

# Synovial Sarcoma of the Tongue: Report of a Case

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This report outlines the workup and management of a 55-year-old woman with a synovial sarcoma of the lateral border of the tongue that was initially diagnosed as a glomus tumor. A review was performed of the literature on synovial sarcomas of the oral cavity and current National Comprehensive Cancer Network guidelines. Synovial sarcomas of the tongue are rare neoplasms, with variable morphologic microscopic types and immunohistochemical profiles. Fluorescence in situ hybridization analysis of the known gene translocation also can be used in diagnosis. According to the literature, resection of the tumor is the current treatment of choice; however, owing to the rarity of this entity, diagnosis and management prove challenging for the oral and maxillofacial surgeon.

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*J Oral Maxillofac Surg* 74:95-103, 2016

Synovial sarcomas of the oral cavity are rare, and diagnosis of these tumors is complicated by their varied microscopic morphology and immunohistochemical profiles. This case report describes the diagnosis and management of a 55-year-old woman with a synovial sarcoma of the right lateral border of the tongue that was initially diagnosed as a glomus tumor. The histology and treatment of these 2 tumors are reviewed.

## Report of Case

The patient was a 55-year-old woman referred by her general dentist to the University of Washington (UW) oral and maxillofacial surgery (OMS) clinic. The patient noticed a 2- × 2-cm nonpainful ulcerated lesion on the right lateral border of her tongue 1 month before presentation, which she believed to be a “canker sore.” The lesion was biopsied at UW and the histologic examination showed a collection of small, round blue cells arranged in small nests surrounded by a rich vascular network that included dilated branching vessels (Fig 1). High mitotic activity was observed and the cells expressed smooth muscle actin by immunohistochemistry. After review by multiple pathologists, including an oral and maxillofacial

pathologist, the working histologic diagnosis was an atypical glomus tumor. Subsequently, the patient was referred to the Harborview Medical Center (HMC) OMS clinic for further evaluation and management.

At presentation to the HMC OMS clinic, the patient reported mild pain and intermittent paresthesia of the right tongue since the biopsy. Intraoral examination showed a 2- × 2-cm mass in the right anterior border and ventral surface of the tongue with an intact epithelial surface, except for the previous biopsy site (Fig 2). The mass was solid and painless on palpation. The floor of the mouth was soft, nontender, and non-elevated. There was no cervical adenopathy and cranial nerves II to XII were intact bilaterally. Magnetic resonance imaging (MRI) showed a 2- × 2-cm mass involving the right tongue and crossing the midline (Figs 3-5). Given the histologic findings of glomus tumor, computed tomographic angiography of the neck was performed with concern for increased vascularity. However, the lesion was not well visualized and streak artifact obscured the supply to the tumor. At the recommendation of interventional radiology, a magnetic resonance angiogram of the neck was obtained the same day and showed that the lesion was supplied bilaterally by hypertrophic

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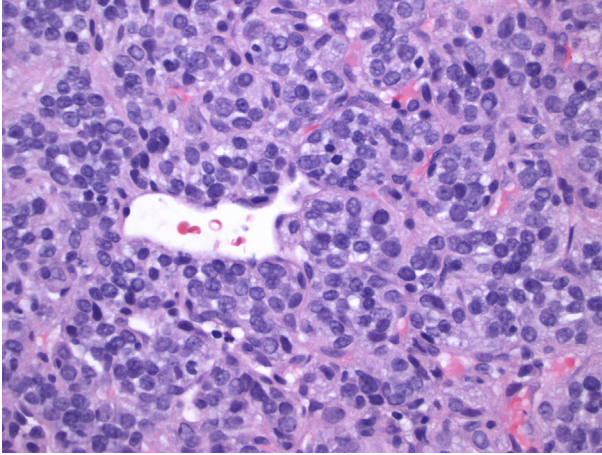
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Received June 22 2015

Accepted June 30 2015

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0278-2391/15/00914-3

<http://dx.doi.org/10.1016/j.joms.2015.06.177>



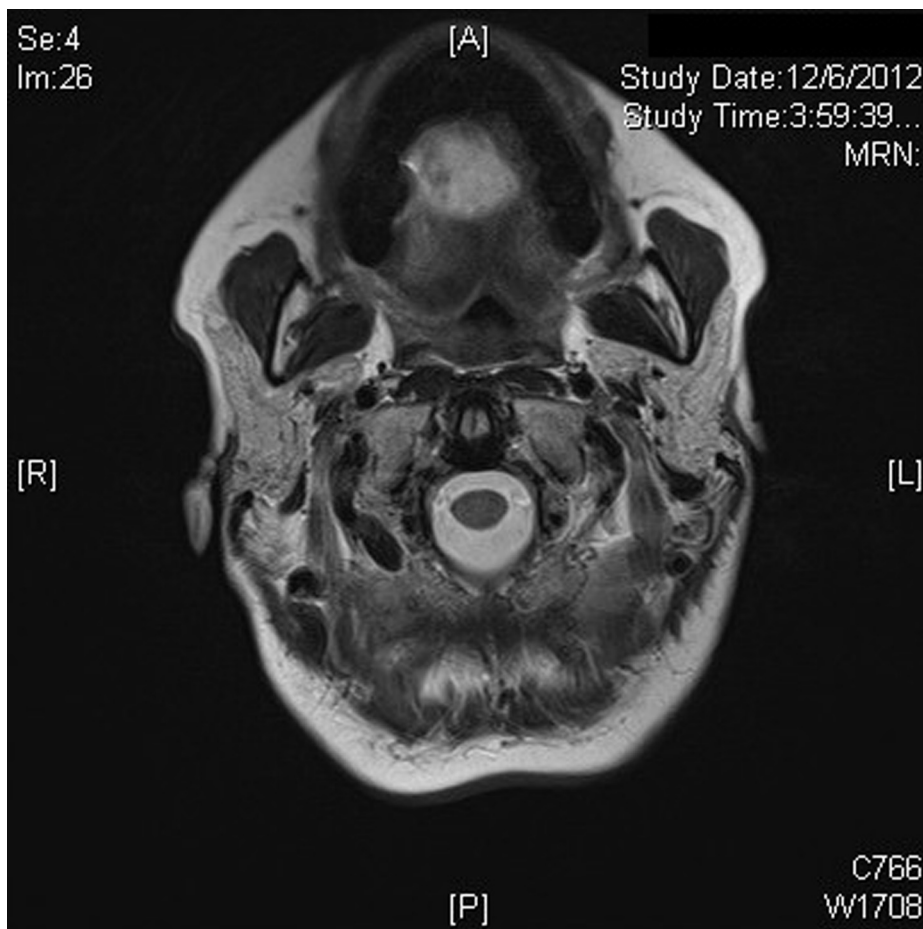
**FIGURE 1.** Initial pathology. Note small round cells arranged in small nests surrounded by a rich vasculature reminiscent of a glomus tumor.

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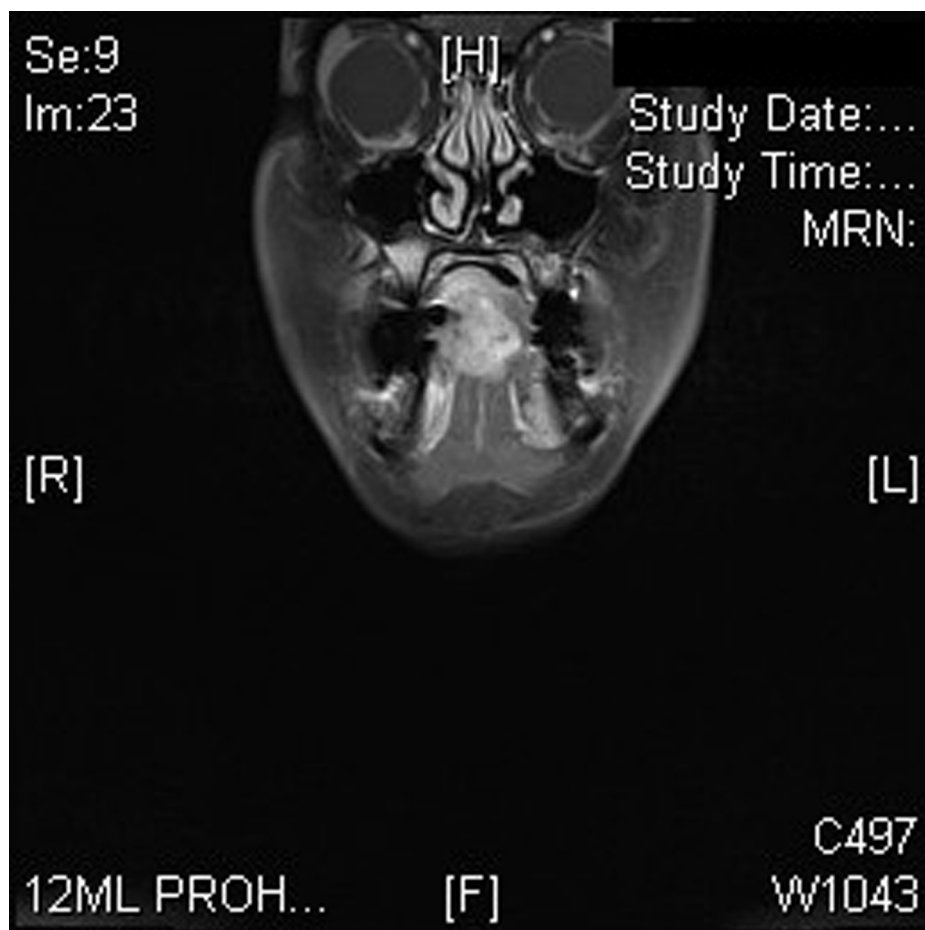
**FIGURE 2.** Initial presentation, mass in the right anterior border and ventral surface of the tongue with an intact epithelial surface.

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**FIGURE 3.** Preoperative T1-weighted magnetic resonance image—axial cut showing a 2-2-cm mass involving the right tongue and crossing the midline.

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**FIGURE 4.** Preoperative T2-weighted magnetic resonance image—coronal cut showing a 2.2-cm mass involving the right tongue and crossing the midline.

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lingual arteries, with the right lingual artery being more predominant.

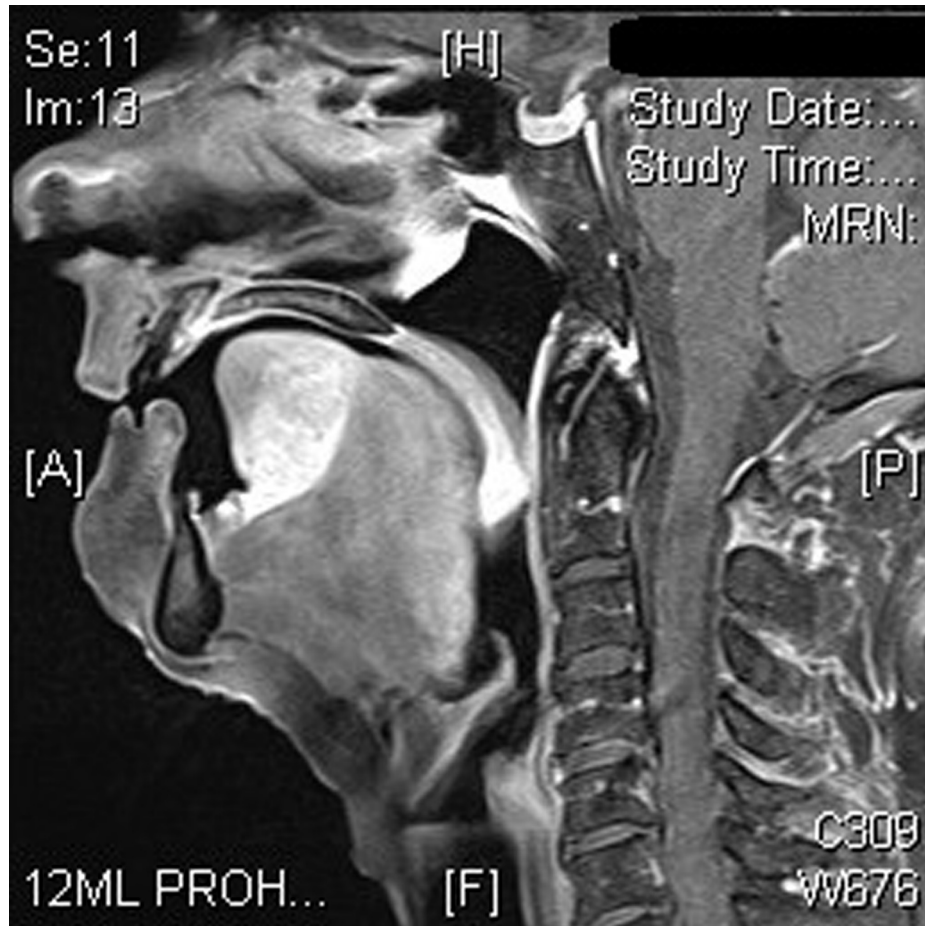
The patient's medical history was noteworthy for hypertension, heart murmur, and previously pharmacologically managed hyperthyroidism. Current medications included lisinopril, hydrochlorothiazide, and a daily multivitamin. She previously underwent a hysterectomy, and her family history showed that her father and her father's brother developed a spinal tumor of unknown etiology while in their late 60s. She was a nonsmoker and occasional drinker.

Owing to the increased vascularity of the lesion, the interventional radiology service performed an embolization of the right and left lingual arteries through the right femoral artery in anticipation of the surgical excision. The patient was scheduled for partial glossectomy with primary closure under general anesthesia 2 days later. Excision was performed using an OmniGuide CO<sub>2</sub> laser (OmniGuide, Inc, Cambridge, MA), observing a 5-mm margin of normal-appearing tissue. Multiple frozen sections were sent from the deep muscle and were negative for tumor. For reconstruction,

the tongue musculature was bisected along its midline to the junction of the posterior third. This posteriorly based tongue tissue was advanced anteriorly and sutured to the remaining tongue as far anteriorly as possible. The remaining left hemitongue was wrapped over the residual defect to re-create the natural tongue shape; this was secured with deep and superficial re-sorbable sutures. The ventral surface was left to granulate (Figs 6-8).

The patient remained intubated overnight for airway precautions and was extubated the following day without difficulty. Her postoperative hospital course was unremarkable and at discharge the patient's tongue movements were grossly normal and she tolerated a full liquid diet.

At her 1-week follow-up clinic visit, the patient reported sensation over the tongue bilaterally, spoke with full comprehension, although with a slight lisp, and maintained a soft diet. The final pathology report described a 2.3-cm right tongue tumor comprised of uniform round cells and cells with spindle cell morphology that had high mitotic activity. Spindle



**FIGURE 5.** Preoperative T1-weighted fat-suppression magnetic resonance image—sagittal cut showing a 2-2-cm mass involving the right tongue and crossing the midline.

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cells were arranged in variably sized fascicles with focal herring-bone architecture alternating with more loosely arranged sheets of spindle cells with variable collagen deposition (Figs 9-11). Large regions of the tumor were composed of round cells arranged in small nests with a rich surrounding vasculature similar to the biopsy findings. The lesional cells stained positive for  $\alpha$ -smooth muscle actin (1A4), S-100, cytokeratin-7, and epithelial membrane antigen (EMA) markers. An immunostain for transducin-like enhancer of split-1 (TLE-1) was remarkable for strong staining of nuclei (Fig 12). Negative immunohistochemical stains included MITE, HMB45, mGFAP, Melan-A-Red, pancytokeratin, CD34, desmin, and myogenin. No evidence of SYT gene rearrangement was noted at fluorescence in situ hybridization (FISH) analysis. No vascular invasion was observed; however, the neoplasm was noted to be 0.2 cm from the deep margin of the specimen.

The differential diagnosis included synovial sarcoma and malignant peripheral nerve sheath tumor. These 2 malignancies can be problematic to distinguish

because of their overlapping morphologic features and immunophenotype. Although evidence of SYT gene rearrangement is specific for synovial sarcoma, 5 to 10% of synovial sarcoma cases can be negative for evidence of gene rearrangement.<sup>1</sup> Ultimately, synovial sarcoma was the favored diagnosis.

The patient's case was presented at the head and neck and sarcoma tumor board at UW. Owing to the lesion's high-grade sarcomatous status and close deep surgical margin (0.2 cm), the radiation oncologists recommended radiotherapy.

The medical oncologists discussed chemotherapy using doxorubicin and ifosfamide; however, given the paucity of scientific data on the treatment of surgically excised oral sarcomas and the risk of negative side-effects, the patient ultimately opted for adjuvant radiotherapy only.

The patient underwent 6 weeks of treatment with a total of 63 Gy. Her primary side-effect was grade 3 mucositis, but she was able to maintain adequate oral nutrition. At her 8-month postoperative OMS clinic follow-up, the patient reported slight paresthesia of



**FIGURE 6.** Intraoperative photographs of the lesion.

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the new tip of her tongue and radiation-induced angular cheilitis. Her tongue functioned without restriction, her speech was intelligible, and her taste sensation had returned to baseline. Routine postoperative MRIs showed heterogeneous enhancement of the surgical bed consistent with surgical scarring with no new pathology observed. Chest imaging thus far has been negative. She will continue to be followed at the HMC OMS clinic every 3 months and by the Seattle Cancer Care Alliance every 6 months, with interval imaging of her head, neck, and chest in accordance with the National Comprehensive Cancer Network (NCCN) 2014 guidelines. She is currently 2 years disease free with no evidence of metastasis (Fig 13).

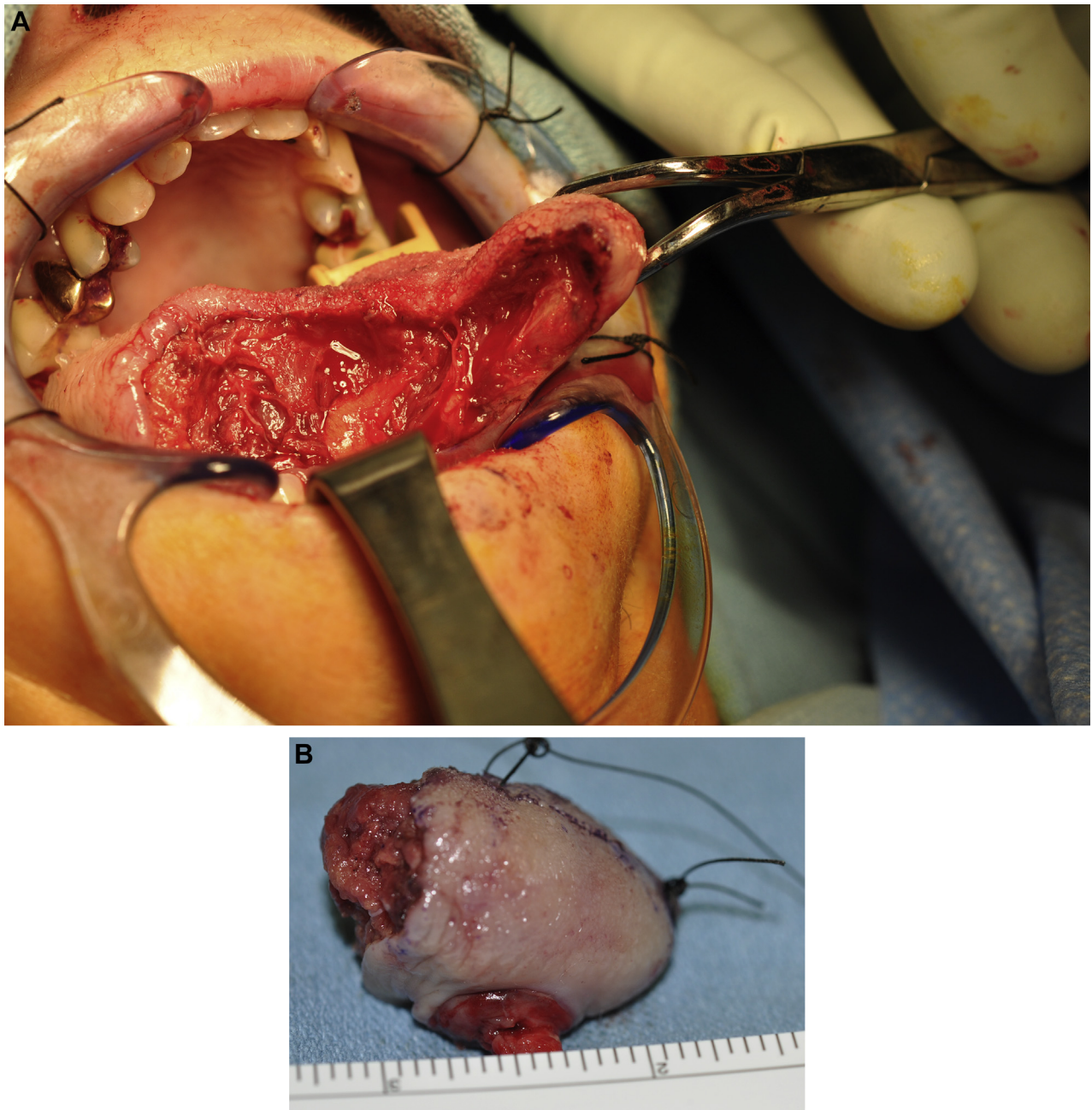
## Discussion

### SYNOVIAL SARCOMA

Synovial tissue is a modified connective tissue derived from the mesenchyme.<sup>1</sup> Synovial sarcomas are malignant neoplasms of this synovial tissue and comprise 8% of all soft tissue malignancies.<sup>1</sup> The World Health Organization defines synovial sarcoma

as a mesenchymal spindle cell tumor with variable epithelial differentiation, including glandular formation and a chromosomal translocation.<sup>2</sup> Approximately 90% of synovial sarcomas occur in the extremities.<sup>1</sup> Of the 3 to 10% found in the head and neck region, synovial sarcomas of the parapharyngeal region are the most common.<sup>1,3</sup> In the oral cavity proper, synovial sarcomas of the buccal mucosa, floor of the mouth, retromolar region, soft and hard palates, submental region, gingivobuccal sulcus, and tongue have been reported.<sup>3,4</sup>

Mir-Abedy<sup>4</sup> first identified a synovial sarcoma of the tongue in 1962. In the following 50 years, Villaroel-Salinas et al<sup>4</sup> noted the English-language publication of only 13 case reports of synovial sarcomas involving the tongue, 2 of which occurred in women. Of these 13 documented tongue cases, 9 involved the base, 3 the lateral border, and 1 the dorsum.<sup>4</sup> Thus, this case is the third reported case of a synovial sarcoma in a woman and the fourth involving the lateral border of the tongue. As in this patient, most synovial sarcomas of the tongue had an insidious presentation, with formation of a painless palpable mass and few other symptoms.<sup>3</sup> Surgical resection is the recommended



**FIGURE 7.** A, Intraoperative photograph of resected tongue specimen. B, Final specimen.

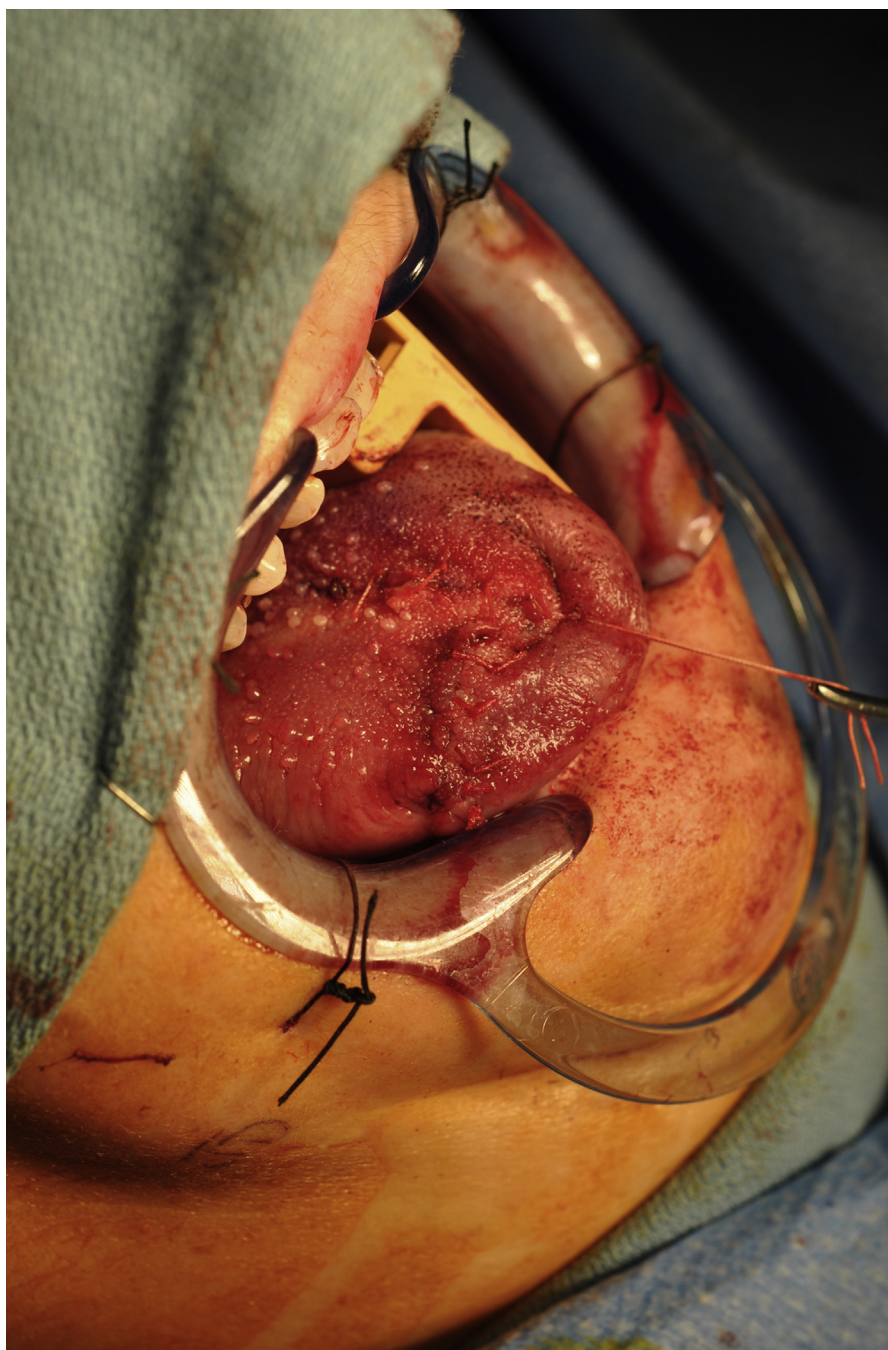
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treatment for these tumors, after which adjuvant radiation with or without chemotherapy can be considered.<sup>1,2</sup>

Synovial sarcomas microscopically present with 2 distinct cell populations. Based on the prevalence of these cell lines, the tumors are described as biphasic (25%), monophasic (fibrous or epithelial, 70%), poorly differentiated (round cell, <5%), and myxoid.<sup>1,3,4</sup> The biphasic synovial sarcomas include epithelial-like cells

in glandular structures and spindle cells.<sup>1</sup> The pathology report for this patient denoted sheets of uniform round cells, spindle cells, and myxoid areas, consistent with a biphasic synovial sarcoma.<sup>3</sup> All previously reported synovial sarcomas of the tongue have been of the biphasic variety, with the exception of the case reported by Villaroel-Salinas et al.<sup>4</sup>

Immunohistochemical staining is an integral part of the accurate diagnosis of a synovial sarcoma and

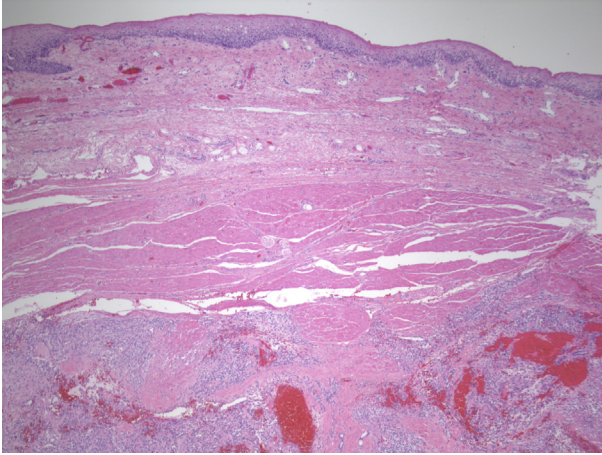


**FIGURE 8.** Final closure.

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imperative in the exclusion of other neoplasms. According to the literature, 90% of synovial sarcomas stain positive for focal cytokeratins or EMA. These stains elucidate the epithelial cells of the biphasic variety, although some spindle cells also might stain positive for these factors.<sup>3</sup> This patient's tumor displayed rare cells positive for cytokeratin-7 and focal cells positive for EMA; it did not stain for cytokeratin-19 or the pancytokeratin cocktail AE1 plus AE3. The spindle cell

component stains positive for vimentin (a nonspecific marker) and fibronectin; these markers were not tested in this patient. Approximately 93% of synovial sarcomas are positive for Bcl-2, for which this patient's specimen was not tested. In addition, 60 to 73% of synovial sarcomas are CD99<sup>+</sup>, although this patient's specimen was negative for this marker.<sup>3,4</sup> Like 21 to 30% of synovial sarcomas, her tumor was variably positive for S-100.<sup>2,4</sup> The TLE-1 antibody nuclear stain

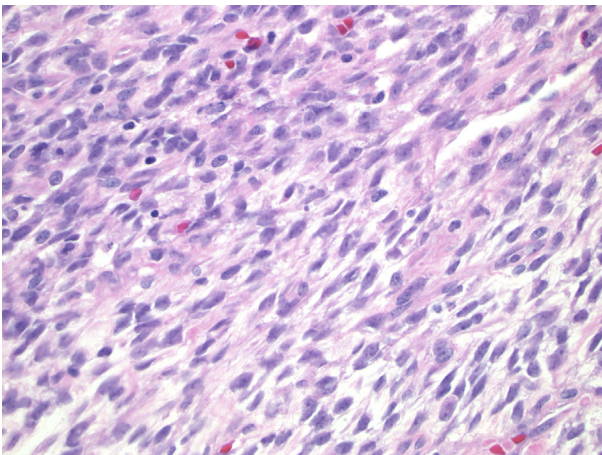


**FIGURE 9.** Low-power view of the resected specimen exhibiting cellular neoplasm within the skeletal muscle of the tongue and an intact overlying squamous mucosa.

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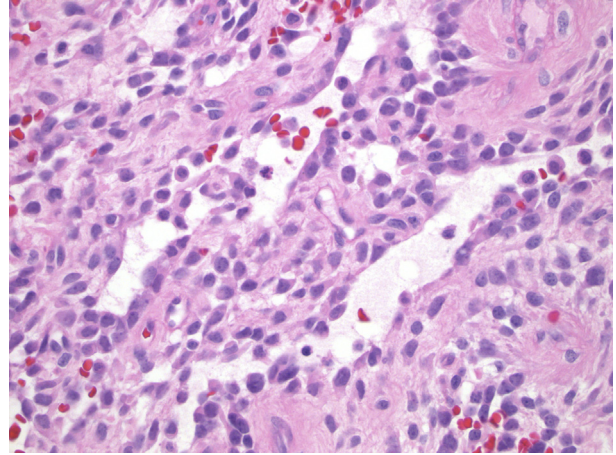
also was variably positive in this patient's specimen, consistent with 90% of synovial sarcomas.<sup>4</sup> Moreover, no synovial sarcomas have been positive for actin (HHF-35), myoglobin, CD34, or desmin<sup>4</sup>; this patient's tumor upholds these data.

Synovial sarcomas yield variable results in immunohistochemical staining, but more than 90% are known to express the balanced reciprocal translocation  $t(X;18)(p11.2q;q11.2)$ .<sup>3</sup> This translocation results in a fusion of the SYT gene on chromosome 18 to the SSX1, SSX2, or SSX4 gene on the X chromosome.<sup>1,3,4</sup> In consequence, this translocation can be identified by FISH analysis. This test was performed for this patient and was negative.



**FIGURE 10.** Spindle cells within the resected tumor arranged in variably sized fascicles and with tapered nuclei and fibroblast-like cytologic features.

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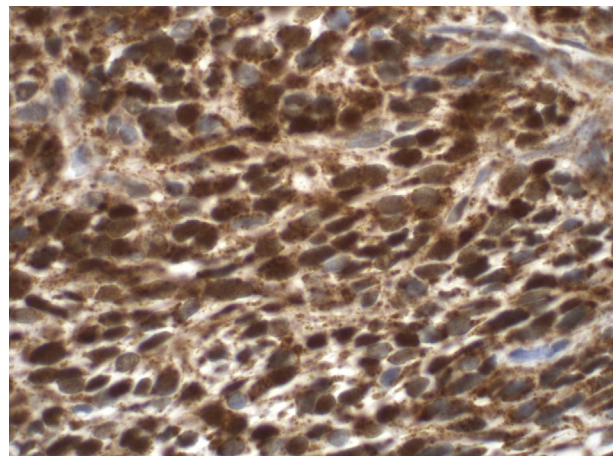


**FIGURE 11.** Round cell area within the resected tumor with features mimicking glomus tumor.

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#### GLOMUS TUMORS

The glomus tumor was first described by Masson<sup>5</sup> in 1924. The stratum reticularis layer of the dermis houses the glomus apparatus, an arteriovenous anastomosis that aids in temperature regulation of the extremities.<sup>5</sup> Fewer than 2% of soft tissue neoplasms are glomus tumors, and these entities are most common in the subungual region of the distal extremities; less commonly, they are found in the stomach, bone, and lung.<sup>2</sup> Glomus tumors are rarely identified in and around the oral cavity, but have been noted to present as generally nonpainful lesions of the upper and lower lips, cheek, gingiva, hard palate, and temporomandibular joint.<sup>5,6</sup> The World Health Organization describes



**FIGURE 12.** Transducin-like enhancer of split-1 histochemical stain.

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**FIGURE 13.** Clinical photograph at patient's 2-year follow-up appointment.

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3 subtypes of glomus tumors depending on the predominance of the cell type. These include glomangioma, glomangiomyoma, and solid glomus tumor.<sup>2</sup> Histologically, glomus cells are round with eosinophilic cytoplasm; the presence of spindled nuclei also is common.<sup>5</sup>

Typically, glomus tumors stain positive for smooth muscle actin, muscle-specific actin, and vimentin; stains for S-100 and epithelial markers are negative.<sup>5</sup> The initial UW pathology report denoted a proliferation of round, blue cells that stained positive for smooth muscle actin. In addition, these cells were negative for EMA, although the en bloc specimen tested positive for EMA. This was likely due to sampling error between the 2 specimens.

#### ADJUVANT THERAPY

The French Federation of Cancer Centers Sarcoma Group system uses the parameters of tumor differentiation, mitotic index, and tumor necrosis to establish a grading classification scheme for soft tissue sarcomas.<sup>7</sup> The tumor grade has been used in conjunction with surgical margins to predict local recurrence and distant metastasis and, according to Coindre,<sup>8</sup> is the most important factor in predicting metastasis risk in synovial sarcomas. Overall, the local recurrence rate of soft tissue sarcomas is 20 to 30%, and the metastasis incidence is 30 to 50%.<sup>8</sup> The 5-year metastasis-free survival rate for grade 3 sarcomas has been reported to be 43.5%.<sup>8</sup> This patient's synovial sarcoma was classified as grade 3. Given the variety of tumor types included in these soft tissue sarcoma studies, the benefit of chemotherapy remains controversial; however, the

grading system remains of paramount importance as a prognostic indicator of metastasis risk.<sup>8</sup>

This patient had a T1N0M0 grade 3 tumor; thus, it is classified as stage IIA by the NCCN guidelines. According to their 2014 soft tissue sarcoma guidelines, tumors of this stage should be managed primarily by en bloc resection followed by radiation therapy.<sup>9</sup> Radiation has been shown to improve disease-free survival, albeit not overall survival.<sup>9</sup> Resection alone is an option for smaller tumors if wide margins can be achieved.<sup>9</sup> In this patient's case, the closest margin was 0.2 cm; thus, postoperative radiation therapy was justified. The NCCN also recommends chest imaging every 6 to 12 months and periodic imaging of the primary tumor location by computed tomography, MRI, or ultrasound scans.<sup>9</sup> Given the rare incidence of oral cavity soft tissue sarcomas, the data for management are largely extrapolated from management of soft tissue sarcomas of the extremity.

Synovial sarcomas of the tongue are rare neoplasms, with variable morphologic microscopic types and immunohistochemical profiles. FISH analysis of the known gene translocation also can be used in diagnosis. According to the literature, resection of the tumor is the current treatment of choice; however, because of the rarity of this entity, diagnosis and management prove challenging for the oral and maxillofacial surgeon.

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