Clinical Case Report

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Mucosa-associated lymphoid tissue lymphoma of the accessory parotid gland presenting as a simple cheek mass

A case report

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Abstract

Rationale: Mucosa-associated lymphoid tissue (MALT) lymphoma, also known as extranodal marginal zone B-cell lymphoma, usually occurs in the gastric mucosa, lung, lacrimal glands, and salivary glands. MALT lymphoma arising from the accessory parotid gland is extremely rare and can therefore be easily confused with other types of soft tissue masses.

Patient concerns: A 56-year-old woman presented with a 1-month history of a mass on the left cheek. The mass was hard and nontender. She had a history of thymectomy 26 years ago due to myasthenia gravis.

Diagnosis: A soft tissue tumor measuring 2.5 × 0.8 cm was identified in the left accessory parotid gland on ultrasonography and enhanced computed tomography (CT). Additionally, CT revealed enlargement of both lacrimal glands and an enhancing mass in the right retropharyngeal space. Under suspicion of a malignant soft tissue tumor, ultrasonography-guided fine needle aspiration biopsy was performed, with findings suggestive of marginal zone B-cell lymphoma of the accessory parotid gland.

Interventions: The patient was transferred to the department of hematology for immunochemotherapy.

Outcomes: The patient has received 6 cycles of rituximab with cyclophosphamide, vincristine, and prednisone chemotherapy. After 6-month follow-up, enhanced CT demonstrated complete remission. Now she is currently under periodic follow-up.

Lessons: Physicians and surgeons should be aware that MALT lymphoma can occur in the accessory parotid gland. When this is suspected, careful history-taking, imaging workup, and biopsy are essential for accurate diagnosis and treatment.

Abbreviations: CT = computed tomography, HL = Hodgkin lymphoma, LDH = lactate dehydrogenase, MALT = mucosa-associated lymphoid tissue, MG = myasthenia gravis, NHL = non-Hodgkin lymphoma, PET-CT = positron emission tomography–computed tomography, R-CVP = rituximab with cyclophosphamide, vincristine, and prednisone.

Keywords: mucosa-associated lymphoid tissue lymphoma, myasthenia gravis, non-Hodgkin lymphoma, salivary gland neoplasm, thymectomy

1. Introduction

Mucosa-associated lymphoid tissue (MALT) lymphoma, a form of extranodal marginal zone B-cell lymphoma, originates from a proliferation of lymphoid tissue caused by chronic inflammation at an extranodal site.[1–3] It usually occurs in the gastric mucosa, but may also develop in other sites, such as the gastrointestinal tract, lung, breast, ocular adnexa, and salivary glands.[4] However, it is unusual for MALT lymphoma to develop in the parotid gland,[1,4,5] and cases of MALT lymphoma in the accessory parotid gland are especially rare[6]; thus, such cases are easily confused with other types of soft tissue masses, such as abscesses, sialoceles, epidermal inclusion cysts, and other benign parotid gland tumors. We report a case of a 56-year-old woman with MALT lymphoma that developed in the accessory parotid gland, which could have easily been mistaken for another type of soft tissue mass.

2. Case presentation

A 56-year-old woman presented with a 1-month history of a mass on the left cheek. The mass was hard and nontender. She had a history of thymectomy 26 years previously due to myasthenia gravis (MG) and had no other neoplastic history. Ultrasonography revealed a lobulated hypoechoic mass measuring 2.5 × 0.8 cm with increased vascularity in the subcutaneous layer of the left cheek (Fig. 1). Enhanced computed tomography (CT) revealed a homogeneously enhancing mass measuring 2.5 × 0.8 cm in the left accessory parotid gland (Fig. 2). Additionally, CT revealed

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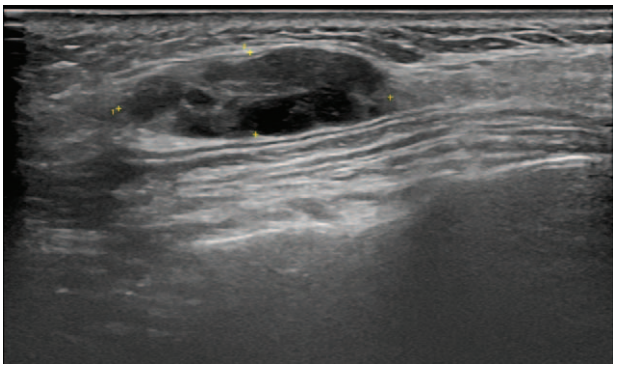

Figure 1. Ultrasonography revealed a lobulated hypoechoic mass measuring 2.5 × 0.8 cm with increased vascularity in the subcutaneous layer of the left cheek.

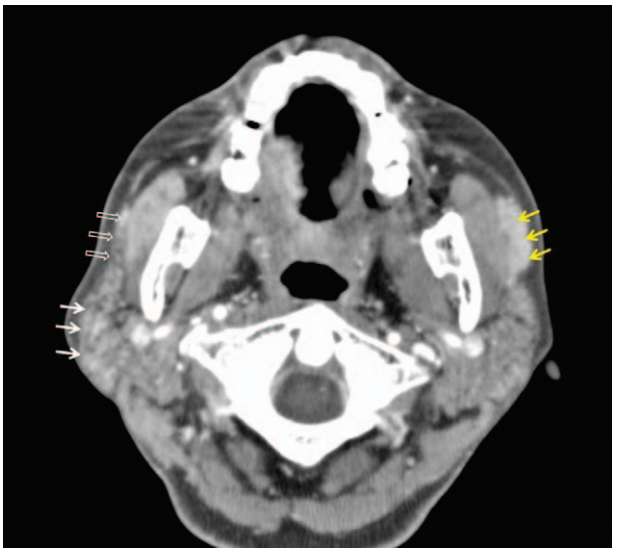

Figure 2. Enhanced computed tomography revealed a homogeneously enhancing mass measuring 2.5 × 0.8 cm in the left accessory parotid gland (yellow arrows). The right parotid gland (white arrows) and the right accessory parotid gland (empty arrows) were intact.

enlargement of both lacrimal glands and an enhancing mass in the right retropharyngeal space. Under suspicion of a malignant soft tissue tumor of the accessory parotid gland, ultrasonography-guided fine needle aspiration biopsy was performed. Histopathological examination showed invasion of atypical lymphocytes into the duct epithelium and formations of lymphoepithelial lesions (Fig. 3A and B). Immunohistochemical staining revealed that these tumor cells were positive for CD20, Bcl-2, and Ki-67, predominantly negative for CD3, and negative for cytokeratin. The tumor cells were also predominantly positive for lambda light chain, rather than kappa light chain (Fig. 4A–D).

The pathological diagnosis of the mass was extranodal marginal zone B-cell lymphoma of the accessory parotid gland. Torso positron emission tomography–computed tomography (PET-CT) was conducted for tumor staging and evaluation of lymphomatous involvement of other organs. In addition to the left accessory parotid gland, focal hypermetabolic lesions were identified in both lacrimal glands and in the right retropharyngeal space, a finding suggestive of lymphomatous involvement (Fig. 5A–C). The subsequent bone marrow section biopsy did not reveal bone marrow involvement. The patient's laboratory values were as follows: white blood cell count of $4000 \times 10^3/\mu L$, hemoglobin level of 14.5 g/dL, platelet count of $290 \times 10^3/\mu L$, and lactate dehydrogenase (LDH) level of 368 IU/L, all of which were within normal limits. Considering the multisite involvement and the staging of the primary lesion (stage IIE), we planned to provide immunochemotherapy rather than surgery or radiotherapy.[7] The patient was then transferred to the Department of Hematology to undergo therapy. She has received 6 cycles of rituximab with cyclophosphamide, vincristine, and prednisone (R-CVP) chemotherapy. After 6-month follow-up, enhanced CT demonstrated complete remission. There was no adverse effect and now she is currently under periodic follow-up.

We obtained the patient's medical records and reviewed the relevant literature. Informed written consent was obtained from the patient for publication of this case report and accompanying images. This study was approved by the Chonnam National University Hospital Institutional Review Board (IRB No. CNUH-2019-041).

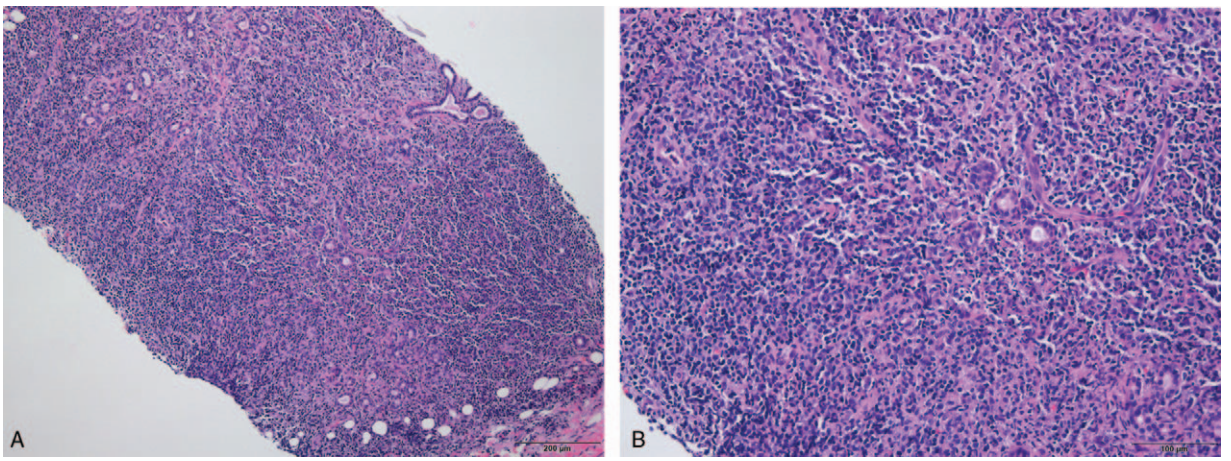

Figure 3. Hematoxylin and eosin staining, ×100 (A) and ×200 (B). Invasion of atypical lymphocytes into the duct epithelium and formation of lymphoepithelial lesions.

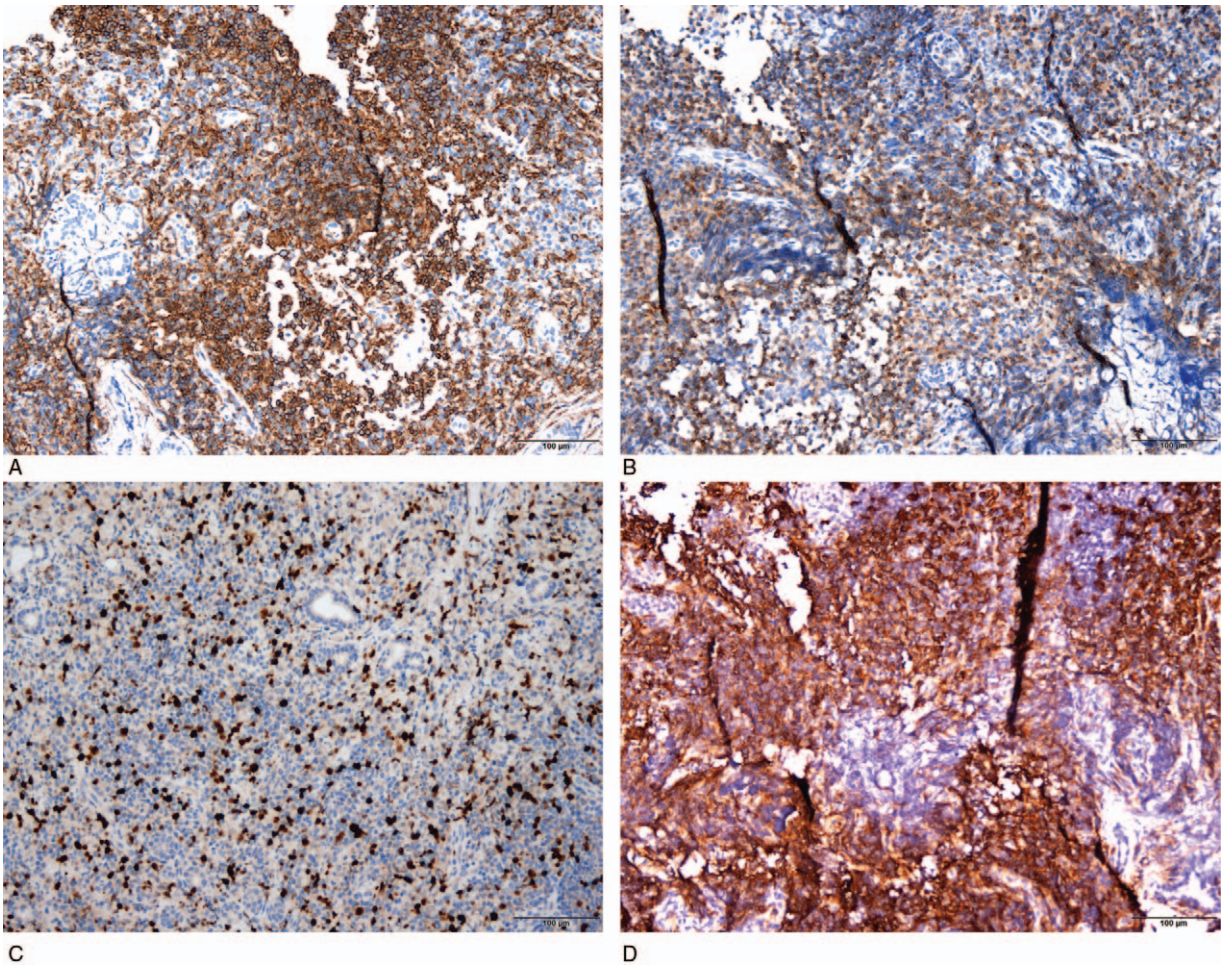

Figure 4. Immunohistochemical staining, ×200. The tumor cells were positive for CD20 (A), Bcl-2 (B), and Ki-67 (C), predominantly negative for CD3, and negative for CK. The tumor cells were also dominantly positive for lambda light chain, rather than kappa light chain (D). CK = cytokeratin.

3. Discussion

According to the World Health Organization classification, malignant lymphoma can be divided into Hodgkin lymphoma (HL) and non-Hodgkin lymphoma (NHL).[8] MALT lymphoma is a form of NHL. While HL usually arises from the inguinal, axillary, and cervical nodes, NHL occurs at extranodal sites.[4]

MALT lymphoma most frequently occurs in the gastric mucosa, but can also develop in the gastrointestinal tract, lung, breast, lacrimal glands, and salivary glands. Possible causes include *Helicobacter pylori*-associated chronic gastritis, gastrointestinal bacterial infections, pulmonary bacterial infections, autoimmune diseases (e.g., Sjogren's syndrome and Hashimoto thyroiditis), and hepatitis C viral infection.[2,6] Such conditions of chronic inflammation induce proliferation of lymphoid tissue, leading to the development of MALT lymphoma.[1,3,9] In our case report, the patient had a history of an autoimmune disease (i.e., MG) and thymectomy.[10] This history of chronic inflammation is thought to have induced lymphoid tissue proliferation, leading to the development of lymphoma.

The accessory parotid gland is a variation of the anteriorly extended parotid gland.[11] This gland may be either continuous with or separated from the main parotid gland.[11] Among the tumors that may arise in the parotid gland, NHL only accounts for 1% to 4%,[1,4] with subtypes including follicular lymphoma, diffuse large B-cell lymphoma, and MALT lymphoma.[6] Of these subtypes, development of MALT lymphoma in the parotid gland is rare[1,5]; further, its development in the accessory parotid gland is especially rare, and such cases have scarcely been reported.[6]

Imaging studies using ultrasonography, CT, and PET-CT must be performed to diagnose MALT lymphoma.[12] However, there are limitations to these tests; therefore, pathological findings are necessary for a precise diagnosis. A simple diagnostic method to obtain pathological findings is fine needle aspiration biopsy.[4,5,12] On cytology, MALT lymphoma is positive for CD20 and CD79a, and negative for CD5, CD10, and cyclin D1.[5,6]

The treatment for nongastric MALT lymphoma varies according to its stage. According to the Ann Arbor staging system, stage I indicates involvement of a single lymph node region (I) or a single organ (IE). Stage II indicates involvement of 2 or more lymph node regions (II) or extranodal organs (IIE) on the same side of the diaphragm. Stage III indicates involvement of 2 or more lymph node regions above and below the diaphragm, and stage IV indicates widespread disease with or without lymph node involvement. According to the National Comprehensive Cancer Network guidelines, radiotherapy must be initially considered in stage I and II tumors,[7,12] and rituximab may be used in certain cases. If the tumor is located in the lung, breast, thyroid, or colon, surgery and additional radiotherapy may be

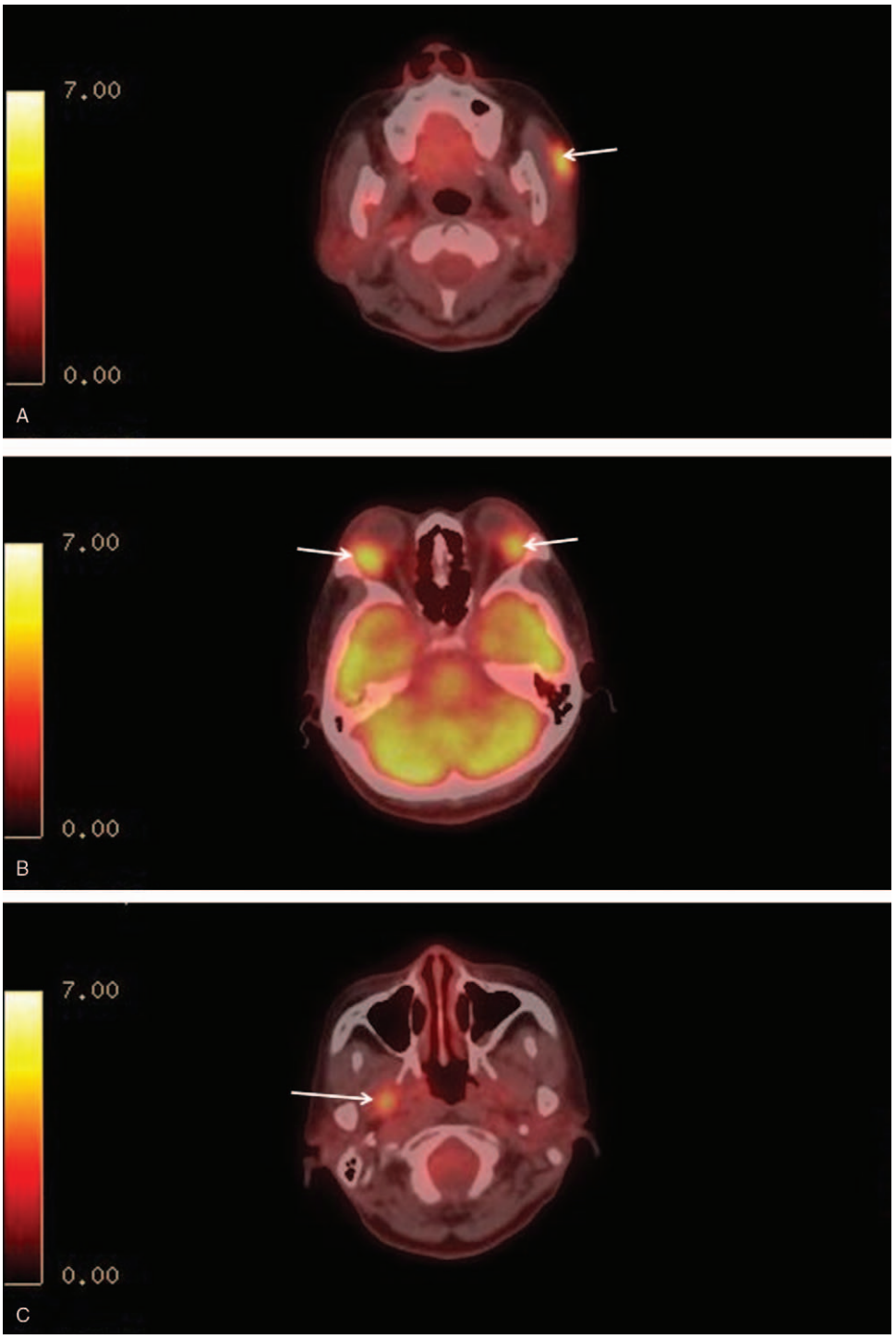

Figure 5. Torso positron emission tomography–computed tomography revealed a focal hypermetabolic lesion in the left accessory parotid gland (A), both lacrimal glands (B), and right retropharyngeal space (C), which was suggestive of lymphomatous involvement.

considered. The treatment for stage III and IV tumors may be either chemotherapy or radiotherapy or even observation in certain cases.[13] Periodic follow-up is necessary after treatment, and radiotherapy is considered in cases of local recurrence.[12] Systemic recurrence can be treated with rituximab or in accordance with the treatment algorithm of marginal zone lymphoma.[12] In addition to the tumor stage, the patient's overall health and age must be considered when determining the treatment method.[12] In our case report, the patient was found to show localized lymphomatous involvement in the lacrimal gland and the retropharyngeal space, consistent with stage IIE. Although radiotherapy is the preferred treatment for stage IIE tumors, the patient was treated with immunochemotherapy using an R-CVP regimen due to the wide range of the lesion sites. Rituximab, a monoclonal anti-CD20 antibody, is effective in the treatment of B-cell lymphoma in combination with conventional

chemotherapy including cyclophosphamide, vincristine, and prednisone.[13–15]

However, when evaluating patients who present with a cheek mass, physicians generally do not consider the possibility of a lymphoma. Because it is extremely difficult to distinguish lymphomas from other masses based on clinical and radiological features, they are often missed and are treated with surgical procedures, such as simple excision or parotidectomy. In such cases, if the intraoperative frozen biopsy reveals malignant and lymphoid tissue, superficial parotidectomy or total parotidectomy is recommended depending on the location of the mass. Adjuvant radiotherapy is also effective.[1,12] Further, PET-CT must be performed to evaluate lymphomatous involvement at other sites.

The complications of MALT lymphoma include local or distant organ involvement, central nervous system involvement, loss of organ function, weakened immune system, and intestinal obstruction. Additionally, the chemotherapy-related complications include dizziness, vomiting, and hair loss. The prevalence rate of dissemination at diagnosis of MALT lymphoma has been reported to be approximately 34%.[16] The recurrence rate is approximately 48%.[17] Furthermore, the 5-year overall survival rates of stage I/II and stage III/IV MALT lymphoma are approximately 94% and 69%, respectively.[16] MALT lymphoma tends to remain localized for a long period and has a low tendency for systemic dissemination,[3] although systemic dissemination can occur in some cases due to delayed diagnosis or treatment. Dissemination to the lymph nodes or bone marrow decreases the overall survival rate,[16] which is why early diagnosis and treatment of MALT lymphoma are clinically important.

Generally, it has been reported that patients with a poor performance status score experience more adverse effects and have a lower survival rate.[12] Additionally, abnormal LDH levels have been reported to be associated with a decreased therapeutic effect.[12] Our patient had a performance status score of 0 and an LDH level of 368 IU/L; thus, we were able to expect good treatment outcomes and a favorable prognosis.

Our study has a few limitations. Several previous studies have investigated the relationship between MG and thymic MALT lymphoma,[2,18,19] as well as the relationship between thymectomy and the development of T-cell lymphoma in patients with MG.[9,20] However, in our case, MALT lymphoma (a form of B-cell lymphoma) developed in the accessory parotid gland after thymectomy for MG treatment, and the relationship between these 2 events was not investigated. Future prospective studies are necessary to identify any such associations.

4. Conclusion

Physicians should be aware that MALT lymphoma can also occur in the accessory parotid gland and that the choice of radiotherapy, chemotherapy, or surgery depends on accurate staging of the tumor. Therefore, when patients present with a cheek mass, careful history-taking and proper imaging workup are essential for its diagnosis. In addition, preoperative fine needle aspiration biopsy or intraoperative frozen biopsy should be performed if there is any suspicion of malignancy for the cheek mass.

Author contributions

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