Primary laryngeal lymphoma: Case report

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Abstract
Extranodal laryngeal lymphoma is extremely rare. We report a case of primary laryngeal lymphoma in a 76-year-old man who had presented with a 7-week history of progressive hoarseness. Laryngoscopy revealed asymmetry of the right false vocal fold. Pathology of a deep biopsy specimen identified a malignant, diffuse, CD20-positive, B-cell lymphoma. The stage 1E lymphoma completely resolved after treatment with CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) and rituximab. Despite its relative rarity, the consequences of a missed diagnosis warrant vigilance for this type of laryngeal tumor.

Introduction
Extranodal lymphoma involving the larynx is exceedingly rare, accounting for less than 1% of all primary laryngeal neoplasms. Most lymphomas involving the larynx involve other sites as well, including the salivary glands, thyroid, nasopharynx, and tonsils.

Recognition of the clinical presentation of laryngeal lymphoma may prevent inappropriate management, particularly if definitive surgical decisions are made on the basis of frozen sections. The treatment of laryngeal lymphoma differs from that of other submucosal lesions such as laryngeal cysts, neurofibromas, lipomas, myxolipomas, hemangiopericytomas, paragangliomas, laryngeal amyloidosis, neurilemomas, and Teflon granulomas. Whereas these other lesions generally require resection, resection is contraindicated in laryngeal lymphoma.

We report this case of laryngeal lymphoma because, despite its relative rarity, the consequences of a missed diagnosis warrant awareness of and vigilance for this type of laryngeal tumor.

Case report
A 76-year-old man was referred to our Department of Otolaryngology–Head and Neck Surgery for evaluation of a 7-week history of progressive hoarseness. He denied any history of dyspnea, dysphagia, fever, night sweats, or weight loss. Indirect and flexible fiberoptic laryngoscopy revealed asymmetry of the false vocal fold on the right side, which made visualization of the true vocal fold difficult. The rest of the larynx appeared to be normal. No palpable lymphadenopathy in the neck was identified. The initial presumptive diagnosis was either a possible early internal laryngocele or a ventricular cyst.

Findings on computed tomography (CT) of the neck were consistent with a right supraglottic tumor (figure 1). A soft-tissue mass measuring approximately 2.8 × 1.7 cm was present at the level of the false vocal fold on the right. The mass extended laterally into the paralaryngeal fat and posteriorly through the cricothyroid notch with effacement of the aerated portion of the right piriform sinus. No adenopathy was seen within the neck.

Microdirect laryngoscopy confirmed that a large, firm, smooth swelling had involved the supraglottic larynx on the right (figure 2). Frozen-section analysis of deep biopsies revealed that the mass was probably a lymphoma. Indeed, the final pathology identified it as a malignant, diffuse, CD20-positive, B-cell lymphoma—probably a large-cell variant (figure 3). After further workup, the tumor was staged as 1E.

The patient was treated with 8 cycles of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) and rituximab weekly for 4 weeks. During treatment, he was also diagnosed with prostate carcinoma, which was treated with radiation implants. He also had a renal mass that was suspected of being a renal cell carcinoma, for which he was closely observed. His response to treatment of the laryngeal lymphoma was excellent, and follow-up 3 years later detected no evidence of recurrence.

Discussion
In our review of 311 lymphomas involving the head and neck, we found that extranodal involvement occurred in 4% of patients with Hodgkin’s disease and in 23% of...
Lymphoma is one of the most common malignancies of the head and neck, second only to squamous cell carcinoma. Extranodal tumors in the head and neck are usually non-Hodgkin's lymphomas. The larynx appears to be a rare site of extranodal lymphoma, accounting for less than 1% of all primary laryngeal neoplasms. By 1976, only 14 cases had been reported in the English-language literature. By 1989, 11 more cases of primary laryngeal non-Hodgkin's lymphoma had been added. As of this writing, the total number of reported cases was approaching 90. In these cases, however, the larynx was not always the only site of involvement, and probably fewer than 35 cases were true stage 1E tumors. Our patient's disease was confined to the larynx.

Our review of the literature also revealed that the median age of patients with laryngeal lymphoma was 60 years (range: 14 to 81). The distribution between males and females was almost equal. The most common symptom at presentation was hoarseness, which had been present from 2 to 18 months. Other reported symptoms were dysphonia, dysphagia, stridor, and cough. Although these symptoms are indistinguishable from those of other laryngeal tumors, the macroscopic appearance of non-Hodgkin's lymphoma of the larynx may raise the suspicion of an attentive clinician.

Figure 1. CT of the neck shows the supraglottic soft-tissue tumor at the level of the false vocal fold on the right. The 2.8 × 1.7-cm mass extends laterally into the paralaryngeal fat abutting the thyroid cartilage and posteriorly with effacement of the aerated portion of the right piriform sinus.

Figure 2. Microdirect laryngoscopy shows the large, firm, smooth, nonulcerated, pale, submucosal tumor before (A) and after (B) biopsy.

Most laryngeal lymphomas present as a submucosal mass or a polypoid tumor; they are smooth, nonulcerated, and gray-white. They are usually located in the supraglottic region, and they have a particular tendency to involve the aryepiglottic folds, although some cases have been reported in the subglottis. While suggestive, none of these features is pathognomonic for a laryngeal lymphoma. Definitive diagnosis depends on histologic examination of a biopsy specimen.

Primary laryngeal lymphomas probably arise from specialized submucosal aggregates of lymphoid cells present in the lamina propria of the supraglottic area and epiglottis. Tumor growth slowly expands the overlying mucosa, which remains intact, and this results in a benign-appearing mass. Squamous cell carcinomas, in contrast, arise in the squamous epithelium and present as an irregularity involving the free margin of the laryngeal structures.

It is characteristic of laryngeal non-Hodgkin's lympho-
mas to remain localized for long periods of time. They can, however, disseminate to distant sites years later, especially to other mucosal sites rather than to peripheral lymphoid tissue.12,13,22,25 This predisposition for other mucosal sites is attributable to the homing properties of the mucosal B lymphocytes.20,22 Recurrences in the gastric mucosa, lung, and orbit have been reported.12,13

A wide spectrum of histologic subtypes of laryngeal lymphomas has been reported. The great majority of laryngeal non-Hodgkin’s lymphomas have been of B-cell lineage; very few T-cell immunophenotypes have been reported.27-29 Using the working classification of these tumors, a high proportion were diffuse large-cell lymphomas.20,22

Historically, radiotherapy has been the primary modality of therapy for these tumors. Results have been fairly good, and long follow-ups have found few recurrences.1,5,22 Considering the systemic nature of most cases of non-Hodgkin’s lymphoma, we believe that chemotherapy has a role, especially in cases of low-grade lymphoma. A definitive diagnosis continues to rely on histologic examination of a biopsy specimen. Care in decision making should be exercised regarding frozen sections. There is little role for surgical resection.

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References

Figure 3. Histopathology identifies the tumor as a malignant, diffuse, CD20-positive, B-cell lymphoma—probably a large-cell variant.