CASE REPORT

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High-Grade Chondrosarcoma of the Larynx with Multiple Metastases: Case Report and Literature Review

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ABSTRACT Chondrosarcoma (CS) is a rare laryngeal malignancy of indolent course. The high-grade CS (HGCS) represents the rarest and the most aggressive type. We present the case of a male patient with a cricoid cartilage HGCS with extralaryngeal invasion and thyroid gland metastases. Three years after hemilaryngectomy and radiotherapy, the patient developed local recurrence treated with salvage laryngectomy. In each of the consecutive years, our patient developed new regional and distant metastases in the tracheal stoma, anterior chest wall, lung and clavicle, which were treated surgically when possible or with radiotherapy. After 8 years, the patient died with the disease, confirming the slow progression of this high-grade malignancy. The treatment for HGCS is total laryngectomy. This tumour is associated with a poor prognosis. Long term follow-up is necessary. Our case is unique by the multitude of loco-regional and distant metastases and the 2 courses of radiotherapy received.

Keywords: Chondrosarcoma; larynx; cricoid cartilage; neoplasm; laryngeal tumour

Chondrosarcoma (CS) is a rare malignancy. The estimated incidence is 1 in 200,000 per year.[1] The most common location in the neck and head area is the laryngeal cartilage (1% of cases).[2] High-grade CS (HGCS) is rare in the literature, with only 20 cases identified.

We present the case of a male patient with HGCS of the larynx with progression to multiple local, regional and distant metastases over 8 years. The patient died with the disease but of unknown causes.

CASE REPORT

A 65-year-old male was referred to our department with longstanding hoarseness and breathing difficulties. His medical history included hypercholesterolemia, emphysema, hepatic steatosis and hypertension. He had a 150-pack year smoking history. Panendoscopy revealed a right sided laryngeal tumour. Deep tissue biopsies confirmed HGCS. Computed tomography (CT) and magnetic resonance imaging (MRI) of the neck were used to evaluate the local extent of the mass and assess for the presence of lymph node involvement. Contrast enhanced axial CT identified a 2 cm bilobed cystic mass originating from the right side of the cricoid cartilage. On MRI, this mass was well circumscribed, adherent to the cricoid cartilage with high T2 signal. There were no abnormal lymph nodes within the neck (Figure 1).

The patient underwent a right hemilaryngectomy and hemithyroidectomy. The histology confirmed a 2 cm HGCS with 4 microscopic thyroid metastasis deposits into the thyroid lobe. Sternothyroid muscle and vascular invasion were present. The MIB proliferation index was 20% confirming its high-grade nature. The patient received adjuvant radiotherapy (66Gy/33Fr). Histopathology images of HGCS de-

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posit into the thyroid lobe are shown in Figure 2, Figure 3.

Eighteen months postoperatively, a supraclavicular skin metastasis was completely excised. A right pyriform fossa recurrence was discovered 3 years after the initial surgery. T1 MRI with contrast demonstrated a 1.8x1.4 cm ring-enhancing hypodense lesion in the region of the right piriform fossa with mass effect in the larynx (Figure 4, Figure 5).

^{18}F-fluorodeoxyglucose positron emission tomography/CT revealed a necrotic mass at the level of the right vocal cord (SUV_{max} 5.3) and a 1.3 cm necrotic lymph node in the right paratracheal region (SUV_{max} 2.7). The patient underwent salvage laryngectomy, right selective neck dissection (levels 2-4) and pectoralis major flap reconstruction. A fixed, invasive tumour was encountered intraoperatively. Histopathology confirmed a multifocal laryngeal recurrent HGCS infiltrating the thyroid cartilage and the left pharyngeal wall without nodal metastases. Histopathology images of the laryngeal specimen are shown below (Figure 6).

At 6 months, and at 1 year post initial surgery, a 5 cm tracheal stoma recurrence and respectively a 3 cm left lung metastasis with focal pleural invasion were surgically excised. In the next consecutive 2 years, a well circumscribed 1.2 cm right epiglottic recurrences, and a 3.5 cm right clavicular head recurrence were diagnosed. A right anterior chest wall

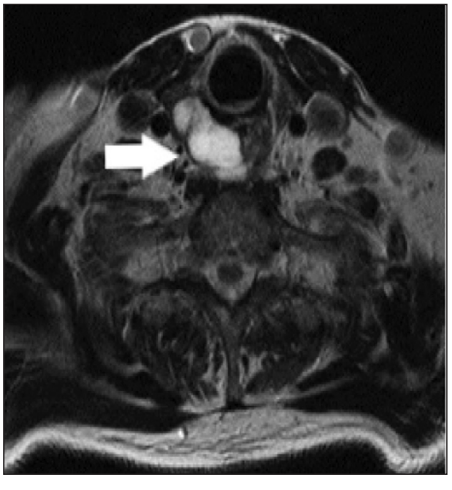

FIGURE 1: Axial T2 magnetic resonance imaging at the level of the cricoid demonstrates a T2 hyperintense mass arising from the cricoid cartilage (white arrow).

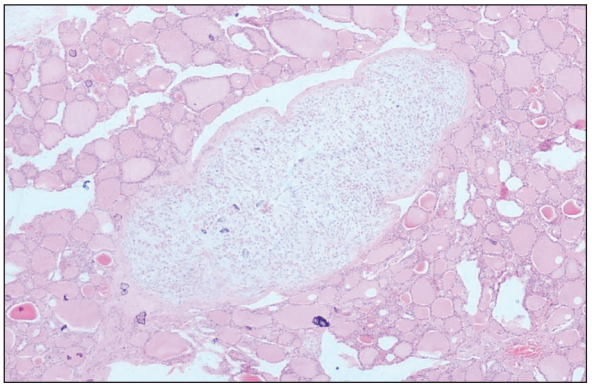

FIGURE 2: Low power of thyroid resection-metastatic deposit of chondrosarcoma infiltrating the thyroid.

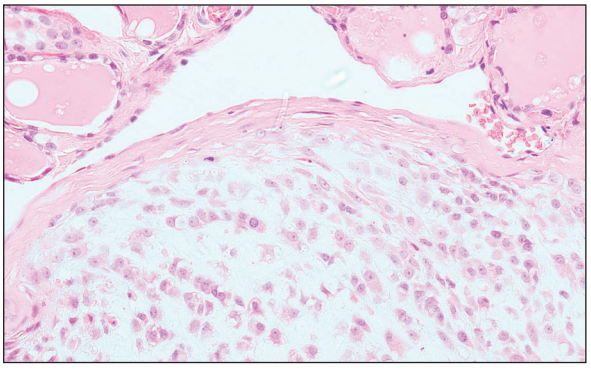

FIGURE 3: High power view of thyroid resection-high grade chondrosarcoma deposit demonstrating high cellularity, cellular atypia, pleomorphism, prominent nucleoli, binucleation and mitotic activity.

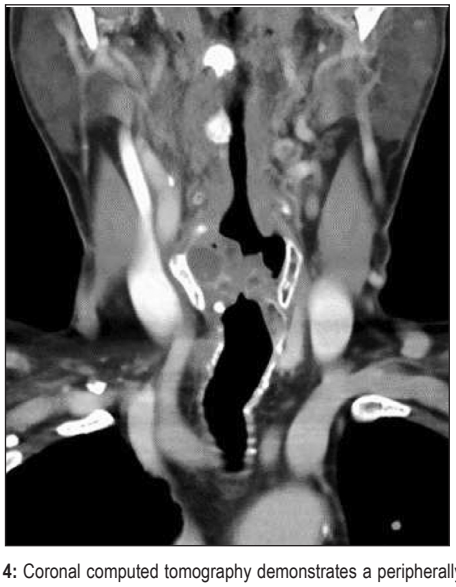

FIGURE 4: Coronal computed tomography demonstrates a peripherally enhancing mass lesion arising from the cricoid cartilage within the right side of the neck.

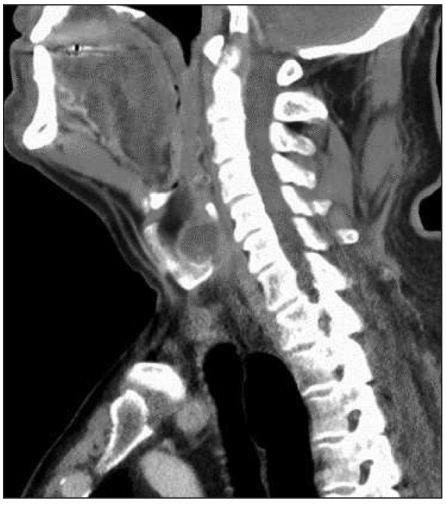

FIGURE 5: Sagittal computed tomography demonstrates a peripherally enhancing mass lesion arising from the cricoid cartilage.

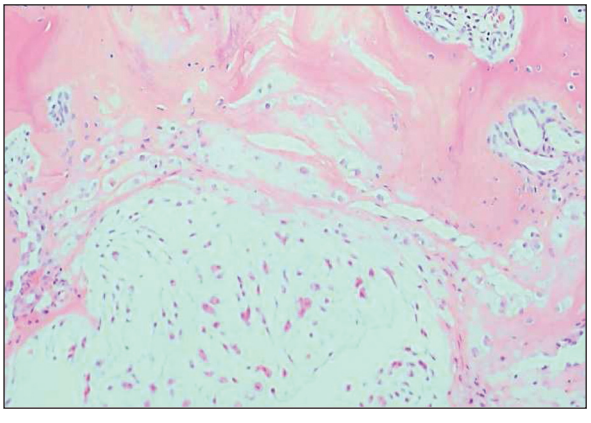

FIGURE 6: High power view of laryngectomy specimen demonstrating high-grade chondrosarcoma with cellular atypia, pleomorphism, prominent nucleoli and binucleation.

metastasis with myxoid matrix was excised. The patient competed 24Gy/8Fr palliative radiation in December 2019. In the following year, he underwent a hemicolectomy with end stoma formation for colonic carcinoma. Oesophageal stricture with total dysphagia was a severe radiotherapy complication. A gastrostomy feeding tube was placed. No further metastases were discovered.

The patient died 8 years later still under ongoing review for HGCS. This report was written after the patient was deceased and an informed consent for publication was not possible.

DISCUSSION

Head and neck CS arises from the cartilaginous structure of the larynx. The most common site is the cricoid cartilage (75%) followed by the thyroid (17%) and rarely the arytenoid (5%) or epiglottis.[2] To the authors knowledge, less than a thousand head and neck CS cases are reported in the literature to date, with only 20 HGCS reported.[3-13]

Their aetiology is unknown, but distorted cartilage ossification is the most recent theory.[8,14] Hyaline cartilage undergoes ossification in time. Other potential causes are prior radiotherapy and smoking. Patients usually present clinically in the 7th decade although younger patients are reported. There is a male predominance.[2,6,9,13]

These slowly growing tumours can reach large sizes before becoming noticeable. Symptoms include hoarseness, dysphagia, airway obstruction or neck masses. Imaging with CT and MRI is useful in tumour localization, assessment for locoregional metastasis and aids surgical planning. MRI delineates more precisely the disease extent.[2]

For laryngeal tumours, tissue biopsy is performed via direct laryngoscopy. Submucosal sampling is necessary due to their deep location. Fine needle aspiration cytology is indicated for investigation of a neck lump. Differential diagnosis includes other chondroid tumours like chondroma or a chondrometaplastic nodule. Macroscopically, they appear as smooth, lobulated, cream/white glistening tumours, with a mucinous centre. The histological diagnosis of HGCS is revealed by the presence of hypercellular cartilage with increased mitotic activity, cellular atypia, and multinucleated chondrocytes.[2] Necrosis and vascular invasion can be present. These tumours are classified in 3 grades, from the least (Grade 1) to the most aggressive form (Grade 3).[15] Grade 3 is the rarest (5-10%). Two other types of CS are even rarer: myxoid and dedifferentiated.

Treatment is surgical consisting of tumour excision with negative margins. The surgical approach depends on tumour site, size and access. Giving the slow progression rate, the current trend is towards an organ preservation approach when feasible. Endo-

TABLE 1: Other HGCS cases described in the literature.

Study	Year	Cases (nr)	Sex	Age	Surgery	RTx	Recurrence	Mets	Origin	Follow up (years)
Verhulst et al.[3]	1996	2	x	x	TL	x	x	yes	x	x
Thompson et al.[4]	2002	6	x	x	x	x	no	x	x	15.1
Saleh et al.[5]	2002	1	M	53	Laryngo-fissure	no	2 months (laryngo fissure), 1 year (TL)	no	x	15
Jacobs et al.[6]	2003	1	x	x	x	x	epiglottis	x	x	x
Jones DA et al.[7]	2003	1	x	x	TL	yes	x	6 monts (lung)	x	6
Casiraghi et al.[8]	2004	1	M	60	TL+ND	x	x	x	cricoid	7
Buda et al.[9]	2012	1	M	24	Subtotal laryngectomy	CTx (Resection +CRTx)	8 years	x	x	14
Oliviera at al.[10]	2014	1	F	73	TL	no	no	no	cricoid	7
Waters et al.[11]	2018	1	M	64	Hemi-laringectomy + tracheal reconstruction	yes	x	x	x	x
Galletti B et al.[12]	2019	1	M	88	TL	no	no	x	x	1.5
Aalling et al.[13]	2020	1 or 5	x	x	x	x	x	x	x	x

TL: Total laryngectomy, ND: Neck dissection, RTx: Radiotherapy, CTx: Chemoterapy, CRTx: Chemoradiotherapy.

scopic approach via CO_2 LASER, robotic surgery or external approach (cricoidectomy, hemilaryngectomy) are recommended methods for small low-grade tumours. Total laryngectomy is reserved for HGCS or recurrences.[1] These tumours are not radiosensitive. Radiotherapy is reserved for incomplete resection or HGCS postoperatively.[2] Chemotherapy has no curative role in these malignancies.

The recurrence rate of HGCS varies (14-65%).[11] Seventy percent of HGCS develop metastases, mainly to the lungs and skeleton.[7] Although CS has a good prognosis overall, HGCS has a survival rate of only 43% at 5 years.[2,12] The case presented here is an aggressive HGCS with multiple metastases developed over 8 years. The metastasis of laryngeal CS in the thyroid gland is extremely rare, with a single case reported.[11] One other particularity of this case represents the 2 courses of radiotherapy administered. Our case is the second HGCS reported in Ireland. The prior described case also had extralaryngeal invasion into the thyroid gland but no recurrence.[11] Table 1 presents other HGCS cases described in the literature.

In our case, the treatment was conservative with salvage laryngectomy after local recurrence. This local recurrence at 3 years post surgery represents tumour re-growth due to microscopic disease, rather than true recurrence. We don't consider adjuvant radiotherapy was helpful in this particular case, and was associated with significant comorbidity. Our patient has developed different metastases each year, confirming the aggressive behaviour of HGCS. The myxoid CS from the patient's chest wall is associated with poor clinical outcome and metastatic spread. The patient was regularly followed up for 8 years, until his recent death.

HGCS is a rare malignancy of the larynx, associated with a poor prognosis. It can present multiple local, regional and distant metastasis, as in our case. Radiotherapy does not influence tumour regrowth rate and leads to severe complications. Lifelong follow-up of HGCS is mandatory to detect recurrences and metastases.

Source of Finance

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vides or produces medical instruments and materials which may negatively affect the evaluation process of this study.

Conflict of Interest

No conflicts of interest between the authors and / or family members of the scientific and medical committee members or members of the potential conflicts of interest, counseling, expertise, working conditions, share holding and similar situations in any firm.

Authorship Contributions

Idea/Concept: *Tom Moran;* ***Design:*** *Andreea Nae;* ***Control/Supervision:*** *Tom Moran, Susan Kennedy;* ***Data Collection and/or Processing:*** *Andreea Nae, Sinead Flanagan, John Duignan;* ***Analysis and/or Interpretation:*** *Andreea Nae;* ***Literature Review:*** *Andreea Nae;* ***Writing the Article:*** *Andreea Nae;* ***Critical Review:*** *Sinead Flanagan, John Duignan, Susan Kennedy, Tom Moran.*

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