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ORAL LEIOMYOSARCOMA PRESENTING AS A RECURRENT HARD PALATE MASS: A CASE REPORT

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Abstract – *Objective:* *Leiomyosarcoma (LMS), a sarcoma with smooth muscle differentiation rarely affects the oral cavity due to the paucity of smooth muscle tissues in the region. Because of the intricacy of the anatomy of the oral cavity, tumors affecting this region usually require complex surgeries. We are thus presenting this case, due to the rarity of the disease and its successful treatment by a multidisciplinary team.*

Case presentation: *A 30-year-old female who was previously diagnosed with a benign smooth muscle neoplasm, had a partial maxillectomy in another institution, came to us for tumor recurrence with a histopathologic report of a smooth muscle tumor of uncertain malignant potential (SmTUMP). Facial and neck CT scan, as well as facial MRI revealed a resectable disease with unremarkable metastatic workup.*

Results: *The clinical aggressiveness of the disease prompted the multidisciplinary team to proceed with infrastructure maxillectomy with the defect covered by a surgical obturator. Final histopathologic report revealed that the tumor is LMS with good margins. Thereafter, the patient underwent adjuvant radiation therapy. At 1-year post-surgery, the patient had minimal speech deficit with good deglutition function and no recurrence.*

Conclusions: *LMS is exceedingly rare in the head and neck region. It is also difficult to diagnose. However, it should be considered a differential diagnosis when dealing with smooth muscle tumors. Successful treatment of this disease entails high index of suspicion and involvement of a multidisciplinary team.*

KEYWORDS: *Oral leiomyosarcoma, Oral smooth muscle tumor, SmTUMP.*

INTRODUCTION

Leiomyosarcoma (LMS) is a soft tissue sarcoma (STS) that originates from smooth muscle cells or from precursor mesenchymal stem cells[1,2]. It is locally aggressive, with propensity for local recurrence and distant metastasis[1,2]. In general, it accounts for 7 – 25% of all STS which in turn represents only 1% of all adult malignancies[1,2]. It is exceedingly rare in the head and neck region which only represents 10% of all leiomyosarcoma, especially in the oral cavity with only 30 – 65 reported cases[3-8].

The 2020 World Health Organization classification of tumors also listed two other smooth muscle neoplasms, leiomyoma and smooth muscle tumor of uncertain malignant potential (SmTUMP) which are benign and intermediate

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grade, respectively[2,9]. These two neoplasms are also infrequent in the oral cavity, with leiomyoma having a reported incidence of 0.065% and SmTUMP with no reported cases[10,11]. Although only LMSa among the smooth muscle tumors is considered malignant, SmTUMP and occasionally leiomyoma may be locally aggressive[10,12].

The primary treatment for these neoplasms is wide excision with radiotherapy and chemotherapy reserved as adjuncts for advance resectable LMS or palliation for unresectable disease[3-8]. The intricacy of the anatomy of the oral cavity, however, makes wide excision difficult in this area[7,8]. Oncologic resection should be made with due regard to the possible loss of function and unacceptable aesthetic outcome.

The purpose of this paper is to present a very rare case of oral leiomyosarcoma successfully treated with surgery and radiation therapy. The success highlights the need for prompt involvement of a multidisciplinary team and early intervention.

CASE PRESENTATION

A 30-year-old-woman with no comorbidities came in for consult at our outpatient department for a hard palate mass. A year earlier, the patient complained of a mass along the medial aspect of her left superior posterior alveolar process adjacent to the second molar tooth, associated with on and off pain (Figure 1A). She was then treated by her dentist with oral antibiotics and underwent tooth extraction, which resulted to the resolution of pain (Figure 1B).

A month after the tooth extraction, the mass was noted to increase in size (Figure 1C). Wedge biopsy was done by the then attending physician, with the histopathologic report revealing that the sample taken was composed of benign salivary and smooth muscle tissues. Thereafter, progression in size of the mass was noted, later involving the left superior posterior alveolar process adjacent to first, second and third molars and part of the hard palate (Figures 1D, 1E, and 1F). The patient was advised and underwent partial maxillectomy at the previous institution (Figure 1G). Histopathologic examination of the specimen revealed that the tumor was a spindle cell neoplasm with 0-1 mitosis per 50/hpf. The tumor stained positive for smooth muscle actin, H-caldesmon and muscle specific actin. On the other hand, the tumor stained negative for STAT6, S100 and CD34. It has 3-5% positivity to Ki67. All of which are consistent with the diagnosis of smooth muscle tumor of uncertain malignant potential (SmTUMP).

Recurrence, however, was noted one month later. The mass progressed in size, later involving the remnant left posterior hard palate (Figures 1H and 1I), thus, the consult in our institution. On inspection the patient had a 3 cm fungating, reddish-pink mass at her left hard palate, crossing the midline and approaching the soft palate posteriorly. The mass was fixed and hard. The left gingivo-buccal sulcus and the retromolar trigone were not involved. There was no palpable cervical lymphadenopathy. Nasal endoscopy noted bulg-

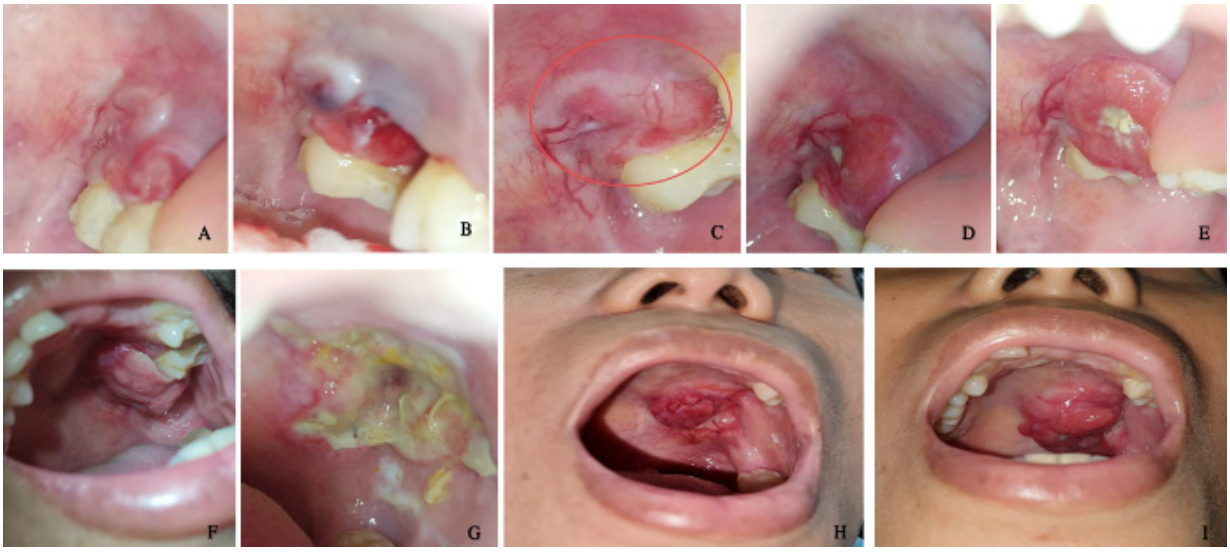


Fig. 1. A, 1 year prior to consult. B, 10 months prior to consult. C, 9 months prior to consult. D, 8 months prior to consult. E, 7 months prior to consult. F, 6 months prior to consult. G, 5 months prior to consult and 1 week after partial maxillectomy. H. 3 months prior to consult. I, Day of consult.

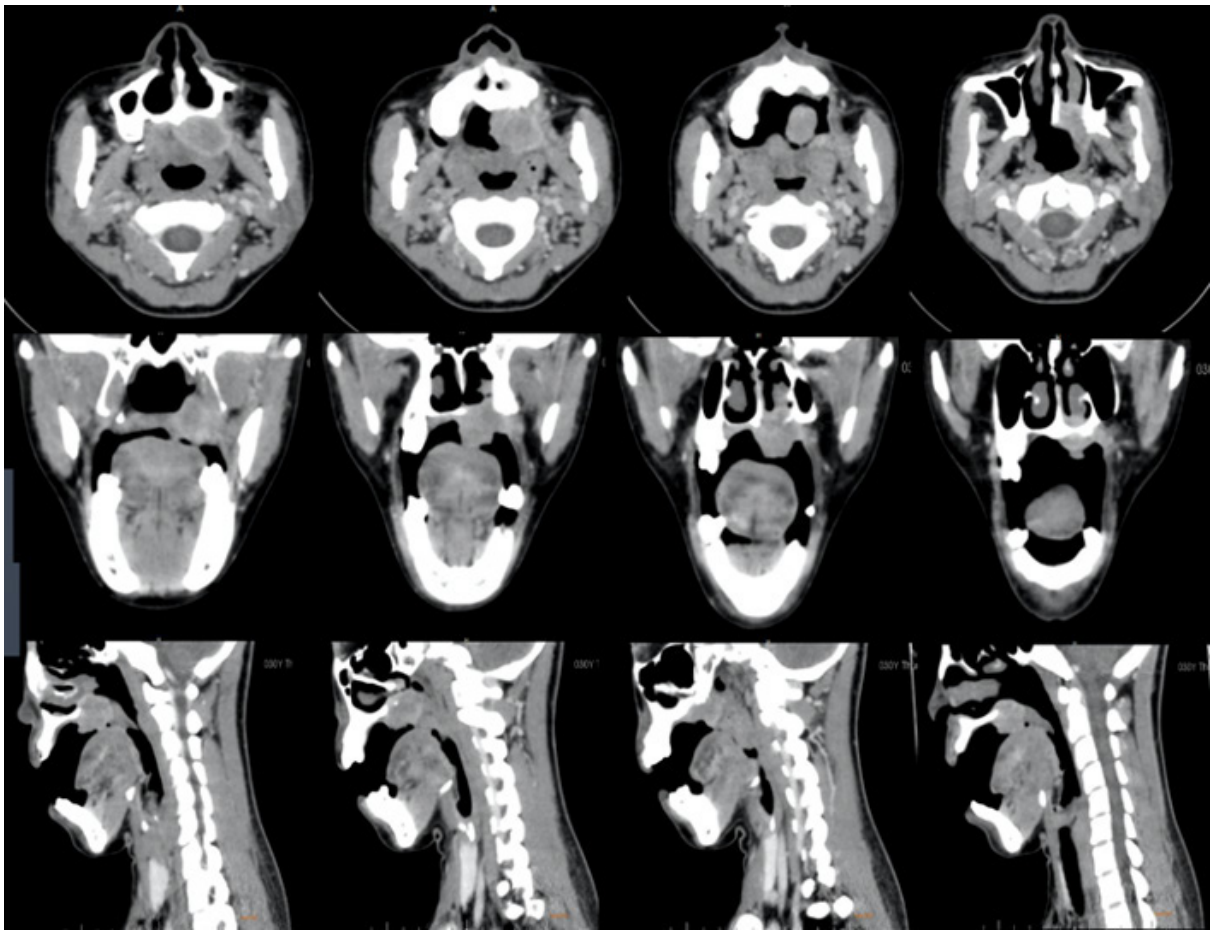


Fig. 2. Facial and neck CT-scan with IV contrast.

ing at the inferolateral surface of the nasal cavity near the left posterior choanae with intact mucosal lining and no color changes.

Facial and neck CT scan with IV contrast (Figure 2) revealed a 2 x 3 x 2 cm fairly defined and heterogeneously enhancing fungating mass with necrotic center, arising from the junction of the left soft and hard palate. Anteriorly, it is seen fungating and encroaching into the anterior oral cavity; posteriorly, it is noted to be abutting the left palatine tonsil; laterally, it is abutting to the left medial pterygoid muscle. However, on facial MRI (Figure 3), the mass had a plane of differentiation from left medial pterygoid muscle. Chest CT scan with IV contrast and liver ultrasound were unremarkable. After evaluation, we have a 30-year-

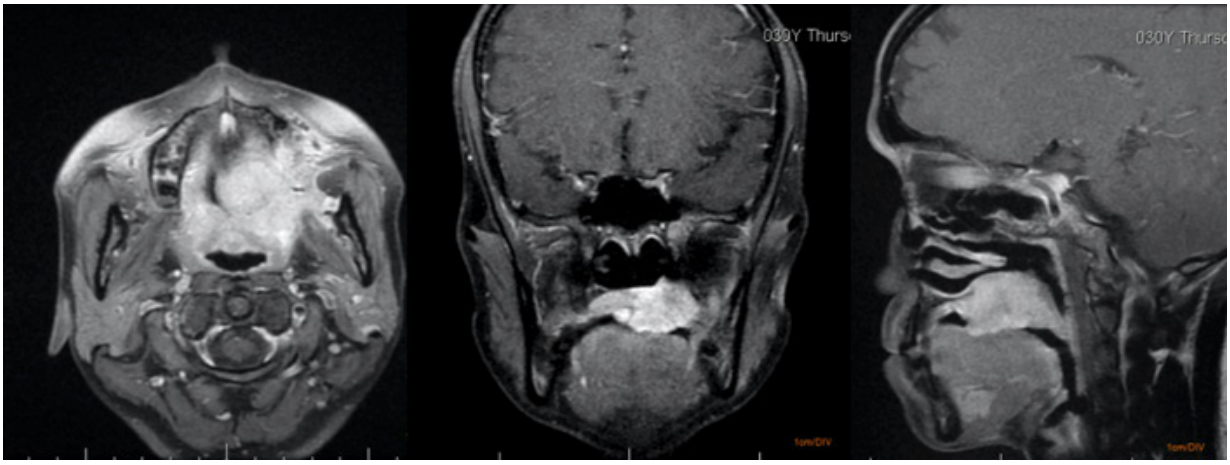


Fig. 3. Facial MRI with contrast.

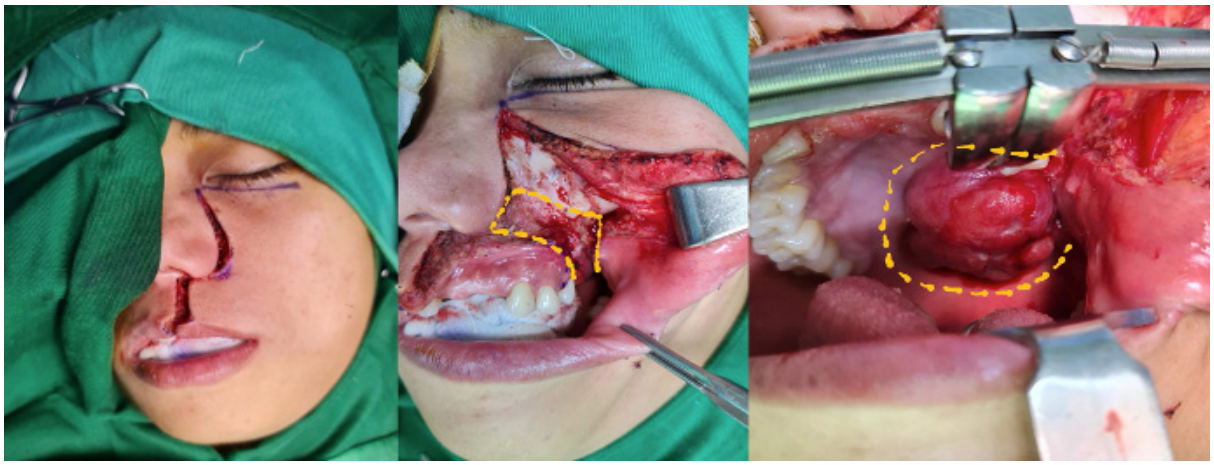


Fig. 4. Extent of the tumor.

old female patient diagnosed with a smooth muscle tumor of uncertain malignant potential (SmTUMP), left hard palate, who was post-partial maxillectomy, left.

After discussion involving a multidisciplinary team, the patient was scheduled for left infrastructure maxillectomy thru a modified Weber-Ferguson-Dieffenbach incision with subciliary extension (Figure 4). Intraoperatively, there is a 3 cm fungating mass, centered on the posterior hard palate left, extending to the anterior portion of the soft palate posteriorly and to the midline of the hard palate medially (Figure 5A). Superiorly, the mass involves the floor of the left maxillary sinus and the floor of the left nasal cavity. The mass also extends to the left medial pterygoid muscle, which was also removed (Figure 5B). There were clear surgical margins on frozen section (Figure 6). Surgical clips were placed on the insertion and origin of the left medial pterygoid muscle (Figure 7). Maxillary packing and a prefabricated surgical hard palate obturator were placed to close the defect.

Histologic examination of the specimen (Figure 8) revealed that the tumor was a high-grade spindle cell sarcoma favoring smooth muscle differentiation - leiomyosarcoma. The tumor size was 2.5 cm in single widest dimension. The mitotic rate was 45-50/10 HPF. There was no necrosis, lymphovascular and perineural invasion. All relevant margins are clear of the tumor. The diagnosis of leiomyosarcoma, left hard palate, Stage IIIB (pT4aN0M0G2) with extension to the left medial pterygoid muscle was made. The patient underwent radiation therapy of 60 Gy over 6 weeks thereafter. Obturators were fabricated, and fitted as healing progressed, allowing progressively improvement of speech and deglutition. The latest obturator **(**Figure 9**)** allows speech with

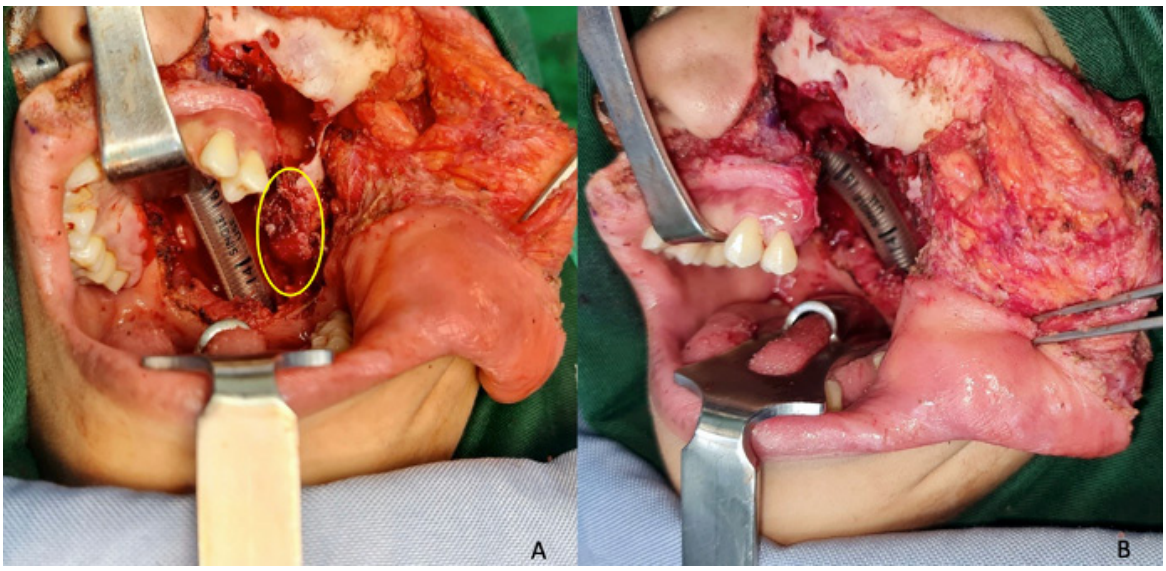
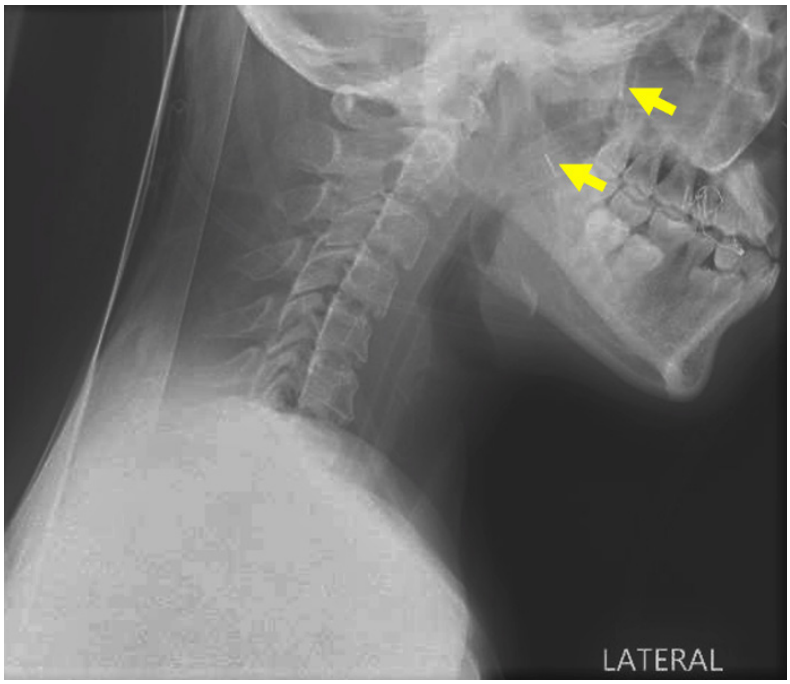


Fig. 5. A. Involved left medial pterygoid muscle. B. Defect after inferior maxillectomy.

Fig. 6. Post-operative radiograph of the surgical field.



minimal deficit and satisfactory deglutition. At 1 year after primary treatment, there is no clinical and radiologic evidence of recurrence.

DISCUSSION

Soft tissue sarcoma (SMS) is a broad group of cancers that have a mesenchymal origin[11]. It is rare, consisting only 1% of adult malignancies[9-12]. On the other hand, leiomyosarcoma (LMS) is a SMS showing distinct smooth muscle features[10]. LMS only accounts for 7 – 25% of all SMS and is extremely rare in the oral cavity due to the paucity of smooth muscles in this region[3-8]. There are only 30-65 reported cases of primary oral LMS to date[6]. LMS of the oral cavity may originate from vascular smooth muscle, myoepithelial cells, or undifferentiated mesenchymal cells[2-8]. Most common sites of oral LMS, according to frequency of occurrence, are the tongue, palate, maxilla, mandible, and rarely, the buccal mucosa and the retromolar trigone[7,8].

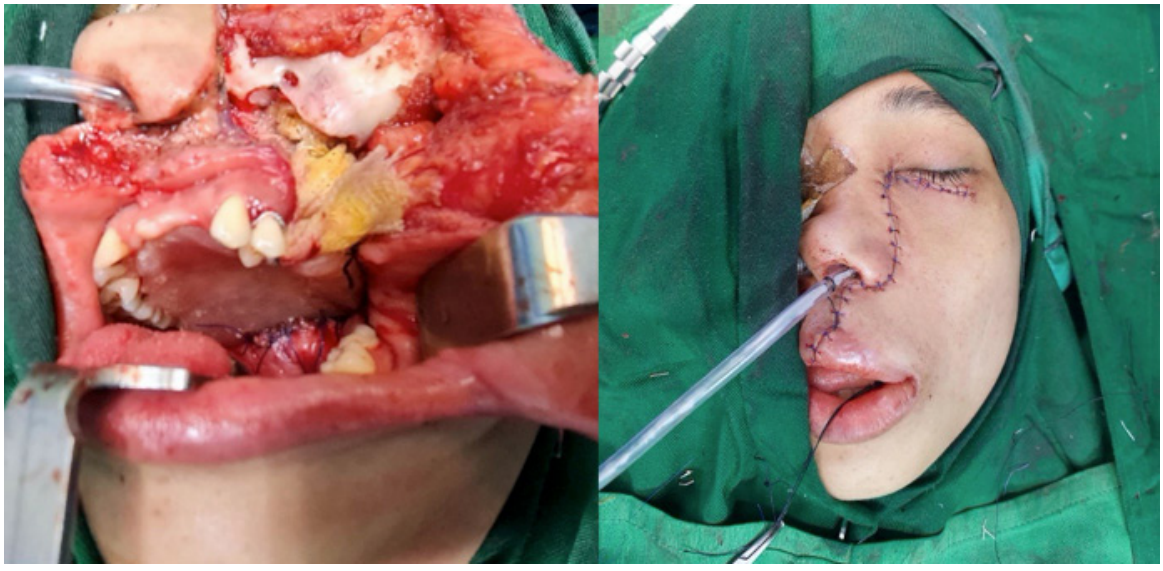


Fig. 7. A, Maxillary packing ang surgical obturator in place. B, Surgical field post-closure.

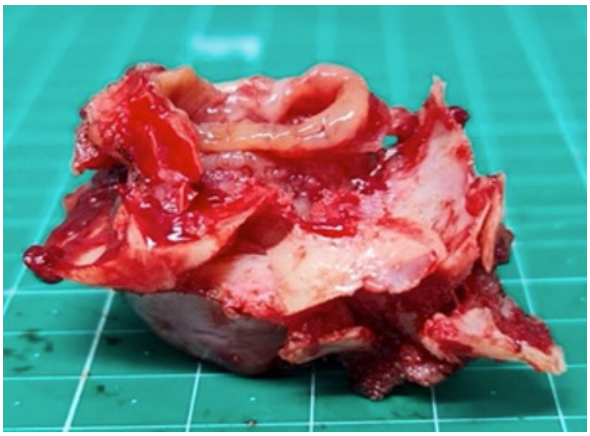


Fig. 8. Gross specimen.

The widely used criteria for the diagnosis of LMS is the Stanford criteria[7]. A typical LMS usually has spindle cells with blunt-ended nuclei and intersecting fascicles on H and E staining with elongated eosinophilic cytoplasm[9,13]. However, in atypical pleomorphic or epithelioid LMS, diagnosis may require desmin or caldesmon reactivity to corroborate smooth muscle differentiation[9,13]. The other necessary criterion for the diagnosis of LMS is proof of malignancy[9,13]. This includes any of the following: cytologic pleomorphism, atypia, tumor cell necrosis or mitotic rate > 4 per 50 hpf[9,13]. In the absence of an evidence of malignancy, a smooth muscle tumor can either be leiomyoma or smooth muscle tumor of uncertain malignant potential (SmTUMP)[9,13]. Leiomyoma is cytologically bland with mitosis of <1 per 50 hpf with no necrosis, while SmTUMP, though cytologically bland, has mitosis of 1-4 mitotic per 50 hpf and is associated with recurrences[10]. It can be assumed that leiomyoma, SmTUMP, and LMS is a continuum of smooth muscle tumor differentiation, representing benign, intermediate and malignant neoplasms[4,5,7,10].

Our case is an oral cavity tumor with three histologic results taken at different points over a period of one year. The first histologic result was for an incision biopsy done with previous consults which was consistent with benign salivary and smooth muscles tissues. The second histologic result was for the partial maxillectomy done in another institution which was consistent with SmTUMP. The third biopsy was for the infrastructure maxillectomy done in our institution consistent with high grade leiomyosarcoma. These three results may be thought to represent different stages of the ongoing tumorigeneses of LMS, wherein malignant properties are conferred to normal cells in an ongoing transitional process that results to a progressively higher and irreversible cancer state[11,14]. Another plausible explanation is that the samples previously taken were not representative of the true tumor characteristics due to intratumoral or spatial heterogeneity which is common among sarcomas[14]. Specimen taken from parts of the tumor may feature varying stages of the disease process which may or may not exhibit malignant characteristics[14]. This is especially problematic for oral sarcomas

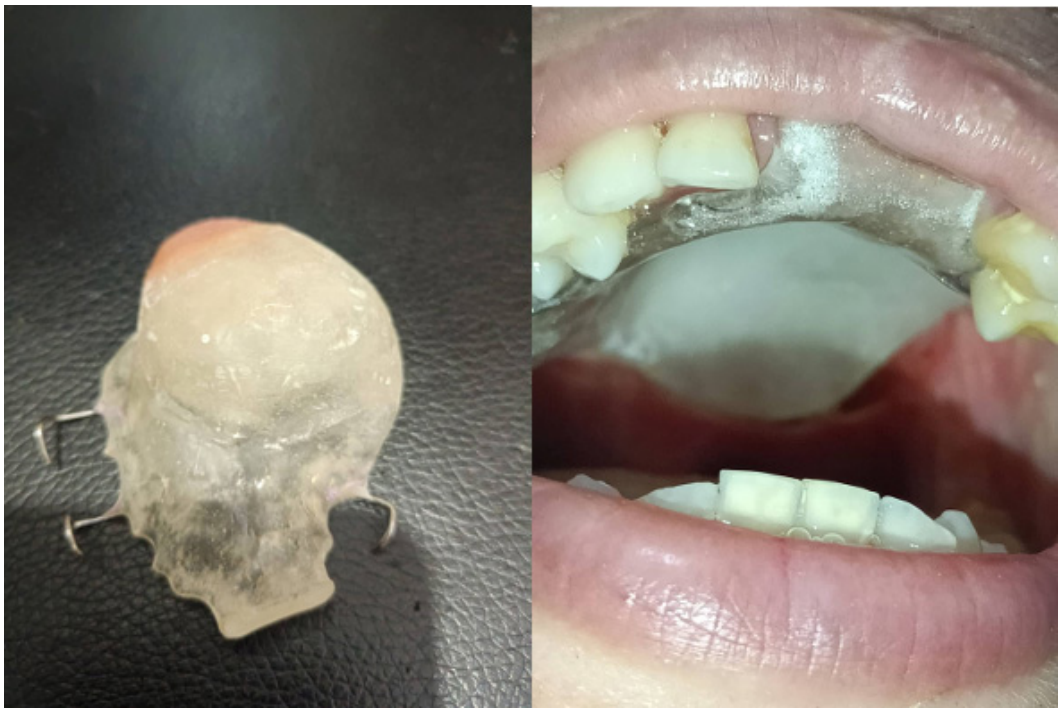


Fig. 9. Latest Obturator.

wherein specimens obtained are often limited[3-6,14]. Regardless of the explanation of the histologic variation, the clinician's dilemma in this case was coming up with a prompt diagnosis in order to give the appropriate treatment.

When the patient presented at our institution, the multidisciplinary team opted to proceed with oncologic resection because of the tumor's clinical behavior in the background of a histologic report consistent with SmTUMP. Infrastructure maxillectomy was decided after resectability was determined and metastasis ruled out. Further tissue diagnosis was not deemed to significantly change the management at that point in time.

Several therapeutic modalities may be utilized in the management of LMS of the head and neck. The National Comprehensive Cancer Network (NCCN) has provided guidelines for the diagnosis and management of soft tissue sarcomas of the head and neck, which depend on the locoregional and distant extent of the disease[15]. Stage 1A and 1B diseases require wide surgical resection for cure, while stage II and III diseases undergo a combination of wide excision surgery and neoadjuvant or adjuvant therapies, which include either radiotherapy, chemotherapy or both[15]. Advance disease requires multimodal treatment with the goal of therapy being palliation with some exceptions[15]. The involved multidisciplinary team, however, determined that our case is a technically resectable disease wherein appropriate oncologic margins can be obtained with an acceptable functional outcome.

Our patient underwent wide resection via infrastructure maxillectomy, which is the mainstay of treatment of SmTUMP as well as LMS of the head and neck across all stages, except for disseminated, advanced diseases[15]. The extent of the excision was planned with due consideration to the post-operative functional and aesthetic outcomes, taking into consideration inputs from dental services and rehabilitation medicine[16-18]. Dissection was made along grossly normal tissues providing 2 cm margin with intraoperative documentation of both surgical and pathological margins[3-8]. Peripheral markers using surgical clips were placed in relevant margins to guide future radiation therapy[1-5]. It should be noted, however, that only with the final histologic report that the diagnosis of leiomyosarcoma was made and the need for radiotherapy was determined. If LMS was diagnosed preoperatively, lymph node dissection was still not indicated because lymph nodes were not clinically involved. Even locally advanced diseases have occult metastases in only 2-5% of cases, which renders lymph node dissection unnecessary[14].

As was mentioned, radiation therapy may be utilized as an adjunct to surgery, which may be given preoperatively or postoperatively depending on the clinical status of the patient[14]. Modalities include external beam radiation, brachytherapy, intraoperative radiation, or intensity-modulated radiotherapy[19,20]. Generally, adjuvant radiotherapy is reserved for patients with poor prognostic features, including large and high-grade tumors which is true in our patient[14].

Systemic therapy, like radiation therapy, may be given preoperatively or postoperatively, as an adjunct to surgery. The preferred first-line regimen for LMS of the head and neck includes the AIM regimen (Doxorubicin, Ifosfamide, Mesna)[14]. For LMS of the oral cavity, however, chemotherapy generally has limited use. In a study by Mitsudo et al[6], inoperable LMS of the maxillary region were treated with super selective intra-arterial chemotherapy using Docetaxel and Cisplatin, which resulted to 50% tumor shrinkage with 80% tumor cell necrosis[4]. This shows that chemotherapy has a role if the main goal of treatment is palliation.

The prognosis of LMS of the oral cavity will depend primarily on tumor grade, size and extent[20]. Tumor size greater than 5 cm, as well as a high-grade histologic status are considered poor prognostic factors[6,11,21]. The estimated five-year overall survival (OS) for primary oral LMS across all stages is at 55 - 61.87%[6,11,21]. These rates are low compared to results obtained in a SEER review on 578 patients with LMS of the head and neck, wherein the five-year disease-specific survival across all stages was 87.6% for well-differentiated tumors, 85.7% for moderately differentiated tumors, and 52.7% for poorly differentiated tumors[6,11,15,21]. However, primary oral LMS limited to soft tissues and gnathic bones with no extension into the paranasal sinuses has a good five-year OS of 94.1%[15]. Thus, the five-year survival of our patient with a completely resected 2.5 cm high grade lesion of the oral cavity extending into the maxillary sinus ranges between 50% and 90%.

CONCLUSIONS

Leiomyosarcoma (LMS), although rare, should be considered as a differential diagnosis in tumors of the oral cavity. It occurs at any oral cavity subsite with predilection to the tongue[7,8]. It is important to the consider the possibility of spatial heterogeneity within the tumor and ongoing tumorigenesis, which may complicate the diagnosis of LMS, as well as other smooth muscle tumors[14].

The case presented had an initial biopsy of benign salivary and smooth muscle tissues, which was determined to be SmTUMP after partial maxillectomy was done in the previous institution, and finally LMS after the infrastructure maxillectomy for the recurrence in our institution. A key to ar-

riving at the correct diagnosis is the consideration of clinical aggressiveness which should prompt further investigation and aggressive treatment. Benign histopathologic finding should not deter oncologic treatment when clinically indicated.

While wide surgical excision with confirmed disease-free margins remains the mainstay to attain cure, a multidisciplinary team is needed at the outset of treatment for a comprehensive management[3-8]. The intricate anatomy of the oral cavity requires due consideration of functional preservation and aesthetic outcome while planning for adequate oncologic resection[6-8]. Thus, appropriate imaging and work up, and the involvement of other specialties are necessary for proper planning and management. Radiotherapy and chemotherapy given either preoperatively or post-operatively should also be considered, which offer certain benefits in advance cases[14].

Finally, because the prognosis of LMS depends on the tumor grade, size and extent, early diagnosis and prompt treatment is necessary[2-8].

Conflict of interest:

The authors have no conflict of interest to declare.

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Ethical approval:

This article was submitted and approved by Ethics Review Board of our Institution.

Informed consent:

Informed consent was obtained from the patient in the study.

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