9}

There are few studies in literature regarding the benefit of chemotherapy in treatment of high-grade chondrosarcoma. No randomised trials have been performed. Chondrosarcoma is an extremely rare tumour, primarily those of grade 2 or 3, so there are few prospective studies with a limited number of cases. Low-grade chondrosarcoma are chemoresistant because of their poor vascularisation, slow growing nature and the expression of multidrug-resistance-1 gene. Thanks to retrospective studies, it is possible to consider that chemotherapy can be useful in patients where surgery is not possible. For Italiano *et al*, systemic chemotherapy treatment significantly improved survival, compared with no treatment controls. Anyway, the overall survival rate for 1 year in all patients was at around 50%.^{14–17} In case of recurrence, the best approach would be a multidisciplinary evaluation with radiotherapists and oncologists to evaluate a new surgical procedure or a chemoradiation therapy.^{5,18}

Recurrence is common and occurs in 35%–40%, while metastasis is rare, the most site is lung.^{19,20}

Disease-specific survival rates for 1, 5, 10 and 20 years were 97.7%, 91.4%, 81.8% and 68.0%, respectively.⁵

In conclusion, high-grade chondrosarcoma of the larynx is an extremely rare tumour associated with a good prognosis, if properly treated. A differential diagnosis with other types of sarcoma is important, histology and immunohistochemistry are gold standard for the final diagnosis. Identifying the final histological result with the correct grading is essential for the correct treatment and management of the pathology. Current best evidence suggests primary surgical resection with negative margins. Chemotherapy may provide some benefit where

surgery is not an option. Radiotherapy may be beneficial if there are margin positive resections or when it is used with palliative intent.

Contributors BG developed the concept and design of the study and treated the patient. FGazia is corresponding author, was preparing the manuscript. DC performed follow-up examinations and literature research. FGalletti critically revised the manuscript for important intellectual content and gave the final approval of the version to be submitted.

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Learning points

- High-grade chondrosarcoma of the larynx is an extremely rare tumour associated with a good prognosis, if properly treated.
- Histology and immunohistochemistry are gold standard for the final diagnosis and the correct grading that are essential for treatment and management of the pathology.
- The best treatment is primary surgical resection with negative margins.
- Chemoradiotherapy may provide some benefit if there are margin positive resections or when it is used with palliative intent.

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