Dedifferentiated Chondrosarcoma of the Larynx

Shiraz S. Fidai¹ · Daniel T. Ginat² · Alexander J. Langerman³ · Nicole A. Cipriani¹

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Abstract Primary dedifferentiated chondrosarcoma occurring in the larynx is a rare head and neck malignancy. The cases reported in the literature suggest male gender predilection and variable clinical outcomes ranging from disease-free survival to disease-related death. Although a calcified matrix is suggestive of chondrosarcoma, the dedifferentiated component is not readily appreciated on conventional imaging modalities and thorough tissue sampling is necessary for confirming the diagnosis. Histologically, there is an abrupt transition from a well-differentiated chondrosarcoma to a high-grade spindle cell component, which can show focal heterologous differentiation. These features are exemplified in this sine qua non radiology–pathology correlation article.

Keywords Primary dedifferentiated chondrosarcoma · Larynx · Head and neck malignancy · Well-differentiated chondrosarcoma · Heterologous differentiation · Cricoid cartilage

Case Description

The patient was a 55 year-old male with no significant past medical history who was transferred to our intensive care unit from an outside emergency room for treatment of a nearly obstructive subglottic mass. Five months prior, the patient presented with shortness of breath and chest x-ray was negative. However, after continued decline in breathing, pulmonary function test 1 month prior to admission revealed an obstructive process. Review of symptoms was notable for progressive hoarseness, throat fullness, discomfort while eating, biphasic stridor, and an unintentional seven pound weight loss. Due to worsening symptoms, the patient presented to an outside hospital emergency department where bronchoscopy revealed a subglottic mass. The patient was then emergently transferred to our intensive care unit. Laryngoscopy revealed a subglottic mass involving the cricoid cartilage, anterior tracheal wall, and subcutaneous tissues anterior to the larynx. Tracheostomy was placed.

Radiographic Features

Contrast-enhanced CT scan revealed a well-defined mass with a calcified matrix arising from the anterior cricoid cartilage. There was associated marked airway narrowing and extension of the tumor into the strap muscles (Fig. 1). There was no evidence of cervical lymphadenopathy.

Diagnosis and Treatment

Partial laryngectomy with resection of stoma was performed. Gross examination revealed a $3.1 \times 2.8 \times 2.5$ cm spherical, white-tan, partially calcified, submucosal mass

✉ Shiraz S. Fidai
shiraz.fidai@uchospitals.edu

¹ Department of Pathology, The University of Chicago, Chicago, IL, USA

² Department of Radiology, Pritzker School of Medicine, The University of Chicago, Chicago, IL, USA

³ Department of Otolaryngology, Vanderbilt University, Nashville, TN, USA

Fig. 1 Axial (a) and coronal (b) contrast-enhanced CT images demonstrate a mass arising from the anterior cricoid cartilage (arrows) with a calcified matrix. There is associated airway narrowing extension of the tumor into the strap muscles

involving the anterior cricoid cartilage and cricothyroid membrane with extension posteriorly along the cricoid. Cut surface was variably white-tan and glistening with focal central degenerative change (Fig. 2). Histologic examination revealed a biphasic neoplasm with invasion into ossified cricoid cartilage and adjacent soft tissue. The major component demonstrated spindle-to-stellate shaped cells in a myxo-chondroid matrix with variable cellularity, cytologic atypia, and necrosis, consistent with low to intermediate grade chondrosarcoma. The minor component showed hypercellular spindle cells with significant nuclear pleomorphism and prominent mitotic activity (up to 6 per 10 high-power fields in the most proliferative area). Some areas were devoid of matrix, while others demonstrated osteoid or myxoid matrix. Overall, the diagnosis was compatible with dedifferentiated chondrosarcoma with focal heterologous osteosarcoma-like differentiation (Fig. 2). All lymph nodes examined were negative and surgical margins were uninvolved. No adjuvant treatment was rendered. He was disease free at last follow-up 8 months following resection.

Discussion

Although it is the most common malignant mesenchymal tumor of the larynx, primary laryngeal chondrosarcoma is rare, comprising only 0.2 % of head and neck malignancies and 1 % of laryngeal malignancies. It shows a predilection for male gender with mean age at presentation between 60 and 64 years. Presenting symptoms depend on the anatomic location and include dyspnea, dysphasia, dysphonia, and cough with hoarseness being the most common symptom (64.9 %) [1]. The etiology of laryngeal chondrosarcomas remains unclear, although ischemic changes in preexisting chondromas are hypothesized to serve as precursors to these lesions [1].

Chondrosarcoma most commonly occurs in the pelvis and long bones of adults. In this setting, dedifferentiation has been reported in 6–21 % of all chondrosarcomas and histologically resembles a high-grade spindle cell sarcoma in a background of well-differentiated chondrosarcoma [2]. Even more rare is dedifferentiated chondrosarcoma of the larynx, with only fourteen cases reported to date in literature; the current case represents the fifteenth [3, 4]. The most common anatomic site of origin is the inner posterior plate or signet of the cricoid cartilage [1, 3]. All reported dedifferentiated chondrosarcomas occurred in male patients [2–4].

On CT, a common feature to identify a laryngeal mass as cartilaginous in nature is the presence of coarse or stippled calcifications, which may be seen in tumors of any grade. This feature is not readily appreciated on MRI, which is more useful for determining tumor extent. However, destructive invasion of cartilage, bone, or soft tissue may suggest that the neoplasm is malignant [1]. Moreover, it is difficult to separate a well-differentiated from a dedifferentiated chondrosarcoma based on imaging alone. Some features such as rapid growth or prominence of soft tissue component may suggest dedifferentiation [5]. A recent study discusses the role of multiple imaging modalities to suggest a dedifferentiated component: hybrid PET/MRI and diffusion-weighted MRI may suggest dedifferentiation due to low ADC values on DW-MRI and high FDG uptake on PET (high SUV) [4].

On histologic examination, chondrosarcomas are defined by the presence of a typical, neoplastic chondrocytes situated in myxoid, basophilic, or metachromatic matrix, with overall loss of normal architecture. Benign laryngeal chondromas are thought to be rare to non-existent in the larynx, and are largely restricted to small (<1 cm), hypocellular, cytologically bland tumors [6]. Depending on the grade of the sarcoma, different morphologic features are seen: grade 1 tumors show slight increase in cellularity with small, hyperchromatic nuclei; grade 2–3 tumors become increasingly

Fig. 2 Cut surface of surgical resection specimen **a** is variably white-tan and glistening with focal central degenerative change. Low power histologic view **b** shows normal cricoid cartilage (*black arrow*) surrounded by conventional chondrosarcoma and dedifferentiated chondrosarcoma (*white arrow*). Both grade 1 (**c**, *bottom left*) and

grade 2 (**c**, *top right*) conventional chondrosarcoma are present. Undifferentiated spindle cell sarcoma areas **d** with mitotic figures (*arrow*) confirm dedifferentiated chondrosarcoma. High-grade malignant cells surrounded by osteoid **e** with mitotic figures (*arrow*) suggest heterologous osteosarcomatous differentiation

hypercellular with cell clustering, nuclear enlargement and hyperchromasia, mitoses, and multinucleation (binucleation is generally not considered specific for chondrosarcoma) [1]. As

seen in dedifferentiated chondrosarcomas arising in other anatomic sites, the histology in primary dedifferentiated laryngeal chondrosarcoma also shows an abrupt transition to a

high-grade spindle cell sarcoma. Morphologically, it can resemble undifferentiated sarcoma, osteosarcoma, rhabdomyosarcoma, leiomyosarcoma, or angiosarcoma [2, 3]. Immunohistochemical findings are inconsistently reported in these cases, but staining for vimentin has exhibited strong positivity in some cases [2].

The main treatment in twelve dedifferentiated laryngeal chondrosarcomas was total laryngectomy; partial laryngectomy was performed in three, including our case [2–4]. In five cases, total laryngectomy was performed only after subsequent development of recurrent tumor at the primary site [2, 4]. Radiation was also performed in four cases [2–4]. Due to the rarity of this disease, it is difficult to determine the best course of treatment and prognosis for these patients. Follow-up reveals a variable clinical course with seven patients (including ours) disease free at variable lengths of follow-up and three patients succumbing to multi-organ metastases and dying of disease; the remaining reported cases were lost to follow up [2, 3]. Our patient is disease free at 8 months following initial diagnosis and resection.

Compliance with ethical standards

Conflict of interest None.

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