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Mucosa-Associated Lymphoid Tissue Lymphoma of the Larynx

A Case Report and Literature Review

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Abstract: The clinicopathological characteristics and rational treatment of primary laryngeal mucosa-associated lymphoid tissue (MALT) lymphoma are still unclear and need to be further defined due to the paucity of this separate lymphoma.

Herein, a supraglottic primary MALT lymphoma was described with detailed clinical course, intervention, and follow-up. To date, research of laryngeal MALT lymphoma has seldom been initiated. Our experience in this case will help to expand our understanding of this unique disease. A 58-year-old female presented with a history of progressive hoarseness for about 10 months. Multiple laryngoscopy examinations revealed severe hypertrophy of left ventricular band. She was admitted to our department with residual MALT lymphoma of supraglottic region after partial resection by laser. After systemic evaluation, she was staged as IEA, International Prognostic Index score 0. Irradiation of intensity modulated radiotherapy technique with a dose of 30.6 Gy/17f to the tumor and 25.5 Gy/17f to the related lymphatic drainage area achieved a complete remission. The disease-free survival has reached to 4 years. The irradiation related acute and late side effects were mild.

Radiotherapy is the first option for limited-stage primary laryngeal MALT lymphoma because of excellent treatment outcome.

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Abbreviations: CHOP = cyclophosphamide, doxorubicin, vincristine, prednisone, CR = complete remission, CT = computed tomography, DFS = disease-free survival, 18F-FDG = 18F-fluorodeoxyglucose, MALT = mucosa-associated lymphoid tissue, NHL = non-Hodgkin lymphoma, PET = positron emission tomography.

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INTRODUCTION

Primary laryngeal mucosa-associated lymphoid tissue (MALT) lymphoma is extremely rare.[1] Given the paucity, little consensus about its clinicopathological features and optimal therapeutic intervention has been established. Here, we present a rare case of supraglottic MALT lymphoma in which radiotherapy alone contributed excellent local control and the patient attained a disease-free survival (DFS) of 4 years. Additionally, related literature was reviewed. Our study helps to expand our understanding of this distinct entity.

METHOD

This was a case report. Ethics committee or institutional review board approval was not obtained. It was not necessary for the case report. The patient signed informed consent for the publication of this case report.

CASE REPORT

A 58-year-old Chinese female who was a retired doctor presented in October 2010 with a history of progressive hoarseness for about 10 months. The patient did not suffer from fever, night sweat, or weight loss. Multiple laryngoscopy examinations in other hospitals revealed severe hypertrophy of left ventricular band. As Figure 1 showed, the left ventricular band and laryngeal ventricle bulged with smooth surface, covering most of the left vocal cord. Her past history was remarkable for rheumatoid arthritis and Sjogren syndrome for many years. Her family and psychosocial history was unremarkable. Partial resection of tumor by laser in another hospital was performed and hoarseness relieved significantly. The postoperative pathology demonstrated neoplastic cells invaded adjacent epithelial cells, forming lymphoepithelial lesion (Figure 2). The immunohistochemical results showed CD3 and CD20 (focally+), κ(diffusely +), λ(−), Ki-67(5−10%). Therefore, the patient was diagnosed as non-Hodgkin MALT marginal zone B-cell lymphoma.

On physical examination, no enlarged superficial lymph nodes were palpated. Laboratory investigations showed a normal complete blood cell count and a generally normal serum biochemical profile. Lactate dehydrogenase was normal. β-2 Microglobulin was 2.47 mg/L (0.7−1.8 mg/L). Erythrocyte sedimentation rate was 41 mm/h (10−20 mm/h). The subsequent thoracic computed tomography (CT) and ultrasound for bilateral neck, armpit, and groin did not reveal any enlarged lymph node. Gastroscopy showed chronic nonatrophic gastritis. The bone marrow aspiration did not find neoplastic involvement. Thus, an MALT lymphoma of larynx, Ann Arbor stage IEA, International Prognostic Index score 0, was diagnosed.

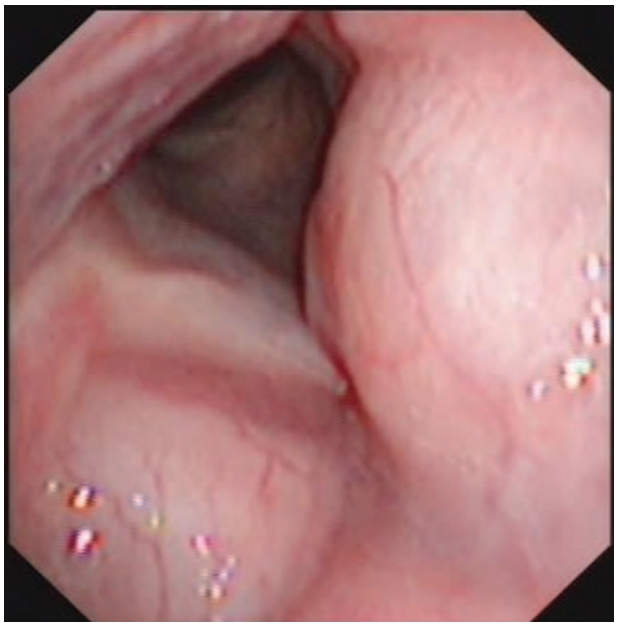

FIGURE 1. Preoperative laryngoscopy demonstrated that the left ventricular band and laryngeal ventricle bulged with smooth surface, covering most of the left vocal cord.

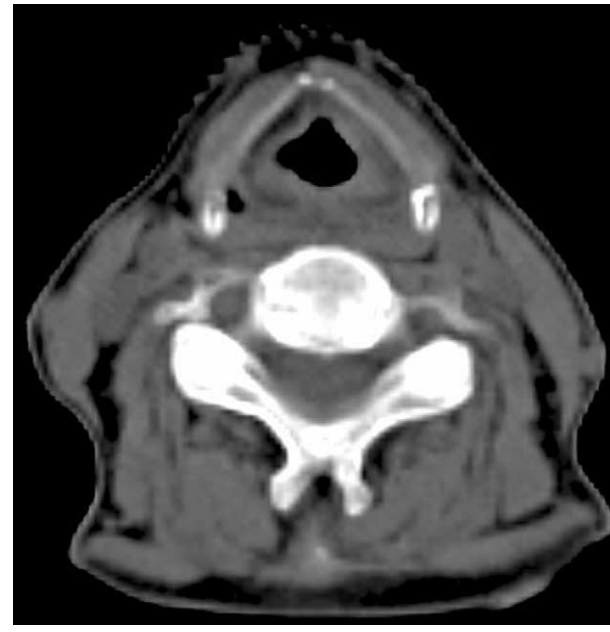

FIGURE 3. The throat CT before radiotherapy revealed the front part of left ventricular band was more hypertrophy than its right counterpart.

One month after surgery, the patient was admitted to our department. Laryngoscopy demonstrated that there was a red mucosa uplift in the left ventricular band, and bilateral vocal cords were normal. The throat CT scan also revealed the front part of left ventricular band was more hypertrophy than its right counterpart (Figure 3). All these findings were consistent with residual tumor. Then irradiation of 7-field intensity modulated radiotherapy technique with a dose of 30.6 Gy/17f to the tumor and 25.5 Gy/17f to the related lymphatic drainage area was carried out. The side effects were mild. The repeated laryngoscopy when she finished radiotherapy showed the tumor disappeared. Radiotherapy alone achieved a complete remission (CR) response. Until now, her condition remains stable and the DFS has reached to 4 years.

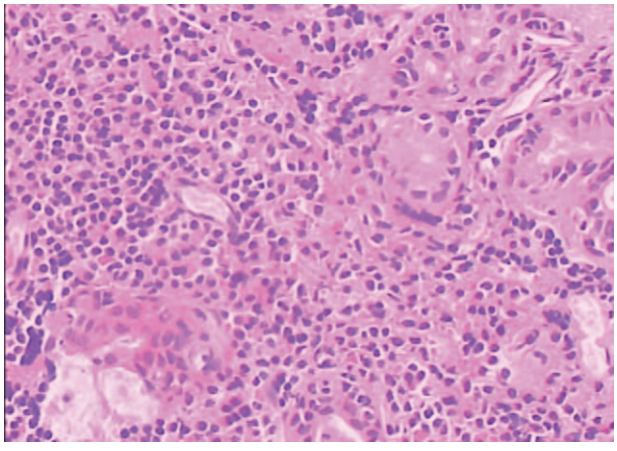

FIGURE 2. The postoperative pathology demonstrated neoplastic cells invaded adjacent epithelial cells, forming lymphoepithelial lesion.

DISCUSSION

Extranodal MALT lymphoma is a rare entity composing about 5% of all the non-Hodgkin lymphomas (NHL). The most common site is gastric. For non-gastric extranodal MALT lymphoma, the sites of involvement include small intestine, parotid gland, lung, ocular adnexa, skin, thyroid, and mammary gland.[2] Primary MALT lymphoma of larynx is exceedingly rare. Since Diebold et al[3] first described such a unique disease in 1990, only 43 cases have been documented to date.[1] The most common presentation is hoarseness and dysphagia.[4] Some patients also suffer from chronic cough unresponsive to oral corticosteroid.[5] Most cases occur in the supraglottic region, subglottic MALT has also been reported.[6] Endoscopic examination usually shows a neoplasm with a smooth surface.[1] Typical imaging characteristics include large uniformly enhanced lesion without central necrosis and cervical lymphadenopathy.[7]

With respect to the pathogenesis, chronic immune simulation by bacteria or autoimmune irritants is viewed as related to MALT lymphoma. MALT lymphoma patients usually have autoimmune disorders or infection of *Helicobacter pylori* and *Chlamydia psittaci*.[8] According to the research by Wöhrer et al,[9] 39% non-gastric MALT lymphoma was associated with an underlying autoimmune disease. Similarly, our patient suffered from a variety of autoimmune diseases, rheumatoid arthritis, and Sjogren syndrome. MALT lymphoma is low-grade malignancy, which can transform to high-grade diffuse large B cell lymphoma.[10] Additionally, MALT lymphoma of the larynx can also coexist with squamous carcinoma.[11] Immunohistochemistry

plays an important role in the accurate diagnosis of MALT lymphoma.

Accurate staging is a prerequisite for rational therapy. Positron emission tomography (PET)-CT has been widely applied in the staging, response evaluation, and surveillance of NHL. However, the value of PET-CT for MALT lymphoma has not been identified yet for its low-grade malignancy. Seven cases of laryngeal MALT lymphoma demonstrated 18F-fluorodeoxyglucose (18F-FDG) avidity.[7,12–14] Despite usually localized behavior, about 7% laryngeal MALT lymphoma showed aggressive process.[1]

Due to the paucity, there has been no retrospective research of primary laryngeal MALT lymphoma yet. Treatment options have to be based on the research results of all the extranodal MALT lymphomas whose original sites distribute at stomach, thyroid, parotid gland, and so on and case reports of primary laryngeal MALT lymphoma. For localized extranodal MALT lymphomas, moderate dose (25–30 Gy [15,16], 30.6–39.6 Gy[17]) radiotherapy is highly effective in local control and long-term outcome. Despite the fact that combined radiotherapy and chemotherapy is more perspective in killing tumor cells, the addition of adjuvant chemotherapy failed to show any benefit of DFS and overall survival in early-staged cases.[18] High radiosensitivity of primary laryngeal MALT lymphoma contributed to excellent outcome of radiotherapy alone. Case reports of primary laryngeal MALT lymphoma also verified that moderate dose radiotherapy could achieve CR response.[13,19–22] This is also proved by our case. However, in some cases, dissemination to other sites can be observed after radiotherapy which emphasizes the imperative of careful follow-up.[21] Additionally, in some cases, chemotherapy also attained CR response.[23–25] However, reports by Zhao et al[12] and Kato et al[21] revealed that the primary treatment of CHOP (cyclophosphamide, doxorubicin, vincristine, and prednisone) chemotherapy was ineffective and switch to radiotherapy contributed to CR response and long-term DFS. This different response to chemotherapy manifested tumor heterogeneity of primary laryngeal MALT lymphoma. Wenzel et al[26] pointed out that aberrant CD5 expression in MALT lymphoma was associated with a more aggressive biological behavior. Furthermore, different expression level of Bcl-2 in lymphoma influenced DNA repair following radiotherapy.[27] In light of the uncertainty of many aspects of primary laryngeal MALT lymphoma, case reports are useful for us to understand more about such a unique entity. Surgery is often done for diagnostic purpose or tracheostomy is performed to relieve dyspnea. For disseminated or recurrent cases, chemotherapy is typically carried out.[19] In IV patients, R-CVP strategy (rituximab, cyclophosphamide, vincristine, and prednisolone) could achieve CR response.[1] Rituximab, anti-CD20 monoclonal antibody, exerted an approximately 70% response rate in marginal zone lymphoma.[8]

CONCLUSION

We presented a rare case of primary laryngeal MALT lymphoma in which radiotherapy alone contributed to favorable local control with mild side effects. To date, DFS has reached to 4 years. Radiotherapy should be recommended for early-staged patients of primary laryngeal MALT lymphoma.

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