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**Massive low-grade myxoid liposarcoma of the floor of the mouth: A case report and review of literature**

Kugimoto T *et al.* Massive oral myxoid liposarcoma

Takuma Kugimoto, Yuko Yamagata, Toshimitsu Ohsako, Hideaki Hirai, Naoto Nishii, Kou Kayamori, Tohru Ikeda, Hiroyuki Harada

**Abstract****BACKGROUND**

Oral liposarcoma is an extremely rare lesion that is often clinically misdiagnosed as a benign tumor due to its asymptomatic and indolent clinical course. Here, we report a case of massive low-grade myxoid liposarcoma (MLS) of the floor of the mouth.

**CASE SUMMARY**

A 71-year-old man presented with a huge mass in the left floor of the mouth. A biopsy was performed, and a diagnosis of a myxoid tumor suspicious for low-grade MLS or myxoma was made. Gadolinium-enhanced T1-weighted magnetic resonance imaging showed an intensely enhanced tumor lesion that occupies the left sublingual space and extends to the submandibular space. Submandibular dissection, tumor resection, and reconstruction with a radial forearm flap were performed. The surgical specimen exhibited histologically low-grade MLS. Fused in sarcoma (FUS, also known as TLS) and DNA damage-inducible transcript 3 (DDIT3, also known as CHOP) break-apart was not detected in the fluorescence *in situ* hybridization analysis. The tumor was

completely encapsulated and did not require additional treatment. Furthermore, no recurrence was reported 40 mo after surgery.

## CONCLUSION

We experienced an extremely rare, massive, low-grade MLS emerging from the floor of the mouth. Oftentimes, an MLS of the floor of the mouth lacks significant clinical findings and is often misdiagnosed. Although no FUS-DDIT3 fusion gene was detected, a low-grade MLS was ultimately diagnosed based on the histological findings.

**Key Words:** Myxoid liposarcoma; Floor of mouth; Surgery; Fluorescence *in situ* hybridization; Sublingual space; A case report

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**Core Tip:** Liposarcoma emerging from the floor of the mouth is extremely rare and often lacks significant clinical findings. This type of liposarcoma is usually misdiagnosed as ranula or benign tumor. In the present case, a definitive diagnosis could not be made preoperatively; however, myxoid liposarcoma was suggested, and complete resection could be achieved with appropriate imaging. A preoperative biopsy can help prevent incomplete resection. Clinical and radiological surveillance is necessary due to the possibility of local recurrence.

## INTRODUCTION

Liposarcomas are among the most common malignant mesenchymal neoplasms of the adipose tissue, which were first described by Virchow in 1857<sup>[1]</sup>. They account for approximately 20% of all soft tissue sarcomas and mostly occur in the lower extremities and retroperitoneum<sup>[2]</sup>; up to 9% of them are detected in the head and neck region<sup>[3]</sup>.

Although more common in other areas, it is rarely seen in the floor of the mouth<sup>[4]</sup>. Liposarcomas can become quite large, but those observed in the head and neck region rarely exceed 10 cm<sup>[2]</sup>. Liposarcoma is categorized into four subtypes: atypical lipomatous tumor/well-differentiated liposarcoma (ALT/WDL), myxoid liposarcoma (MLS), pleomorphic liposarcoma (PLS), and dedifferentiated liposarcoma (DDLs)<sup>[5]</sup>. Here we report a rare case of a massive low-grade MLS of the floor of the mouth in a 71-year-old male patient.

## **CASE PRESENTATION**

### ***Chief complaints***

A 71-year-old male presented to his physician stating that a mass had started to develop in the left floor of his mouth a year before and had slowly continued to enlarge.

### ***History of present illness***

The patient was referred to our division 3 mo later.

### ***History of past illness***

The patient had hypertension and alcoholic liver disease, but no other chronic disease.

### ***Personal and family history***

The patient heavily consumed alcohol, approximately 1000 mL of beer daily for 50 years. He denied any family history of malignant tumors.

### ***Physical examination***

Physical examination upon presentation showed an 8.0 cm × 7.0 cm elastic, hard tumor extending from the submental to the submandibular region. The left-side floor of the mouth was elevated by the painless, smooth, nontender tumor.

### ***Laboratory examinations***

The laboratory tests conducted were as follows: blood routine test, RBC:  $5.32 \times 10^{12}/L$  and HCT: 47.5%; biochemical test,  $\gamma$ -GTP: 82 U/L.

### *Imaging examinations*

Contrast-enhanced computed tomography (CT) showed an unenhanced cystic lesion separating from the surrounding muscle tissue (Figure 1A and B). Gadolinium-enhanced T1-weighted magnetic resonance imaging (MRI) revealed an intensely enhanced tumor lesion with a well-circumscribed solid mass. The tumor had compressed the genioglossus, digastric, and mylohyoid muscles and occupied the sublingual space and extended to the submandibular space (Figure 1C and D). A malignant salivary gland tumor emerging from the sublingual gland was suspected. 2-Deoxy-2-[ $^{18}F$ ]fluoro-D-glucose positron emission tomography/CT (FDG-PET/CT) showed a slight uptake in the tumor but no abnormal uptake in other organs. The maximum standardized uptake value ( $SUV_{max}$ ) was 3.0.

### **MULTIDISCIPLINARY EXPERT CONSULTATION**

Incisional biopsy of the floor of the mouth revealed a myxoid tumor, and a low-grade MLS or myxoma was suspected. Preoperative assessment was performed at the Oral Oncology Conference, which was attended by oral surgeons, radiation therapists, pathologists, and oncologist, who jointly decided on a treatment policy.

### **FINAL DIAGNOSIS**

We ultimately diagnosed this patient with MLS.

### **TREATMENT**

Submandibular dissection, tumor resection, and reconstruction with a forearm flap were performed. The tumor was resected based on the transoral and transcervical approaches. The floor of the mouth was reconstructed using a vascularized forearm flap following tumor resection. The tumor had a capsule, and the muscle tissue was

excluded; no infiltration into the compressed mylohyoid, genioglossus, geniohyoid, and hyoglossus muscles was seen. These muscles, except for mylohyoid, were preserved. The lingual and hypoglossal nerves were not affected by the tumor and were therefore preserved. The periosteum of the mandible in contact with the tumor was resected as a margin (Figure 2). The resected tumor had a size of 8.5 cm × 6.5 cm × 5.5 cm (Figure 3A).

The macroscopic and histological features of the tumor are presented in Figure 3B-E, respectively. The tumor cells lacked nuclear pleomorphism, and the mitotic activity was low. The immunohistochemical staining results are presented in Figure 4. Fused in sarcoma (FUS, also known as TLS) and DNA damage-inducible transcript 3 (DDIT3, also known as CHOP) break-apart was not detected in the fluorescence *in situ* hybridization (FISH) analysis. However, based on the histological findings, including the presence of Oil Red O (ORO)-positive lipoblasts, a low-grade MLS was ultimately diagnosed. No cervical node metastasis was histopathologically observed.

### **OUTCOME AND FOLLOW-UP**

At the 48-mo follow-up, the patient remained free of the disease, with no obvious signs of recurrence on clinical examination.

### **DISCUSSION**

Oral liposarcoma is extremely rare<sup>[2,6,7]</sup>. Ohta *et al*<sup>[4]</sup> reviewed 120 cases of oral liposarcoma and found that the most common subtypes are ALT/WDL (60.8%), MLS (17.5%), DDLS (6.7%), and PLS (3.3%). The most common location was the tongue (40.7%), followed by the cheek/buccal mucosa (31.4%), gingiva (7.6%), palate (5.9%), floor of the mouth (5.1%), lip (4.2%), and other areas (5.1%). Since 1960, eight cases of liposarcoma of the floor of the mouth have been reported in the English-language literature<sup>[7,8-13]</sup> (Table 1). Clinically, liposarcoma presents as a soft, painless mass with a slow growth and relatively well-defined boundaries; it is also covered with a pseudocapsule. Liposarcoma is commonly known to often lack significant clinical



findings. In fact, in a past report of liposarcoma of the floor of the mouth, five patients were clinically diagnosed with ranula or benign tumor and underwent excisional biopsy (Table 1). In the present case, the tumor developed in the deep part of the floor of the mouth. It grew asymptotically, forming a massive mass occupying the sublingual space and extending to the submandibular space, and malignant salivary gland tumor was suspected. This was a rare case in which the clinical diagnosis of a malignant tumor was made.

MRI and CT scan are commonly employed to diagnose liposarcoma. Among them, MRI is the most useful as it can reveal tumor features that suggest malignancy. On MRI, liposarcoma is clearly demarcated; has thick, fibrous septa; and appears nodular and lobulated. The presence of bleeding, edema, and/or necrotic areas in addition to these findings is suggestive of malignancy. A low-grade liposarcoma tends to show a slight enhancement compared with a high grade liposarcoma, which usually enhances contrast very well. On FDG-PET/CT, MLS commonly presents as a mildly FDG-avid mass with overlapping metabolic characteristic. Due to the low FDG activity of a primary MLS lesion, the usefulness of FDG-PET/CT in tumor follow-up is questionable<sup>[14]</sup>. In the present case, MRI showed an uneven enhancement inside the tumor, and FDG-PET/CT showed a slight uptake in the tumor; both the MRI and PET/CT findings were consistent with the characteristics of MLS.

Although each liposarcoma <sup>2</sup> subtype has its own pathological features, <sup>5</sup> the key to diagnosis is the presence of lipoblasts. The myxoid variant comprises <sup>5</sup> proliferating lipoblasts at varying stages of differentiation, signet-ring cells, a plexiform capillary pattern, and a myxoid matrix<sup>[15]</sup>. The smallest cell morphology is considered a low-grade tumor and is usually enriched with spindle-shaped cells. Large cell morphology is considered to be of high grade and usually shows abundant round cells. Many soft tissue neoplasms, whether benign or malignant, can demonstrate myxoid changes, including extraskeletal myxoid chondrosarcoma, myxofibrosarcoma/myxoid-type malignant fibrous histiocytoma, aggressive angiomyxoma, WDL with myxomatous change, and myxoma, and making a definitive histological diagnosis is sometimes

difficult. In the present case, myxoma was part of the differential diagnosis of MLS, and it was difficult to make a definitive diagnosis in the small biopsy specimen.

MLS is characterized by a reciprocal translocation that generates a fusion transcription factor oncogene. In more than 95% of cases, a translocation, t (12;16) (q13;p11), which indicates fusing FUS with DDIT3, is present<sup>[16]</sup>. In the present case, we conducted FISH analysis to determine whether the FUS-DDIT3 fusion gene was present, but the break-apart between FUS and DDIT3 was not detected. Based on the histological findings, including the presence of ORO-positive lipoblasts, low-grade MLS was ultimately diagnosed. The fusion gene would have been detectable with polymerase chain reaction analysis, but we did not have a chance to conduct such an analysis. However, specific gene mutation is not found in all cases of each tumor type, and if histological diagnosis is reliable, it may not be necessary to change the diagnosis depending on the presence or absence of the gene mutation<sup>[17-19]</sup>. We ultimately made the diagnosis of MLS. Genetic testing for soft tissue tumors should be conducted in a well-controlled facility in close proximity to histological and clinical findings.

Liposarcoma is known to have a small island-shaped tumor tissue around the main tumor tissue, and inadequate excision is considered as the main reason for local recurrence, estimated at approximately 30%<sup>[20,21]</sup>. The optimal treatment for head and neck liposarcoma is surgery with negative margins; however, in the head and neck region, radical surgical approaches can cause functional and aesthetic disorders and may not provide sufficient resection margins. As MLS is radiosensitive, preoperative radiotherapy is considered effective to achieve a negative margin<sup>[22]</sup>. However, in the present case, a definitive diagnosis of MLS was not made preoperatively, and preoperative irradiation was not performed due to unclear tumor boundary and possibility of complete resection. Postoperative irradiation is considered for large tumors, but the efficacy of radiation therapy has been obscure due to the absence of systemic studies comparing the outcomes of treatment with or without radiotherapy<sup>[23]</sup>. Although metastasis is unlikely, local recurrence is common, with the MLS recurrence



rates ranging from 33% to 53%<sup>[8,24]</sup>. Lymph node metastases are quite rare<sup>[25]</sup>; thus, neck<sup>1</sup> dissection is not necessary unless there is specific evidence of lymph node metastasis.

The 5-year disease-specific survival rate is 100% for ALT/WDL, 100% for MLS, 60% for round cell liposarcoma, and 45% for PLS in the head and neck region<sup>[26]</sup>. Tumor sizes > 5.0 cm<sup>[27]</sup> and > 3.6 cm<sup>[28]</sup> have been reported to be poor prognostic factors for liposarcoma in the oral region, and careful follow-up is thus needed, as done for the patient in the present case.

## CONCLUSION

In conclusion, we treated an extremely rare, massive, low-grade MLS<sup>12</sup> of the floor of the mouth. Oftentimes, an MLS of the floor of the mouth lacks significant clinical findings and is misdiagnosed. A preoperative histological diagnosis *via* incisional biopsy allows the largest possible primary resection. In the present case, complete resection was performed, and no lymph node metastasis was observed; however, a tumor size > 5 cm is a risk factor for poor prognosis; thus, careful follow-up is essential. Although no FUS-DDIT3 fusion gene was detected, low-grade MLS was ultimately diagnosed based on the histological findings.

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