

Imaging Characteristics of Primary Non-Hodgkin's Lymphoma of The Larynx

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Abstract

Purpose

This study aimed to report the computed tomography (CT) and magnetic resonance imaging (MRI) characteristics of primary Non-Hodgkin's Lymphoma (NHL) of the larynx.

Materials and methods

The radiographic examinations of five patients (2 men, 3 women; median age, 68 years) with histopathologically proven NHL of the larynx were retrospectively reviewed. CT and MRI images were analyzed qualitatively (Tumor distribution, Local tumor invasion, Tumor appearance, Cervical lymphadenopathy of NHL).

Results

CT and MRI images showed no obvious signs of vascular and laryngeal cartilage invasion. Three cases (1 MALT, 2 diffuse large B-cell lymphomas (DLBCL)) were centered in the supraglottic region involved the glottis (3/3) and subglottic (1/3). Two cases (MALT) were centered in the glottis involved the subglottic. The laryngeal tumors involved the true cords (5 cases), aryepiglottic folds (3 cases), ventricles and false cords (3 cases), anterior commissure (2 cases). On MRI (4 cases), all NHL presenting as homogeneous intermediate T1-weighted, heterogeneous slightly high T2-weighted mass with homogeneous moderate to evident enhancement. The mucosa with more obvious enhancement and smooth surface could be seen. On CT (1 plain and 3 contrast-enhanced), all tumors were homogeneous moderate density, and no necrosis or calcifications were seen. Lymphadenopathy was presented in two patients of DLBCL without necrosis.

Conclusions

On MRI or CT, when the laryngeal mass is located under the mucosa with uniform density or signal intensity, smooth surface, moderate to obvious homogeneous enhancement without cystic, necrosis, calcification and cartilage destruction, the radiologist should consider that it is likely to be NHL, especially when the mass spreads upwards to the oropharynx, nasopharynx and Webster's lymphoid ring. Further studies however are needed to confirm our findings obtained in a limited number of patients.

Introduction

Primary laryngeal non-Hodgkin's lymphoma (NHL) accounts for less than 1% of laryngeal malignant tumors, while more than 90% of laryngeal malignancies are squamous cell carcinoma [1]. Some cases of NHL of the larynx have been reported in the literature, but a few for the imaging characteristics. Improving

the diagnostic and evaluation accuracy of laryngeal NHL can effectively reduce unnecessary tracheotomy and help clinical doctors choosing appropriate treatment strategies, because lymphoma is mostly treated by radiotherapy and chemotherapy rather than surgery [2].

Our purpose is to provide and identify more imaging characteristics of NHL of the larynx through CT and MRI images of another five additional patients, so as to help to distinguish them from other laryngeal malignant tumors, and help clinicians to correctly diagnose this rare tumor and choose appropriate treatment in the early stage. In the end, it can help patients avoid unnecessary surgery and obtain more long-term benefits.

Materials And Methods

General information

The imaging data of five patients with NHL (two males, three females) proved by immunohistochemistry in our hospital from January 2010 to January 2020 were retrospectively reviewed. One case was consulted by UCLA. All patients signed informed consent before receiving imaging examination. The average age of these patients was 68 years old (range, 53–83 years). All 5 cases came to the hospital with hoarseness.

CT/MRI Examination and Parameters

Four cases underwent 64-row spiral CT scanning, and the axial image thickness was 1 mm. Coronal and sagittal images were reconstructed by multiplanar reconstruction (MPR). Contrast-enhanced CT imaging (three cases) was obtained after intravenous injection of contrast media at a dose of 1.0ml/kg.

All MR imaging (four patients) was performed on 1.5T or 3.0T unit to produce transverse T2-weighted sequences with fat suppression and T1-weighted sequences before enhancement. After injection of Gd-DTPA with a dose of 0.2mmol/kg, axial, coronal and sagittal enhanced T1-weighted images (thickness = 4mm) were obtained.

CT/MRI assessment

All images were analyzed by two experienced radiologists (with 8 years and 23 years of imaging diagnosis experience) working in consensus using a picture archiving and communication system (PACS) workstation. MR and CT images were assessed for distribution, appearance, local extension, and cervical lymphadenopathy. Besides, the clinical manifestations, histological features and prognosis were analyzed retrospectively also.

Results

Clinical Features and Pathological types

None of the patients had a history of HIV and EB virus infection and had no B symptoms (i.e. unexplained fever > 38 C; night sweating; weight loss > 10%). Two patients confirmed by pathology as MALT-lymphoma suffered from laryngeal obstruction (3 degrees [one case] and 2 degrees [one case]) and underwent emergency tracheotomy. The last one of the 3 cases of MALT-lymphoma involved not only the larynx but also the orbit. The other 2 cases were diffuse large B-cell lymphoma (DLBCL). Both cases of diffuse large B-cell lymphoma (DLBCL) were older than 80 years old (Table 1).

CT and MR Features

Tumor distribution. All the tumors were based in the submucosa and mucosa, One case of MALT-lymphoma showed no invasion of blood vessels and mucosal epithelium. In the remaining four patients, the blood vessels and mucosal epithelium was not specified on pathology reports. CT and MRI images showed no obvious signs of vascular invasion. Three cases, including one MALT-lymphoma, two diffuse large B-cell lymphomas (DLBCL), were centered in the supraglottic region but also involved the glottis (3/3) and subglottic (1/3). The other two cases of MALT-lymphoma were centered in the glottis but also involved the subglottic. In the five cases, all tumors invaded the true cords. Other involved location included the ventricles and false cords (three cases), aryepiglottic folds (three cases), and anterior commissure (two cases). Among them, all three cases of MALT-lymphoma grew across the midline (Fig. 1–3). No laryngeal vestibule was involved in all cases.

Local tumor invasion. NHL extended outside the larynx to involve the hypopharynx and oropharynx in one patient (Fig. 4), and the invasion sites included ipsilateral tonsils, pyriform fossa, posterior pharyngeal wall, epiglottic valley, paralaryngeal fat space and extralaryngeal muscles. In another case of lymphoma, multiple thyroid nodules were seen, while Color Doppler flow imaging (CDFI) demonstrated that blood flow signals were not abundant. Unfortunately, thyroid lesions have no pathological results. The pathological type of the above two cases were both diffuse large B-cell lymphoma (DLBCL). A case of laryngeal MALT-lymphoma accompanied with concomitant Wechsler's ring and ocular MALT-lymphoma also. It is noteworthy that no obvious invasion or destruction of laryngeal cartilage was observed in all cases.

Tumor appearance. Four contrast-enhanced MR imaging, one plain CT and three contrast-enhanced CT studies were reviewed. MR imaging demonstrated homogeneous moderate signal intensity on T1WI, heterogeneous slightly high signal intensity on fat suppressed T2WI, with homogeneous moderate to evident contrast enhancement characteristics. In addition, the surface mucosa with more obvious enhancement and smooth surface could be seen (Fig. 1). CT images revealed that all tumors were homogeneous moderate density similar to muscle tissue, with moderate to obvious contrast enhancement. In all cases, the enhancement degree of MALT-lymphoma centered in subglottic region was more obvious in two cases. CT examination showed no clear signs of calcification and necrosis.

Cervical lymphadenopathy. Lymphadenopathy was present in two patients of diffuse large B-cell lymphoma (DLBCL). Diffuse large B-cell lymphoma (DLBCL) had bilateral lymphadenopathy, one

involved from level II to IV zone, the other one involved from level II to VII zone, without obvious necrosis. In the remaining three cases of MALT-lymphoma, small lymph nodes were found on both sides of the neck, but the short diameter was less than 8 mm.

Table 1
Clinical data

Case (No.)	Age(y) /Sex	Clinical Symptoms	Pathology	Treatment	Outcome
1	53/F	Hoarse voice; Laryngeal obstruction 3°	MALT	Tracheotomy Radiation	Disease-free at 24 months
2	80/M	Hoarse voice	DLBCL	Refuse treatment	
3	83/F	Hoarse voice	DLBCL	Operation	Recurrence occurred 9 months later
4	74/F	Hoarse voice; Laryngeal obstruction 2°	MALT	Operation	Lost to follow-up
5	53/M	Hoarse voice	MALT	Chemo-radiation	Disease-free at 12 months
F: female; M: male; DLBCL: diffuse large B-cell lymphoma; MALT: mucosa-associated lymphoid tissue					

Pathologic Findings

Discussion

Lymphomas are a heterogeneous group of malignant tumors which are mainly composed of two major categories: Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL). The subtypes of lymphoma can be divided into B-cell lymphomas, T-cell and natural killer-cell lymphomas (T/NK-NHL) and HL based on the cell of origin [3–5]. MALT-lymphoma and diffuse large B-cell lymphoma (DLBCL) mentioned in this paper are subtypes of non-Hodgkin lymphoma (NHL) stemming from marginal zone B-cells. Approximately 30% of NHLs show heterogeneous extra-nodal manifestations. Besides the gastrointestinal tract, head and neck is the second most frequently involved extranodal site in NHL. NHL of the head and neck mostly occurs within the Waldeyer' ring, paranasal sinuses, salivary glands, thyroid gland and orbit. The larynx is a very rare site for NHL, and its incidence rate is less than 1% in all laryngeal tumors [6, 7]. The diffuse large B-cell lymphoma (DLBCL) and the MALT-lymphoma are the most common primary tumors of larynx originating from hematopoietic system [8, 9].

The presenting symptoms and signs of laryngeal lymphoma varied from site to site. The most common symptom was hoarseness (70.2%), followed by throat pain (26.3%), dyspnea (17.5%), and dysphagia (17.5%). B-symptoms (including night sweats, weight loss and fever) were rare (14.0%) [1]. In this study, all patients developed hoarseness without B symptoms. Indirect laryngoscopy often shows a polypoid submucosal mass without ulcer or other particular diagnostic characteristics. Two-thirds of the tumors tend to invade supraglottic regions, especially the epiglottis and aryepiglottic folds [10]. This is because the lesions mostly originate from the mucosa associated follicular lymphoid tissue in the lamina propria of the supraglottic region. NHL is speculated to originate from two parts of the larynx: 1) the special lymphoid tissue aggregates in submucosa, mainly B-cell line, or 2) mucosa-associated lymphoid tissues (MALT), mainly originated from the epiglottis and aryepiglottic folds [11].

Laryngeal lymphoma is usually characterized by submucosal mass in the supraglottic region, resulting in narrowing of the laryngeal cavity. The lesions may involve the glottic and subglottic areas downward, and the pharyngeal lymph ring may also be involved upward. In our series of study, imaging findings revealed that all the patients with laryngeal diffuse large B-cell lymphoma (DLBCL) had supraglottic and glottis involvement. The tumor most involved the false cords, aryepiglottic folds and true cords. In our other three cases of MALT-lymphoma, two cases were centered in the subglottic, involving the glottic region, resulting in laryngeal obstruction. One case was centered in the supraglottic region and involved the glottic region at the same time. This is not consistent with the imaging findings previously reported by Takayama et al and King et al that laryngeal lymphoma rarely originated from subglottic region [10, 12]. It may be because there were too few MALT-lymphomas in their cases of study. It was not surprising that NHL of larynx were not restricted to the glottis in our cases, because lymphatic vessels were very scarce in the true vocal cords. As showed in our cases of study, glottic tumors were often secondary to the spread of tumor tissues in adjacent areas. Among the seven reported cases of B-cell lymphomas causing laryngeal stenosis, five cases were MALT-lymphoma located in the subglottic region [13–19]. This is consistent with the results of our study, which may indicate that most of the NHL located in the subglottic region and causing laryngeal stenosis are MALT-lymphoma.

Compared with the pathological classification and image morphological characteristics, diffuse large B-cell lymphoma (DLBCL) and MALT-lymphoma showed mass formation at corresponding sites. One case of diffuse large B-cell lymphoma (DLBCL) extended to the hypopharynx, and one case of MALT-lymphoma had the same type of lesions in the orbit, and this extensive involvement should raise the suspicion of lymphoma. Because of its submucosal origin, the surface of the lesions is mostly smooth [7, 12, 20]. In all of our enhanced MRI images, the smooth surface of the tumor was observed with more obvious linear enhancement of the mucosa. On CT plain scan, the lesions showed homogeneous and medium density similar to muscle tissue, and moderate homogeneous enhancement was found on contrast-enhanced scan. No obvious cystic degeneration, necrosis, calcification and cartilage destruction were the typical features. The results showed that the high signal intensity of laryngeal NHL on T1WI was homogeneous or slightly lower than that of muscle, while on T2WI it was inhomogeneous and slightly hyperintense. The mucosal layer with high signal intensity on enhanced T1WI was clearly displayed and continuously smoothed, indicating that the lesion originated from submucosa [10]. In this study, diffuse

large B-cell lymphoma (DLBCL) was more prone to have cervical lymphadenopathy than MALT-lymphoma. The density, signal intensity and enhancement of the enlarged lymph nodes were consistent with those of the primary lesions, which were also confirmed in the literatures of NHL in other parts of the head and neck [20, 21].

The imaging findings of laryngeal NHL are easy to be confused with other laryngeal lesions. Due to the lack of research on imaging manifestations of this disease, all the above five cases were misdiagnosed as squamous cell carcinoma at the initial diagnosis, and the diagnostic coincidence rate was low. Laryngeal squamous cell carcinoma (LSCC) originated from the mucous layer. The surface of the lesion was not smooth. It showed uneven moderate or significant enhancement on enhanced scan. It was easy to invade laryngeal cartilage. The primary lesion and enlarged lymph nodes were mostly accompanied with necrosis and showed ring enhancement [22]. Besides lymphoma and squamous cell carcinoma, it is also necessary to differentiate them from other laryngeal masses located in the mucosal or submucosal with homogeneous enhancement [12]. Neuroendocrine tumor-atypical carcinoid, paraganglioma, schwannoma, adenoid cystic carcinoma and other minor salivary tumors, sarcoma, tuberculoma, tumor-like lesions (Brown tumor and inflammatory myofibroblastic tumor), and inflammatory lesions should all be considered [23].

With the progress of MRI technology, DWI, ADC and dynamic contrast-enhanced MRI (DCE-MRI) are more and more used in the diagnosis and differential diagnosis of head and neck lymphoma [24, 25]. Based on the principle of different attenuation coefficient of the same material under different X-ray energy, Dual-Energy CT (DECT) collect data at the same time with high and low energy scanning scheme, and obtains iodine based image, water-based image, energy spectrum curve and virtual plain scan image by post-processing methods such as material separation and reconstruction technology. In addition, the parameters such as iodine concentration, overlay value and slope of energy spectrum curve obtained can provide additional information for disease identification. Seidler et al. has shown that machine learning assisted-DECT texture analysis can distinguish metastatic lymph nodes of head and neck squamous cell carcinoma from lymphoma, normal lymph nodes, or inflammatory [26]. Perhaps these techniques may be helpful in differentiating NHL from other laryngeal lesions.

Conclusion

Although NHL of the larynx is rare, there are certain imaging characteristics that should suggest it. When the lesions occur under the mucosa, the density and signal are uniform, the surface is smooth, and the enhanced scan shows moderate homogeneous enhancement without cystic change, necrosis, calcification and cartilage destruction, the probability of diagnosis of NHL should be increased, especially when it spreads upward to the oropharynx, nasopharynx and Webster's lymphoid ring. However, Further studies are needed to confirm our findings obtained in a limited number of patients.

Declarations

Ethics approval and consent to participate

This study has passed the ethical review of the human body research ethics committee of the Second Affiliated Hospital of Zhejiang University School of Medicine.

Consent for publication

Not applicable

Availability of data and materials

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

Pingding Kuang, Qiaoling Ding, Zijian Wang analyzed and interpreted the patients' images, Xinyi Chen consulted relevant materials, and was a major contributor in writing the manuscript. All authors read and approved the final manuscript. Biao Jiang is the corresponding author.

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Figures

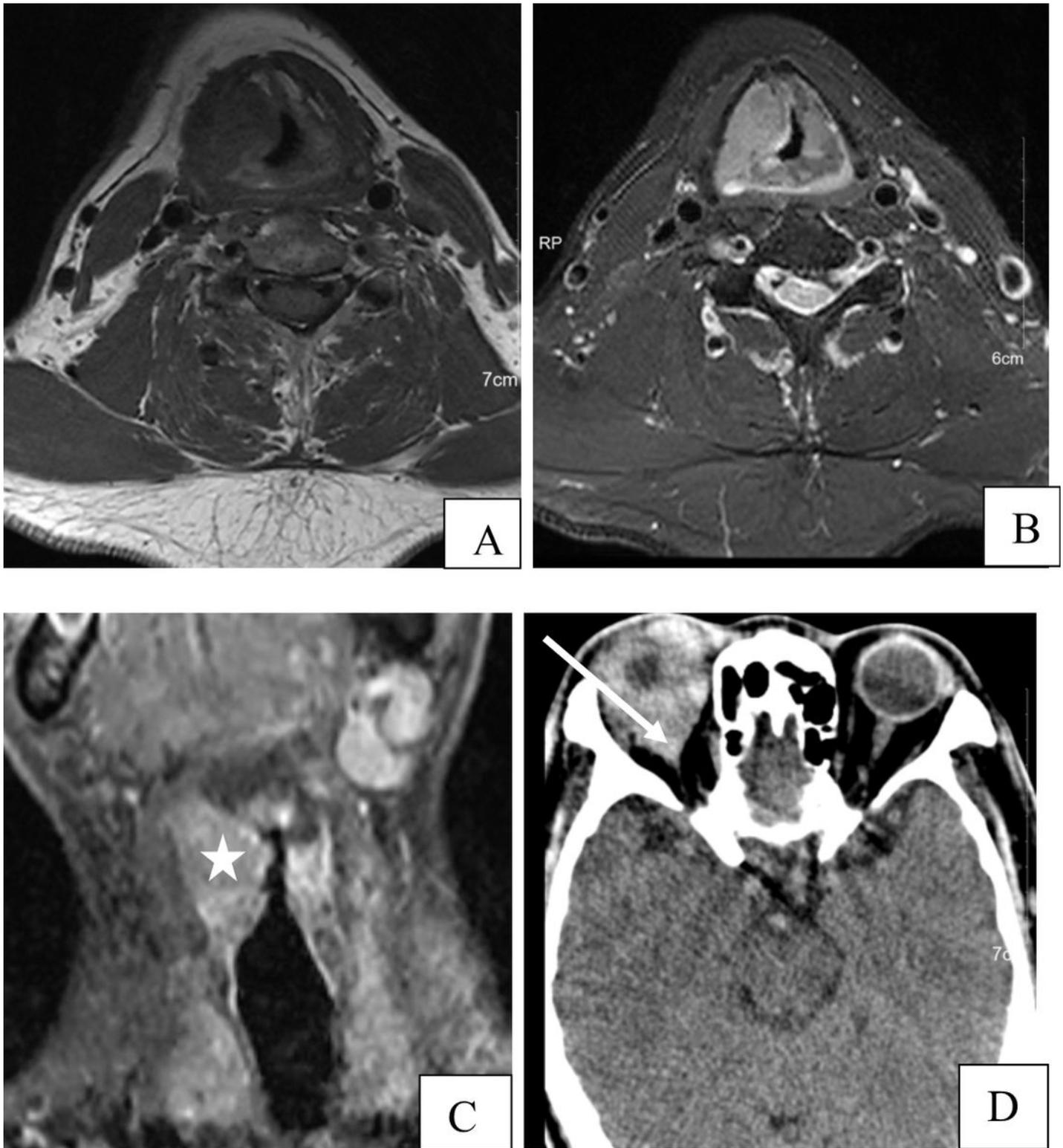


Figure 1

A 53-year-old man with laryngeal MALT-lymphoma. A, Mass shows intermediate signal intensities on both T1WI and B, Fat-saturated T2WI with smooth surface mucosa. C, Enhanced coronal T1-weighted MR image demonstrated obvious enhancement of the supraglottic lesion (asterisk), especially in the surrounding mucosa. D, Plan CT shows lesion of the same histopathological type in the right orbit (white arrow).

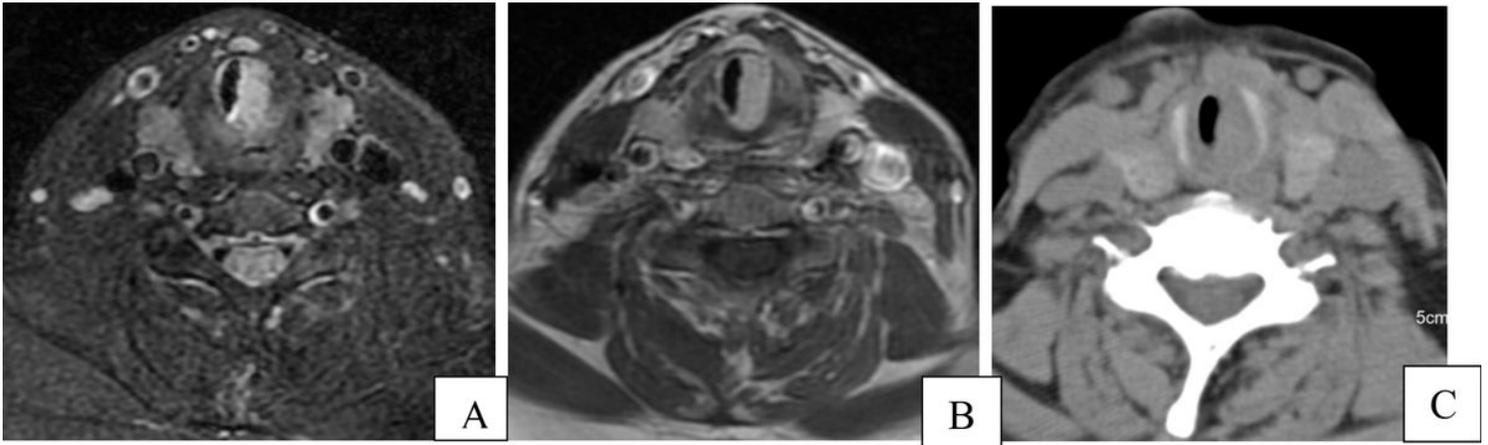


Figure 2

A 53-year-old woman with laryngeal MALT-lymphoma. A, The lesion locate in the subglottic region with heterogeneous slightly high signal intensity on fat-saturated T2WI image, growing across the midline and B, homogeneous moderate to evident contrast enhancement characteristics. C, CT image shows that tumor with smooth surface and homogeneous moderate density similar to muscle tissue.

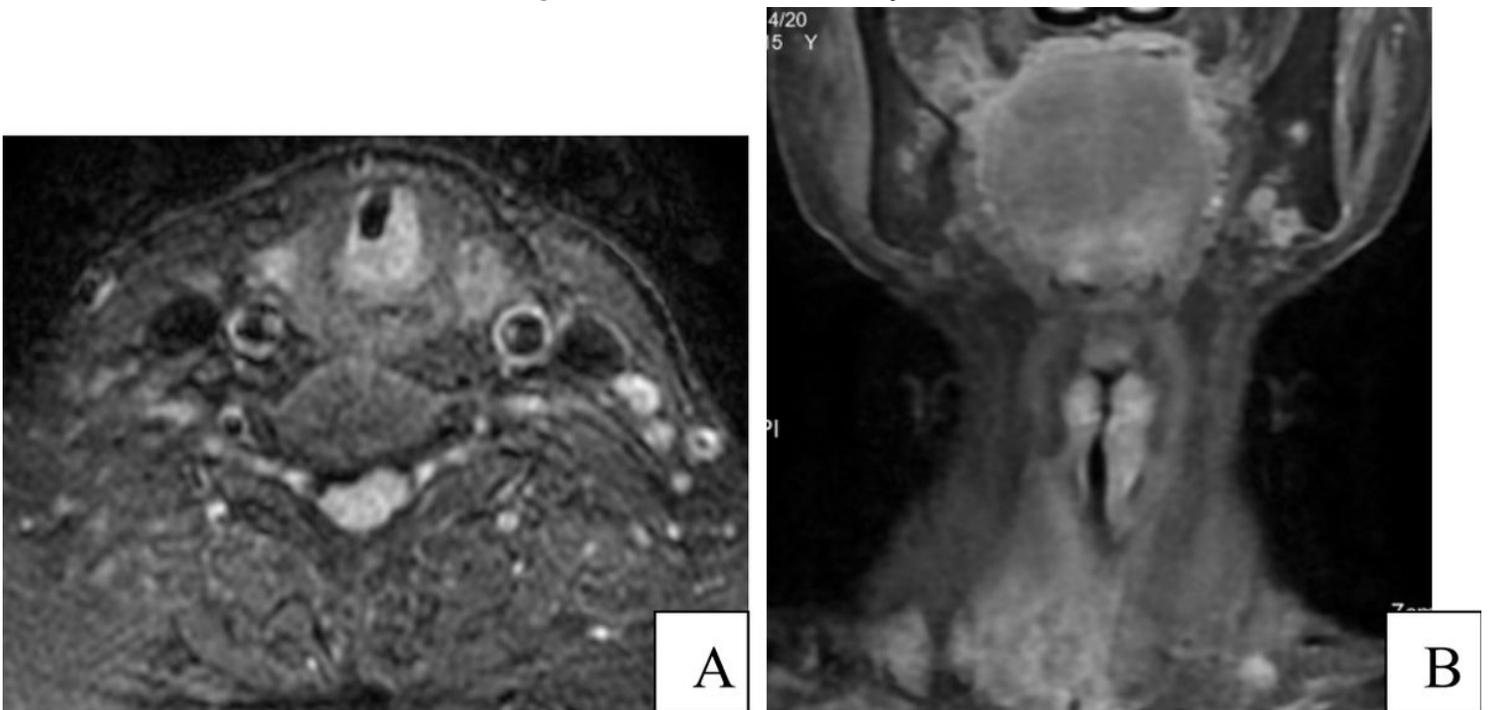


Figure 3

A 74-year-old woman with laryngeal MALT-lymphoma. A, Fat-saturated T2WI image demonstrates a subglottic laryngeal tumor. B, Enhanced coronal T1-weighted MR image demonstrates that the mass was uniformly enhanced and extended to the glottic region, resulting in significant airway stenosis.

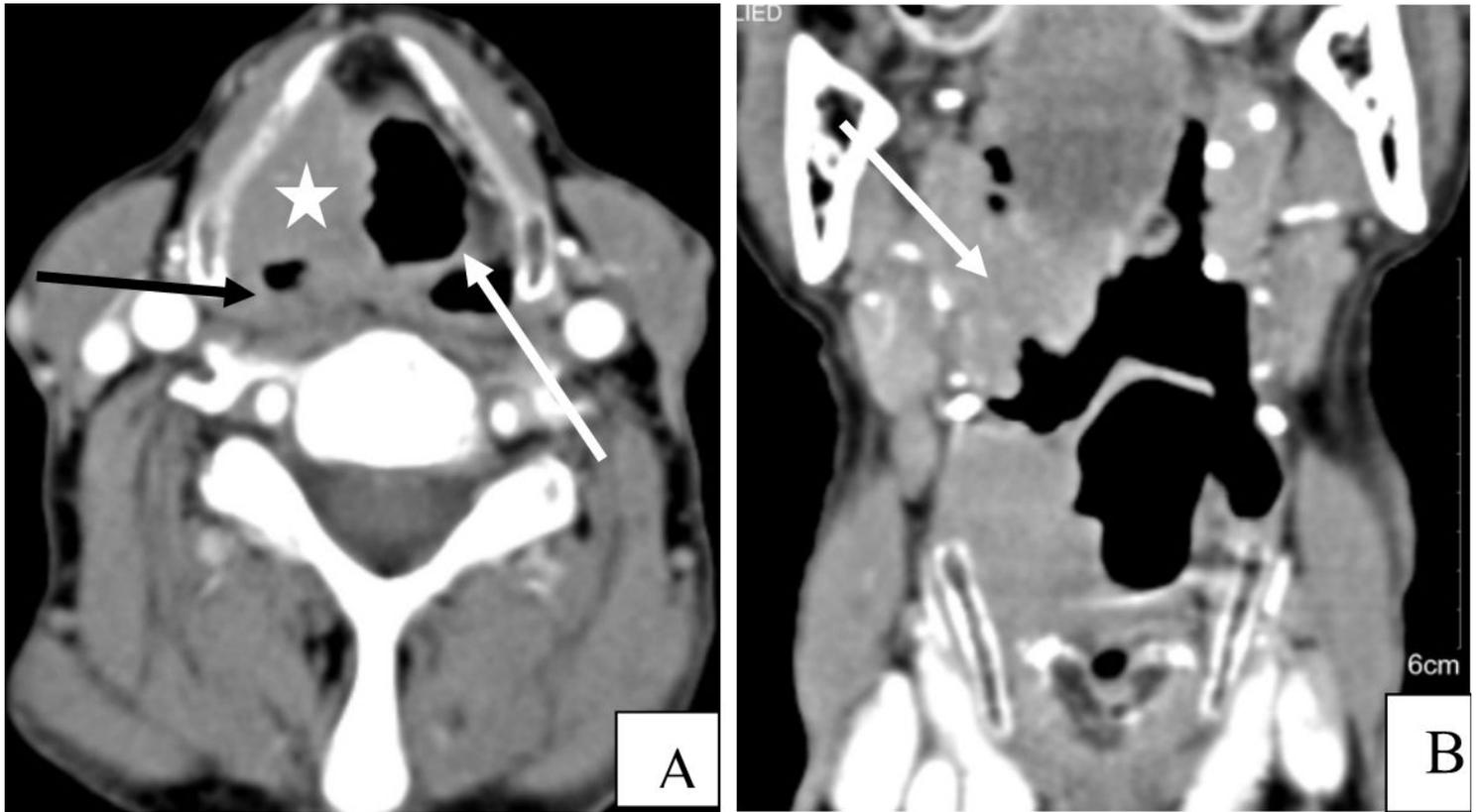


Figure 4

An 80-year-old man with diffuse large B-cell lymphoma of the larynx. A, Axial CT scan shows moderate uniform enhancement mass (asterisk) in the right supraglottic region, involving the right aryepiglottic fold, the right piriform fossa (black arrow), the right false vocal cord and the true vocal cord, infiltrating into the subglottic area. The normal shape of the right aryepiglottic fold is not visible, while the normal configuration of the left aryepiglottic fold remained (white arrow). B, Enhanced coronal T1-weighted MR image demonstrates the supraglottic mass (asterisk) extending to the oropharynx (white arrow).