Synovial sarcoma of the tongue: report of a case and review of the literature

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ABSTRACT

This report outlines the work-up and management of a 35-year-old man with a synovial sarcoma of the lateral border of the tongue. Synovial sarcoma of the tongue is an extremely rare tumour with variable morphological microscopic types and characters of immunohistochemical profile. There have only been 15 cases previously reported. This report aims to update the literature on this subject and explore the best treatment options.

KEYWORDS

Synovial sarcoma – Immunohistochemistry

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Introduction

Synovial sarcoma is a soft tissue sarcoma with variable morphological and genetic characteristics. Synovial sarcoma often occurs in the head and neck, including the parapharyngeal space and parotid gland. Synovial sarcomas of the tongue are extremely rare and diagnosis of these tumours is complicated. We describe the diagnosis and management of a 35-year-old man with a synovial sarcoma of the lateral left side of the tongue, which was initially diagnosed as a haemangioma. Given its rarity, we believe that this case is worthy of reporting and comparison with previously reported cases located in the same anatomical site to explore the best treatment options.

Case history

A 35-year-old man noticed a mildly painful, non-mobile lump on the left side of his tongue one year before presentation. The patient described the initial tumour as being the size of a quail's egg. The tumour produced a progressive speech impairment and led to difficulty in food intake. One month after first noticing the lump, the patient underwent a magnetic resonance imaging (MRI) examination at the local hospital. Haemangioma was diagnosed. Subsequently, he underwent further evaluation and management at the Stomatological Hospital of Shandong University. Blood analysis indicated that he had hepatitis b. The patient denied smoking and drinking.

Intraoral examination revealed a 4 × 4 × 3 cm mass located on the posterior third of the left side of the tongue. The mass was solid and painless on palpation. The colour

of the mucosa of lingual dorsum was normal. Tongue movements were partially restricted (Fig 1). No enlarged lymph nodes were noted on either side of the neck. MRI of the head and neck revealed the presence of a large tumour occupying the left side of the tongue (Figs 2 and 3). The panel of oral and maxillofacial surgery experts assessed the patient and recommended surgical excision of the tumour. The malignant nature and vasculature of the tumour was not clear, as assessed by clinical manifestation and MRI. Given that a preoperative biopsy may have led to excessive bleeding, we prepared an intraoperative frozen biopsy.

No capsule was present around the tumour and it infiltrated peripheral tissue (Fig 4). The pathology result did not exclude a low degree of malignancy, but a clear diagnosis was not obtained. We decided to remove the tumour completely. Given the defective tissue, we used local flap repair to remodel the tongue (Fig 5).

The histopathological report of the surgical specimen revealed a synovial sarcoma of the tongue. Immunohistochemical analysis was positive for epithelial membrane antigen (EMA) and CD99. The pathology report confirmed wide tumour-free surgical margins.

According to the 2017 National Comprehensive Cancer Network (NCCN) Clinical Practice Guidelines in Oncology of soft tissue sarcoma, this patient had a T2N0M0 tumour. The tumour was classified as stage IIB based on NCCN guidelines. Tumours of this stage should primarily be managed by en-bloc resection to obtain oncologically appropriate margins, followed by radiation therapy and adjuvant chemotherapy. However, there are limited and conflicting data regarding the potential benefits of adjuvant

Figure 1 Initial presentation showing a mass in the left side of the tongue

chemotherapy at stage II.¹ The patient ultimately chose adjuvant radiotherapy alone. After receiving a course of radiation therapy, the patient was reviewed at our hospital. The incision healed well and his tongue movement improved. MRI revealed no enlarged lymph nodes in the neck. The patient received regular follow-up with routine blood examination and interval imaging of his head and chest to assess for relapse or pulmonary metastasis. He

Figure 3 Preoperative T2-weighted magnetic resonance image; the mass can be seen occupying the middle and posterior third but not extending to the base of the tongue

Figure 2 Preoperative T2-weighted magnetic resonance image showing a well-defined, ovoid, circumscribed mass can be depicted

Figure 4 Intraoperative image of resected tongue specimen; there was no capsule around the tumour

continues with a follow-up regimen: every two months for two years, then every six months for the following two years, and then annually. He is currently one-year disease-free with no evidence of metastasis.

Figure 5 Final closure

Discussion

Synovial sarcoma is a soft tissue sarcoma with characteristic morphological and genetic features. Synovial sarcoma often occurs in the limbs near the joints, head and neck, parapharyngeal space and parotid gland. In the oral cavity, synovial sarcomas can occur in the buccal mucosa, gingivobuccal sulcus, soft and hard palates, floor of the mouth, retromolar region, submental region and tongue.² However, less than 100 cases have been reported in the literature. Involvement of the tongue by synovial sarcoma is a rare event. Only 15 cases of synovial sarcoma originating in the tongue have been reported (Table 1).^{5–12} An analysis of these cases reveals a striking male predilection. Approximately 81.25% patients are male and the average age of morbidity is 27 years. The base of the tongue appears to be the most frequent site for synovial sarcoma (62.5%). The most common treatment is surgical excision with adjuvant radiotherapy and three of these patients with metastases received follow-up by survey.

Early tumour growth is slow and the location is deep. A sudden increase in symptoms is often noted many years

Table 1 Analysis of reported cases of synovial sarcoma of the tongue

Case	Reference	Year	Age (years)	Gender	Site	Size (cm)	Management	Follow-Up
1	Mir-Abedy	1962	23	F	Base of tongue	5	Surgery	Alive and well, 3 years
2	Novotny and Fort	1971	20	M	Base of tongue	3.5 x 2	Radiotherapy	Alive and well, 2 years
3	Moussavi and Ghodsi	1974	21	M	Base of tongue	6 x 5 x 5	Surgery, radiotherapy	Alive and well, 1.3 years
4	Guzman Patraca <i>et al.</i>	1975	21	M	Base of tongue	7	Surgery	A with metastases, 1 year
5	Shmookler <i>et al.</i>	1982	16	M	Dorsal tongue	1.2	Surgery	Alive and well, 8 years
6	Engelhardt and Leafstedt	1983	25	M	Base of tongue	NR	Surgery	Not recorded
7	Holtz and Magielski	1985	16	M	Base of tongue	6 x 5 x 4	Surgery, radiotherapy, chemotherapy	Dead of disease, 37 months after surgery with metastases
8	Bridge <i>et al.</i>	1988	31	M	Base of tongue	3 x 3	Surgery	Not recorded
9	Carrillo <i>et al.</i>	1993	13	M	Lateral tongue	1.1 x 5 x 5	Surgery	Alive and well, 1 year
10	Fortuño-Mar <i>et al.</i>	2000	26	M	Base of tongue	5	Surgery, radiotherapy	Alive and well, 18 months
11	Komis <i>et al.</i>	2008	49	M	Lateral tongue	3 x 4.5 x 4	Surgery	Alive with metastases to lung 2 years
12	de Almeida-Lawall <i>et al.</i>	2009	26	M	Lateral tongue	1 x 1	Surgery	Alive and well, 18 months
13	Agarwal <i>et al.</i>	2009	22	M	Base of tongue	5 x 3 x 2	Surgery, radiotherapy	Not recorded
14	Villaroel-Salinas <i>et al.</i>	2012	32	F	Base of tongue	3.5 x 2 x 2	Surgery	Not recorded
15	Basile <i>et al.</i>	2016	55	F	Lateral tongue	2 x 2	Surgery, radiotherapy	Alive and well, 2 years
16	Present case	2017	35	M	Lateral tongue	4 x 3.5 x 2	Surgery, radiotherapy	Alive and well, 1 year

Figure 6 A) Low-power microphotograph of the histological specimen (hematoxylin and eosin stain; $\times 200$). B) Higher magnification of the same lesion. Biphasic pattern of synovial sarcoma with a mixture of epithelial cells and spindle-shaped cells (narrow) (hematoxylin and eosin stain; $\times 400$). C) Positivity of epithelial component for epithelial membrane antigen (EMA stain; $\times 400$). D) The immunohistochemical stain with the nuclear antigen shows strong positivity (CD99 stain; $\times 400$)

after tumour initiation and this early growth process can occur for one to four years. Its clinical manifestations are related to the tumour growth site and include a tumour mass, dysphagia, pain, hoarseness, headache and hearing loss. Surgical resection is recommended, followed by consideration of adjuvant radiotherapy with or without chemotherapy.¹⁵

Synovial sarcoma imaging is not specific, but MRI is significant for determining the primary site and presence of adjacent tissue infiltration and lymph node metastasis. MRI is the most commonly used imaging method for the diagnosis of soft tissue tumours and the boundaries of soft tissue tumours are depicted.^{14,15} Synovial sarcoma has no characteristic diagnostic markers. Thus, several antibody markers are often used to exclude many morphologically similar sarcomas or carcinomas. Histologically, synovial sarcoma is mainly described as biphasic (25%), monophasic fibrous or monophasic epithelial (70%), poorly differentiated (less than 5%) or myxoid variant.^{16,17} These tumours present microscopically with two distinct cell populations, contain epithelial-like cells in glandular structures and spindle cells, and exhibit biphasic differentiation. Migration is noted between spindle cells and epithelial-like cells (Fig 6a,b). Immunohistochemical staining is necessary for the accurate diagnosis of synovial sarcoma. According to available reports, 90% of synovial sarcomas stain positive for focal cytokeratins and EMA. EMA is the most sensitive indicator of synovial sarcoma expression markers with a sensitivity of

91% (74% of which is clearly stained) and specificity of 82%. The overall sensitivity of cytokeratins was 70% and specificity was 68%.¹⁸ In this case, immunochemistry revealed that the tumour was positive for EMA and CD99 (Fig 6c,d). Negative immunohistochemical staining also has a diagnostic value in excluding morphological similar tumours. Immunoreactivity for cytokeratins, smooth muscle actin, desmin and myogenin has not been described. After consultation with pathologists, the disease was diagnosed as synovial sarcoma.

Synovial sarcomas yield variable results in immunohistochemical staining, but chromosomal studies revealed that the balanced reciprocal translocation $t(X;18)(p11.2;q11.2)$ is found in more than 90% of all synovial sarcoma subtypes.¹⁹ This translocation results in a fusion of the *SYT* or *SSXT* gene from chromosome 18 to the *SSX1*, *SSX2* or *SSX4* genes from the X-chromosome. The *SYT-SSX* fusion transcript has high diagnostic value in synovial sarcoma. Molecular testing is not required, however, if the diagnosis of synovial sarcoma is certain and based on clinical and histological evaluation. Thus, this testing was not performed for this case.

Surgery is an important means of treating head and neck synovial sarcoma, which is key to reducing recurrence and metastasis, but the recurrence rate is very high (greater than 70%).²⁰ The reasons for this finding include the following points. The lack of capsule formation leads to incomplete surgical removal, especially at the base of the skull and infratemporal fossa. The head is rich in blood vessels and nerves, and widespread removal of the tumour may result in dysfunction or even death. The tumour is easily misdiagnosed, which causes repeated recurrence after surgery, thereby increasing the risk of distant metastasis and lymph node metastasis, eventually leading to treatment failure. Most scholars believe that the surgical margin and tumour size are key factors that affect disease prognosis.^{16,21} Reduced lymph node metastases are noted in synovial sarcoma of the head and neck. Unless distinct enlarged lymph nodes are present, preventive cervical lymph node dissection is not recommended.²¹ Fayda *et al.* believe that chemoradiotherapy is a better option for treating head and neck synovial sarcoma. The recommended total dose is 65 Gy and ifosfamide is the main chemotherapy.^{23,24}

Radiotherapy improves disease-free survival in the majority of patients.²⁵ According to the 2017 NCCN Clinical Practice Guidelines in Oncology of soft tissue sarcoma (version 2),¹ postoperative radiotherapy in the range of 45 Gy for a low-dose rate or a high-dose equivalent is recommended. If the dose is too high, it will lead to adverse effects, such as radiation mucositis, ulceration and osteoradionecrosis.²⁶ The clinical and radiological manifestations of synovial sarcoma are not easily distinguished from those of other soft tissue sarcomas and its pathophysiology is diverse. Doctors are less aware of this condition, which is highly misdiagnosed. The clinical and radiological manifestations are determined by fluorescence in situ hybridisation when necessary and this test should be used to reduce the risk of misdiagnosis. Given its rarity, the treatment plan efficacy should be verified in

more cases. Further studies are needed to determine the long-term outcome.

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