

CASE REPORT

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# Primary giant mucosa-associated lymphoid tissue lymphoma of the lower lip: a case report and literature review

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## Abstract

Oral lymphomas are rare and difficult to diagnose, with Mucosa-Associated Lymphoid Tissue (MALT) lymphoma most commonly affecting older adults, particularly women. MALT lymphoma of the lip is exceptionally rare, and its cause is poorly understood. We present a case of primary giant MALT lymphoma of the lower lip, explore its clinicopathological features, and review relevant literature. An 83-year-old woman developed a painless, pea-sized swelling on the right lower lip over three years, which gradually increased in size without discomfort. She had no history of chronic infections or autoimmune diseases, and all investigations were unremarkable. Examination revealed a spherical, indurated mass on the left lower lip, measuring 8 cm, with no regional lymphadenopathy. Histology and immunohistochemistry confirmed extranodal marginal zone B-cell lymphoma of MALT. This case underscores the need to consider lymphoma in the differential diagnosis, even without systemic symptoms. Patients with oral MALT lymphoma often achieve complete remission after treatment, but diagnosing it can be challenging, requiring immunohistochemical testing for confirmation.

**Keywords** Oral mucosa, Mucosa-associated lymphoid tissue (MALT), Lymphoma, Non-Hodgkin lymphoma, Lip

## Introduction

Mucosa-associated lymphoid tissue (MALT) lymphoma is classified as a non-Hodgkin lymphoma and was first described by Isaacson and Wright in 1983 [1]. This type of lymphoma is classified as extranodal marginal zone B-cell lymphoma of MALT in the new World Health Organization classification [2]. Although relatively rare, MALT lymphoma constitutes about 0.2–8% of total B-cell lymphomas, according to various studies [3, 4]. It is a low-grade lymphoma that typically remains localized, accounting for approximately 8% of malignant lymphomas. However, it can progress to diffuse large B-cell lymphoma, which has the potential to metastasize to other organs [5–7].

The most frequent site for these lymphomas in the gastrointestinal tract is the stomach, which is often associated with *Helicobacter pylori* infection. However, MALT

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lymphomas can also develop in other common areas, such as the salivary glands, lungs, head and neck mucosa, ocular adnexa, skin, thyroid, and breast [8, 9]. Additionally, the risk of MALT lymphoma is elevated in individuals with autoimmune disorders like Sjögren's syndrome (SS), Hashimoto's thyroiditis, or lymphoepithelial sialadenitis [5, 6, 10, 11]. In the oral soft tissues, the salivary glands are most commonly affected [12], with the parotid gland being the primary site and the minor salivary glands being the least affected [13]. MALT lymphomas of the lip are exceedingly rare, with only a handful of cases documented in the literature [4, 14, 15]. Most cases occur in adults over 60, with very few reported in children under 10 [5, 16]. Furthermore, a female predominance is seen in both pediatric and adult cases [4, 13].

There is only sparse information regarding clinical presentation, diagnosis, disease course, and outcome in the lymphoma of the lips—all the reported cases of MALT lymphoma of the lip present as small, isolated masses. Here, we describe a rare case of primary giant MALT lymphoma that developed in the lower lip and provide a review of the related literature.

### Case presentation

An 83-year-old female presented to a local dental hospital with a painless, pea-sized swelling on the right lower lip, first noticed three years ago. The swelling gradually increased in size without causing discomfort. The patient declined inpatient treatment and opted for self-administered traditional Chinese medicine; however, the mass continued to enlarge, remaining painless. She was subsequently referred to the Department of Oral and Maxillofacial Surgery at Xiangya Hospital, Central South University, for further evaluation and treatment. Upon admission, the initial diagnosis was mucoepidermoid carcinoma of the minor salivary glands.

The patient's medical history includes hypertension managed with Amlodipine Besylate 2.5 mg daily for over 10 years and Parkinson's disease treated with Levodopa Benserazide 25 mg and Benzhexol Hydrochloride 4 mg, both taken once daily for more than a decade. Additionally, she has a 20-year history of trigeminal neuralgia, for

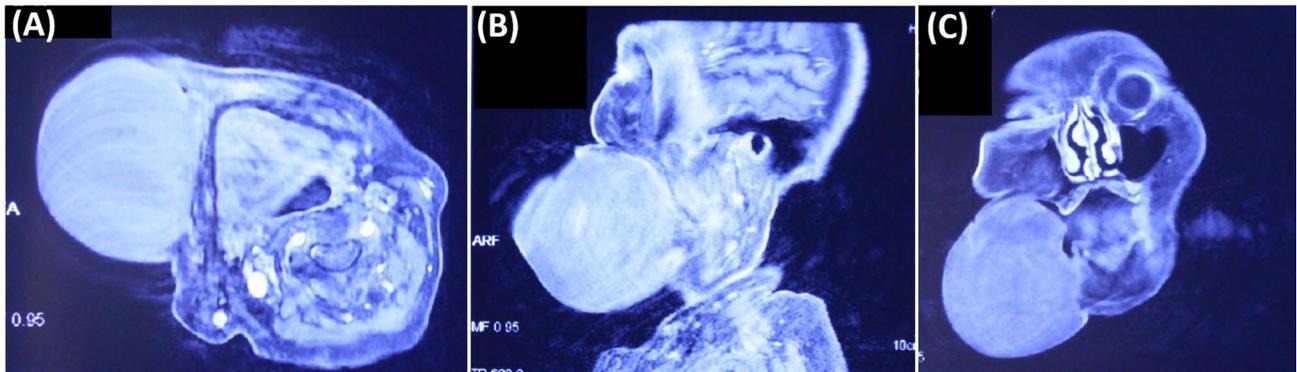
which gamma knife surgery was performed over 10 years ago. The patient recall any history of diabetes, heart disease, blood transfusions, or allergies and does not provide details regarding her vaccination history. There is no family history of oral lesions or autoimmune conditions. Clinical examination revealed facial asymmetry with a firm, indurated, spherical mass on on the left lower lip measuring approximately 5 cm × 8 cm × 8 cm, with no signs of regional lymphadenopathy. The overlying skin exhibited visible vascular dilation, and the mass demonstrated fluctuation upon palpation with well-defined borders and no significant tenderness (Fig. 1). The bilateral temporomandibular joints were non-tender and free of clicking, and the patient's mouth opening was within normal limits. Intraoral examination reveals edentulous jaws with healthy mucosa and no tenderness or numbness. No other notable abnormalities were detected.

Magnetic resonance imaging (MRI) revealed a round to oval lesion in the right cheek and lower lip with iso-T1 and mildly hyperintense T2 signals. The lesion has well-defined borders and heterogeneous internal signals and extends beyond the skin surface, measuring 74 mm × 92 mm × 85 mm, with a larger transverse diameter. Mild, uniform enhancement is noted, while adjacent central areas show irregular, patchy, long T1 and T2 signals without enhancement and poorly defined borders (Fig. 2).

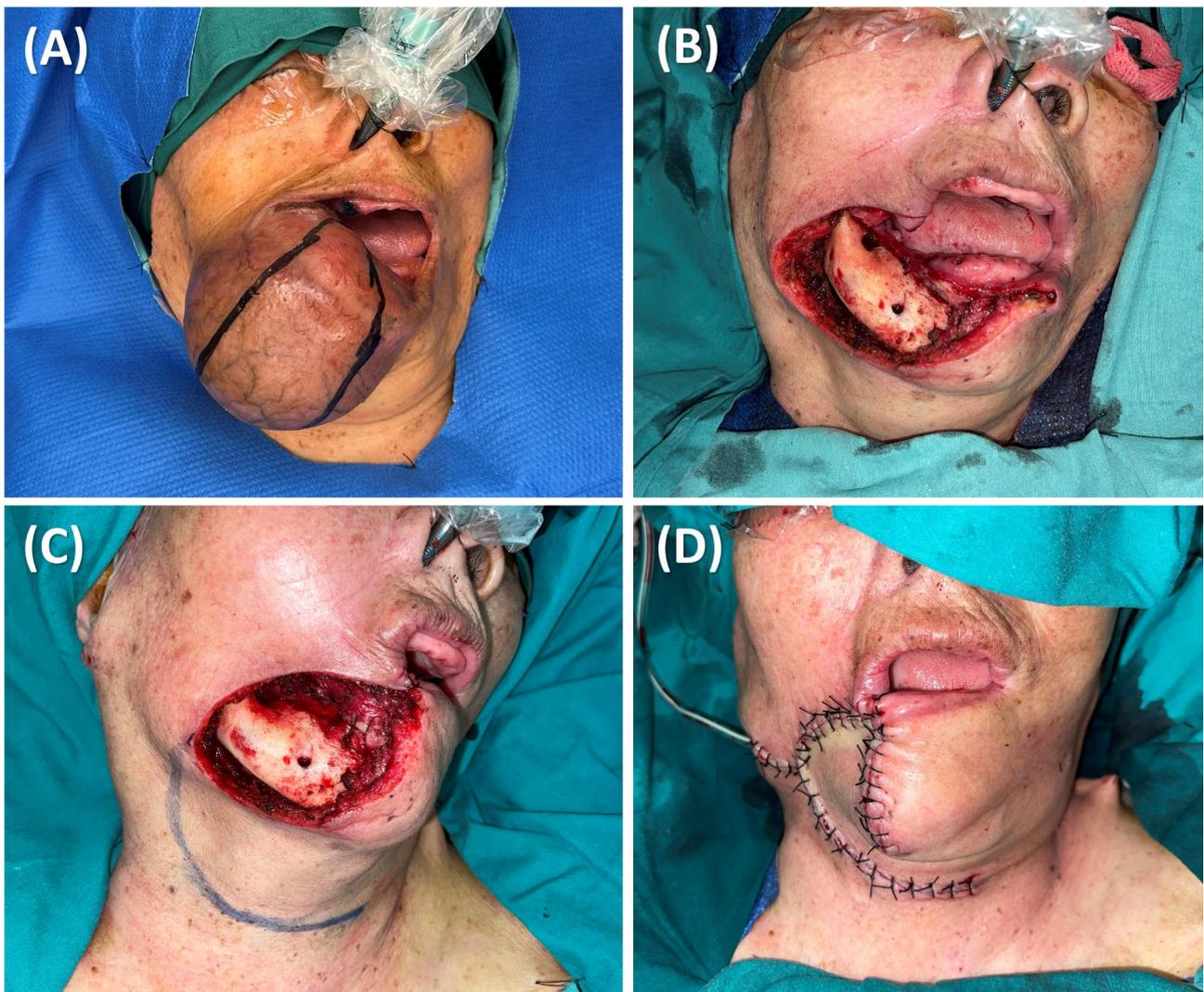
A surgical resection of the lower lip mass was performed under general anesthesia. The skin overlying the mass was incised, and an attempt was made to dissect the mass (Fig. 3, A). However, no distinct boundary or capsule could be identified, and the mass was found to be highly adherent to the skin. As a result, both the mass and the overlying skin were excised along the lower lip margin and sent for frozen pathological analysis. The preliminary report suggested a possible lymphohematopoietic tumor, with confirmation pending further with immunohistochemistry. An extended resection of the soft tissue over the mandible was then carried out (Fig. 3, B). Due to excessive tension, direct suturing was not feasible, prompting an incision from the beard area extending to the neck to create a local pedicled flap (Fig. 3, C). Enlarged submandibular lymph nodes were identified



**Fig. 1** The preoperative extraoral photograph reveals a well-defined, fluctuant mass on the right lip with visible vascular dilation and minimal tenderness



**Fig. 2** MRI scan in axial (A), sagittal (B), and coronal views (C) revealing a round to oval well-defined lesion in the right cheek and lower lip measuring 74 mm x 92 mm x 85 mm



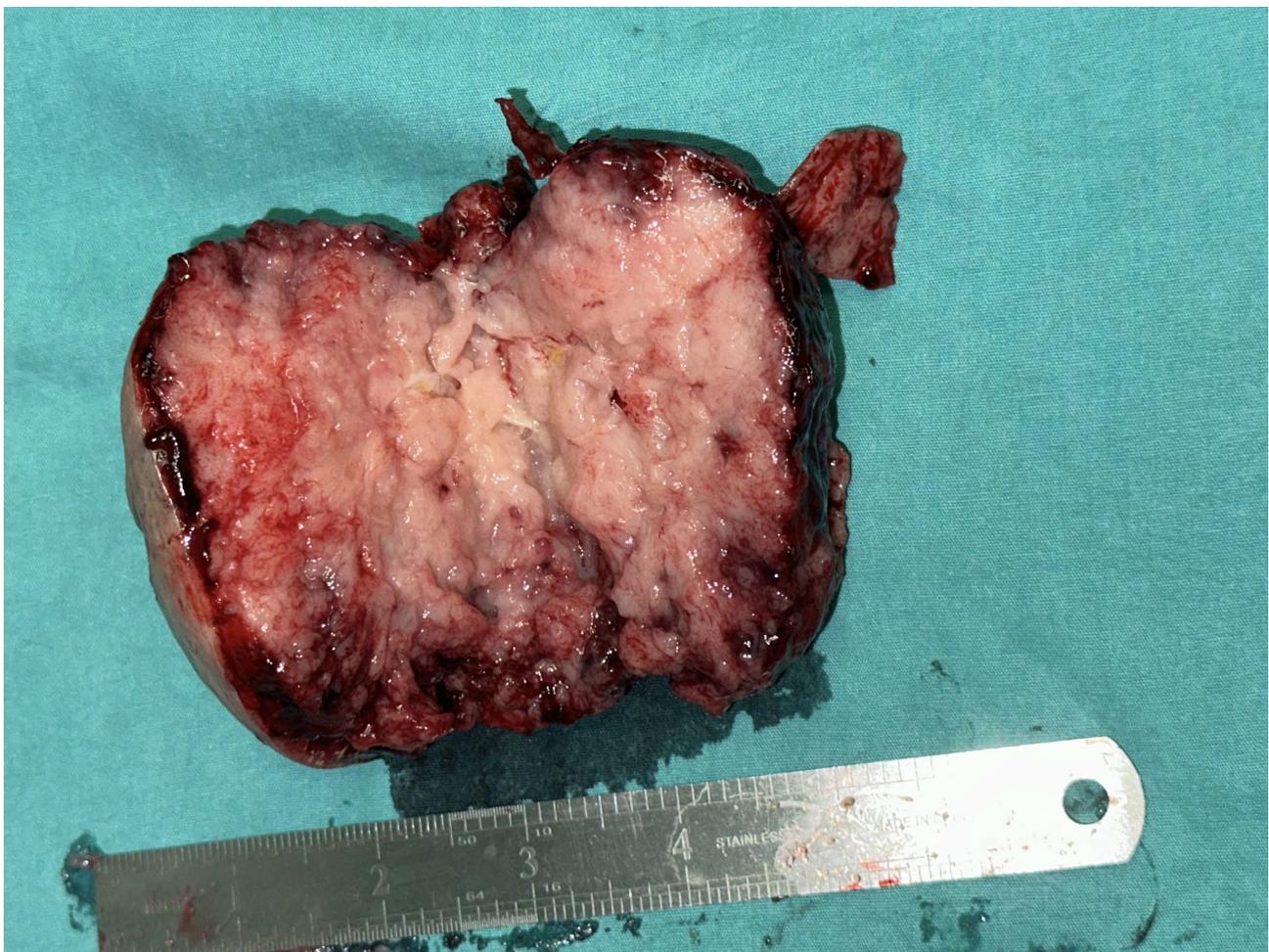
**Fig. 3** An intraoperative photo shows (A) the mass during primary resection with attempted dissection from the overlying skin, (B) the mass completely removed without adhesion during extended resection, (C) direct closure deemed unfeasible, leading to the design of a local pedicled flap, and (D) reconstruction of the defect with the pedicled flap and surface layer suturing

during this process, excised, and sent for routine pathological examination. The pedicled flap was rotated to repair the defect in the right lower lip, and the wound was successfully closed in layers (Fig. 3, D). The gross surgical specimen of MALT lymphomas was sent for histopathological analysis (Fig. 4). The patient had a smooth postoperative recovery and was discharged 7 days after surgery without complications (Fig. 5).

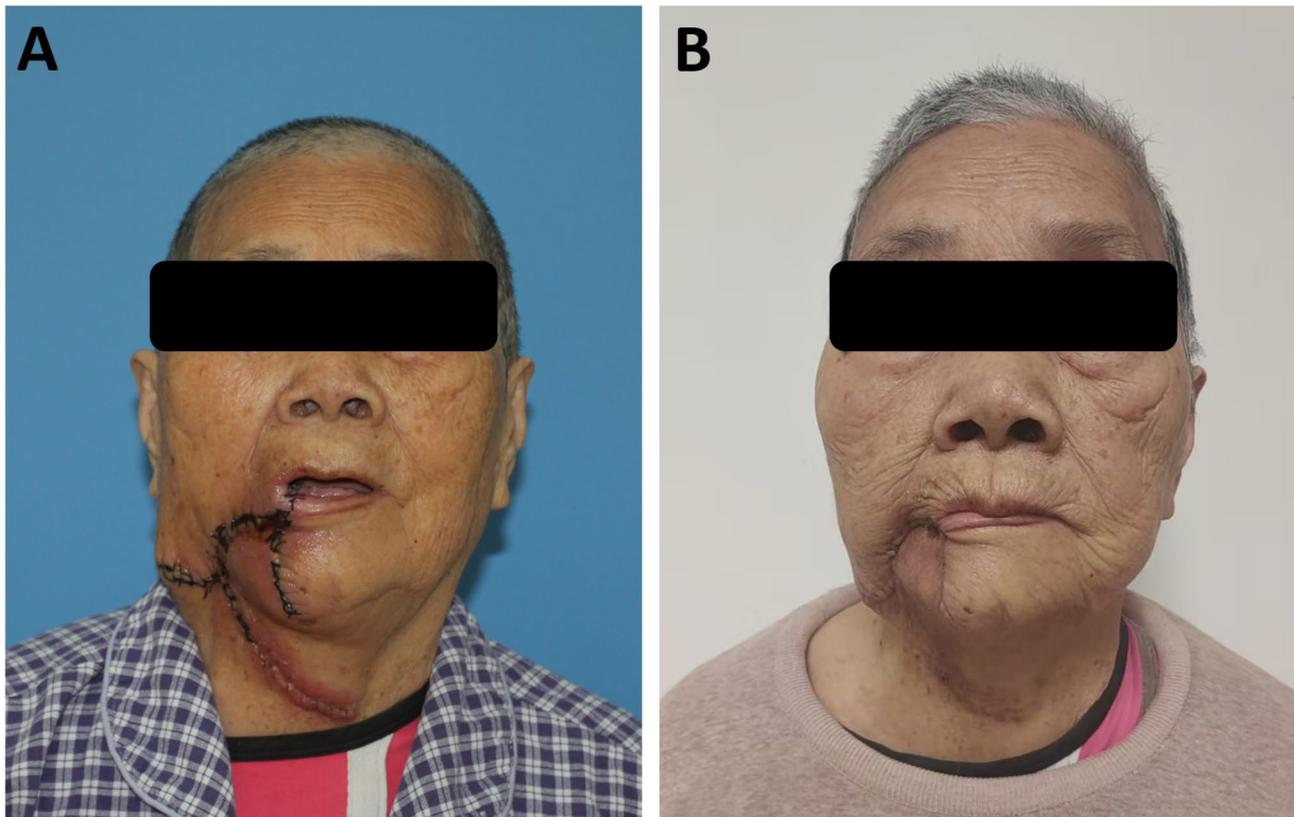
The histopathological examination revealed a diffuse proliferation of small to medium-sized lymphoid cells interspersed among reactive hyperplastic lymph follicles with germinal centers, with some neoplastic cells colonizing these follicles. The infiltrating lymphoid cells were small to medium-sized centrocyte-like cells, some showing a monocytoid appearance with pale, abundant cytoplasm (Fig. 6A, B, C). Immunohistochemical analysis showed positive reactions for CD20, CD5, PAX-5, and Bcl-2 (Fig. 6D, E, F) and negative results for Cyclin D1, SOX11, CD10, CD21, CD3, CD30, CD4, CD8, MUM1, Bcl-6, and ALK (Fig. 6G, H). Staining of lambda and kappa light chains revealed lambda light chain restriction

in plasma cells ratio exceeded 10:1, and the Ki-67 labeling index of tumor cells was approximately 20% (Fig. 6I). A negative EBER (FISH) result indicated no detection of Epstein-Barr Virus in the lymphoma cells (Fig. 6J, Supplemental Fig. 1). A pattern of immunoglobulin heavy chain (IGH) gene was detected through clonal gene rearrangement in B-cell lymphoma, often accompanied by clonal immunoglobulin kappa (IGK) or lambda (IGL) rearrangements, which is a key diagnostic marker for B-cell lymphoma (Supplemental Fig. 2). A comprehensive assessment of the clinical and pathological findings led to the final diagnosis of extranodal marginal zone lymphoma of MALT type.

Examinations for infections, including HIV, hepatitis B, hepatitis C, and *Helicobacter pylori*, as well as evaluations for other immunologic disorders, all returned negative. Based on the patient's clinical features and MRI findings, along with normal serum levels of Immunoglobulin G (IgG), Immunoglobulin E (IgE), and anti-SS-A and anti-SS-B antibodies, SS was ruled out. Due to the patient's advanced age, she declined any adjuvant



**Fig. 4** The gross surgical specimen of MALT lymphoma from the lower lip



**Fig. 5** (A) Frontal view photograph of the patient 7 days postoperatively, (B) Two months after surgery with satisfactory result

therapy. Regular follow-up over the 12 months post-surgery revealed no recurrence, and the patient remained asymptomatic throughout.

### Discussion

MALT lymphoma is generally considered a low-grade malignant tumor originating in lymphoid tissue, and it typically has a favorable prognosis. However, in some cases, MALT lymphoma can occur at multiple sites or progress into diffuse large B-cell lymphoma, making early diagnosis of the disease crucial [17]. MALT lymphoma is most commonly detected in the stomach (43%), followed by the lungs (14%) and various soft tissues such as the salivary glands, orbital adnexa, colon, skin, thyroid, and mammary gland, among others [18]. A study by Anacak et al. [13] examined 63 patients with salivary gland MALT lymphoma and found that the parotid gland was a more frequent site of occurrence than the submandibular gland, with multiple gland involvement observed in 9 patients. MALT lymphoma may develop in individuals with inflammatory or autoimmune conditions; for example, gastric MALT lymphoma is often associated with chronic gastritis caused by *Helicobacter pylori* infection, while salivary gland MALT lymphoma is frequently linked to SS [15, 19, 20].

The occurrence of MALT lymphoma as a primary tumor in the oral cavity mucosa is extremely rare [21]. It is most commonly seen in women over 60, though cases have been reported in children. These tumors typically present as mass-like swellings or nodular lesions in the lip and often manifest as isolated oral MALT lymphoma without any associated autoimmune or infectious diseases, as highlighted in the English-language literature and summarized in Table 1. Generally, they have a slow, indolent progression, with only a small number of cases spreading to other areas, typically after long disease-free intervals [4]. Most non-Hodgkin lymphomas of the lips exhibit these characteristics, although a subgroup has been identified in children, suggesting a bimodal age distribution with peaks around ages 10 and 60. All MALT lymphomas of the lips tend to follow a prolonged, indolent disease course and should be managed conservatively.

Oral cavity MALT lymphomas can be categorized into two types: one originating from a pathological lymphocyte infiltrate in the minor salivary glands and another developing from lymphoid cells in the mucosa, unrelated to salivary gland inflammation. Under normal conditions, the salivary gland parenchyma lacks lymphocyte infiltrates; however, this can occur in inflammatory conditions, particularly in SS, a systemic autoimmune

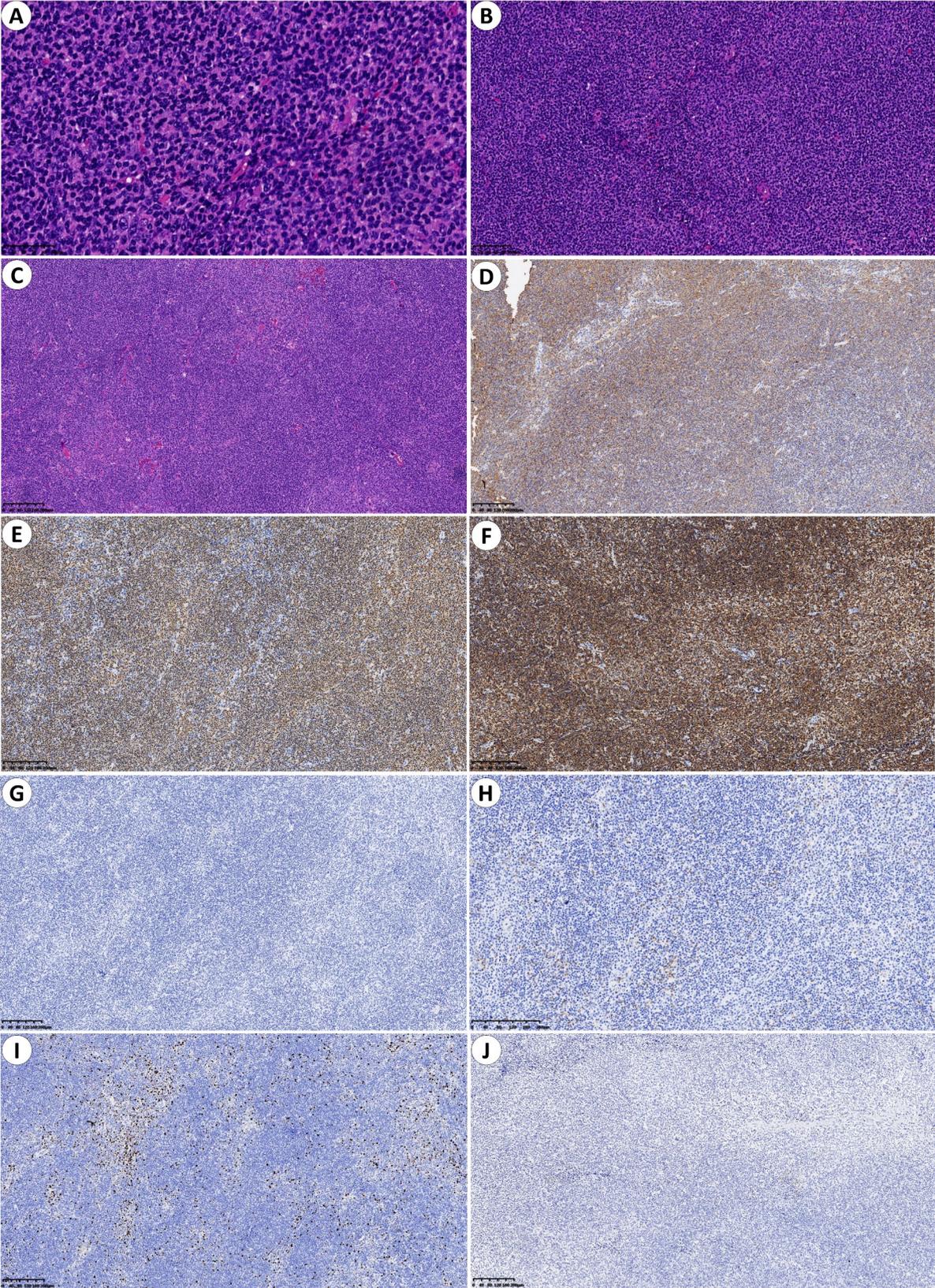


Fig. 6 (See legend on next page.)

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**Fig. 6 (A, B, C)** A hematoxylin and eosin (H&E) stained section shows a diffuse proliferation of small to medium-sized tumor cells with a uniform appearance and no residual salivary gland tissue. **(D, E)** Immunohistochemical staining demonstrates diffuse and uniform expression of CD20 **(D)**, with membrane positivity, and PAX-5 **(E)**, with nuclear staining in the tumor cells. **(F)** The tumor cells exhibit strong and diffuse positivity for BCL-2. **(G)** Markers associated with follicular center B cell differentiation are not expressed in the tumor cells. **(H)** Scattered T lymphocytes within the tumor population are CD3-positive. **(I)** The Ki67 proliferation index is low within the tumor cells. **(J)** EBER (FISH) testing is negative

disorder marked by lymphoepithelial sialadenitis [22]. Other chronic conditions, such as sclerotic sialadenitis or localized inflammation, may also lead to such infiltration [23]. Our patient histopathological result showed no

evidence of minor salivary gland lobules or inflammatory infiltrates, and the SS markers were within normal limits.

The histologic features of salivary gland MALT lymphoma include the proliferation of marginal zone B cells around the ductal epithelium, solid sheets of these cells,

**Table 1** Summary of the literature evaluating the clinical and pathological characteristics of reported cases of MALT lymphoma in the lips, without any association with autoimmune or infection diseases

Authors/Year	Country	Age (yrs)	Sex	Tumor Location	Clinical manifestation	MSG involvement	CD5	Type of NHL	Management	Follow up
Bombeccari et al. [28] (2011)	Italy	11	M	Lower Lip	Mass, 1.5 cm	NO	–	EMZB- MALT	Surgical resection	3 years
Crandley et al. [29] (2010)	USA	9	F	Lower Lip	Painless mass, 1 cm	YES	UK	EMZB- MALT	Surgical resection	More than 2 yrs
Frazier et al. [30] (2017)	USA	50	M	Upper and Lower Lip	Mass, 3.0 cm	NO	–	EMZB- MALT	Surgical resection	UK
Berrebi et al. [15] (1998)	France	10	M	Lower Lip	Mass, 3.0 cm	YES	UK	EMZB- MALT	Surgical resection	1 yr
Gabali et al. [31] (2013)	USA	11	M	Lower Lip	Mass, 1.5 cm	YES	–	EMZB- MALT	Surgical resection	NK
Ruy et al. [4] (2009)	Korea	7	F	Lower Lip	Mass	NO	–	EMZB- MALT	Chemotherapy	6 months
Gerami [10] (2007)	USA	56	F	Lower Lip then involved Upper Lip	Painless swelling	NO	–	UN	Chemotherapy	6 months
Kaplan et al. [32] (2019)	Israel	59	F	Lower Lip	UK	YES	–	EMBZ- MALT	Chemotherapy + anti-CD20	11 yrs
		87	F	Lower Lip	Firm mobile mass, 2 cm	YES	–	EMBZ- MALT	Surgical resection	1yr
		82	F	Upper Lip	Firm mass, 0.5 cm	YES	–	EMBZ- MALT	Surgical resection	UK
		82	F	Lower Lip	Mass, 1 cm	YES	–	EMBZ- MALT	Surgical resection	2 yrs
		66	F	Lower Lip	Firm mass, 0.5 cm	YES	–	EMBZ- MALT	Surgical resection	UK
		79	F	Lower Lip	Mass, 3 cm, paresthesia	YES	UK	DLBC CD30+	Surgical resection	9yrs
Kawasaki et al. [33] (2014)	Japan	27	M	Upper Lip and Lower Lip	Two masses, 0.6 and 0.8 cm	YES	UK	EMZB- MALT	Chemotherapy and radiotherapy	29 months
Mo et al. [5] (2004)	USA	12	M	Lower Lip	Mass, 1.7 cm	YES	–	EMZB- MALT	Chemotherapy	1 year
Zambrano et al. [34] (2006)	USA	14	M	Upper Lip	Mass, 1.1 cm	NO	+	EMZB- MALT	UK	UK
Bianco et al. [35] (2018)	Italy	82	M	Upper Lip	Swelling	NO	–	EMZB	Chemotherapy and Radiotherapy	UK
Present Case (2024)	China	83	F	Lower Lip	Giant painless mass, 9.2 cm	NO	+	EMZB- MALT	Surgical resection	12 months

**Abbreviations:** NHL; non-Hodgkin lymphoma, EMZB-MALT; extra nodal marginal zone B cell lymphoma of Mucosa associated Lymphoid Tissue, DLBC; diffuse large B cell lymphoma, MSG; minor salivary gland, absence (–) or presence (+) of marker expression CD5, UK; Unknown

and prominent lymphoepithelial lesions [4]. Cytologically, MALT lymphoma shows variability, with small to medium-sized cells often having irregular nuclei (centrocyte-like), monocytoid cells with pale cytoplasm, or cells resembling small mature lymphocytes. Occasionally, larger cells like centroblasts, immunoblasts, and plasma cells may also be present [24]. Lymphoepithelial islands infiltrated by neoplastic lymphoid cells are characteristic, and cytokeratin stains aid in their identification. A dense infiltrate of CD20-positive cells and destruction of normal gland parenchyma further support the lymphoma diagnosis.

Immunohistochemistry is a critical tool for diagnosing lymphoma. Unfortunately, there is no specific immunohistochemical marker for MALT lymphoma, so the diagnosis is based on recognizing its morphological features and combining immunostaining results [24]. The expression of CD5 by MALT lymphomas is not frequent. To differentiate MALT lymphoma from other CD5-positive small-cell lymphomas, such as mantle cells and small lymphocytic lymphomas, the absence of cyclin D1 and CD10 is crucial. MALT lymphomas are typically negative for CD5, CD10, BCL6, and cyclin D1 (Table 1). A study by Silva et al. [25] found CD5 positivity associated with extragastric MALT lymphomas and a tendency for dissemination, though none involved the oral cavity. Nevertheless, CD5-positive oral MALT lymphomas have been linked to disseminated forms, with cases expressing both kappa and lambda light chains showing more aggressive behavior and recurrence [26]. Tanaka et al. [27] reported a case where an initially CD5-positive oral MALT lymphoma expressed a kappa light chain, then both kappa and lambda in recurrence. In our patient, the oral MALT lymphoma was CD5-positive and negative for CD10, BCL6, and cyclin D1.

Active treatment options for MALT lymphoma include surgery, radiotherapy, chemotherapy, immunotherapy, and combination therapies. The treatment choice is based on the disease stage and primary anatomical site. Among the 19 reported cases of MALT lymphoma of the lip without associated autoimmune or infectious diseases, including our case, the treatments and outcomes were as follows: 12 patients underwent surgical resection alone, 4 received chemotherapy, and 2 were treated with a combination of chemotherapy and radiotherapy, and one case did not report the outcome (Table 1). In our case, a biopsy was not performed initially due to the patient's overall health condition, which presented significant risks and contraindicated a more invasive procedure. Instead, a frozen section was used, as it provided sufficient diagnostic information while minimizing the risk of complications. The frozen section suggested the possibility of lymphoma, allowing us to move forward with treatment planning. Regarding the choice of surgical

excision, it was deemed the preferred option despite the preliminary lymphoma diagnosis. This decision was made because the patient declined radiotherapy and chemotherapy, even as adjunctive treatments following surgery. Given these preferences, surgical excision was considered the most appropriate course of action, offering the potential for local disease control. In such cases, surgery can still provide substantial therapeutic benefit, particularly when more aggressive therapies like chemotherapy or radiation are not part of the treatment plan.

## Conclusions

We presented a rare case of giant MALT lymphoma in the lower lip, showing features of a specific non-Hodgkin lymphoma subtype that warrants further attention. These lesions are usually asymptomatic, slow-growing submucosal masses without ulceration. Lymphoma should be considered in the differential diagnosis, even without systemic symptoms. While localized MALT lymphoma of the lips generally has a good prognosis, some patients may relapse or progress to high-grade or systemic lymphoma, making long-term follow-up essential.

## Abbreviations

MALT lymphoma	Mucosa-associated lymphoid tissue
SS	Sjögren's syndrome
IgG	Immunoglobulin G
IgE	Immunoglobulin E
IGK	Immunoglobulin kappa
IGL	Immunoglobulin lambda

## Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s12903-025-05799-5>.

**Supplementary Material 1: Supplemental fig. 1.** The FISH test result of the MALT1 gene was negative, and the picture showed that the proportion of MALT1 gene signal separation was about 1%, indicating no break in the MALT1 gene.

**Supplementary Material 2: Supplemental fig.2.** B cell lymphoma clonal gene rearrangement detected IGH, IGK, and IGL clonal rearrangement.

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Not applicable.

## Author contributions

Conceptualization: MAA, LBH, JC; formal analysis and investigation: MAA, NL; Data curation: MAA, LBH; writing original draft preparation: MAA, CHJ, JW, writing—review and editing: MAA, NL, CHJ; supervision: CHJ, JW.

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## Data availability

The datasets used and/or analyzed during the current study available from the corresponding author on reasonable request.

## Declarations

### Ethics approval and consent to participate

The Institutional Review Board reviewed and approved the research protocol. The Research Ethics Committee endorsed the informed consent process, and participants provided written informed consent.

### Consent for publication

A written informed consent for publication was obtained from the patient to publish all clinical data and any accompanying images and also a written consent to publish this information was obtained from study participant.

### Competing interests

The authors declare no competing interests.

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