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Case Report

Dedifferentiated Laryngeal Chondrosarcoma: Combined Morphologic and Functional Imaging With Positron-Emission Tomography/Magnetic Resonance Imaging

Bela S. Purohit, MD; Pavel Dulguerov, MD; Karim Burkhardt, MD; Minerva Becker, MD

Chondrosarcoma of the larynx is a rare, low-grade malignancy in terms of histology and clinical behavior. We present an unusual case of laryngeal chondrosarcoma, which developed a large dedifferentiated component on recurrence after primary surgery. The diagnosis of dedifferentiation was suggested in view of the morphological and metabolic findings on hybrid positron-emission tomography/magnetic resonance imaging (PET/MRI) and was subsequently confirmed surgically. Whole-organ, slice-by-slice radiologic–histologic correlation revealed excellent delineation of the well-differentiated and dedifferentiated tumor components with PET/MRI. PET/MRI can provide additional functional information to supplement the morphological mapping and histopathology of these tumors.

Key Words: Positron-emission tomography/magnetic resonance imaging; dedifferentiated chondrosarcoma; larynx.

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INTRODUCTION

Chondrosarcomas are rare tumors accounting for about 0.5% of all laryngeal neoplasms. Unlike their counterparts in other head and neck locations, laryngeal chondrosarcomas are slow growing, low-grade tumors, and local excision is curative in most cases.[1–3] We describe a rare case of dedifferentiation or malignant mesenchymal component within a laryngeal chondrosarcoma. Although there are a few previous reports describing the pathological findings in dedifferentiated laryngeal chondrosarcomas, to our knowledge, this is the first report that describes the findings and role of multimodality imaging with hybrid positron-emission tomography/magnetic resonance imaging (PET/MRI) including diffusion-weighted MRI (DW MRI) in the diagnosis of dedifferentiation in laryngeal chondrosarcoma.

From the Department of Radiology (B.S.P., M.B.), Department of Otorhinolaryngology–Head and Neck Surgery (P.D., M.B.), and Department of Clinical Pathology (K.B.), Geneva University Hospital, Geneva, Switzerland.

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Send correspondence to Minerva Becker, MD, Department of Radiology and Department of Otorhinolaryngology–Head and Neck Surgery, Geneva University Hospital, Rue Gabrielle Perret Gentil 4, CH-1211 Geneva 14, Switzerland. E-mail: minerva.becker@hcuge.ch

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CASE REPORT WITH IMAGING AND PATHOLOGY

A 69-year-old male patient presented to our hospital in 2012 with a long-standing history of dysphonia, which had increased in severity over 2 months. He also complained of increasing respiratory stridor. Computed tomography (CT) study showed a 3.0 × 1.6-cm-sized, well-circumscribed, submucosal mass arising from the right cricoid cartilage with expansile lytic destruction and stippled calcifications. There was no involvement of the vocal cords or esophagus and no cervical adenopathy. Imaging findings and endoscopic biopsy were consistent with a grade 1–2 chondrosarcoma. The patient underwent cricotracheal resection (4.8-cm craniocaudal length), with sacrifice of the right recurrent laryngeal nerve and tracheostomy. Histologic evaluation of the resected specimen revealed a grade 2 chondrosarcoma with a microscopic focus of dedifferentiation. Five months later, he presented with slightly increasing dyspnea and peritracheostomal bleeding. Endoscopy showed right vocal cord palsy, a submucosal glottic bulge covered by intact mucosa, and posterior commissure synechia. Endoscopic biopsy was negative for tumor, and the posterior synechia was resected. Despite the negative biopsy and in view of the previous history, informed consent was obtained and the patient underwent a total body PET/MRI examination on a Philips Ingenuity TF scanner as part of an ongoing clinical study protocol. PET/MRI showed a large lobulated mass involving the larynx and trachea. The mass showed two distinct components (Fig. 1): a small, well-circumscribed, T1 hypointense, T2 hyperintense component involving the right ala of the

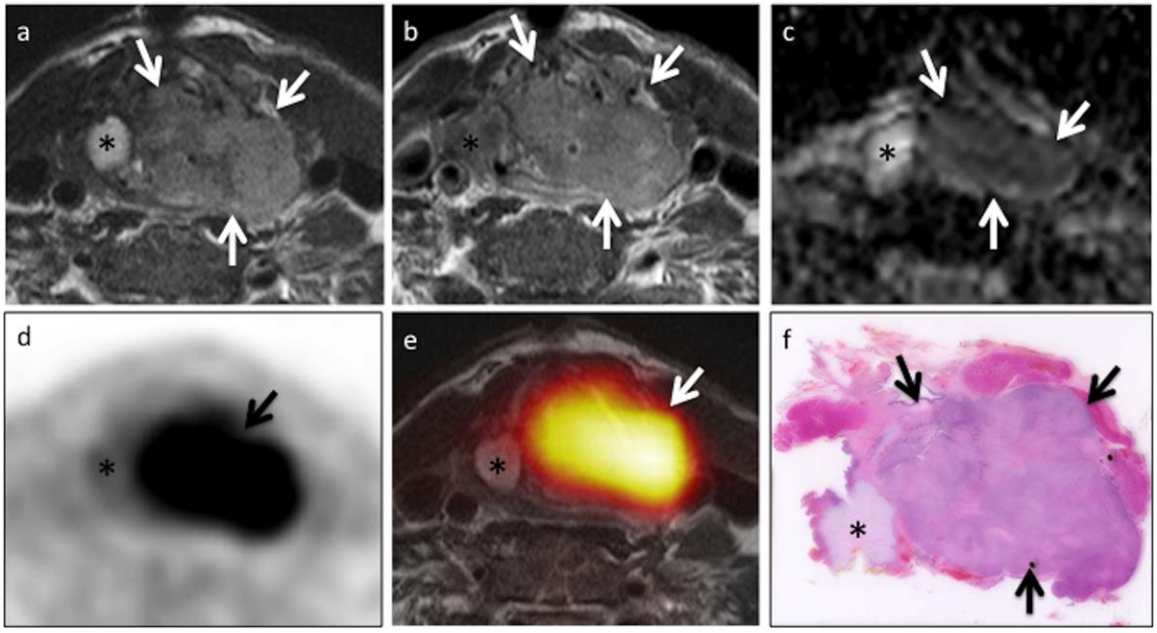

Fig. 1. (a) Axial T2-weighted magnetic resonance imaging (MRI) shows a laryngeal mass with a small, rounded, well-circumscribed, T2-hyperintense component on the right side (asterisk) and a large, lobulated, intermediate signal-intensity component on the left (white arrows). (b) Contrast-enhanced axial T1-weighted MRI shows nonspecific enhancement of the small right-sided component (asterisk) and of the lobulated left-sided component (white arrows). Note the tumor spread into the prelaryngeal strap muscles and hypopharynx. (c) Axial apparent diffusion coefficient (ADC) map shows high ADC values (ADCmean = 2.11×10^{-3} mm^2/s) within the right-sided component (asterisk) and very low ADC values (ADCmean = 0.945×10^{-3} mm^2/s) within the left-sided component (white arrows). (d) Axial fluorodeoxyglucose (FDG)/positron-emission tomography (PET) image shows very high FDG uptake (standardized uptake value [SUV]mean = 24; SUVmax = 32) within the large left-sided component (black arrow) in keeping with very high tumor metabolism. In contrast, moderate uptake was seen in the region of the right-sided component (asterisk, SUVmean = 3.7; SUVmax= 4.7). (e) Fused axial PET/MRI shows very high FDG uptake within the large left-sided tumor component (white arrow). This is in sharp contrast to the small, round, right-sided component (asterisk), which shows minor FDG uptake. (f) Axial whole-organ histologic slice of the surgical specimen obtained at the same level as images 1a through 1e shows the biphasic tumor with a well-differentiated, low-grade chondrosarcoma component (asterisk) and the large dedifferentiated component (arrows). [Color figure can be viewed in the online issue, which is available at www.laryngoscope.com.]

thyroid cartilage, as well as a larger, poorly marginated, lobulated component on the left. The left-sided component showed intermediate T1 and T2 signal intensity and heterogeneous contrast enhancement. It involved the left ala of the thyroid cartilage, with infiltration into the left pretracheal soft tissue, strap muscles, and thyroid gland as well as the left pyriform sinus and proximal esophagus. On DW MRI, the two components of the mass showed distinct behavior (Fig. 1c): the right-sided component showed high apparent diffusion coefficient (ADC) values, whereas the left component showed low ADC values. Although the smaller right-sided component appeared consistent with a classic chondrosarcoma, the large left-sided component was considered to be suspicious for a more aggressive high-grade tumor. Fused fluorodeoxyglucose (FDG) PET and MRI images showed intense tracer uptake in the left-sided component, with high standardized uptake values (SUVs) and moderate FDG uptake in the small right-sided component (Fig. 1e). These findings supported the diagnosis of dedifferentiation within the left part of the recurrent tumor. PET/MRI further revealed absence of lymph node metastases and absence of distant metastases.

Repeat deep endoscopic biopsy on the left confirmed the presence of dedifferentiated chondrosarcoma. The patient underwent a total laryngectomy with further tracheal resection, total thyroidectomy, and noncircumferential resection of 5 cm of the upper esophagus. Because an additional 4 cm of trachea were resected, a tracheal composite graft made of radial free flap armed with split costal cartilage was performed. Part of the radial free flap was used for pharyngoesophageal closure. A soft tracheotomy tube, used for stenting of the tracheal graft, was removed 2 months after the procedure. The patient underwent postoperative radiochemotherapy.

Histopathology with whole-organ serial slices performed every 3 to 4 mm to match the axial PET/MRI imaging plane confirmed the presence of dedifferentiation in the left portion of the recurrent chondrosarcoma as suggested by imaging (Fig. 1f). Histologic slice-by-slice analysis revealed an excellent correlation between PET/MRI and microscopic findings with regard to the delineation of well-differentiated and dedifferentiated components and regarding invasion of laryngeal and extralaryngeal structures. Histopathology further revealed that the well-differentiated part had a characteristic chondroid matrix with lacunae containing chondrocytes with rare mitoses typical of a chondrosarcoma grade 2. The dedifferentiated portion had markedly pleomorphic spindle cells with large nuclei, giant cells, and numerous mitoses, in part atypical. Vascular and lymphatic spread were equally present. As depicted by PET/MRI, there was an abrupt transition between the two tumor components.

DISCUSSION

Laryngeal chondrosarcomas are rare tumors accounting for <0.2% of all head and neck malignancies and about 0.5% of all laryngeal tumors. Unlike other head and neck chondrosarcomas, laryngeal chondrosarcomas are low-grade tumors (grade 1 and 2) that generally follow an indolent clinical course.[1–5] The cricoid cartilage is involved more often than the thyroid cartilage, and the tumors are typically submucosal.[3,4] They commonly present with hoarseness, dysphagia, or a neck mass in older men who have had symptoms for about 2 years.[1–5] On MRI, laryngeal chondrosarcomas appear similar to chondrosarcomas in other body locations, with the tumor matrix showing high T2 signal corresponding to hyaline cartilage.[4] Small areas of intralesional low signal correspond to intratumoral stippled calcifications, seen even more elegantly on CT.[2,4] The enhancement pattern of chondrosarcomas is variable.[4] Laryngeal chondrosarcomas portend an excellent overall prognosis, and conservative voice-sparing surgery is usually curative.

Rarely, an additional aggressive malignant mesenchymal component or dedifferentiation may develop within a chondrosarcoma. Dedifferentiation occurs in about 5% to 10% of all chondrosarcomas and has been more commonly described in bones, where the dedifferentiated components are osteosarcomas, fibrosarcomas, or malignant fibrous histiocytomas.[1,2,5] The origin of the dedifferentiated and cartilaginous components is still controversial; some studies show that they arise from a common precursor cell, whereas others suggest separate genotypic lineages, thus raising the possibility of a collision tumor. The histological hallmark of dedifferentiated chondrosarcomas consists of a cartilaginous component juxtaposed to the high-grade, noncartilaginous, dedifferentiated component, with abrupt transition between the two tissue types, as seen in the current case. The cartilaginous component may constitute a very small proportion of the dedifferentiated chondrosarcoma, and therefore careful histological evaluation of the entire tumor specimen is mandatory.[1–3,5] In our case, histopathology was typical of dedifferentiation, where a biphasic pattern of neoplastic cartilage was seen juxtaposed to a large spindle cell component with pleomorphism, vesicular nuclei, giant cells, and numerous mitoses.

Dedifferentiation in laryngeal chondrosarcomas has been described as a rare occurrence in literature. In contrast to low-grade tumors, the prognosis of dedifferentiated laryngeal chondrosarcomas is poorer, with higher tendency for recurrence, the propensity for distant metastases, and poorer survival rates.[1–3,5] Total laryngectomy is considered as the treatment of choice for dedifferentiated chondrosarcomas. There have been a few reports mentioning radiotherapy for these tumors; however, its role is still unclear.[1–3,5]

Sakai et al.[2] have mentioned that the CT imaging features of a dedifferentiated chondrosarcoma may be very similar to a well-differentiated chondrosarcoma. In our case, however, MRI showed a prominent, aggressive-appearing soft-tissue component, which did not display the typical morphologic features of a low-grade chondrosarcoma. In addition, findings on DW MRI clearly indicated low ADC values and therefore high cellularity in the left, larger tumor component. DW MRI is a recent functional MRI technique based on the assessment of random (Brownian) motion of water molecules, which is impaired (restricted diffusion) in hypercellular tissue, resulting in low ADC values. Despite the fact that DW MR images may be degraded by swallowing, breathing, and susceptibility artifacts, quantitative measurements of ADCs have been shown to be reproducible in head and neck tumors[6] and lower ADCs are observed with increasing dedifferentiation. In the current case, the ADC map correctly reflected the microstructural architecture of the laryngeal chondrosarcoma with its two distinct components: a highly cellular component with low ADC values and a low cellularity component with high ADCs.

The pattern of FDG uptake on PET is known to act as a valuable adjunct in identifying aggressive cartilage tumors. Well-differentiated grade 1–2 chondrosarcomas show low–moderate FDG uptake (low SUVs) reflecting their hypometabolism, regardless of their size. In contrast, high-grade and dedifferentiated chondrosarcomas show high SUV values equaling that of osteosarcomas, fibrosarcomas, and Ewing sarcomas.[7] Although integrated morphological and functional imaging is often performed for evaluating bony chondrosarcomas, its role in laryngeal chondrosarcomas has not yet been described. In our case, PET/MRI provided additional functional information by identifying the hypermetabolic, aggressive dedifferentiated component in contrast to the closely apposed, small, hypometabolic, low-grade component. Although the idea to combine PET and MRI arose even before the implementation of PET/CT, the introduction of commercially available clinical hybrid PET/MRI systems was possible only very recently.[8–10] A few research groups have already reported the feasibility of this emerging technology in patients with head and neck tumors.[9] Although the reported results are based on a small number of patients, combining functional and anatomic information from MRI with metabolic information from PET—as in the current case—may thus provide additional precision in noninvasive cross-sectional imaging.

CONCLUSION

Dedifferentiation within a laryngeal chondrosarcoma is a rare entity. We describe the role of integrated morphological and metabolic imaging with PET/MRI in its diagnosis. PET/MRI can provide additional functional information to supplement the morphological mapping and histopathology of these tumors.

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