

Synovial Sarcoma of the Tongue: Report of a Case and Review of the Literature

Constantine Komis, DDS,* George A. Lagogiannis, MD, DDS,†
Gregory Faratzis, MD, DDS, MSc,‡ and
Alexander D. Rapidis, MD, DDS, PhD§

Although a rare entity, synovial sarcoma (SS) is one of the most common malignant mesenchymal neoplasms affecting soft tissues of the human body. Soft tissue is defined as mesenchymal extraskelatal tissue excluding the reticuloendothelial, glial, and parenchymal organ supporting tissue. Tumors arising from soft tissue are classified according to their postulated histologic origin, typically based on the adult tissue they most resemble.¹

Soft tissue tumors include a heterogenous group of mesenchymal lesions whose classification continue to evolve as a result of incorporating advances in cytogenetic and molecular techniques.² Synovial tissue is a modified connective tissue that is formed from a development of cavities in pre-existing mesenchyme. The progenitor mesenchyme differentiates into 2 recognizable components: an inner "epithelioid" cell layer and an outer, also specialized, connective tissue component. Committed cells from these 2 compartments possess properties that distinguish them from other offspring of mesenchyme, and while the cells may appear as separate entities, they are considered interchangeable.³ SS constitutes approximately 8% of all soft tissue tumors and usually presents during early adulthood. In more than 90% of cases, SSs are located in the upper and lower extremities. The head and neck area is the site of origin for 3% to 10% of SS and the most common anatomic location is the parapharyngeal area.³⁻⁶ Its intraoral appearance is rare.⁷ The

tongue is an equally uncommon location for SS to develop, with only 10 cases being reported in the literature over a 40-year period.⁷⁻¹⁷ Because of the rarity of these lesions, we considered it worthwhile to report an additional case treated in our department.

Report of a Case

An otherwise healthy 49-year-old Caucasian male presented to our department (Department of Maxillofacial Surgery, Greek Anticancer Institute, St Savvas Hospital, Athens, Greece) complaining of a painful bleeding mass located in the left side of the tongue of 4 months' duration. The lesion had a rapid clinical progression with an accelerated increase in size over the last 6 weeks. The enlarging tumor was producing a progressive speech impairment and difficulty in food intake. The patient denied smoking and reported moderate alcohol consumption.

Intraoral examination revealed a painless, diffuse, partially ulcerated firm mass located on the posterior third of the lateral left side of the tongue measuring $3 \times 4.5 \times 4$ cm (Fig 1). Movements of the tongue were partially restricted by the dimensions of the tumor. No other pathology was detected from the oral cavity, nasopharynx, and laryngopharynx. There were no palpable lymph nodes in either of



FIGURE 1. Clinical preoperative intraoral photograph of the tongue lesion at presentation.

Komis et al. *Synovial Sarcoma of the Tongue*. *J Oral Maxillofac Surg* 2008.

Received from the Department of Maxillofacial Surgery, Greek Anticancer Institute, St Savvas Hospital, Athens, Greece.

*Fellow in Maxillofacial Surgical Oncology.

†Senior Registrar in Maxillofacial Surgery.

‡Registrar in Maxillofacial Surgery.

§Professor and Chairman Department of Maxillofacial Surgery.

Address correspondence and reprint requests to Dr Rapidis: Department of Maxillofacial Surgery, Greek Anticancer Institute, St Savvas Hospital, 171 Alexandras Ave, Athens 115 22, Greece; e-mail: rapidis@usa.net

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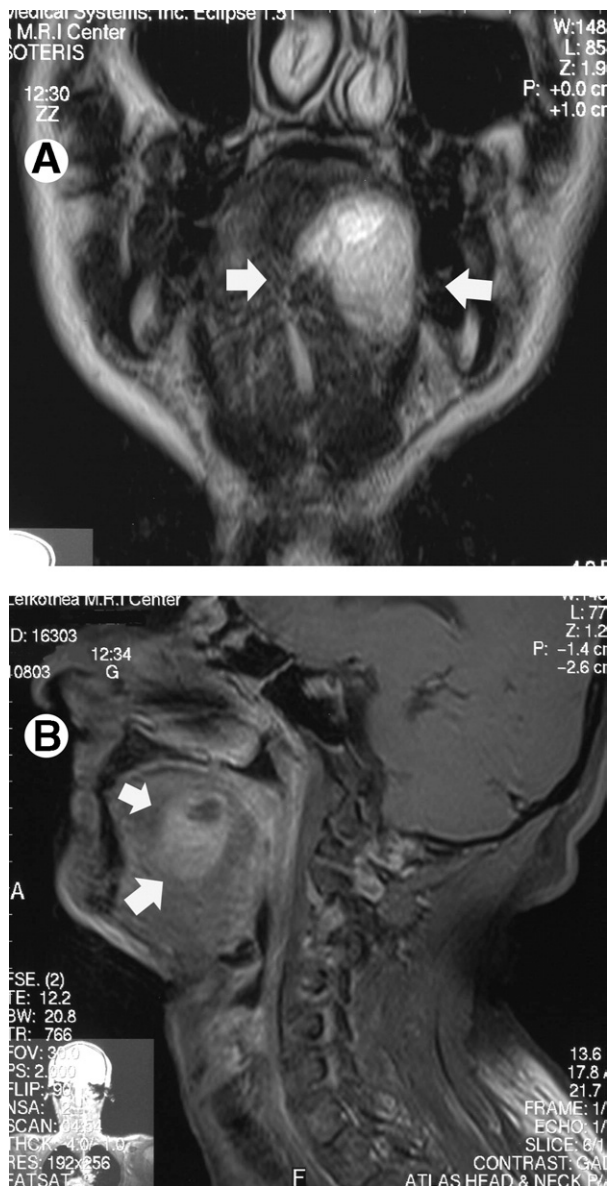


FIGURE 2. A, Coronal MRI (T_2 mode). A well delineated, ovoid, circumscribed lesion inside the tongue can be depicted (arrows). B, Lateral MRI (T_1 mode). The lesion can be seen inside the musculature of the tongue occupying the middle and posterior third but not extending to the base of the tongue (arrows).

Komis et al. Synovial Sarcoma of the Tongue. *J Oral Maxillofac Surg* 2008.

the necks. Magnetic resonance imaging (MRI) of the head and neck revealed the presence of a large tumor occupying the left side of the oral tongue (Fig 2). The lesion extended to the midline of the tongue and produced no cervical lymphadenopathy. An incisional biopsy was performed under local anesthesia and the histopathologic examination reported an SS of the tongue. The tumor consisted of 2 morphologically different types of cells forming the typical biphasic pattern of epithelial cells with a surrounding spindle component (Fig 3). Additional examinations (computed tomography scan of the lungs, bone scan, abdominal ultrasonography) were negative for regional or distant metastases.

The patient was assessed by the Tumor Board, which recommended surgical excision of the tumor without post-

operative additional treatment of either chemotherapy or radiotherapy. Surgical treatment planning included a hemiglossectomy with excision of part of the floor of the mouth via a paramedian mandibular split and immediate reconstruction of the created surgical defect of the tongue. Because sarcomas of the head and neck rarely, if ever, give regional neck metastases, the reconstructive options included either a radial forearm free flap or a submental island skin flap. In cases where a selective neck dissection of either I-III or I-IV neck levels was to be performed, the island flap would have not been feasible because its vascular pedicle would have most probably been severed during neck dissection. The option of the island flap was favored and the patient was scheduled for surgery.

In the time period awaiting hospitalization, the patient developed 2 hemorrhagic attacks from the tumor site that regressed spontaneously. The hemorrhage from the tumor resulted in an extensive intralesional bleeding that produced a sudden increase in the size of the tumor. The tumor developed an exophytic and bluish appearance and increased the patient's symptomatology regarding speech and swallowing. Hospitalization was hastened and after a routine preoperative workup, which was within normal limits,

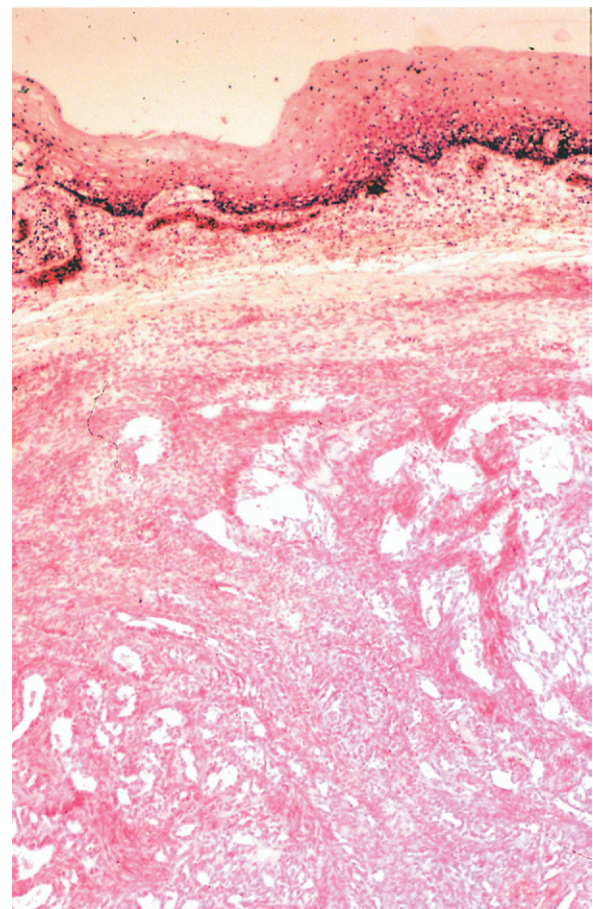


FIGURE 3. Microphotograph of the histologic slide from the incisional biopsy. A classical biphasic SS can be seen under an overlying stratified squamous oral tongue epithelium. A fibrous connective tissue lining separates the basal lamina from the tumor. (Hematoxylin-eosin stain; magnification $\times 150$.)

Komis et al. Synovial Sarcoma of the Tongue. *J Oral Maxillofac Surg* 2008.

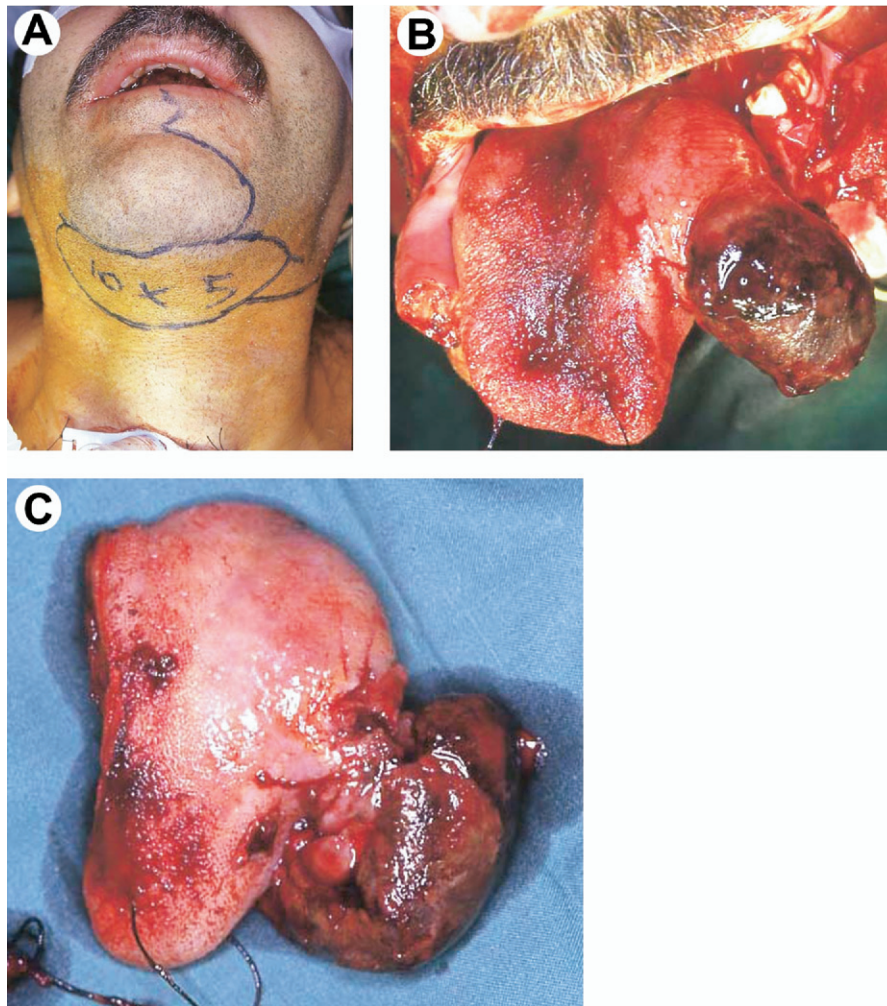


FIGURE 4. A, Intraoperative photograph showing the incision lines of the midline split and the island skin flap. A tracheostomy is performed to facilitate surgical resection. B, Intraoperative photograph showing the distortion of the tumor from the intralesional hemorrhage. A paramedian mandibular split has been performed. C, The excised specimen of hemiglossectomy is shown. A generous, clinically free surgical margin surrounding the tumor is evident.

Komis et al. Synovial Sarcoma of the Tongue. J Oral Maxillofac Surg 2008.

the patient was rushed to surgery. A temporary tracheostomy was performed and a 10×5 cm fasciocutaneous submental island flap was raised along with its left-sided vascular pedicled supply. A median lip split incision was created and, via a left paramedian mandibular osteotomy, a hemiglossectomy along with lateral floor of the mouth resection was performed (Fig 4). The submental island skin flap was transported intraorally along its vascular pedicle and was sutured to cover the created defect of the tongue. The patient made an uneventful recovery, tracheostomy was removed on the second postoperative day, and he was discharged from hospital on day 6 after surgery. The histologic report of the surgical specimen showed a classic or biphasic SS characterized by a dual differentiation into epithelial nests of cells and spindle cell collections surrounding the epithelial components. The tumor stained positively in high and low molecular weight cytokeratin antigens and to the epithelial membrane antigen (Fig 5). The patient's tumor was not tested for its molecular and cytogenetic characteristics. The pathology report confirmed wide tumor-free surgical margins.

The functional and esthetic results were very satisfactory apart from the need of intraoral shaving of the skin of the flap (Fig 6). The patient was therefore followed-up regularly with clinical, laboratory, and radiographic examinations. During the eighteenth postoperative month, the patient, residing in an isolated part of the country, developed a progressive respiratory insufficiency that required hospitalization into a local hospital near his residence. Chest x-rays and computed tomography raised the suspicion of lung metastases, which were not confirmed because the patient denied bronchoscopy. However, his clinical picture improved with medical treatment and the patient remains symptom-free 2 years postoperatively.

Discussion

SS is composed of 2 morphologically distinct but histogenetically related cell types responsible for the characteristic biphasic pattern. Depending on the rel-

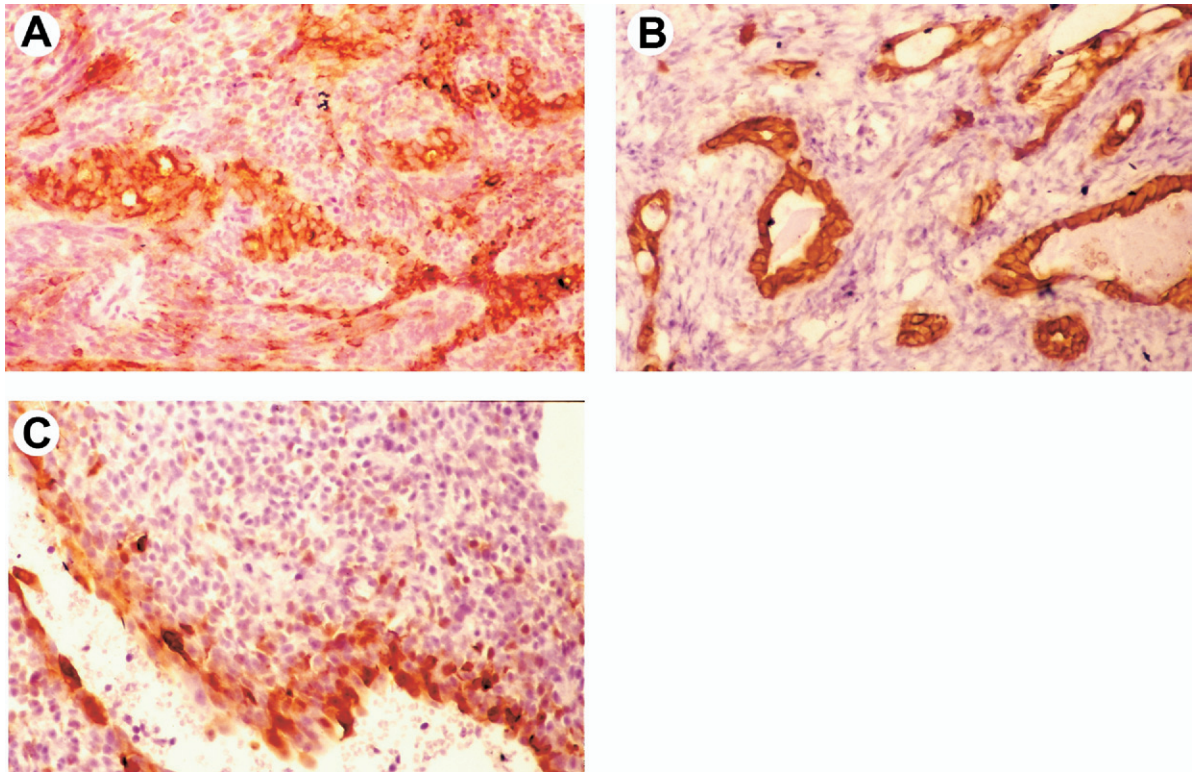


FIGURE 5. Microphotograph of the histologic specimen. A, The immunohistochemical stain with the epithelial membrane antigen shows strong positivity. (EMA stain; magnification $\times 250$.) B, The immunohistochemical stain with high and low molecular weight cytokeratin. (AE₁/AE₃ stain; magnification $\times 150$.) C, Higher magnification of the same histologic slide (B). The strong positive staining of the cell population is clearly evident. (Magnification $\times 400$.)

Komis et al. *Synovial Sarcoma of the Tongue*. *J Oral Maxillofac Surg* 2008.

ative prominence of the 2 cell populations and the degree of differentiation, these tumors form a continuous histopathologic spectrum; this spectrum can be divided into biphasic, monophasic fibrous, monophasic epithelial, and poorly differentiated (round cell) types.¹³ A myxoid variant has also recently been described.¹⁸ The monophasic type of SS is composed of spindle and rarely from epithelial cells. All previously reported SSs of the tongue, including the present case, had the typical biphasic histologic pattern consisting of epithelial-like cells arranged in glandular structures and a spindle cell component. Immunohistochemically, the epithelial-like cells are positive for cytokeratins and epithelial membrane antigen, and the spindle cells are positive for vimentin and fibronectin.¹³

The first reported case of SS in the tongue was that by Mir-Abedy in 1962.¹⁶ Meer et al¹³ reviewed 29 oral SS and added 2 more patients. From the 31 reviewed cases of oral SS, 10 (30%) presented with tumors located in the tongue. From the 11 reported cases of tongue SS, 7 had the base of the tongue as the anatomic site of the primary tumor (Table 1). The male predominance observed in tongue and other intraoral SSs is not a characteristic of all soft tissue sarcomas,

which show an equal male to female ratio for both head and neck and other anatomic sites.^{1,5,19} SS of the oral tissues affect patients between the ages of 10 and 50 years, whereas SS in all sites have a range between 5 and 87 years and a median age at presentation of 32 years.¹⁹

It has been hypothesized that patients of advanced age present with tumors of both unusual histologic patterns and poorly differentiated cell morphology. This not only presents diagnostic difficulties, but also results in a more aggressive biological behavior of the tumor with poorer prognosis and frequent distant metastases than in cases presenting in young patients.²⁰

High-grade SS should be histologically differentiated from Ewing sarcoma, primitive neuroectodermal tumor, and malignant peripheral nerve sheath tumor.²¹ SS with predominantly epithelioid appearance may mimic carcinomas or myoepitheliomas. While the microscopic diagnosis of SS in its classic biphasic form poses no difficulties, monophasic epithelioid variants of SS and poorly differentiated SS can mimic, even immunohistochemically, spindle cell sarcomas, round cell sarcomas, myoepitheliomas, and epithelioid fibrosarcomas.

There is recent evidence that soft tissue sarcomas can be divided into 2 major genetic groups: sarcomas

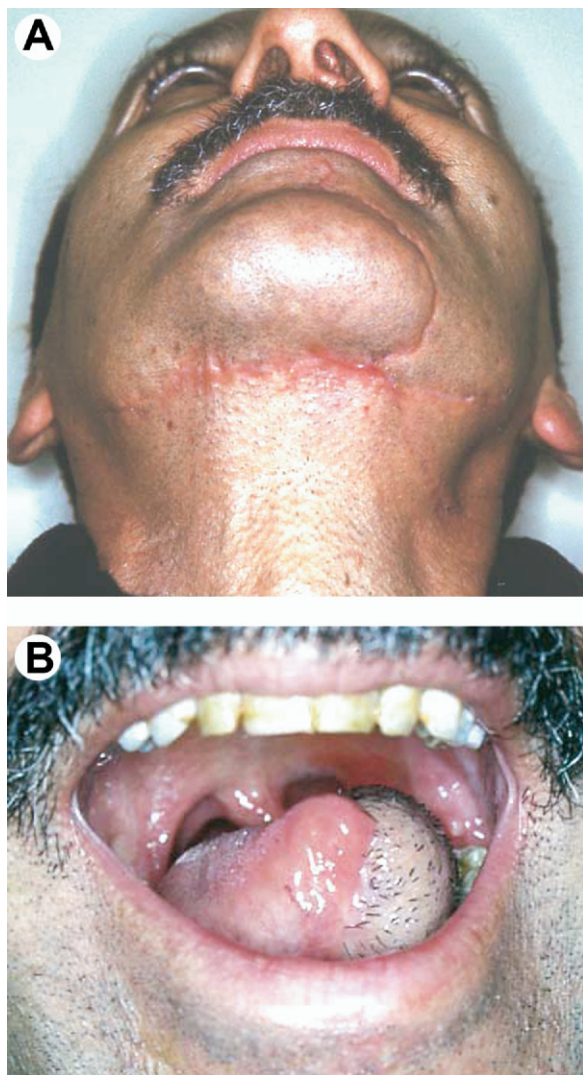


FIGURE 6. Postoperative clinical photograph of the patient. A, Eighteen months postoperatively, the donor site defect presents minimal functional and esthetic impairment to the patient. B, The flap produces minimal deficiency in the patient regarding speech and swallowing. However, the intraoral hair growth in the skin flap needs regular shaving.

Komis et al. *Synovial Sarcoma of the Tongue. J Oral Maxillofac Surg* 2008.

with specific genetic alterations and specific oncogenic mutations and sarcomas with nonspecific genetic alterations and complex unbalanced karyotypes.² Cytogenetically, SS is characterized by an (X; 18) translocation resulting in fusion between the SYT gene on chromosome 18 and most often either SSX1, SSX2, or SSX4 on the X chromosome.^{4,5} The identification of the translocation gene, which can be accomplished in more than 95% of SSs, can also provide a highly reliable diagnosis of the tumor.²²

Regardless of the relatively slow growth pattern of the tumor, overall survival of SS is poor and the 5-year survival rate is reported to be between 40% and 50%.³

The head and neck area is not a privileged site with regard to a more favorable outcome from other anatomic sites. According to Carrillo et al,⁷ the generally less aggressive course of SS located in the tongue has been attributed to the early detection, small size, and young age of patients. Patients often develop blood-borne metastases, particularly to the lungs, which is the common cause of death.¹ Sarcomas rarely give regional neck metastases.²³ This also applies to SS, although an increased risk of lymphatic spreading compared with other soft tissue sarcomas has been reported.^{1,24} Elective neck dissection is indicated only in the presence of palpable nodes, when the neck is accessed during surgical resection or when a need for microvascular free tissue transfer is indicated for the reconstruction of the created surgical defect.¹

Local recurrence is generally associated with positive surgical margins and is considered one of the most important prognostic factors not only for SS but for all head and neck sarcomas.²⁵ Local recurrences usually occur during the first 2 postoperative years or even later.^{3,5}

Even though SS is considered and treated as a high-grade sarcoma, recent studies suggest that the biologic behavior of the lesion is associated with various patient-related parameters that influence disease outcome. Negative prognostic factors have been identified to be the large tumor size (>5 cm), treatment in a noncancer-specific hospital, patient age above 25 years, and the poorly differentiated histologic appearance of the tumor. The presence of the SYT-SSX1 gene fusion transcript is related to a metastasis-free disease outcome.^{5,21,26,27}

Surgical treatment of oral SS, as in other types of oral sarcomas, is the treatment of choice.^{3,23,28} Local resection with an adequate disease-free margin safeguards the absence of local recurrence and distant metastases. The submental island flap, used for the reconstruction of our patient, was conceived and described in 1993 by Martin et al.²⁹ The flap is used as an alternative to the cervical skin flaps of the platysma, the supraclavicular, and infrahyoid island flaps.^{30,31} The flap receives its vascular supply from the submental artery, a branch of the facial artery and drains via the submental vein into the facial vein, which represents an anastomotic branch of the external jugular vein.³²⁻³⁴ The flap can be used either as a pedicled or a free flap in sizes up to 20 × 10 cm and has been used for the reconstruction of extraoral defects of the lower lip, the cheek, forehead, temporal and orbital region, ear and external auditory canal, upper lip, and the nose, and intraorally for the reconstruction of the oral tongue, floor of the mouth, the palate, the glottis and supraglottic area, and the cervical esophagus.^{35,36}

The flap can be harvested as a composite, with an osseous part of the lower border of the mandible, or

Table 1. CLINICOPATHOLOGIC CHARACTERISTICS OF SYNOVIAL SARCOMAS OF THE TONGUE

Study	Year	Age/ Gender	Location	Size (cm)	Treatment	Follow-Up (mos)	Distant Metastases	Outcome
Mir-Abedy ¹⁶	1962	23/F	Base of tongue	5	Surgery	36	NR	AND
Novonty and Fort ¹⁰	1971	20/M	Base of tongue	3.5 × 2	Surgery/Radiotherapy	72	NR	AND
Mousavi and Ghodsi ⁹	1974	40/M	Base of tongue	6 × 5 × 5	Surgery/Radiotherapy	4	NR	AND
Guzman et al ¹⁷	1975	21/M	Base of tongue	7	Surgery	12	Lungs	AWD
Engelhardt and Leafstedt ¹¹	1983	25/M	Base of tongue	NR	Surgery	NR	NR	NR
Smookler et al ¹⁵	1982	16/M	Mobile tongue	1.2	Surgery	96	NR	AND
Holtz and Magielski ⁸	1985	16/M	Base of tongue	6 × 5 × 4	Surgery/Radiotherapy/ Chemotherapy	37	Multiple sites	DOD
Bridge et al ¹²	1988	31/M	Base of tongue	3 × 3	Surgery	NR	NR	NR
Carrillo et al ⁷	1992	13/M	Middle third	1.1 × 5 × 5	Surgery	12	NR	AND
Fortuno-Mar et al ¹⁴	2000	26/M	Unspecified	NR	Surgery	NR	Lungs	AWD
Present case	2006	49/M	Middle third	5.8 × 4.5 × 2.8	Surgery	24	Lungs	AWD

NOTE. Data from Meer et al.¹³

Abbreviations: AND, alive no disease; AWD, alive with disease; DOD, died of disease; NR, not reported.

Komis et al. *Synovial Sarcoma of the Tongue. J Oral Maxillofac Surg* 2008.

only as fasciocutaneous or along with the ipsilateral anterior belly of the digastric muscle. The submental vessels usually run deep to the anterior belly of the digastric muscle, giving perforating branches to the skin paddle. When the muscle is included with the flap the venous drainage is better.³⁴ When a neck dissection is needed, the raise of the submental island flap as a pedicled flap is very difficult because its vascular supply from the facial artery and vein must be preserved during both the excision of the submandibular gland and the submental and submandibular lymph nodes (levels I and II). In these cases, another type of flap should be considered.

We favored the reconstruction of the tongue with the submental island flap, despite its known postoperative disadvantage in male patients of hair growth on the skin paddle. A radial forearm free flap or another type of fasciocutaneous free flap, usually less hairy, would have required additional surgery for the free tissue transfer and would be related to donor site morbidity. Postoperatively, the submental island flap showed the same functional results as those of a radial free forearm flap. Despite the 10 × 5 cm skin defect of the chin area, the mobilization of the submental and submandibular skin allowed a direct proximity closure and created a minimal disfigurement to the patient. The mandibulotomy via a lip split incision performed in our case is not necessary to transport the submental island flap intraorally, as this can be performed via a blunt dissection of the mylohyoid muscle and the floor of the mouth. The mandibulotomy in our case was judged necessary in order to access the enlarged tumor due to its intralesional

hemorrhage and the fear of leaving positive margins during resection.

Malignant mesenchymal tumors, and especially sarcomas, affecting intraoral tissues have a different biologic behavior than that of squamous cell carcinoma of the same anatomic sites. Oral squamous cell carcinomas have a tendency to spread into the adjacent lymphatics of the neck in 30% to 40% of cases developing neck metastases. In patients with negative necks who submit to elective neck dissections, micro-metastases are found in 20% to 30%.³⁷⁻³⁹ On the contrary, sarcomas show a rare pattern in metastasizing to the lymph nodes of the neck and their metastases are in distant sites. Therefore, it is oncologically safe for patients with an intraoral sarcoma with negative neck to locally resect the tumor along with a generous clinically free tumor area and not perform a simultaneous ipsilateral neck dissection.

The role of postoperative radiotherapy is still a debatable issue. However, in inoperable cases or those with incomplete resection and positive surgical margins, radiotherapy seems to improve locoregional control of the disease.^{1,5,19,24,40,41}

SS is believed to be a soft tissue tumor sensitive to chemotherapy, although results from prospective studies with large cohorts of patients are lacking in the literature because of the rarity of the disease. On the contrary, tumors appearing during early childhood are usually treated with chemotherapy, which seems to reduce the rates of local recurrences and distant metastases.⁴¹⁻⁴⁶

Recent studies on the genetic and molecular profiles of patients with SS, and especially the identi-

fication of the chimeric protein produced by the fusion of the SYT-SSX genes, represents a future target for antigen-directed, individualized, antineoplastic immunotherapy.⁴⁷⁻⁴⁹ This type of treatment along with targeted therapies will definitely be the oncologic management of the future of head and neck malignancies.

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