Dear Editors.

Thank you for your review of our manuscript entitled "**Massive Low-Grade Myxoid Liposarcoma of the Floor of the Mouth: Case Report and Review of Literature**" (79770), which we would like to resubmit after revisions. We have provided below a detailed response to the reviewer's comments and have made the necessary revisions to the manuscript as well.

79770-Answering Reviewers

Reviewer 1

Lines 38-9

"The tumor was completely encapsulated and no additional treatment was performed." Treatment is performed when required.

The tumor was completely encapsulated and no additional treatment was required.

→ Thank you for your comment concerning English refinement. Changed as fellows: "The tumor was completely encapsulated and did not require additional treatment." (p2, lines 40-41)

Core Tip: Liposarcoma arising from the floor of mouth is extremely rare and often lacks significant clinical findings. Previous reports of the floor of mouth liposarcoma have been misdiagnosed as ranula or benign tumor. A low-grade myxoid liposarcoma (MLS) or myxoma was suspected on an incisional biopsy. We performed submandibular dissection, tumor resection, and reconstruction with a forearm flap. The surgical specimen revealed histologically low-grade MLS. We conducted FISH analysis, 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.

‘Core Tip’ is advice pertinent, and not what management (diagnosis & treatment) done.
Kindly modify.

→ Thank you for your comment concerning Core Tip modifies. Changed as follows: “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.” (p2, lines 51-p3, lines 55)

FURTHER DIAGNOSTIC WORK-UP

An incisional biopsy of the floor of mouth was diagnosed as a myxoid tumor, and a low-grade MLS or myxoma was suspected. Preoperative assessment was conducted at the Oral Oncology Conference, which was attended by oral surgeons, radiation therapists, pathologists, and oncologist, who jointly decided upon a treatment policy.

A standard Surgery Textbook states:
“In addition, for some radiosensitive histologic subtypes, such as myxoid liposarcoma, preoperative radiation therapy may shrink the tumor, facilitating resection with negative margins”.
[Reference: Gonzalez RJ, Gronchi A, Pollock RE. Soft tissue sarcomas. In: Brunicardi FC, Andersen DK, Billiar TR, Dunn DL, Hunter JG, Kao LS, et al, editors. Schwartz’s Principles of Surgery. New York: McGraw-Hill Education. 2019;p 1577.]

Was pre-operative radiotherapy considered?

→ Thank you for your comment and detailed references regarding preoperative radiotherapy. In this case, preoperative radiotherapy was not performed because MLS was not diagnosed preoperatively. In the DISCUSSION, I referred to the references provided and explained the reason why preoperative radiotherapy was not performed. “As MLS is radiosensitive, preoperative radiotherapy is considered effective to achieve a negative margin [22]. 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 [23]." (p7, lines 183-189)

TREATMENT

Lines 117-8
However, based on the histological findings, including the presence of Oil Red O (ORO)-positive lipoblasts. No cervical node metastasis was observed.

Based on the histological findings, what was done/interpreted is not clear.

Clinically or histo-pathologically?

→ Thank you for your comment concerning the response after the histopathological findings. Added as follows: "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." (p5, lines 119-121)

DISCUSSION

Lines 185-7

Tumor sizes > 5.0 cm [25] and > 3.6 cm [26] have been reported to be poor prognostic factors for liposarcoma in the oral region, and careful follow-up is needed for the patient in the present case.

It sounds that it (follow-up) is not needed by other patients with similar tumour sizes.

Tumor sizes > 5.0 cm [25] and > 3.6 cm [26] have been reported to be poor prognostic factors for liposarcoma in the oral region, and careful follow-up is needed, as done for the patient in the present case.

→ Thank you for your comment concerning English refinement. Changed as follows: "Tumor sizes >5.0 cm [27] and >3.6 cm [28] 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." (p8, lines 194-197)

CONCLUSION

In conclusion, we treated an extremely rare, massive, low- grade MLS of the floor of mouth. MLS of the floor of mouth often lacks significant clinical findings and is often misdiagnosed.

Conclusion guides further practice.
Myxoid liposarcomas frequently present as slow-growing tumours. Early management is always advisable.

Modification needed.

Thank you for your comment concerning COCLUSION modifies. Changed as follows: "A preoperative histological diagnosis via incisional biopsy allows the largest possible primary resection." (p8, lines 201-202)

CONCLUSION

In the present case, complete resection was performed, and there was no lymph node metastasis; however, a tumor size > 5 cm may be a risk factor for poor prognosis; thus, careful follow-up is necessary.

Conclusions should be strong and firm.

Late manifestations of metastasis and recurrence are common with large tumour sizes.

In the present case, complete resection was performed, and there was no lymph node metastasis; however, a tumor size > 5 cm is a risk factor for poor prognosis; thus, careful follow-up is necessary.

→ Thank you for your comment concerning English refinement. Changed as follows: "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". (p8, lines 202-206)

Reviewer 2

Liposarcoma of the Floor of Mouth: case report and review of literature) presents a very important and interesting study of this very rare case in the floor of mouth, yet there few points to be addressed before publication

– " It therefore remains unclear whether the present case had the fusion gene".Page7, Line169， delete this sentence.

→ Thank you for your comment. As you pointed out, it has been deleted.

- Figure 3: lens magnification should be mentioned in the legend.

→Thank you for your comment concerning Figures. As you pointed out, I added the lens magnification and scale bar to the legend.