# Primary extranodal laryngeal lymphoma: description of two cases

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**Abstract**

The larynx is a delicate organ which functions not only to vocalize, but more importantly for airway protection. Its structural integrity is comprised of a musculo-cartilaginous framework and an overlying epithelium, with a broad spectrum of pathologies ranging from benign mucosal retention cyst to rare soft tissue tumours. Primary haematological malignancy involving the larynx remains a rare phenomenon due to its limited lymphatic supply. The authors present two cases of primary non-Hodgkin lymphoma of the larynx which manifested with non-identical symptoms and clinical findings. Clinicians should be aware of the various forms of localized throat symptoms as well as the gross tumour appearance in a primary haematological malignancy of the larynx.

## Introduction

Primary laryngeal lymphoma represents a rare entity, constituting less than 1% of all laryngeal neoplasms.[1-3] Fewer than 100 cases of primary laryngeal lymphoma have been reported worldwide to date.[1-5] Its rare occurrence can be attributed to the low lymphoid content in the larynx compared to other areas along the respiratory tract.[1,5] Non-Hodgkin lymphoma within the larynx is presumed to originate from the submucosa, which contains an abundant aggregation of predominantly B-cell lineage lymphoid tissues, as well as mucosa-associated lymphoid tissue (MALT).[4,5]

Primary laryngeal lymphoma may present with various forms of localized throat symptoms that range from just foreign body sensation to difficulty in breathing due to airway obstruction, similar to any other laryngeal neoplasm. The tumour characteristics may appear benign with smooth overlying mucosa or malignant with fungating mass: thus histopathology examination is the only avenue of confirming a diagnosis of laryngeal lymphoma. Herein, we report two cases of primary non-Hodgkin lymphoma of the larynx which manifested with non-identical symptoms and clinical findings.

## Case 1

A 54-year-old male was brought to the emergency department for worsening foreign body sensation in the throat and shortness of breath for the past two weeks. He denied other associated symptoms such as changes of voice, odynophagia, dysphagia, or neck swelling. Further history did not reveal preceding foreign body ingestion, laryngeal trauma, previous intubation, recent upper respiratory tract infection, or constitutional symptoms. Upon physical examination, he appeared well-built with no clinical evidence of anaemia. There was a striking feature of intermittent inspiratory stridor with the usage of accessory respiratory muscles, indicative of impending airway obstruction. A complete head and neck examination, along with lung auscultation, were unremarkable. A flexible nasoendoscopy (Figure 1) revealed a smooth-surfaced mass occupying the laryngeal surface of the epiglottis. The mass was partially obstructing the laryngeal inlet, hindering a complete visualization of the vocal folds.

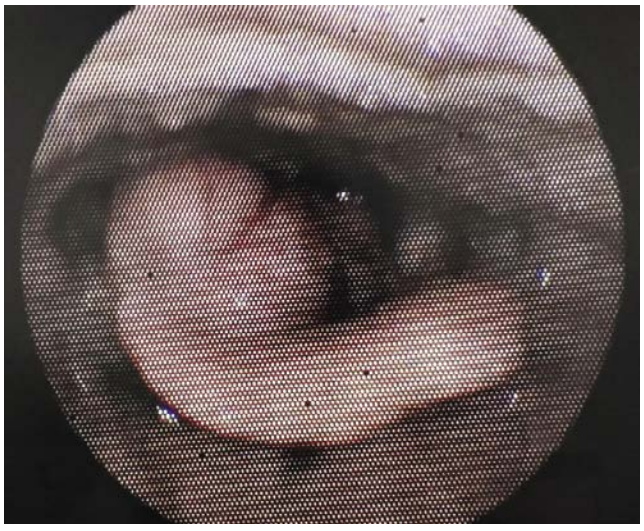

**Figure 1.** Flexible nasoendoscopic view of the laryngeal inlet of case 1 reveals a mass over the laryngeal surface of epiglottis (arrow). Its smooth glistening surface with a well demarcated border deceptively resembles a benign lesion, masking its true malignant nature.

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Following informed consent, the patient was brought to the operating theatre, with the purpose of airway security under a controlled setting. An attempted awake fibreoptic nasotracheal intubation was futile, so a tracheostomy under local anaesthesia was performed. The mass was seen originating from the laryngeal surface of the epiglottis upon direct laryngoscopy. It was yellowish, smooth, and hard on palpation. Other subunits of the supraglottic, glottic, and subglottic region were normal. The mass was excised and sent for histology analysis. A telescopic study of the trachea showed normal finding. Histopathological examination revealed grade 3 Non- Hodgkin follicular lymphoma with a high proliferative index (Ki-67 of 50%). The tumour sample was positive for CD20, CD23, and B-cell lymphoma-2 (BCL-2) while negative for CD3, CD5, CD15, and CD30 (Figure 2). Computerized tomography (CT) staging unveiled disease confined within the larynx (Figure 3). Bone marrow aspiration and trephine (BMAT) showed absence of lymphomatous infiltration. The patient was referred to the tertiary haematological disease centre and was treated with six cycles of chemotherapy of RCHOP regime (rituximab, cyclophosphamide, doxorubicin hydrochloride, vincristine and prednisolone). He was successfully decannulated at one-month post-treatment, with flexible nasoendoscopy surveillance showing a patent airway with mobile vocal folds. A subsequent follow up at six months post-treatment revealed no clinical evidence of recurrence.

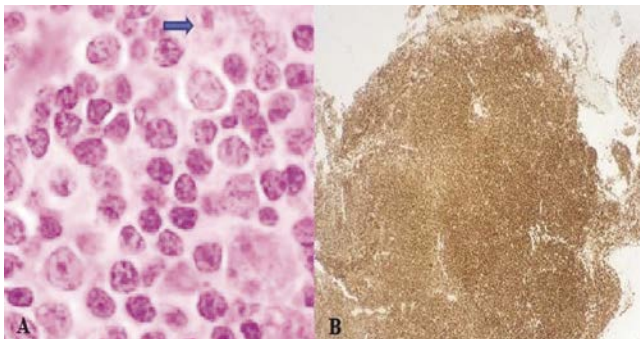


**Figure 2.** (Panel A) Hematoxylin & eosin (H&E) image of case 1 in high power shows homogenous infiltration of small to moderate mononuclear cells with centroblasts (arrow in blue). The small cells are mostly cleaved with hyper-chromatic, inconspicuous nucleoli and scant cytoplasm, while the centroblasts are non-cleaved with round to oval vesicular chromatic, peripherally located nucleoli. (Panel B) Immunohistochemistry staining of case 1 with a positive result for B-cell lymphoma-2 (BCL-2).

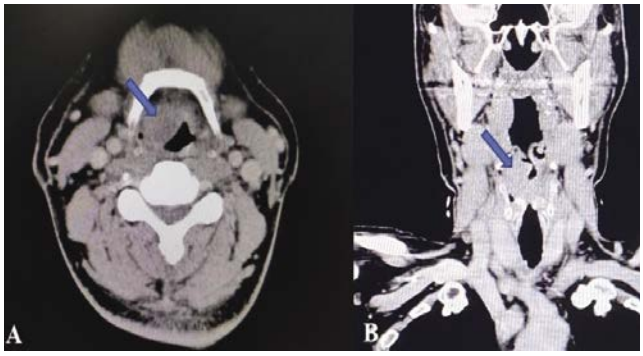


**Figure 3.** Axial view (panel A) and coronal view (panel B) of a contrast-enhanced CT of the neck of case 1 showing homogenous enhancing lesion at the right side of the epiglottis (blue arrows).

## Case 2

A 28-year-old male chronic smoker was referred to the otorhinolaryngology department for further evaluation of a suspicious laryngeal mass following an ineffectual endoscopic transoral biopsy. He presented with worsening sore throat and odynophagia of three months duration. He also noticed a new onset of left otalgia of one-month period. He denied voice changes, dyspnoea, dysphagia, and constitutional symptoms. Further history suggested neither recent foreign body ingestion nor neck trauma. His past medical and family history was unremarkable. On examination, he spoke with a normal voice and appeared comfortable with stable vital signs. Oral cavity examination and neck palpation were normal. A flexible nasoendoscopy showed an exophytic lesion along the left aryepiglottic fold, with lateral extension to the medial wall of the left pyriform sinus (Figure 4). The vocal fold movement remained normal. He underwent contrast CT of the neck, which revealed a homogeneously enhanced lesion involving the left aryepiglottic fold and pyriform sinus (Figure 5).

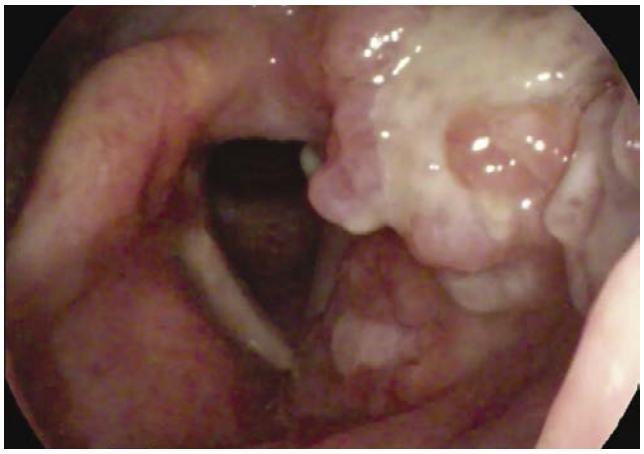

**Figure 4.** Videoendoscopic view of the laryngeal inlet of case 2 showing a diffuse fungating mass along the left aryepiglottic fold and arytenoid.

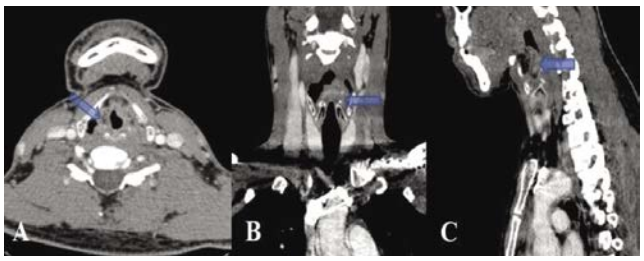


**Figure 5.** Axial (panel A), coronal (panel B) and sagittal view (panel C) of a contrast-enhanced CT of the neck of case 2 showing homogenous enhancing lesion on the left aryepiglottic fold. It has extended laterally into the left pyriform sinus (blue arrows).

A transoral examination of the larynx under general anaesthesia showed a friable fungating tumour from the left aryepiglottic fold and the pyriform sinus. The mobility of the cricoarytenoid joints were normal on palpation. The glottis and subglottic remained free from disease. Biopsy of the lesion confirmed the diagnosis of a NK/T cell laryngeal lymphoma with high proliferative index (Ki-67 of 60%). The specimen revealed malignant lymphoid cells

with prominent nucleoli, which were positive for immunostaining of Epstein-Barr encoding region (EBER), CD3, CD5, T-cell intracellular antigen 1 (TIA1), and CD56, while negative for CD20, CD4, CD8 and anaplastic lymphoma kinase (ALK). A subsequent positron emission tomography/computerized tomography (PET/CT) and BMAT showed localized laryngeal disease. He was planned for six cycles of chemotherapy of GELOX regime (gemcitabine, L-asparaginase, and oxaliplatin) with radiotherapy.

## Discussion

The age of diagnosis of primary laryngeal lymphoma ranges widely from 4 to 81 years, with an average age of diagnosis at 70.1,[5] Reports show varied gender predominance.6 The most frequent site of involvement remains within the supraglottis, comprising 47%, followed by the glottis, of 25%.[5] The paraglottic and subglottic area, on the other hand, has been rarely reported.[5]

The clinical manifestation of a laryngeal lymphoma is indifferent from other laryngeal pathologies. Localized symptoms that have been described are namely hoarseness, odynophagia, dysphagia, and foreign body sensation, which may mimic squamous cell carcinoma.[1,5,6] Similar to the first presenting case, catastrophic presentations of an impending airway obstruction which requires immediate surgical intervention has also been reported.1 Azzopardi et al. described two cases of laryngeal lymphoma with different clinical manifestations, of which one presented with progressive hoarseness while the other presented with respiratory distress secondary to an obstructed airway that necessitated an emergency tracheotomy. On the other hand, both cases reflect how systemic symptomatology such as loss of weight and night sweats is rather uncommon.[1,2,5] The literature suggests that most reports of lymphoma involving the larynx report limited stage disease.[5,6] The first presenting case gave a history of a short duration of foreign body sensation, which turned out to be laryngeal lymphoma. Contradictory to its deceiving benign-looking appearance, the final histology examination confirmed the diagnosis of haematological malignancy. The laryngeal mass in the second case, however, appeared fungating in a cauliflower-like cluster, implicating a possible malignant pathology. Various macroscopic features of the tumour have been described in the English-language scientific literature. These include a smooth submucosal mass, papillomatous lesion, and laryngeal ulcer.[1-3] Therefore, laryngeal appearance may not serve as an ideal diagnostic indicator in laryngeal lymphoma.

Histopathological examination remains the gold standard to diagnose a primary laryngeal lymphoma.[5] A generous and deep biopsy should be undertaken as the lesion is originated from the submucosa layer.[1] Imaging modalities remain imperative in delineating its regional infiltration as well as distant metastasis. The radiological features of a laryngeal lymphoma include the presence of a homogenous mass, which enhances with contrast during CT.[4,6] Magnetic resonance imaging (MRI) may aid the diagnosis of a submucosal mass.[6] PET/CT is invaluable in the diagnosis, staging, and assessing the response to therapy in laryngeal lymphoma, especially in high grade lymphomas.[7] The management of lymphoma is largely dictated by the histopathology, rather than the anatomic location. Due to the limited number of reported cases, there is no definite consensus in the treatment of laryngeal lymphoma. However, radiotherapy or in combination with chemotherapy appears to be the emerging preferred modality of treatment.[1,2,5,6] The role of surgical intervention is merely for diagnostic purpose and airway security in the event of impending airway obstruction.[3]

## Conclusion

Despite its rare occurrence, primary laryngeal lymphoma should be contemplated when generating a differential diagnosis of a laryngeal mass. A high clinical suspicion index amongst physicians is imperative as overlooking this entity may result in catastrophic consequences.

## References

1. Azzopardi CP, Degaetano J, Betts A, et al. Laryngeal lymphoma: the high and low grades of rare lymphoma involvement sites. Case Rep Med. 2014;1-4. doi: 10.1155/2014/284643.
2. Word R, Urquhart AC, Ejercito VS. Primary laryngeal lymphoma: case report. Ear Nose Throat J. 2006 Feb;85(2):109-11.
3. Izadi F, Parvas E, Derakhshandeh V. Lymphoma of larynx presented with hoarseness: case report. Med J Islam Repub Iran. 2014;28(21):1-3.
4. Siddiqui NA, Branstetter BF, Hamilton BE, et al. Imaging characteristics of primary laryngeal lymphoma. AJNR Am J Neuroradiol. 2010 Aug;31(7):1261-5. doi: 10.3174/ajnr.A2085.
5. Khamassi K, Mahfoudhi M, Jaafoura H, et al. Primary lymphoma of the larynx: a case report and literature review. Open J Clin Diagn. 2015 Jun;5(2):81-5.
6. Junior NT, Zago TM, Pauna HF, et al. Non-Hodgkin lymphoma in supraglottis: case report. Otolaryngol (Sunnyvale). 2017;7(1):285. doi: 10.4172/2161-119X.1000285.
7. Zhou ML, Zhao K, Zhou SH, et al. Role of PET/CT in the diagnosis, staging, and follow-up of a nasal type natural killer T-cell lymphoma in the larynx: a case report and literature review. Int J Clin Exp Med. 2014 Nov;7(11):4483-91.