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Synovial Sarcoma in the Oral and Maxillofacial Region: Report of 4 Cases and Review of the Literature

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Synovial sarcoma (SS) is a well-defined tumor that accounts for up to 10% of all soft tissue sarcomas. It arises primarily in the extremities,[1] with a predilection for sites in proximity to large joints such as the knee.[2] The oral and maxillofacial region is an unusual site for this tumor. Here we report 4 cases of SS in the oral and maxillofacial region and also present a review of the literature.

Report of Cases

CASE 1

A 32-year-old man had a 9-month history of a progressively growing tumor on the left side of his face. Physical examination revealed a 5 cm × 4 cm, firm, slightly tender, nonmobile tumor in the left preauricular region. Facial asymmetry and left facial swelling were observed. The maximum possible amount of mouth opening was 20 mm. The regional lymph nodes were not enlarged. A computed tomography (CT) scan revealed destruction of the normal structure of left condylar process (Fig 1). The patient underwent surgery under general anesthesia. Interoperative frozen results were consistent with a diagnosis of malignant tumor originating from mesenchymal tissue. The tumor was excised with wide margins. Histopathologic examination showed that tumor had infiltrated the condylar process (Fig 2A) and was composed of epithelial cells and spindle-shaped cells (Fig 2B). Immunohistochemical examination revealed diffuse tumor cell positivity for vimentine (Fig 2C) and CD99 (Fig 2D), with no reactivity for cytokeratines, smooth muscle actin (SMA), desmin, or CD34. A diagnosis of primary biphasic SS was made on the basis of the histopathologic and immunohistochemical findings.

CASE 2

A 31-year-old woman was referred to our institution due to aggravating left temporal region pain of 6 months' duration. Four weeks earlier, the patient had presented with mouth-opening limitation and left lower lip numbness. The patient's medical history, family history, traumatic history, and review of systems were noncontributory.

Physical examination revealed slight swelling and tenderness in the left temporal region. The maximum possible amount of mouth opening was 15 mm. The occlusal relationship was normal. No appreciable lymphadenopathy was detected. Magnetic resonance imaging (MRI) demonstrated a 5 cm × 4.9 cm × 2.4 cm mass occupying

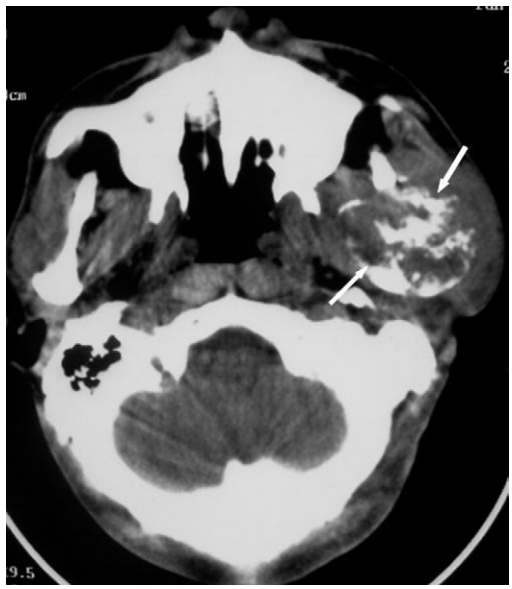

FIGURE 1. Case 1. Axial CT showing a nonhomogeneous area in the left condylar process (*arrow*). The normal structure of the left condylar process was destroyed, obscuring the border of the mass.

Wang et al. Synovial Sarcoma in the Oral and Maxillofacial Region. J Oral Maxillofac Surg 2008.

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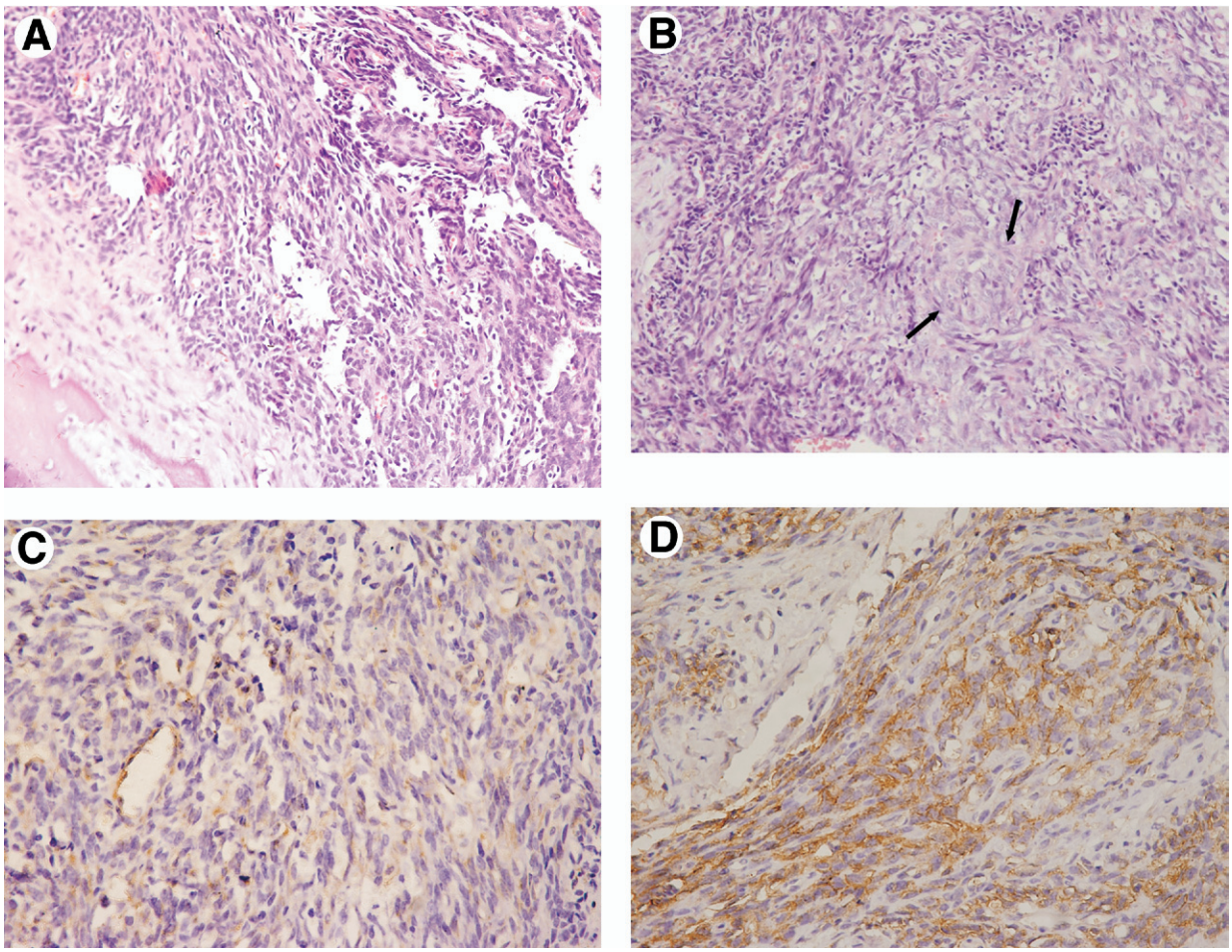

FIGURE 2. Case 1. Microphotograph of SS in the condylar process. (*A*) A solid cellular mass infiltrating the condylar process. (Hematoxylin and eosin; original magnification ×60.) (*B*) Histological view showing a mixture of epithelial cells (*arrow*) and spindle-shaped cells. (Hematoxylin and eosin; original magnification ×50.) (*C* and *D*) Immunohistochemical staining showing vimentin-positive (*C*) and CD99-positive (*D*) immunoreaction. (Original magnification ×100.)

Wang et al. Synovial Sarcoma in the Oral and Maxillofacial Region. J Oral Maxillofac Surg 2008.

the left infratemporal fossa space (Fig 3). The patient underwent surgery with a marginal excision.

Light microscopic examination revealed that the tumor cells were composed of spindle cells (Fig 4A). Immunohistochemistry was positive for epithelial membrane antigen (EMA) (Fig 4B), vimentin (Fig 4C), CD99, and Pan-CK (cytokeratin) but negative for SMA. Based on the histopathological and immunohistochemical findings, a diagnosis of monophasic (spindle cell) SS was made.

CASE 3

A 34-year-old man was referred with suspected recurrence of right cheek SS to our hospital in November 2005. The symptoms had been present for approximately 2 months. The patient reported noticing a swelling of the right cheek 6 years earlier, but that he had not paid much attention to it. In 2003, he began to experience local pain, and sought care at the local hospital. The final diagnostic result was not available. One year later, the tumor recurred and was re-excised at the local hospital. The specimen was sent to the Department of Pathology, West China Hospital for consultation. Light microscopy showed that the tumor comprised 2 alternating components, spindle cells and epithelial cells (Figs 5A,B). Immunohistochemically, the spindle cell components were positive for vimentin and the epithelial cell components were positive for EMA (Fig 5C), whereas tumor cells were negative for SMA, desmin, and S-100. Based on these features, the tumor was classified as a biphasic SS.

At 10 months after the patient's second surgery, another cheek mass reported as SS was removed in another institution. The tumor had recurred again 2 months earlier. Physical examination revealed a 5 cm × 2.5 cm firm, nonmobile mass in the right cheek. Mouth opening was limited, a maximum of 10 mm. Submandibular and preauricular operative scarring were evident. Chest radiographs did not reveal any metastatic change. The regional lymph nodes were not enlarged. Enhanced CT revealed a tumor in the right masseteric space (Fig 6). The diagnosis of recurrence was considered, and the patient underwent surgery with wide tumorectomy, including the overlying cheek soft tissues, zygomatic bone, and the zygomatic arch, along with segmental resection of the right mandibular ramus and local flap reconstruction.

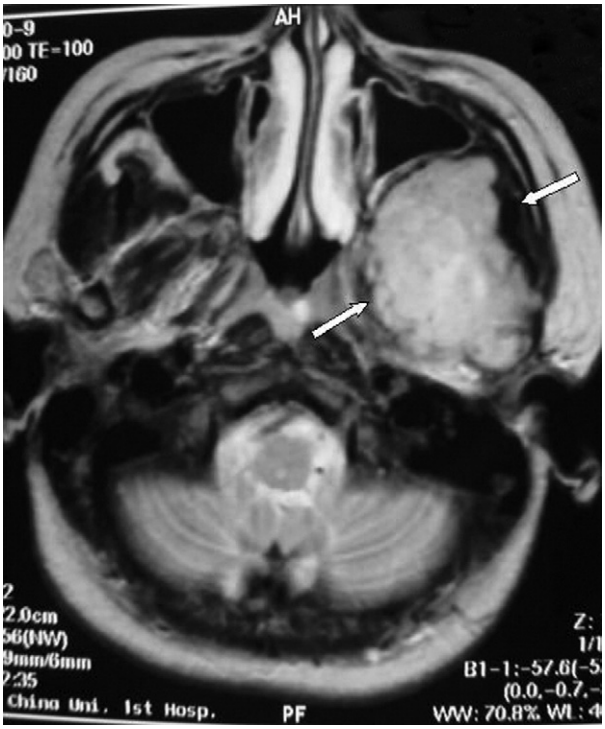

FIGURE 3. Case 2. MRI showing the mass occupying the left infratemporal fossa space (*arrow*), without complete inner encapsulation of the lesion.

Wang et al. Synovial Sarcoma in the Oral and Maxillofacial Region. J Oral Maxillofac Surg 2008.

CASE 4

On November 3, 2005, a 30-year-old woman complained of swelling of 2 months' duration in the left parotid region. Physical examination revealed a firm, tender, 1.5 cm × 1.5 cm tumor in the left parotid gland region. Facial nerve function was normal. CT showed a mass in the left parotid gland region involving the temporomandibular joint and infratemporal fossa. The lesion was excised and a specimen sent for histological examination. Histologically, tumor cells were found infiltrating the parotid gland and nerve tissue (Figs 7A,B). Biphasic features including nesting-like epithelial cells and spindle cell components were observed (Fig 7C). Immunohistochemical examination revealed tumor cell positivity for Pan-CK (cytokeratin) but no reactivity for S-100, CD31, CD34, and desmin. Considering the morphological and immunohistochemical features, a diagnosis of primary left parotid gland SS was made.

Discussion

SS is a highly invasive tumor, but only 3% of all cases occur in the head and neck region. In the last few years, an increasing number of primary SSs have been detected in oral and maxillofacial sites, including the buccal mucosa,[3] maxillary sinus,[4] mandible,[5,6] tongue,[7] and floor of the mouth.[8] The typical clinical presentation of these lesions is a slow-growing, deep-seated, palable mass associated with pain in about 50% of cases.

In the 4 cases presented here, 2 occurred in males and the other 2 in females. The patients ranged in age from 30 to 34 years. The 4 lesions were located in the left condylar process, left infratemporal fossa, right cheek, and left parotid gland. The clinical presentation of all 4 cases was that of a gradually growing tumor. Case 3 had 3 recurrences. The biphasic type of SS is more common than the monophasic type; of the 4 cases presented here, 3 were biphasic and 1 was monophasic. To date, 6 cases of cheek SS and 2 cases of parotid SS have been reported in the English literature (Table 1).[9-12] Occurrence in the infratemporal fossa or condylar process as illustrated in the current cases appears to be extremely rare.

SS is not restricted to periarticular sites; it sometimes appears in locations unrelated to the synovium, such as the tongue and soft palate. Thus, the histogenesis of SS remains controversial. Intercellular junctions, microvilli, external lamina, and epithelial differentiation are rarely observed in normal synovium but can be seen in tumors.[13] According to Leader et al,[14] SSs can be more appropriately classified as carcinosarcomas. It is now generally accepted that SSs originate from undifferentiated or pluripotent mesenchymal cells with a dual differentiation capacity, both epithelial and mesenchymal.[14,15] Variants of SS are subclassified into 4 types: (1) biphasic type with distinct epithelial and spindle cell components present in various proportions and patterns, (2) monophasic spindle cell type with little or no evidence of epithelial differentiation, (3) monophasic epithelial type, and (4) poorly differentiated type.

Immunohistochemically, the spindle cells of SS strongly and uniformly express mesenchymal marker (vimentin) with occasional evidence of cytokeratin markers, particularly in biphasic tumors. In contrast, the epithelial cells usually demonstrate strong expression of epithelial markers (ie, CK7, CK19, EMA). At least 1 of these 2 epithelial markers is expressed in 90% of SSs. CD99 is expressed in most Ewing's sarcomas and peripheral neuron-ectodermal tumors; however, CD99 immunoreactivity also can be detected in the cytoplasm of cells in many SSs.

A biphasic SS is easily identified by its histological features. A monophasic spindle cell neoplasm, the most common variant of SS, is usually more problematic. Immunohistochemistry is a very useful tool in classifying these lesions. The tumor cells in SS are generally positive for epithelial markers (ie, cytokeratins and EMA) that are mostly absent in other soft tissue sarcomas, such as fibrosarcomas.

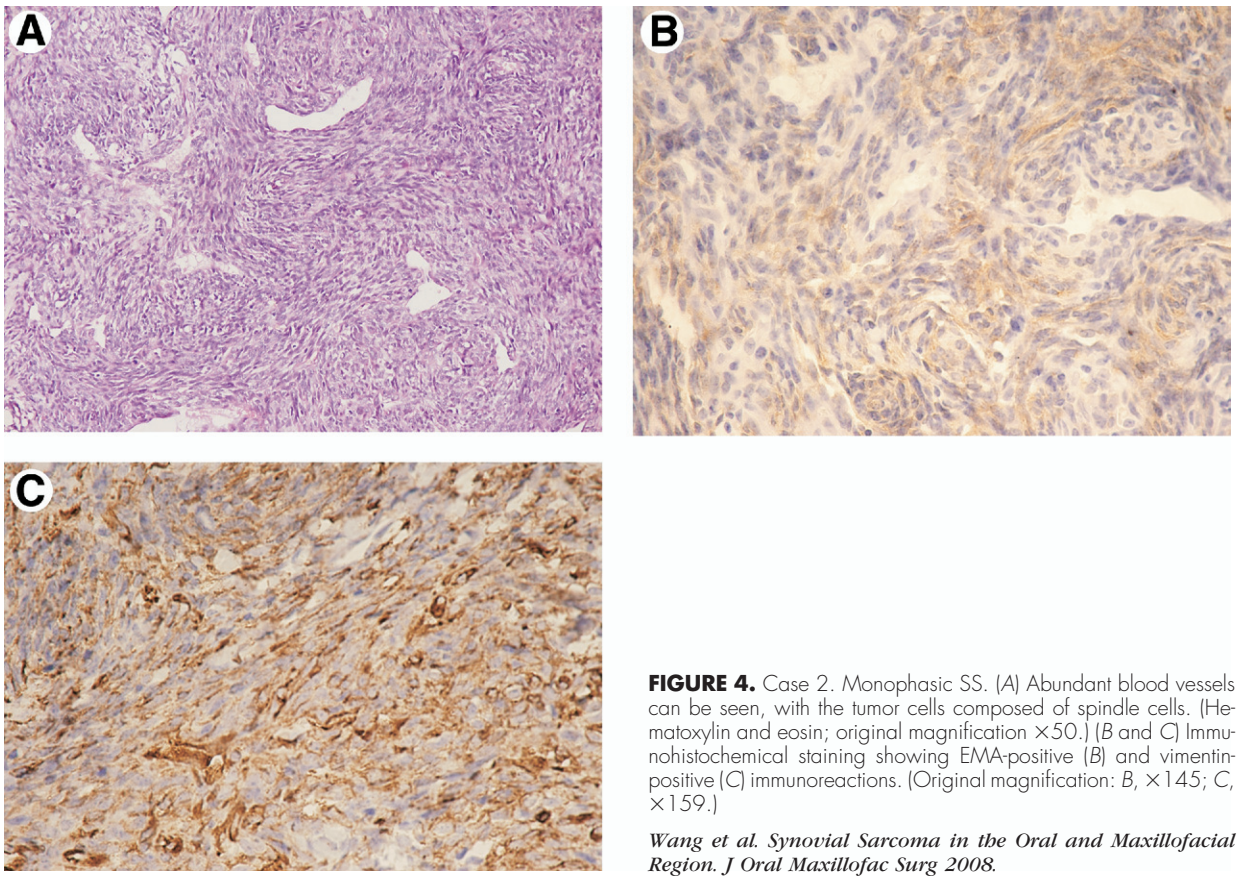

FIGURE 4. Case 2. Monophasic SS. (*A*) Abundant blood vessels can be seen, with the tumor cells composed of spindle cells. (Hematoxylin and eosin; original magnification ×50.) (*B* and *C*) Immunohistochemical staining showing EMA-positive (*B*) and vimentin-positive (*C*) immunoreactions. (Original magnification: *B*, ×145; *C*, ×159.)

Wang et al. Synovial Sarcoma in the Oral and Maxillofacial Region. J Oral Maxillofac Surg 2008.

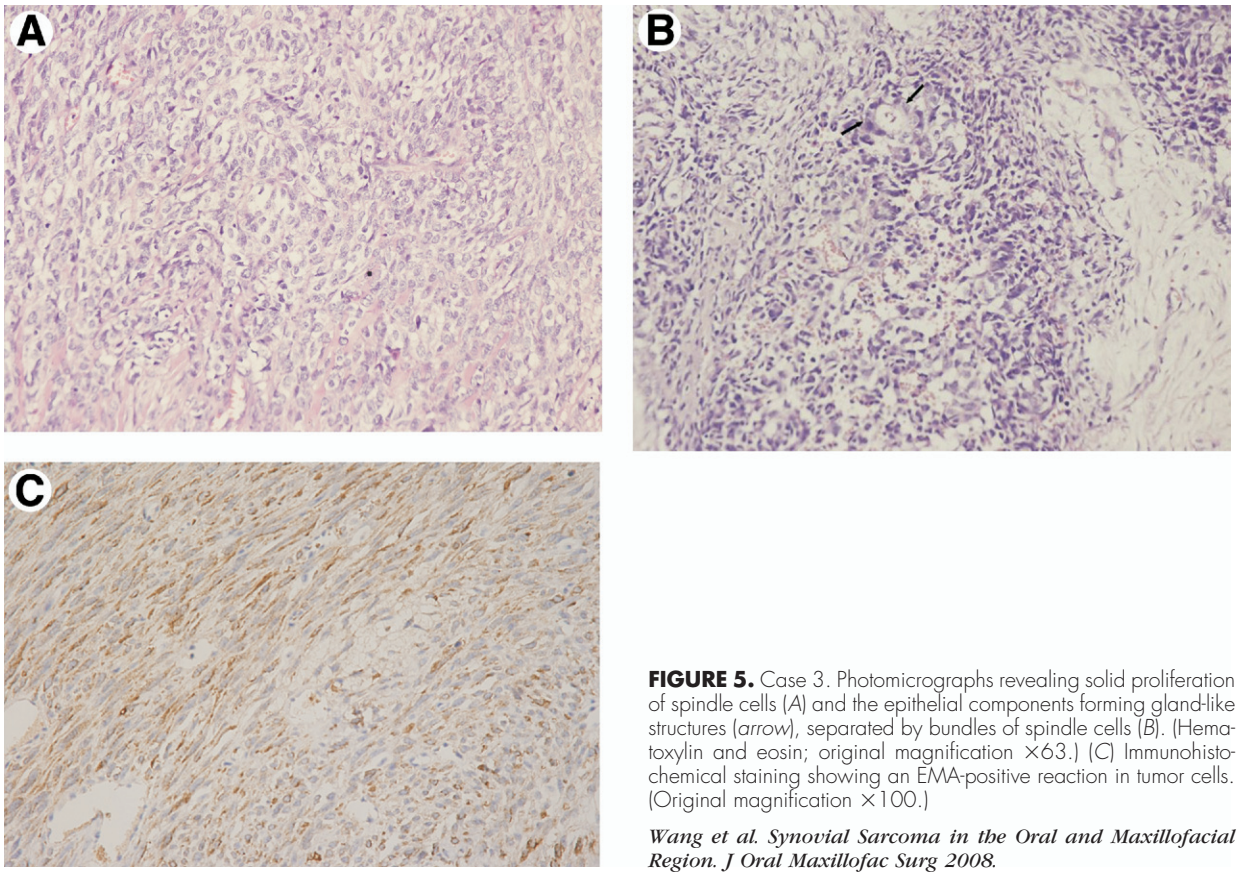

FIGURE 5. Case 3. Photomicrographs revealing solid proliferation of spindle cells (*A*) and the epithelial components forming gland-like structures (*arrow*), separated by bundles of spindle cells (*B*). (Hematoxylin and eosin; original magnification ×63.) (*C*) Immunohistochemical staining showing an EMA-positive reaction in tumor cells. (Original magnification ×100.)

Wang et al. Synovial Sarcoma in the Oral and Maxillofacial Region. J Oral Maxillofac Surg 2008.

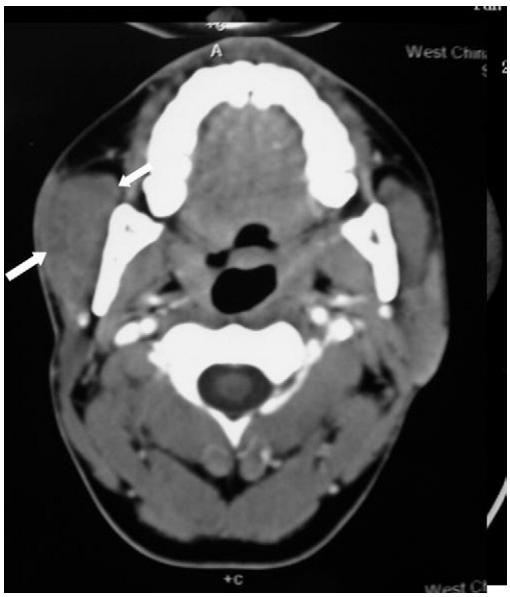

FIGURE 6. Case 3. Enhanced CT scan showing the tumor located in the right masseteric space (*arrow*), with the surrounding bone intact.

Wang et al. Synovial Sarcoma in the Oral and Maxillofacial Region. J Oral Maxillofac Surg 2008.

Muscle-associated markers (eg, desmin, SMA) can be detected in leiomyosarcoma but are rarely seen in SS. S-100 protein is expressed in most malignant peripheral nerve sheath tumors. Considerable prognostic information can be provided by immunohistochemical analysis of tumor proliferation. A Ki-67(MIB-1) index greater than 10% may be significantly correlated with the development of metastatic disease.[16]

Cytogenetically, SS is characterized by the specific t(X;18) (p11.2;q11.2) chromosomal translocation, found in more than 95% of the tumors. At the molecular level, this translocation results in rearrangements of the *SYT* gene in 18q11 and 1 of the *SSX1*, *SSX2*, or *SSX4* genes in Xp11, creating a *SYT-SSX1*, *SYT-SSX2*, or *SYT-SSX4* chimeric gene.[17] The *SYT-SSX2* fusion is usually associated with the monophasic type, and the *SYT-SSX1* fusion is present in tumors of biphasic or monophasic type. This relationship is not absolute, however; biphasic tumors with *SYT-SSX2* fusion have been reported.[17-19] The *SYT-SSX* fusion transcript is a defining diagnostic marker of SS and thus is of high diagnostic value.[20-22] However, molecular testing is not required if the diagnosis of SS is certain or probable based on clinical, histological, and/or immunohis-

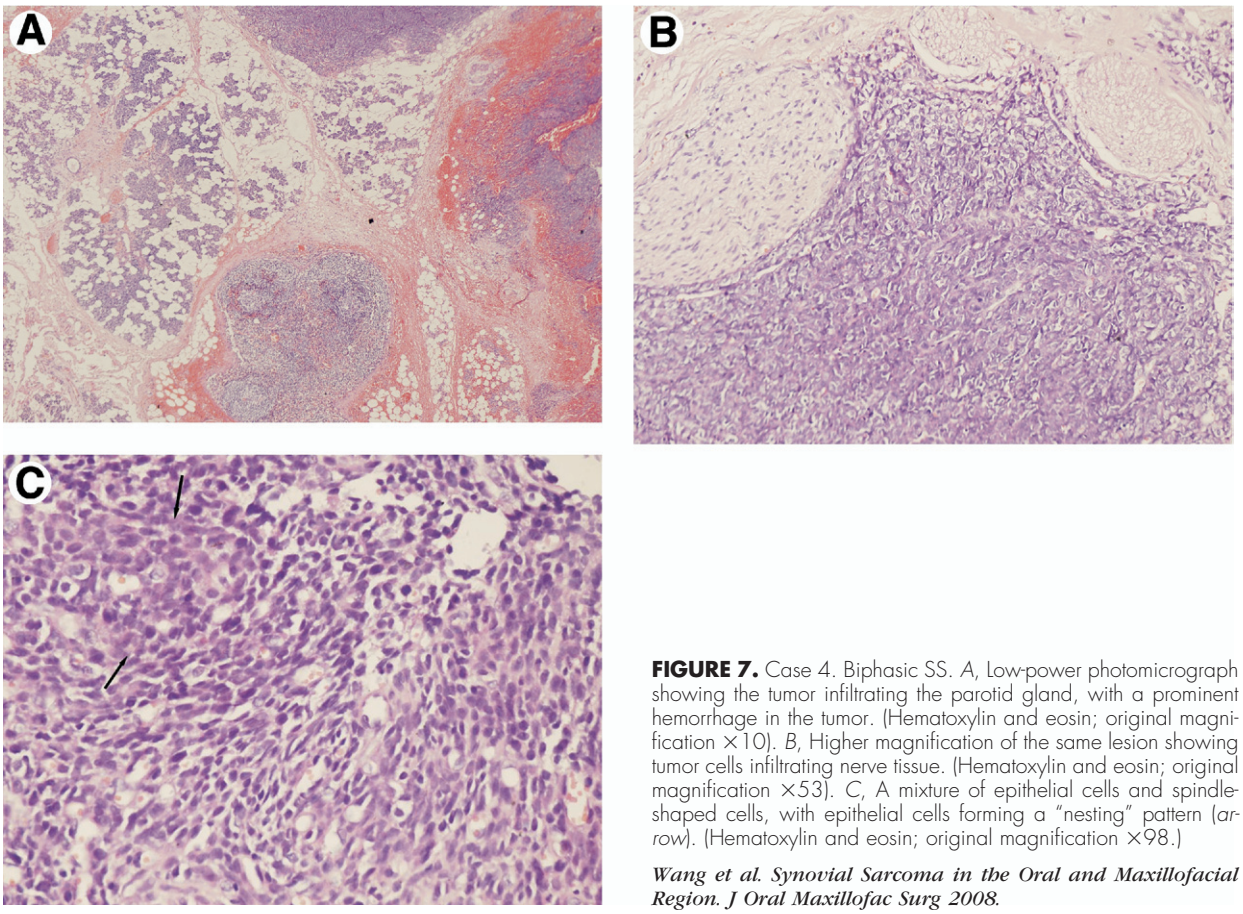

FIGURE 7. Case 4. Biphasic SS. *A*, Low-power photomicrograph showing the tumor infiltrating the parotid gland, with a prominent hemorrhage in the tumor. (Hematoxylin and eosin; original magnification ×10). *B*, Higher magnification of the same lesion showing tumor cells infiltrating nerve tissue. (Hematoxylin and eosin; original magnification ×53). *C*, A mixture of epithelial cells and spindle-shaped cells, with epithelial cells forming a "nesting" pattern (*arrow*). (Hematoxylin and eosin; original magnification ×98.)

Wang et al. Synovial Sarcoma in the Oral and Maxillofacial Region. J Oral Maxillofac Surg 2008.

Table 1. SUMMARY OF CLINICAL FEATURES OF 8 PREVIOUSLY REPORTED CASES OF RELATED REGIONS OF SS

Reference	Age	Gender	Location	Management	Histological type	Follow-Up
Lee et al[9]	15	F	Cheek	SX	INA	A&W/15 years
Lockey[10]	11	F	Cheek L	SX, RTX, CTX	B	Dead/0.7 years
Nunez-Alonso et al[11]	48	M	Cheek R	SX, RTX	B	A&W/1.8 years
Shmookler et al[12]	27	F	Cheek L	SX	B	A&W/1.3 years
Shmookler et al[12]	36	M	Cheek R	SX, RTX, CTX	B	Dead/2.1 years
Shmookler et al[12]	26	M	Cheek-pterygomaxillary fossa, R	RTX, SX, CTX	B	Dead/2.6 years
Shmookler et al[12]	19	M	Parotid region, L	RTX, CTX, SX	B	Dead/2.9 years
Shmookler et al[12]	49	M	Parotid region, R	SX, RTX	B	A&W/2.3 years

Abbreviations: SX, surgical excision; RTX, irradiation therapy; CTX, chemotherapy; A&W, alive and well; B, biphasic type; INA, information not available.

Wang et al. Synovial Sarcoma in the Oral and Maxillofacial Region. J Oral Maxillofac Surg 2008.

tochemical evaluation.[21] Genetic trials were not carried out for the 4 cases reported here. The fusion type presented by SS is a major prognostic indicator. The *SYT-SSX1* fusion gene is associated with more aggressive tumor growth and poor outcome. Patients with *SYT-SSX1* fusion genes have been reported to have shorter metastasis-free survival compared with patients with *SYT-SSX2* fusion genes.[17,18,23,24]

Owing to the paucity of cases of SS in the oral and maxillofacial area, the information regarding appropriate therapy for this tumor is limited. At present, adequate surgical excision appears to the most appropriate procedure to prevent local recurrence. In the head and neck, radical excision generally cannot be done without sacrificing vital structures. For this reason, the therapeutic strategy frequently avoids radical and mutilating surgery but includes postoperative radiation and adjuvant chemotherapy after conservative excision of the tumor.

Post-treatment recurrence rate for SS arising from all body sites is about 50%. Most cases recur in the first 2 years after treatment. Five-year survival rate is about 36% to 51%. Prognosis is affected by tumor size, location, patient age, histological subtype, extent, mitotic activity, and margin of resection.[1,17,25] Tumor size is the most important prognostic factor. Patients with tumors of maximum diameter greater than 5 cm have a poorer prognosis than those with tumors less than 5 cm in diameter.[26] Despite advances in the treatment of local disease, distant metastasis remains the predominant cause of death. Recently, some investigations revealed that epidermal growth factor receptor (EGFR) and human epithelial growth factor receptor 2 (HER-2/neu) may play roles in the tumorigenesis of SS. Thus, antigrowth factor antibody therapies may provide a previously unrecognized therapeutic approach to these tumors.[27,28]

In summary, this report has presented 4 cases of SS in different oral and maxillofacial regions. All 4 patients underwent surgical resection with negative margins. The final diagnoses were confirmed by histological and immunohistochemical findings. Data on post-treatment recurrence and survival rate were not obtained, because all 4 patients were lost to follow-up.

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Malposed Teeth in the Pterygomandibular Space: Report of 2 Cases

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Malposed teeth are well-documented in the literature.[1] Normal canines and third molars are most frequently found in an abnormal position. Supernumerary teeth can also be found in unusual locations, as can teeth that have been displaced by the growth of odontogenic cysts or tumors. We report 2 cases of mandibular third molars that were located in the pterygomandibular space. Although both apparently had some connection with the oral cavity, neither seems to have been displaced by a cyst or a tumor.

Report of Cases

CASE 1

A 49-year-old woman presented to her general dentist with acute right mandibular pain, trismus, and a foul taste in her mouth. Periapical films showed periodontal bone loss distal to the mandibular right second molar. When a periodontal pocket was noted in this location, she was treated with scaling, root planing, and oral clindamycin. Symptoms resolved temporarily but returned 2 weeks later, and the patient was referred to an oral and maxillofacial surgeon. A panoramic radiograph revealed a third molar high in the ascending ramus of the right mandible (Fig 1A). The practitioner believed that this represented a cyst, which he could not manage in his office. He referred the patient to our department for care.

A malposed tooth was obvious on x-ray, but a cystic lesion could not be discerned. We obtained a computed tomographic (CT) scan of the mandible (Fig 1B), which showed the third molar crown to be outside of the bone, in the pterygomandibular space. The tooth was inverted, with its root apices attached to bone just below the sigmoid notch. No associated cyst or tumor was noted. Sclerosis in the adjacent mandible was consistent with chronic infection. At surgery, the tooth was easily removed from the area between the lingula and the sigmoid notch. Attachment to bone was observed at the root apices. The crown was blackened and occlusal caries was present, indicating a connection with the periodontal pocket distal to the mandibular right second molar. The patient was treated with a cephalosporin and made a rapid recovery, with resolution of all symptoms.

CASE 2

A 55-year-old woman was referred to our department by her dentist after 3 days of rapidly increasing left facial swelling, pain, fever, and trismus. No evidence of a dental cause was noted, and the patient reported no previous dental symptoms. An urgent CT scan was obtained, which

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