Case report

Laryngeal chondrosarcoma treated with conventional radiotherapy – case report and review of the literature

Agata Roch-Zniszczoł[1], Dorota Księżniak-Baran[2], Ewa Chmielik[3], Maria Goleń[1], Natalia Amrogowicz[2], Dorota Gabryś[1]

[1]Department of Radiotherapy, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland
[2]1st Radiation and Clinical Oncology Department, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland
[3]Tumour Pathology Department, Maria Sklodowska-Curie National Research Institute of Oncology, Gliwice Branch, Gliwice, Poland

We report a case of a 68-year-old patient with laryngeal chondrosarcoma, whose first symptoms were hoarseness and gradually increasing dyspnoea, but there was no sign of disease in clinical examination, which postponed the diagnosis. The patient underwent complete laryngectomy and adjuvant conformal radiotherapy with a total dose of 70 Gy. The pathological assessment confirmed advanced laryngeal chondrosarcoma originating from thyroid cartilage. Imaging studies and directoscopy were performed, and they did not reveal recurrence or metastases of the disease for 6 years. Distant metastatic spread in the liver and lungs was confirmed 7 years after diagnosis, which caused hepatic insufficiency and led to death.

Key word: laryngeal chondrosarcoma, radiotherapy.

Introduction

Laryngeal chondrosarcoma is a rare neoplasm of the head and neck region, which represents less than 1% of malignant tumours of the larynx and 75% of sarcomas confirmed in this localization [1–6]. Most often laryngeal chondrosarcoma develops in cricoid cartilage, less commonly in the thyroid cartilage and arytenoid cartilage [3, 5, 7, 8]. It is usually diagnosed in patients between 50 and 70 years old, and it predominates in males [2, 7–11].

Aetiopathological factors determining the development of these tumours has not been clearly identified. It is suggested that previous irradiation, chronic inflammation, disorganized ossification, mechanical stress, and smoking are important risk factors; moreover, there has been some debate on whether chondromas are benign precursor lesions that transform into chondrosarcomas [8, 12]. Clinical symptoms are not distinctive and usually appear after a few years of latency. Most often patients demonstrate hoarseness and dyspnoea (varied intensity) [8]. Dysphagia, caused by oesophageal constriction, and a visible lump of the neck are less common signs. Laryngological examination reveals a firm tumour mass characterized by submucous infiltration and expanding growth that leads to narrowing of the larynx.

Chondrosarcomas of the larynx originate as a result of neoplastic transformation of the hyaline cartilage. Histopathologically they are divided into well (G1), moderately (G2), and poorly (G3) differentiated tumours (classification based on the assessment of mitotic index and cellular/nuclear atypia) [10, 13]. Well-differentiated chondrosarcomas comprise around 80% of all cases [5, 6, 10]. The slow growth of the tumour makes early detection difficult

and delays the correct diagnosis [14]. We describe a patient with such a problem when early complaints were not confirmed in clinical examination and postponed the correct diagnosis by few months. Due to the advanced stage of the disease the patient underwent a complete laryngectomy with negative margins. Radical surgery plays an essential role in the treatment of patients with chondrosarcoma, but the role of radiotherapy is unclear. Our patient was referred for such a combined treatment, which resulted in long recurrence-free survival. Subsequently the patient died of metastatic disease to the liver and lung.

Case presentation

A 68-year-old male with confirmed laryngeal chondrosarcoma was admitted to the Cancer Centre and Institute in Gliwice in February 2012. The first symptoms appeared in February 2011. The patient suffered from hoarseness and gradually increasing dyspnoea. There were no abnormalities detected in clinical examination and laboratory tests. Complaints aggravated in July 2011; thus, a head and neck computed tomography (CT) was performed. Tomography revealed a lesion, in diameters of 26 × 37 × 52 mm, localized on the right side, in the lateral part of the larynx. The tumour mass was situated at the laryngeal inlet with infiltration of the surrounding tissues and osteolytic destruction of the right side of the cricoid cartilage. Penetration of the tumour caused a significant narrowing of the laryngeal lumen at the distance of 40 mm, preserving a tight space of 7 mm. Normal lymph nodes were described bilaterally along the neck vessels. Chest CT did not confirm any abnormalities. An urgent tracheotomy was performed and samples for histopathological examination were taken. The pathological assessment confirmed laryngeal chondrosarcoma. The tumour originated from thyroid cartilage, infiltrated the surrounding larynx wall and soft tissues, and adhered to the thyroid, but it did not destroy the thyroid capsule. The tumour consisted of atypical chondrocytes arranged in a lobular pattern in the cartilaginous matrix material. Hyperchromatic nuclei and binucleation were features

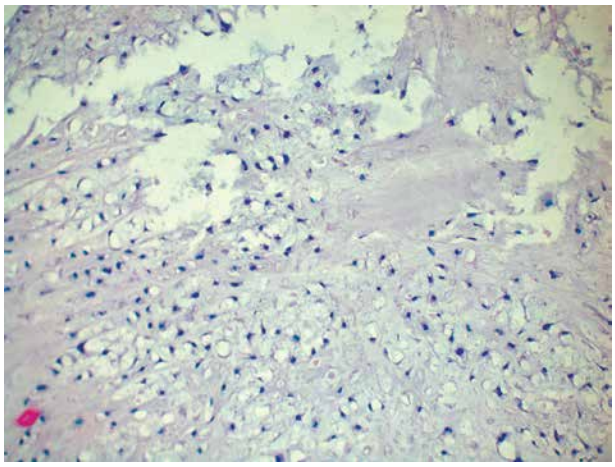

Fig. 1. The microscopic picture consisted of low-grade chondroid neoplasm, chondrosarcoma G-1. Haematoxylin and eosin staining; magnification 20×

of the tumour. Small fields of necrosis were noted. Myxoid areas were not identified. Calcifications were seen in tumour parts near the larynx mucosa. The microscopic picture consisted of a low-grade chondroid neoplasm, chondrosarcoma G-1 (Fig. 1). In March 2012 complete laryngectomy was performed. In postoperative histopathological evaluation, a tumour of the posterior commissure, 50 × 40 × 30 mm in size, spreading on the right vocal fold, and invading prelaryngeal muscles was described. Laryngeal chondrosarcoma, pT3, G1, was confirmed. Pharyngocutaneal fistula occurred in the postoperative period. Despite negative surgical margins, adjunctive radiotherapy was taken under consideration because of the size of the tumour and the prelaryngeal muscle invasion. Conformal radiotherapy with the use of a 2/70 Gy fractionation schedule (for postoperative tumour bed) was planned and performed (Fig. 2). Early radiation injury of the skin, as the only observed toxicity, was noticed and described as moderate. The patient was examined in 3- to 6-month intervals after receiving radiotherapy. Performed imaging studies and directoscopy did not reveal recurrence or metastatic spread of the disease for 6 years. In the seventh year of follow-up clinical symptoms of hepatic insufficiency were observed. A distant metastat-

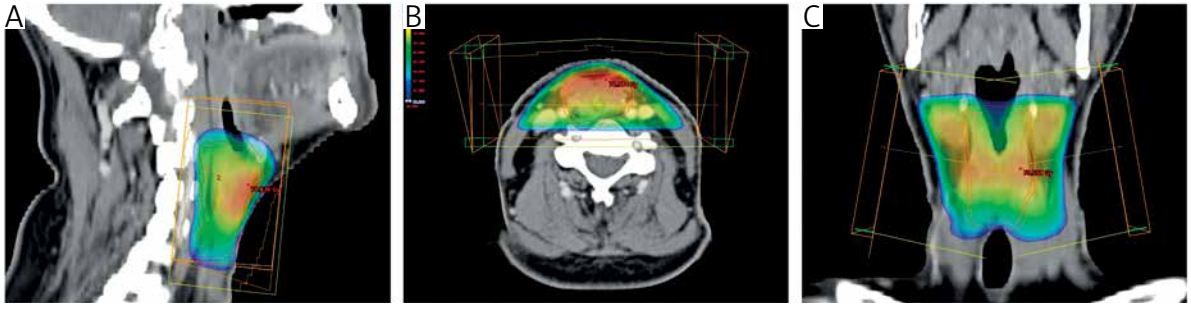

Fig. 2. Dose distribution. A) Transversal. B) Sagittal. C) Coronal. Dose shown as wash colours with minimum dose set to 66.5 Gy

ic spread in the liver and lungs was confirmed. Poor general condition and laboratory parameters did not allow systemic treatment or radiotherapy. Palliative care was suggested. The patient died in November 2018, 7 years after diagnosis.

Discussion

In the case of our patient, a typical lack of characteristic symptoms and their very slow growth led to a late diagnosis. Meticulous assessment of the clinical, radiological, and pathological picture is crucial in obtaining a correct diagnosis. In computed tomography, chondrosarcoma appears as a hypodense mass with localization below normal mucosa. Typically, contrast enhancement does not occur, although characteristic calcifications are described in 80% of cases [2, 10, 15]. This type of change was confirmed in the CT examination of our patient, and a significant advancement of the neoplastic process in the form of infiltration of the surrounding tissues and osteolytic destruction of the cricoid cartilage was observed.

In histopathological examination, chondrosarcomas was present with the following: immature chondrocytes, atypia, mitoses, necrosis, and infiltration [16]. In the differential diagnosis for this tumour, we took into consideration chondroma, chondrometaplasia, and tracheopathia osteoplastica. In the case of clinically, radiologically, and pathologically difficult cases, chondrosarcoma should be taken into account in tumours larger than 2 cm [4, 5, 14]. Differentiation between low-grade chondrosarcoma and chondroma can be extremely difficult or even impossible. Analysis of the entire specimen after resection is crucial and helpful in differential diagnosis. Usually, chondromas are smaller than chondrosarcomas. Smaller cellularity and lower pleomorphism are characteristic for chondromas rather than chondrosarcomas. Benign cartilaginous neoplasms do not present mitoses and necrosis [17]. Chondromas are distinguished from normal laryngeal cartilaginous structures in that they show increased cellularity, and the chondrocytes are often arranged in clusters. A recent study by Velez Torres based on analysis of 16 conventional chondrosarcomas revealed that up to 60% of laryngeal chondrosarcomas arise in association with pre-existing chondromas [18]. Chondrosarcoma is characterized by a slow progressive growth, with frequent recurrences, which are related to incomplete surgical excision or higher tumour grade [17]. Laryngeal tumours in the prevalence subset are well-differentiated and characterized with a favourable course. Thus, surgery performed via endoscopic or open access remains the main treatment modality [6]. Most often, surgical removal of the tumour with appropriate margins is performed. Consequently, maximal sparing of the healthy tissues is achieved [5, 19]. In the case of our patient, the surgical procedure was also applied in the first-line treatment, especially because the previously obtained biopsy material showed signs of significant malignancy.

Although chondrosarcomas are considered low-radiosensitivity tumours, irradiation is considered in cases of contraindications for surgery, unresectable tumours, and after the unradical surgical procedure [2, 5, 7, 20]. Some investigators suggest applying adjuvant radiotherapy even after radical surgery, although data on this are limited to case reports [5, 8, 10, 21–23]. The main indications for radiotherapy comprise the following: low degree of histopathological differentiation (G3), positive surgical margins, tumours larger than 5 cm (T2), inoperable cases, and confirmed tumour recurrence [23, 24]. In the case of the patient treated in our centre, we decided to add radiotherapy despite the radical nature of the surgery, due to the initial advancement of the disease (size of the tumour 5 cm and prelaryngeal muscle invasion). Application of adjuvant radiotherapy with a high dose (70 Gy) was probably of great importance to the absence of local relapse during the long-term observation of our patient. In contrast to skeletal lesions, chondrosarcomas of the larynx do not progress aggressively. Typically, they present slow growth and lack significant metastatic potential [15]. However, cases of distant metastases have been observed in poorly differentiated tumours [5, 6]. Chemotherapy is used very rarely as a treatment of laryngeal chondrosarcomas, and the results are not encouraging [2, 25]. Conventional chemotherapy has very limited efficacy in patients with advanced chondrosarcoma, with the highest benefit in mesenchymal and dedifferentiated chondrosarcoma [26].

The five-year survival rate for laryngeal chondrosarcomas ranges between 79 and 90% [27, 28]. Recurrences or metastases after applying radical surgical treatment are found in 8–14% of cases [2, 27]. In the case of our patient, despite the pathological diagnosis of low-grade malignancy, relapse of the disease occurred in the form of distant metastases. Therefore, the role of systemic therapy should be further investigated.

Conclusions

Given the good tolerability of the radiotherapy used and its local efficacy, it seems appropriate to use this form of treatment as adjuvant therapy in specific clinical cases. Patients diagnosed with low-grade chondrosarcoma with the co-existence of additional risk factors should be subject to frequent follow-up visits and checks for early detection of distant metastases.

Acknowledgment

The authors would like to thank Prof. Leszek Miszczyk, our mentor and boss, for participating

in the creation of this work, and whose premature death makes us sad.

The authors declare no conflicts of interest.

REFERENCES

1. Hong P, Taylor SM, Trites JR, et al. Chondrosarcoma of the head and neck: report of 11 cases and literature review. J Otolaryngol Head Neck Surg 2009; 38: 279-285.
2. Moerman M, Kreps B, Forsyth R. Laryngeal chondrosarcoma: An exceptional localisation of a not unfrequent bone tumor. Sarcoma 2009; ID 394908.
3. Kanotra SP, Kanotra S, Paul J, Jamwal PS. Chondrosarcoma of the arytenoid cartilage. Ear Nose Throat J 2010; 89: 94-100.
4. Bathala S, Berry S, Evans RA, et al. Chondrosarcoma of larynx: review of literature and clinical experience. J Laryngol Otol 2008; 122: 1127-1129.
5. Thompson LDR, Gannon FH. Chondrosarcoma of the larynx: a clinicopathologic study of 111 cases with a review of the literature. Am J Surg Pathol 2002; 26: 836-851.
6. Lewis JE, Olsen KD, Inwards CY. Cartilaginous tumors of the larynx: clinicopathologic review of 47 cases. Ann Otol Rhinol Laryngol 1997; 106: 94-100.
7. Oudidi A, Hachimi H, El Alami MN. Chondrosarcome laryngé. Cancer/Radiother 2005; 9: 343-346.
8. Chin OY, Dubal PM, Sheikh AB, et al. Laryngeal chondrosarcoma: a systematic review of 592 cases. Laryngoscope 2017; 127: 430-439.
9. Qinying W, Haihong C, Shuihong Z. Chondrosarcoma of the larynx: report of two cases and review of the literature. Int J Clin Exp Pathol 2015; 8: 2068-2073
10. Buda I, Hod R, Feinmesser R, Shvero J. Chondrosarcoma of the larynx. Isr Med Assoc J 2012; 14: 681-684.
11. Casiraghi O, Martinez-Madrigal F, Pineda-Daboin K, et al. Chondroid tumors of the larynx: a clinicopathologic study of 19 cases, including two dedifferentiated chondrosarcomas. Ann Diagn Pathol 2004; 8: 189-197.
12. Duzcu SE, Cosgun Z, Astarci HM. Laryngeal chondrosarcoma of the thyroid cartilage. Turk Patoloji Derg 2021; 37: 178-182.
13. Evans HL, Ayala AG, Romsdahl MM. Prognostic factors in chondrosarcoma of bone. A clinicopathologic analysis with emphasis on histologic grading. Cancer 1977; 40: 818-831.
14. Nao EEM, Bozec A, Vallicioni J, et al. Laryngeal chondrosarcoma: report of two cases. Eur Ann Otorhinolaryngol Head Neck Dis 2011; 128: 191-193.
15. Potochny EM, Huber AR. Laryngeal chondrosarcoma. Head Neck Pathol 2014; 8: 114-116.
16. Batsakis JG, Kevin Raymond A. Cartilage tumors of the larynx. South Med J 1988; 81: 481-484.
17. Zidar N, Gale N. Update from the 5th edition of the World Health Organization Classification of Head and Neck Tumors: Hypopharynx, Larynx, Trachea and Parapharyngeal Space. Head Neck Pathol 2022; 16: 31-39
18. Velez Torres JM, Martinez Duarte E, Diaz-Perez JA, et al. Primary sarcomas of the larynx: a clinicopathologic study of 27 cases. Head Neck Pathol 2021; 15: 905-916.
19. Thomé R, Thomé DC, De La Cortina RAC. Long-term follow-up of cartilaginous tumors of the larynx. Otolaryngol Head Neck Surg 2001; 124: 634-640.
20. Dailiana T, Nomikos P, Kapranos N, et al. Chondrosarcoma of the larynx: treatment with radiotherapy. Skeletal Radiol 2002; 31: 547-549.
21. Waters DK, Elliott JA, O'Duffy F, O'Dwyer T. High-grade chondrosarcoma of the larynx: a case report and literature review. J Surg Case Reports 2018; 2018: 1-3.
22. Semmar A, Mouden K. Laryngeal chondrosarcoma: a case report. J Clin Case Reports 2016; 6: 1-2.
23. Oliveira JF dos S, Branquinho FAPL, Monteiro ARRTN, et al. Laryngeal chondrosarcoma – ten years of experience. Braz J Otorhinolaryngol 2014; 80: 354-358.
24. Pellitteri PK, Ferlito A, Bradley PJ, et al. Management of sarcomas of the head and neck in adults. Oral Oncol 2003; 39: 2-12.
25. Gripp S, Pape H, Schmitt G. Chondrosarcoma of the larynx. The role of radiotherapy revisited – a case report and review of the literature. Cancer 1998; 82: 108-115.
26. Italiano A, Mir O, Cioffi A, et al. Advanced chondrosarcomas: role of chemotherapy and survival. Ann Oncol 2013; 24: 2916-2922.
27. Baatenburg de Jong RJ, van Lent S, Hogendoorn PCW. Chondroma and chondrosarcoma of the larynx. Curr Opin Otolaryngol Head Neck Surg 2004; 12: 98-105.
28. Miloundja J, Lescanne E, Garand G, et al. Chondrosarcoma of the cricoid. Ann Otolaryngol Chir Cervicofac 2005; 122: 91-96.

Address for correspondence

Dorota Gabryś
Department of Radiotherapy
Maria Sklodowska-Curie National Research
Institute of Oncology, Gliwice Branch
Wybrzeże Armii Krajowej 15
44-101 Gliwice, Poland
Phone: +48 322788051
Fax: +48 322788082
e-mail: Dorota.Gabrys@io.gliwice.pl