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Case Report

Head and Neck Solitary Fibrous Tumor Presenting as Salivary Gland Tumor: Two Case Reports and Review of the Literature

Kensuke Suzuki[a] Yuri Noda[b] Tomofumi Sakagami[a] Masao Yagi[a]
Kimihide Kusafuka[c] Hiroshi Iwai[a]

[a]Department of Otolaryngology, Head and Neck Surgery, Kansai Medical University, Hirakata, Osaka, Japan; [b]Department of Pathology, Kansai Medical University, Hirakata, Osaka, Japan; [c]Department of Pathology, Shizuoka General Hospital, Shizuoka, Japan

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Solitary fibrous tumor · Head and neck · Parotid gland · Buccal space · STAT6

Abstract
Solitary fibrous tumors (SFTs) are soft tumors (mesenchymal origin) that most likely develop from adult mesenchymal stem cells. SFTs are not common in the head and neck region, and the characteristics of tumors in this location are unclear. The present study describes the clinicopathological findings of 2 cases of SFTs arising in the parotid gland and buccal space, presenting as salivary gland tumors. The first case is a 76-year-old man presenting with a painless tumor on the right parotid gland who subsequently underwent partial superficial parotidectomy. According to the results of histopathological analysis, the tumor consisted of stellate and spindle-shaped cells proliferating on a mucous-like substrate. Immunohistochemical staining revealed that neoplastic cells were positive for CD34, vimentin, Bcl2, and STAT6. The second case is of a 64-year-old man presenting with a painless lump on his right cheek. Based on the findings of fine needle aspiration cytology, a tumor derived from myoepithelial cells of the minor salivary gland or a nonepithelial tumor was suspected. The patient underwent surgical resection via an intraoral approach. Histopathologically, the tumor consisted of spindle-shaped cells with rod-shaped or irregular nuclei. Immunohistochemical staining revealed that the neoplastic cells were positive for CD34, CD99, Bcl2, and STAT6. Briefly, SFT should be considered in the differential diagnosis of a well-marginalized lesion in the salivary gland and oral cavity. STAT6 immunohistochemistry is the most specific and sensitive method of diagnosing SFT. A thorough understanding of the morphological changes associated with SFT and their correlation with clinical, immunohistochemical, and molecular characteristics is important to avoid misdiagnosis.

Correspondence to:
Kensuke Suzuki, suzukken@hirakata.kmu.ac.jp

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Introduction

In 1931, solitary fibrous tumors (SFTs) were described by Klemperer and Rabin as tumors of the pleura [1]. SFTs are neoplasms of mesenchymal origin, probably derived from adult mesenchymal stem cells [2]. Recently, the molecular marker of SFT has been found to be a repetitive fusion of the NAB2 and STAT6 genes located in the chromosomal region 12q13 [3, 4].

SFTs have been identified in almost every anatomical region of the human body. Among these, the pleura is the most common site of SFT occurrence, accounting for >30% of the cases. Other sites of occurrence of SFTs are meninges (27%), abdominal cavity (20%), trunk (10%), extremities (8%), and the head and neck region (5%) [5]. In particular, SFTs in the head and neck region are uncommon, and the characteristics of tumors at this location are unclear [6]. This study reports clinicopathological findings from 2 cases of SFTs arising in the parotid gland and buccal space with a brief review of the literature to improve knowledge on the diagnosis of this rare entity. The CARE Checklist has been completed by the authors for this case report, attached as online supplementary material (for all online suppl. material, see https://doi.org/10.1159/000531067).

Case Presentation

Case 1

A 76-year-old man presented with a 10-year history of a painless, palpable mass on the right side of the parotid gland. On physical examination, the tumor was found to be elastic, hard, and movable, measuring approximately 30 mm in diameter. Magnetic resonance imaging (MRI) scan revealed a well-circumscribed regular mass of 32 × 30 × 24 mm in the right parotid gland (Fig. 1). The patient underwent partial superficial parotidectomy. Notably, the gross resected specimen was a grayish-white solid tumor (Fig. 2a). Histopathological examination revealed that the tumor was extensively vitiated and comprised stellate and spindle-shaped cells proliferating with a branching vascular network (Fig. 2b, c). The surrounding salivary gland tissue was also observed (Fig. 2b). The mitotic rate was found to be 1 per 10 high-power fields (HPFs), and no tumor necrosis was noted. Immunohistochemical staining revealed that the neoplastic cells were negative for AE1/AE3, α-SMA, p63, and S100 protein but positive for CD34, vimentin, Bcl2, and STAT6 (Fig. 2d, e). The final histopathological diagnosis was SFT. The surgical margins were negative, and no adjuvant therapy was administered. Notably, there was no local recurrence or metastatic disease during the 6-year follow-up period.

Case 2

A 64-year-old man presented with a 1-month history of a painless tumor on his right cheek. His physical examination revealed a tumor in the right buccal submucosa and subcutaneous area that was elastic, hard, movable, and approximately 40 mm in diameter. MRI scan revealed a well-defined regular mass of 40 × 36 × 31 mm in the right buccal space (Fig. 3). Based on the findings of fine needle aspiration cytology, a tumor derived from myoepithelial cells of the minor salivary gland (e.g., pleomorphic adenoma) was suspected; however, it was difficult to distinguish the tumor from a nonepithelial tumor (Fig. 4). The patient underwent surgical resection of the mass via an intraoral approach. The buccal mucosa on the surface of the tumor and the masseter muscle were partially resected. The gross resected specimen was a yellow-white tumor (Fig. 5a). Histopathological examination revealed that the tumor comprised spindle-shaped cells with rod-shaped or irregular nuclei

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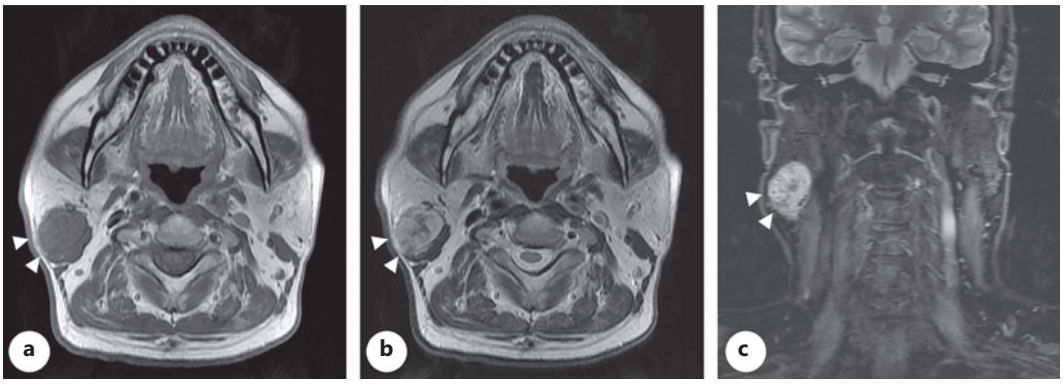

Fig. 1. A preoperative MRI scan of case 1. MRI scans showing a well-defined and regular tumor in the right parotid gland (**a–c**). Axial T1-weighted (**a**) and T2-weighted (**b**) images of the mass showing hypointense and hyperintense signal intensities, respectively. **c** A hyperintense signal in the mass is visible on the coronal STIR image. Arrowheads indicate the tumor mass. MRI, magnetic resonance imaging; STIR, short TI inversion recovery.

and a densely hyalinized collagenous stroma (Fig. 5b, c). The surrounding tissue, including a few muscles, was observed; conversely, normal salivary gland tissue was not observed (Fig. 5b). The mitotic rate was found to be 14 per 10 HPFs, and no tumor necrosis was detected. Immunohistochemical staining revealed that the neoplastic cells were negative for AE1/AE3, α-SMA, p63, calponin, and S100 protein but positive for CD34, CD99, Bcl2, and STAT6 (Fig. 5d, e). The final histopathological diagnosis was SFT. The surgical margin was partially positive, and vascular invasion was detected. Further, additional resection was performed, but no residual tumor was detected. Notably, no local recurrence or metastatic disease was observed during the 20-month follow-up period.

Discussion

SFT is recognized as a soft tumor of mesenchymal origin that rarely affects the parotid gland, with only 43 cases reported in the relevant literature [7–23]. Moreover, SFTs in the oral cavity, including the buccal space, are rare. According to a previous study, SFT in the oral region accounts for 3% of all cases of SFTs [24]. In particular, SFTs in the head and neck region are more likely to be identified at earlier stages and are smaller in size than SFTs in the intrathoracic region owing to their anatomic location [25].

SFT typically affects middle-aged individuals but is also observed in young individuals [7, 26]. Clinically, patients with SFT usually present with a slow-growing, hard, well-defined, and painless mass for a few months to a few years [7], similar to the cases presented in this report. In general, radiological findings of SFTs are nonspecific, with most patients presenting with a well-circumscribed and lobulated mass [27]. MRI usually shows intermediate signal intensity in T1-weighted images and an enhancement in T2-weighted images [12].

The histologic and immunophenotypic characteristics of SFTs are comparable, regardless of the anatomic site [7, 28]. Microscopically, these tumors have a patternless arrangement of spindle-shaped cells on a collagenous background with prominent blood vessels. Further, the cell nuclei are round to oval in shape with open vesicular chromatin. Histological features suggesting malignancy include a high mitotic rate, hypercellularity, moderate-to-marked atypia and nuclear pleomorphism, tumor necrosis, and infiltrative boundaries [11, 15].

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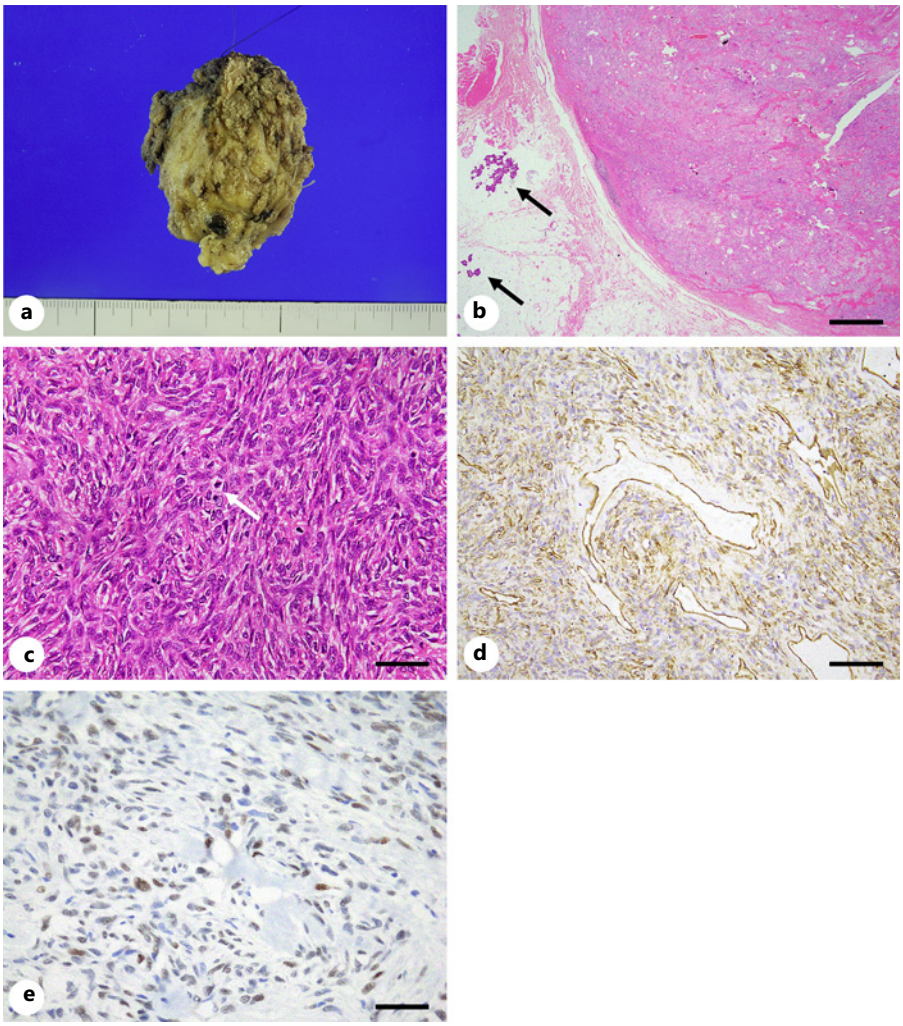

Fig. 2. Histological findings of case 1. **a** The gross resected specimen is a grayish-white hard tumor. **b** The tumor is surrounded by adipose tissue, including salivary glands, according to H/E staining (black arrows). The tumor is composed of stellate and spindle-shaped cells proliferating with a branching vascular network (**b**, **c**). **c** Mitosis is observed (white arrow). Immunohistochemical staining shows that neoplastic cells are positive for CD34 (**d**) and STAT6 (**e**). Scale bars, 1 mm (**b**); 50 μm (**c**); and 100 μm (**d**, **e**). H/E, hematoxylin and eosin.

Notably, SFTs exhibit a wide range of histological characteristics, often leading to a broad differential diagnosis and frequent misdiagnosis [7, 28]. The differential diagnosis of SFT includes cellular pleomorphic adenoma, myoepithelioma, schwannoma, neurofibroma, benign fibrous histiocytoma, nodular fasciitis, fibromatosis, myofibroblastoma, meningioma, fibrosarcoma, spindle cell squamous cell carcinoma, spindle cell melanoma, Kaposi sarcoma, and monophasic synovial sarcoma [7, 15]. Although no normal salivary gland tissue was found in the surgical specimen of case 2, both SFT cases presented here exhibited radiological or cytological evidence of tumors growing from the major or minor salivary gland, which required differentiation from more common diseases, such as pleomorphic adenoma.

Immunohistochemically, a combination of CD34, CD99, and Bcl2 has been commonly used to diagnose SFTs, but none of these markers are sufficiently sensitive or specific to discriminate between these tumor types [17]. Notably, malignant SFTs tend to have less CD34 immunoreactivity [29]. STAT6 IHC stain has been proven to be a valuable surrogate marker

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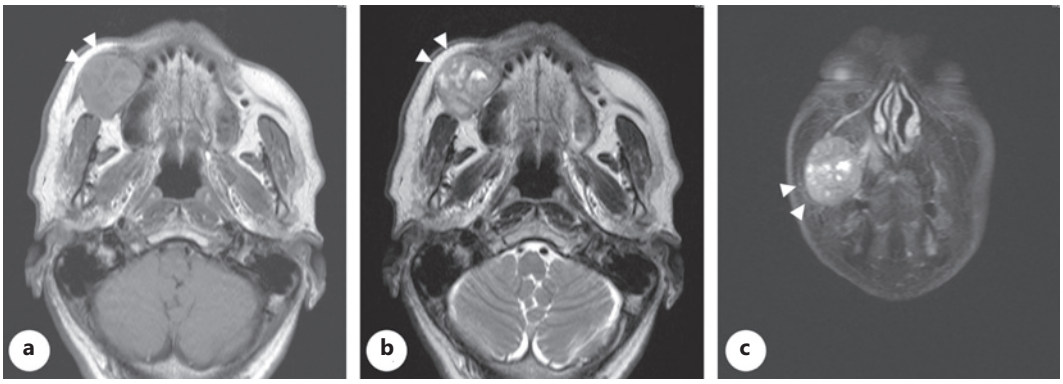

Fig. 3. A preoperative MRI scan of case 2. MRI scan showing a well-defined regular mass in the right buccal region (**a–c**). Axial T1-weighted (**a**) and T2-weighted (**b**) images of the mass showing pale hyperintense and heterogeneous hyperintense signal intensities, respectively. **c** Coronal STIR image shows a heterogeneous hyperintense signal in the mass. Arrowheads indicate the tumor mass. MRI, magnetic resonance imaging; STIR, short TI inversion recovery.

for the fusion of the NAB2-STAT6 gene, which has high sensitivity and specificity and is even expressed in malignant cases [30]. In a large study, Demicco et al. assessed STAT6 expression in 1781 non-SFT mesenchymal tumors and found remarkable nuclear expression in only 4% of the cases [31]. STAT6 expression in SFT is predominantly nuclear; however, other tumors may be positive on both nuclear and cytoplasmic staining [31]. The lack of pancytokeratin and myoepithelial markers (e.g., S100 protein and calponin) can help exclude other differential diagnoses [17]. Similar to the results of previous reports, on staining, the 2 cases presented in this report were positive for CD34, Bcl2, and STAT6 but negative for pancytokeratin and S100 protein.

Recently, many studies using whole-exome sequencing or RT-PCR have identified a recurrent fusion of the NAB2-STAT6 gene on chromosome 12 in SFT [3, 4]. This gene fusion has variable breakpoints and induces STAT6 nuclear expression [32], which is thought to be an initial event in the development of SFT tumors [33].

There is no consensus on the treatment of SFTs [34] due to the lack of treatment methods and randomized controlled trials. The most commonly used treatment approach for benign and malignant SFTs is complete surgical excision with negative microscopic margins [7, 15]. Furthermore, postoperative radiation and/or chemotherapy may be recommended in cases of incomplete resection or malignant histologic features [15–17].

The development of multivariate risk models has resulted in a better prognostication than the conventional distinction between benign and malignant tumors [35]. The most widely used model for metastatic risk includes determination of mitotic count (≥4 mitoses/10 HPFs), patient age (≥55 years), tumor size stratified by 5 cm, and necrosis grades to classify tumors into low-, intermediate-, and high-risk groups [36, 37]. Based on the risk assessment, the 2 cases presented here were classified into the low-risk group, indicating a very low likelihood of metastasis. Further, additional external validation of such criteria is required for prognostic assessment of head and neck SFTs because they both account for only a small subset of these studies [25]. The median overall survival time of patients with extrathoracic SFTs ranged from 59 to 94 months in one study, with 5-year and 10-year survival rates of 89% and 73%, respectively [36]. Because recurrence and metastasis can manifest after several years, regular clinical and imaging follow-up is recommended [27].

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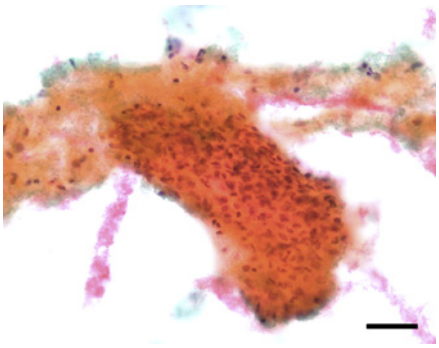

Fig. 4. Cytomorphology of fine needle aspiration. Smear showing multilayered clusters of oval- to spindle-shaped nuclei. Pleomorphic adenoma – a type of myoepithelial tumor – is suspected. Papanicolaou stain. Scale bar, 50 μm.

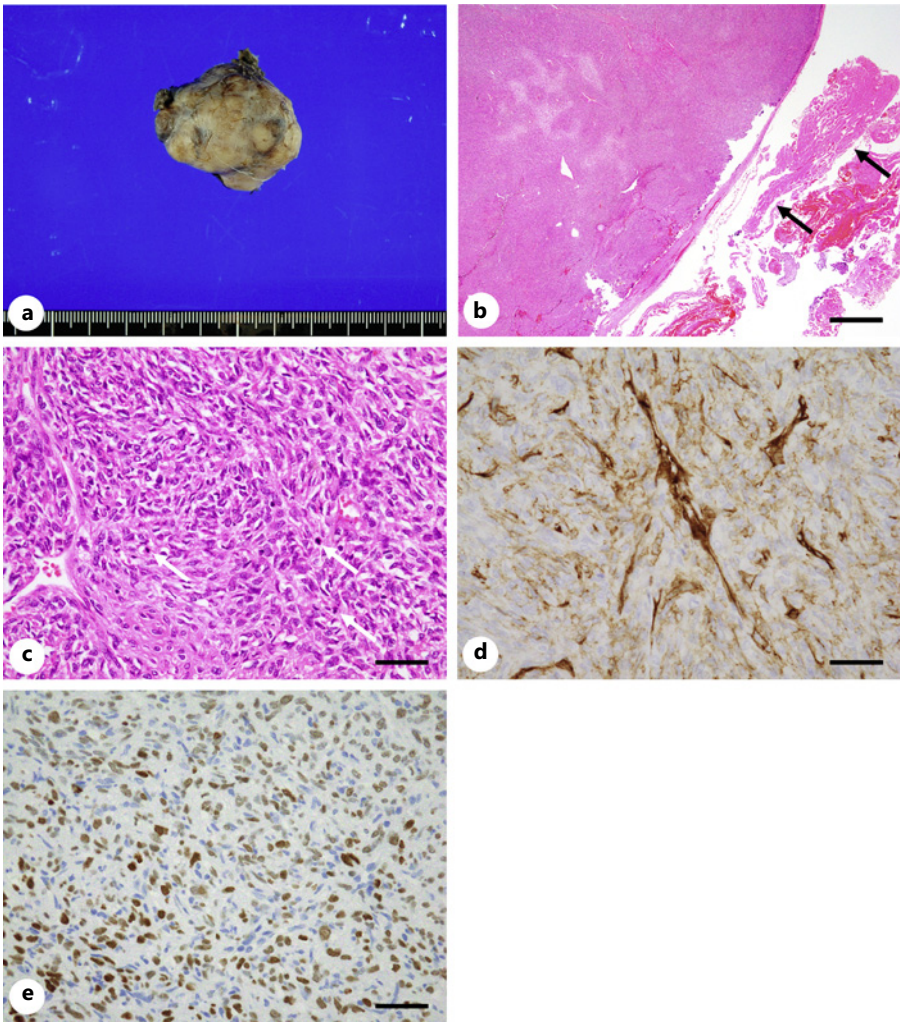

Fig. 5. Histological findings of case 2. **a** The gross resected specimen is a yellow-white tumor. **b** H/E staining showing muscles surrounding the tumor (black arrows). Spindle cells with rod-shaped or irregular nuclei and densely hyalinized collagenous stroma can be seen (**b**, **c**). **c** Mitosis is observed (white arrows). Immunohistochemical staining shows that neoplastic cells are positive for CD34 (**d**) and STAT6 (**e**). Scale bars, 500 μm (**b**) and 50 μm (**c–e**). H/E, hematoxylin and eosin.

In conclusion, this study presented the clinicopathological findings of 2 cases of head and neck SFTs occurring in the parotid gland and buccal space. We suggest that SFT should be considered in the differential diagnosis of a well-marginated lesion in the salivary gland and oral cavity. Further, we found that STAT6 immunohistochemistry is the most sensitive and specific method for SFT diagnosis; moreover, it is the most convenient and cost-effective method. Finally, a thorough understanding of the morphological changes associated with SFT and their correlation with clinical, immunohistochemical, and molecular characteristics is important to avoid misdiagnosis.

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Statement of Ethics

This study was approved by the Kansai Medical University Ethics Committee (approval # 2015103). Written informed consent was obtained from the patient or the patient's next of kin for publication of the details of their medical case and any accompanying images.

Conflict of Interest Statement

The authors have no conflicts of interest to declare.

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Author Contributions

K.S. and H.I. designed the study. K.S., Y.N., and H.I. drafted and revised the manuscript. K.S., Y.N., T.S., M.Y., and K.K. collected, examined, and interpreted the data. All authors approved the final manuscript.

Data Availability Statement

All data generated or examined during this investigation were contained in this article. Further inquiries can be directed to the corresponding author.

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