Received: 8 July 2022 | Revised: 8 August 2022 | Accepted: 11 August 2022

DOI: 10.1002/ccr3.6293

CASE REPORT

Clinical Case Reports Open Access WILEY

MALT lymphoma of the sublingual gland: A case report with current overview of diagnostic and therapeutic strategies

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Abstract

Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT) is a low-grade B-cell lymphoma. MALT lymphomas involving the sublingual gland are extremely rare. Herein, we report a case of MALT lymphoma of the sublingual gland. Additionally, we discuss challenging diagnostic aspects as well as current treatment strategies.

KEYWORDS

extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue, flow cytometry, malignant lymphoma, non-Hodgkin lymphoma, salivary gland

1 | INTRODUCTION

Extranodal marginal zone lymphoma (MZL) of mucosa-associated lymphoid tissue (MALT), a subtype of MZL, is a low-grade B-cell lymphoma accounting for 5%–8% of all B-cell lymphomas and may invade various extranodal sites.[1] The stomach is the most common organ involved in MALT lymphoma and is primarily associated with *Helicobacter pylori* infection. Additional significant etiological factors include autoimmune diseases, such as Sjögren's syndrome and Hashimoto thyroiditis.[2] The salivary gland is the typical site of head and neck involvement.[3] While the parotid gland is primarily associated with salivary gland MALT lymphomas, the involvement of the sublingual gland is quite rare.[4] Moreover, even in the oral and maxillofacial lesions, MALT lymphoma of the sublingual gland is uncommon.

This report presents a rare case of MALT lymphoma involving the sublingual gland, diagnosed in an older male patient without a medical history of autoimmune disease. Most tumors that arise in the sublingual gland are malignant,[5] and the management of these tumors differs greatly from that of lymphomas. This raises many challenges for physicians not only in the diagnosis of MALT lymphomas but also in the treatment decision. The purpose of this case report is to shed light on the rare occurrence of lymphomas in the sublingual gland and enlighten the readers regarding appropriate diagnostic and therapeutic strategies.

2 | CASE REPORT

An 81-year-old Japanese man presented to the Oral and Maxillofacial Surgery Clinic of Aichi Gakuin University with the chief complaint of swelling in the floor of the mouth for 3 weeks. He did not have a medical history and was not under any medication. On examination, firm and painless enlargement of the right sublingual gland was noted (Figure 1). There was no enlargement of the parotid and submandibular glands or cervical lymph adenopathy. Computed tomography (CT) scan showed a tumor-like image on the right side of the floor of the mouth. Additionally, magnetic resonance imaging revealed a 25 mm × 15 mm × 18 mm mass in the right sublingual gland (Figure 2). Sublingual gland tumor was tentatively diagnosed, and malignant lymphoma was suspected after examining an incisional biopsy specimen taken from the mass. Subsequently, surgical removal of the right sublingual gland and surrounding tissue was performed as an initial treatment, and a definitive diagnosis was obtained (Figure 3). Histopathological evaluation showed that no lymphoepithelial lesions were seen in the surgical specimen but there was infiltration of intermediate to small lymphoid cells between lymph follicles, which was compatible with low-grade B-cell lymphoma of the MALT type (Figure 4). Immunohistochemical patterns were as follows: CD20+, CD3-, CD5-, CD10-, BCL2+, CCDN1-, and EBER-ISH-. The patient was referred to the hematology department for further work-up and treatment. Positron emission tomography (PET)-CT scan showed no evidence of tumor (Figure 5). According to the Ann Arbor staging system, the tumor was considered to be a stage IE MALT-type lymphoma. Additional treatment was not planned by the hematology department. The patient has been tumor-free for more than 5 years after the surgical treatment.

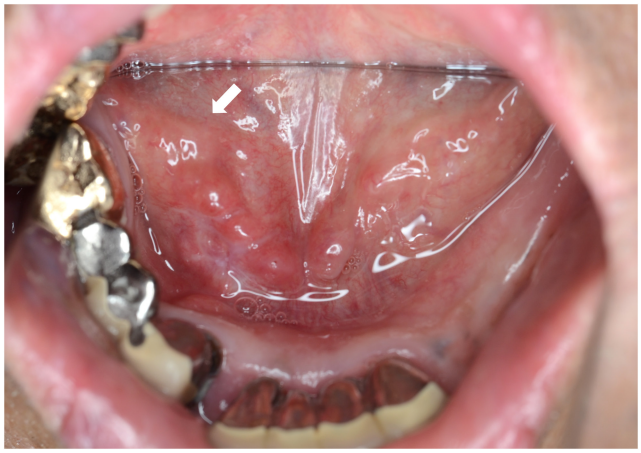

FIGURE 1 Preoperative intraoral view showing a mass (arrow) on the floor of the mouth (mirror image)

3 | DISCUSSION

Although salivary tissues do not contain lymphocytes under normal circumstances, they can acquire lymphocytes during inflammation. MALT lymphoma is commonly associated with preexisting autoimmune diseases, such as Sjögren's syndrome, or with chronic immune stimulation of the salivary gland, which accounts for 52% of MALT lymphomas in the maxillofacial region.[6,7] Several genetic abnormalities that result in the amplification of NF-κB and NOTCH signaling have been recently reported as possible causes.[8,9] For instance, frequently

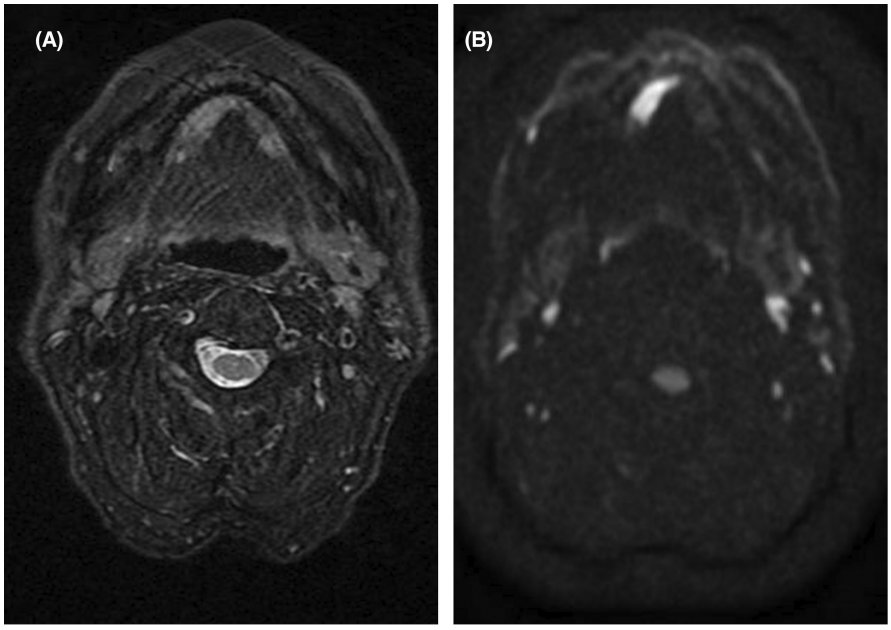

FIGURE 2 Preoperative images. Mass lesion detection in the right sublingual gland on MRI. The lesion shows higher intensity on T2-weighted imaging (A) and STIR (B) in comparison with that in the left sublingual gland

occurring translocations, such as t(11;18)(q21;q21), t(14;18)(q32;q21), and t(1;14)(p22;q32), which deregulate MALT1, BCL10, and BIRC3 have been reported to activate NF-κB signaling.[10] Additionally, a recent study identified that 16% of MALT lymphomas of the salivary gland had recurrent somatic mutations in the G-protein-coupled receptor 34 (GPR34), showing a relationship between immune receptor signaling and mutations, which might contribute toward the pathogenesis of the disease.[11] Although genetic analysis of the current case was not performed, the patient was not associated with immunological diseases and had no significant medical history. Therefore, the etiology of this case could not be specified.

In the present case, the histological type of the malignant lymphoma was not identified at the time of incisional biopsy. The histological type of malignant lymphomas cannot be clarified without a sufficiently large specimen of high quality. Therefore, we performed excisional biopsy as the initial treatment and confirmed the diagnosis.

MALT lymphomas gradually progress from the primary site; the early stages are usually localized for long periods.[12] The National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines for B-cell lymphomas (version 3.2022) indicate that radiation therapy is preferred for non-gastric MALT lymphomas in stages I–II; surgery may be considered for certain sites, including the lung, breast, thyroid, colon, and small bowel.[13] The salivary glands were not included in the organ groups.[13] However, this guideline also states that surgical excision for adequate diagnosis may be an appropriate treatment, which is in line with the treatment policy of the current case. Previous reports have also described that patients with localized lymphomas (stages I and II) in the salivary glands are generally treated with surgery and/or radiotherapy, with excellent local control.[14,15] Moreover, they have shown nearly equivalent outcomes of surgery in comparison with radiation therapy.[15] Our patient had early-stage MALT lymphoma of the sublingual gland which is usually not dysfunctional due to surgical resection as opposed to the parotid gland. Therefore, diagnostic surgical excision was performed in this case, and the patient was carefully monitored without any additional treatment. Optimal treatment choices based on the disease stage and primary anatomical site are necessary for initial stage MALT lymphomas.

Although MALT lymphoma does not have a specific immunophenotype,[16] immunophenotyping by immunohistochemistry (IHC) panel or flow cytometry (FCM) is essential for the diagnosis of malignant lymphoma. Since there are differences in antibody specificity between IHC and FCM, the both tests should be performed. Advantages of FCM include the ease of multicolor staining and the ability to detect expression intensity and frequency. Furthermore, FCM provides immediate results for testing, usually on the same day. Rapid immunophenotyping is also important to determine the need for additional genetic analysis. Additionally, FCM is a useful tool for determining the indication for immunotherapy, especially in anti-CD19 chimeric antigen receptor (CAR) T-cell therapy, which is a relatively new treatment option.[16] Because FCM is able to detect lower expressed antigens than IHC, FCM is preferred to proceed with this therapy. To date, CAR-T-cell therapies have been approved for treating refractory B-cell lymphomas; however, they have not been approved for MALT lymphoma treatment. Although anti-CD19 CAR-T-cell therapy is not currently the first-line treatment for B-cell lymphomas, laboratory tests need to be planned using a biopsy specimen of primary lesion to

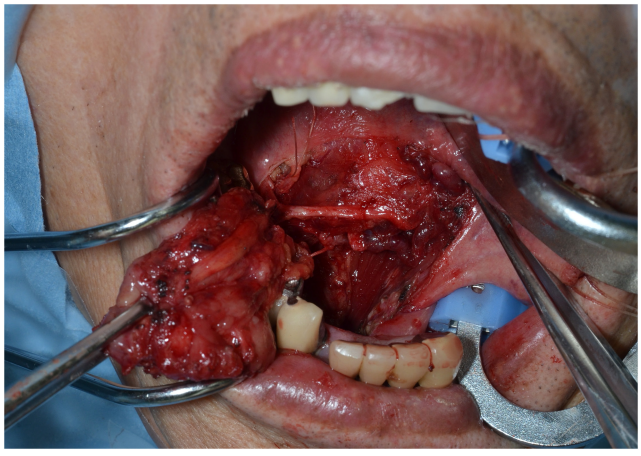

FIGURE 3 Intraoperative photograph

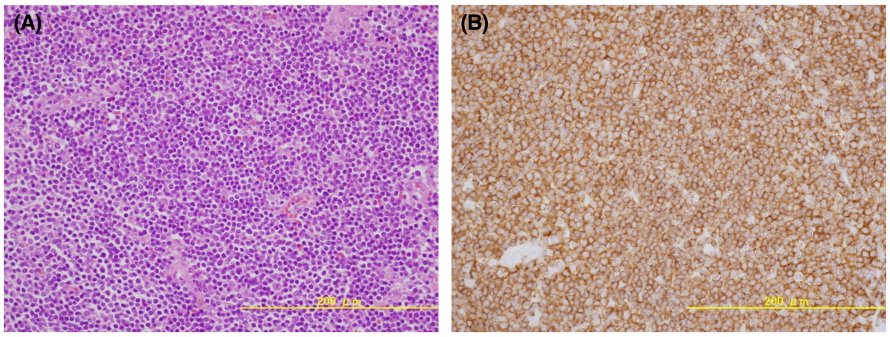

FIGURE 4 No lymphoepithelial lesions are seen, but there is infiltration of intermediate to small lymphoid cells between lymph follicles. (H&E) (A) and immunohistochemical staining of CD20 showing positive expression (B)

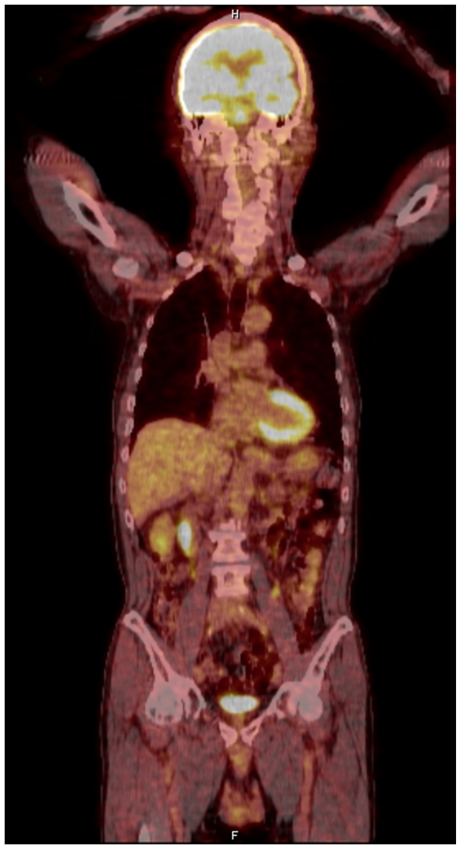

FIGURE 5 Postoperative PET-CT image showing no evidence of tumor

figure out immunophenotype which would help to choose good treatment options. Because, if it is impossible to biopsy recurrent or metastatic lesions, the treatment indication must rely on the biopsy specimen of primary lesion. Therefore, unfixed specimens are essential for the diagnoses of malignant lymphomas with an undetermined histologic type. The failure to perform FCM should be regretted in this case.

Although MALT lymphomas in the salivary gland are generally described as low-grade malignancies exhibiting an indolent clinical course, a high rate of late relapse has been reported, suggesting the need for long-term patient observation.[14] Even if the patient has early-stage lymphoma localized at the primary site, as in the current case, careful follow-up should be considered. The NCCN Clinical Practice Guidelines for B-cell lymphomas recommend follow-up every 3–6 months for 5 years and then yearly or as clinically indicated.[13] Physical examination is most important for lesions on the body surface, as in this case. PET-CT is also essential to detect distant metastases.

In conclusion, MALT lymphomas rarely occur in the sublingual gland, as shown in the present case. We performed diagnostic excisional biopsy as the initial treatment because the lesion was localized, and the histological type of the malignant lymphoma was unclear preoperatively. Surgeons need to know useful tools for the diagnosis of malignant lymphomas and chose optimal treatment based on the disease stage and primary anatomical site. Additionally, MALT lymphoma has a slow progression from the primary site, and local treatment approaches are important.

AUTHOR CONTRIBUTIONS

Shoya Ono: Manuscript preparation. Mitsuo Goto: Patient treatment, manuscript editing and review. Satoru Miyabe: Manuscript editing and review. Hiroyuki Makihara: Patient treatment, manuscript editing and review. Katsutoshi Kubo: Pathological diagnosis, manuscript editing and review. Toru Nagao: Manuscript editing and review.

ACKNOWLEDGMENT

We sincerely thank Dr. Satomi Sahashi, Hematologist, from Gifu Prefectural Tajimi Hospital for performing general examination and providing clinical support. We would like to thank Editage [https://editage.com/] for editing and reviewing this manuscript in English language.

CONFLICT OF INTEREST

The authors declare no conflicts of interest associated with this manuscript.

DATA AVAILABILITY STATEMENT

Data availability statement: Data sharing is not applicable to this article as no new data were created or analyzed in this study.

ETHICAL APPROVAL

Ethics approval is not applicable to this article as an observational study in which individuals are not identified.

CONSENT

Written informed consent was obtained from the patient for publication.

PERMISSION TO REPRODUCE MATERIAL FROM OTHER SOURCES

Reproduction is not permitted.

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How to cite this article: Ono S, Goto M, Miyabe S, Makihara H, Kubo K, Nagao T. MALT lymphoma of the sublingual gland: A case report with current overview of diagnostic and therapeutic strategies. *Clin Case Rep*. 2022;10:e06293. doi: 10.1002/ccr3.6293