

Peer Review File

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Reviewer A

1: I am pleased to review this interesting manuscript with a subject that has been little studied. The authors describe a case series of patients with one of the most common benign salivary gland tumors in an unusual location (the lip).

The message of the manuscript is stringently described and unambiguous.

Reply: We thank you sincerely for the insightful comments on our paper. We feel the comments have helped us significantly improve the paper.

2: It would be desirable to highlight the limitations, especially with regard to Figure 4. The figure provides interesting information and should be included in the manuscript, but there is considerable selection bias in this regard.

Reply: We agree with you and have incorporated this suggestion. In fact, the original Figure 2 that we presented is the result of our oral surgery only, and we also examined only resected lesions. I think this needs to be clarified. Thank you for pointing this out.

Changes in the text: (Results) We have added text about study limitations as advised (see Page 9, line 174-178).

3: Did the authors find cases in the literature where recurrence or malignant degeneration occurred in the lip area?

Reply: Of the 35 previously reported cases of lip PA we examined, five had malignant findings. None of them showed postoperative recurrence. We felt your points needed to be clearly stated due to the nature of the PA pathology. I appreciate your pointing this out.

Changes in the text: (Discussion) We have added our text as advised (see Page 12, line 244-250).

4: It would be desirable for the authors to describe whether the removal of the tumors was performed under local or general anesthesia.

Reply: The surgery for all of our cases was performed under local anesthesia.

Changes in the text: (Results) We have added one sentence about this for each of the three patients (see Page 7, line 138; Page 8, line 159).

5: At what intervals do the authors follow-up patients with PA in the lip? Are ultrasounds or MRIs performed as part of the follow-up?

Reply: There is no set view on the lip PA follow-up interval. This is because postoperative recurrence of PA rarely occurs within the first few years, but often occurs 5–10 years or more later. We initially followed up each patient every other week until we were sure that the wound was completely healed. After that, we encouraged the patients to visit the clinic every six months, but there are cases in which patients stop coming in halfway through the

follow-up. We believe that one of the reasons for this is that the patients themselves no longer feel the need to follow up. Therefore, we need to fully explain the pathophysiology of PA. On the other hand, few articles clearly describe the need for imaging studies (US, MRI, etc.) as a means of postoperative follow-up. Schapher et al. have shown that the use of US as a follow-up for parotid PA can provide an early detection of recurrent findings (34). However, since the lips are the easiest area in the oral cavity to self-examine, the patient's own tendency to notice abnormalities should be included in the consideration of follow-up intervals and the need for imaging studies.

Changes in the text: (Discussion) Reflecting the above, we have modified and added our text and cited additional relevant and important references (see Page 12,13, line 254-267, refs. 35-37).

Reviewer B

1: The authors give a detailed account of clinical picture and a comprehensive literature review on the rare cases of lip pleomorphic adenoma.

Reply: Thank you very much for taking the time to review this paper. Your precise points have added a richness to the content.

2: There are few points which require authors' attention and clarification:

1) In line 94, the ratio should be written as "1:1" instead of "3:3."

Reply: Thank you for your suggestion.

Changes in the text: (Materials and methods) We have modified our text (see Page 5, line 94).

3: In line 190, the ratio should be written as "4:3" instead of "20:15".

Reply: Thank you for your suggestion.

Changes in the text: (Discussion) We have modified our text as advised (see Page 10, line 198).

4: in line 234-235, the authors state that they performed only removal with complete inclusion of the capsule in the three present patients. However, in the case history of patient 3, the authors report that the surgical margin was unclear (line 158), which implies that there was incomplete inclusion of capsule. Fig 3F also raises the suspicion of incomplete excision. The authors should clarify their statement of complete inclusion of capsule and surgical since it is relevant to the appropriateness of their clinical management. The completeness of capsule and surgical margin significantly increases the risk of local recurrence and affect clinical management.

Reply: We agree with you. This is an important opinion. Indeed, in Patient 3, we did not completely remove the resected material with its entire capsule. We needed to correct this

discrepancy between the Results and Discussion. Thank you for pointing this out.

Changes in the text: (Discussion) We have modified our text as advised (see Page 12, line 251-254).

Reviewer C

1: The survey results clearly showed that pleomorphic adenomas should be considered on the lips and the need for follow-up.

The writing was objective and clear and there is relevance in the presentation

Reply: We are thankful for the time and energy you expended. We hope that this revision of the paper has resulted in even better content.

Reviewer D

1: I read the paper "Lip Pleomorphic Adenomas: Case Series Study and A Literature Review" with pleasure. Authors conclude that preoperative diagnosis of the lip pleomorphic adenoma is more difficult compared to palatal lesions, is also prone to long-term neglect, and has the potential for recurrence and malignant transformation. It is thus necessary to perform an excision that includes the capsule and surrounding tissues, and careful postoperative follow-up should be continued.

Reply: Thank you very much for providing important comments. As you say, there are cases in which a preoperative diagnosis of lip PA is difficult or where the treatment plan is cautious in terms of recurrence or malignancy.

2: Generally, diagnosis and treatment of the pleomorphic adenoma is well known and now widely used worldwide. Nevertheless, the topic of lip pleomorphic adenoma is still relevant due to the rarity of the occurrence of this tumor in the lip and oral cavity. The authors carried out a thorough analysis of the available literature in a generally accepted manner (AME Case Series Checklist – Adapted from CARE Checklist and PROCESS Checklist), which significantly increases the value of this work.

Undoubtedly, this topic requires further research on larger groups of patients. However, in my opinion, it is a very well-written research paper in all respects. Therefore, without a doubt, I recommend this work for publication.

Reply: We are very happy to hear your kind words. Indeed, our present study alone may not be sufficient to support this content. We will strive to carry out our research with certainty by conducting a broader survey in the future. We hope that this paper, as improved through this peer review, will meet your expectations.