J Oral Pathol Med (2007) 36: 538–42

doi: 10.1111/j.1600-0714.2007.00568.x

www.blackwellmunksgaard.com/jopm

Solitary fibrous tumor of the oral cavity: the need for an extensive sampling for a correct diagnosis

Lorenzo Lo Muzio[1], Massimo Mascolo[2], Saverio Capodiferro[3], Gianfranco Favia[3], Eugenio Maiorano[4]

[1]*Department of Surgical Sciences, University of Foggia, Foggia, Italy;* [2]*Pathology Section, Department of Biomorphological and Functional Sciences, Faculty of Medicine and Surgery, 'Federico II' University, Naples, Italy;* [3]*Department of Dental Sciences and Surgery, University of Bari, Bari, Italy;* [4]*Department of Pathological Anatomy, University of Bari, Bari, Italy*

BACKGROUND: Solitary fibrous tumor (SFT) is an uncommon but well-characterized soft tissue tumor that was first described as a pleural lesion and now is considered ubiquitous, having been detected at many extra-pleural sites (abdominal cavity, orbit, upper respiratory tract, and oral cavity). Histologically, SFT may show wide morphological variability of both its cellular and stromal components, which may lead to incorrect diagnosis especially when dealing with small incisional biopsies.

MATERIALS: We report on the clinical, morphological and immunohistochemical features of eight SFT occurring in the oral cavity.

RESULTS: Microscopically all eight tumors showed widely variable morphological features in terms of cellular density and stromal architecture, thus simulating benign fibrous histiocytoma, schwannoma, hemangiopericytoma or low-grade sarcoma in distinct areas of the same lesion. Among these eight cases, five had been diagnosed as SFT, two as benign fibrous histiocytoma and one as low-grade sarcoma.

CONCLUSIONS: In consideration of the heterogeneous morphological appearance of SFT, inaccurate sampling of the mass may lead to misdiagnosis and inappropriate treatment. Therefore, an accurate histological examination of multiple tissue sections is advised, along with the use of appropriate immunostains.

J Oral Pathol Med (2007) **36:** 538–42

Keywords: extensive sampling; immunohistochemistry; oral cavity; solitary fibrous tumor

Introduction

Solitary fibrous tumor (SFT) is an uncommon mesenchymal neoplasm, originally reported in the pleura or other serosal sites (e.g. peritoneum and pericardium). Even if the microscopic features of SFT were first detailed by Wagner in 1870, who suggested the mesothelial origin of SFT, it was only in 1931 that Klemperer and Rabin more appropriately described this neoplasm as a subpleural lesion distinct from mesothelioma (1, 2).

Solitary fibrous tumor is a benign neoplasm exhibiting a variegation of histological patterns, low mitotic index but no cytologic atypia or necrosis, which very rarely may show a more aggressive clinical course (3–7).

Less than 800 pleural SFT (5, 8) have been reported so far, along with cases arising in the peritoneum, pericardium, mediastinum and in several extra-serosal sites as orbit, liver, thyroid, male reproductive system, breast, skin and, more rarely in the cervico-facial district (7–17). Even more rarely SFT has been described in the oral cavity (tongue, hard palate and cheek) (18–29).

The clinical presentation and the morphological and immunohistochemical profiles of oral SFT are comparable with those of pleural and extra-pleural SFT. Microscopically, these neoplasms show an extremely broad range of morphologic patterns, alternating hypercellular areas with storiform or fascicular pattern, characterized by thin collagen bands disposed parallely, with hypocellular areas, which contain abundant and dense keloid-type collagen. The vascular component may be abundant and surrounded by prominent stromal cells in a hemangiopericytoma-like pattern. Multinucleated giant cells can be present within the stroma.

The morphological appearance of STF may be extremely variable from tumor to tumor and within the same tumor and can possibly lead to misdiagnosis with other benign or malignant soft tissue neoplasms.

Besides the study of Alawi et al. (18), we report on the largest series of oral SFT, consisting of eight cases, with the aim of further illustrating the morphological variability of this entity and of stressing the importance

Correspondence: Lorenzo Lo Muzio, Dipartimento delle Scienze Chirurgiche., Università degli Studi di Foggia, Via Carelli 28, 71100 Foggia, Italy. Tel: +39 881 685809, Fax: +39 881 685809, E-mail: llomuzio@tin.it
Accepted for publication April 15, 2007

of tumor sampling in view of accurate diagnosis and appropriate treatment of oral SFT.

Materials and methods

Subjects

The original histological preparations (stained with hematoxylin–eosin and Gomori's reticulin) of all benign mesenchymal intra-oral tumors included in the files of Pathology Department of the University of Bari between 1975 and 2000, with the exception of pure lipomas, were retrieved. A total of 128 cases were subjected to morphological re-evaluation and those fitting into the criteria of Chan et al. (4) and Alawi et al. (18) were selected for further immunohistochemical analyses. Briefly, the above criteria for inclusion in this study were tumor circumscription, presence of alternating foci of hypercellular and hypocellular areas composed of bland-looking spindle or ovoid cells, evidence of fascicular or storiform arrangement of the spindle cell component, intimate admixture of collagen fibrils with spindle cells, low ($<4/10$ high-power fields) mitotic activity.

Based on these features, eight cases were selected, whose salient clinical characteristics are reported in Table 1.

Methods

A representative formalin-fixed, paraffin-embedded block from each case was selected, cut at 4 μm and collected on positively charged slides. These were dewaxed and then pre-incubated in a microwave oven three times for 5 min in 10 mM, pH 6.0 citrate buffer. Subsequently, the sections were incubated with the primary antibodies (all purchased from Dako, Glsotrup, Denmark) illustrated in Table 2, for 30 min at 37°C. A standard avidin–biotin peroxidase procedure (ABC standard, Vector Laboratories Inc., Burlingame, CA, USA) was employed using diaminobenzidine as the chromogen. Negative controls were obtained by substituting the specific primary antibodies with pre-immune serum and appropriate positive controls were included in the procedure.

Table 1 Salient clinical data of the cases selected for immunohistochemical analyses

Case no.	*Age*	*Sex*	*Location*	*Size (cm)*
1	71	F	Cheek	2
2	37	M	Cheek	3
3	58	F	Cheek	7
4	38	M	Tongue	5
5	19	M	Hard palate	2
6	44	F	Cheek	5
7	75	M	Tongue	2
8	71	F	Cheek	1.5

Table 2 Primary antibodies used for immunophenotyping

Antibody	*Clone*	*Dilution*
bcl-2	124	1:1000
CD34	QBEnd 10	1:500
CD68	PG-M1	1:2000
CD99	O13	1:2000
Cytokeratin	AE1/AE3	1:200
Desmin	D33	1:3000
S-100 protein	polyclonal	1:600
Vimentin	V9	1:1000

Results

Patients' characteristics

Following review of 128 mesenchymal intra-oral neoplasms, except for lipomas, eight cases were identified that fitted into the morphological diagnosis of SFT. Five of these had been originally diagnosed as SFT, two as benign fibrous histiocytoma and one as low-grade sarcoma, consistent with leiomyosarcoma. At presentation, all patients were asymptomatic and showed a firm subepithelial mass measuring from 1.5 to 7 cm in diameter. In one case, only the surface epithelium showed focal ulceration (Fig. 1a) while bone involvement, as detected by ortopantomography and computed tomography, was absent in all patients (Fig. 1b). All patients had undergone conservative surgical treatment and were disease free after a minimum follow-up of 3 years.

Pathological findings

Gross examination revealed a well-circumscribed, variable-sized, ovoid or round submucosal masses (Fig. 1c) covered by intact surface epithelium in all but one case affected by a larger tumor that was responsible for chronic dental trauma. The cut surface was variable in color, from white-tan to reddish, to brown.

Microscopically, the eight tumors were characterized by a widely variable morphological appearance (Fig. 1d–f), although all of them shared some common features, such as tumor circumscription, predominant spindle cell component with variable density, deposition of dense keloid-type collagen and presence of at least focal hemangiopericytoma-like areas as opposed to the lack of significant cytologic atypia and necrosis. Interestingly, all cases also showed at least minimal areas composed of tightly packed spindle cells closely adjacent to thin and elongated bands of sclero-hyaline collagen (the so-called 'ropey collagen'). The above morphological features, although shared by all tumors, were represented in very variable proportions in each of them and such morphological variability was also evident in distinct areas of the same tumor. Very rarely, occasional and typical mitotic figures were present.

In addition, three such tumors were characterized by a prominent vascular component, mainly consisting of thin-walled, small- to medium-sized blood vessels showing perivascular hyalinization. In half of the cases, myxomatous stromal changes were present, dense sclerotic bands were detected in two, while isolated multinucleated giant cells were present in two different cases and bland chronic inflammatory infiltration in two other cases.

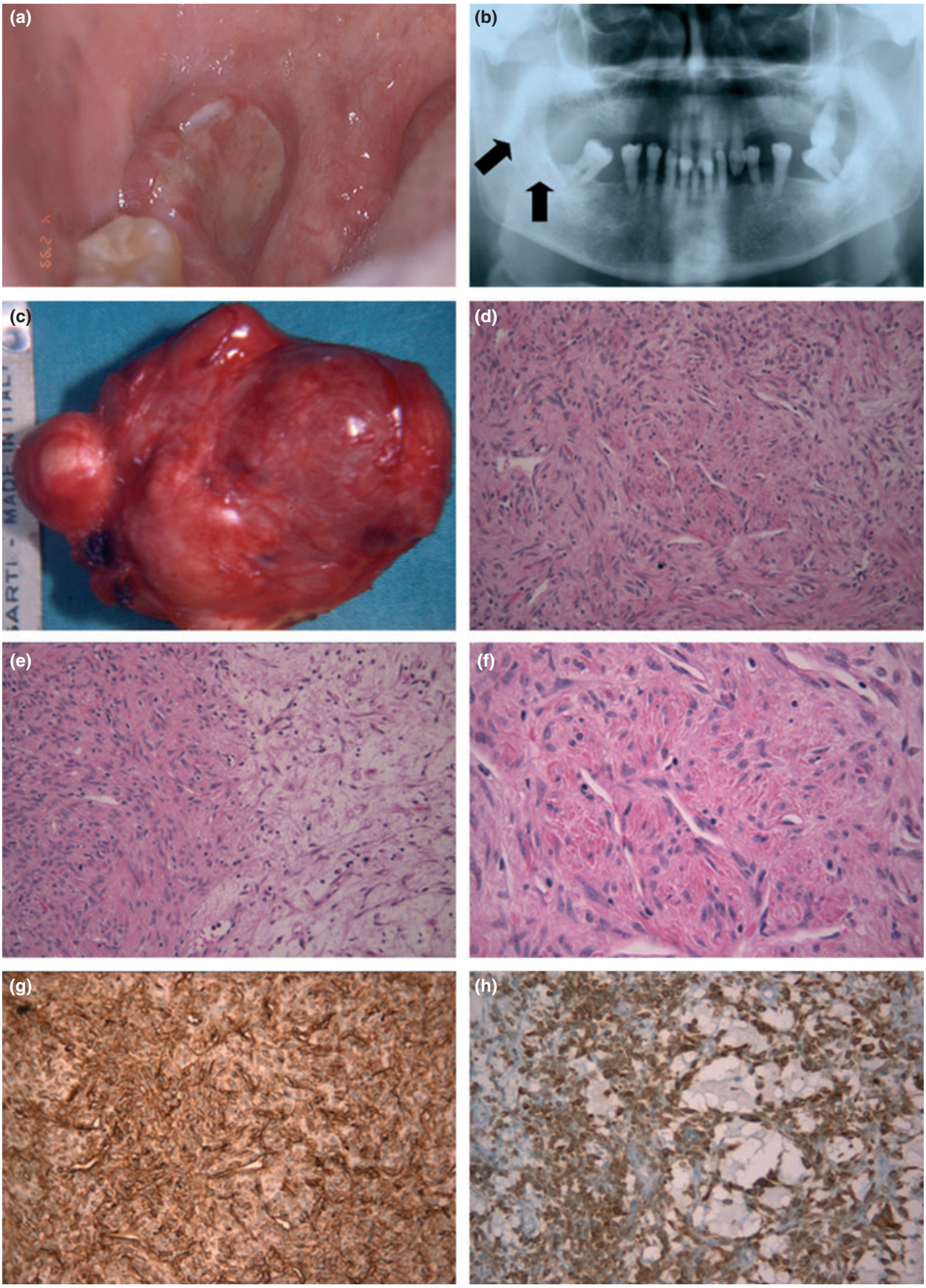
(a)
(b)
(c)
(d)
(e)
(f)
(g)
(h)

Table 3 Immunohistochemical profile of SFTs included in this series

Antibody	*1*	*2*	*3*	*4*	*5*	*6*	*7*	*8*
Vimentin	+ + +	+ +	+ + +	+ +	+ +	+ + +	+ + +	+ + +
CD34	+ +	+ + +	+ + +	+ +	+ +	+ + +	+ +	+ + +
bcl-2	+	–	+ +	+	+	–	+	+
CD99	+ +	–	+	+ +	+	–	–	+
CD68	–	–	–	–	–	–	–	–
Cytokeratins	–	–	–	–	–	–	–	–
Desmin	–	–	–	–	–	–	–	–
S-100 protein	–	–	–	–	–	–	–	–

Immunohistochemical findings

Moderate-to-strong immunohistochemical expression of vimentin and CD34 was detected in all cases (Fig. 1g), while bcl-2 immunoreactivity was present in six (Fig. 1h) and CD99 positivity in five cases (Table 3). CD68, cytokeratins, desmin and S-100 protein immunoreactivity were undetectable, with the exception of residual normal structures included in the samples. Interestingly, inter-tumoral and intra-tumoral variability of CD34, bcl-2 and CD99 immunoreactivity was a prominent feature of all cases and clusters of cells manifesting intense staining were frequently adjacent to areas devoid of any positivity.

Discussion

Solitary fibrous tumor is a unique neoplastic entity and its heterogeneity of microscopic features represents a prime example of morphological diversity.

The definition of uniform criteria for the correct diagnosis of SFT is a relatively recent event: in 1997, Chan et al. (4) proposed those that today are considered 'essential diagnostic criteria' for diagnosing pleural and extra-pleural SFT: tumor circumscription, presence of alternating foci of hypercellular and hypocellular areas composed of bland-looking spindle or ovoid cells, evidence of fascicular or storiform arrangement of the spindle cell component, intimate admixture of collagen fibrils with spindle cells, low ($<4/10$ high-power fields) mitotic activity. The same criteria were adopted by Alawi *et al.* who reported the largest series of oral SFT (18) and by our group for case selection in the current study.

Moreover, the broad spectrum of morphological features that characterize SFT and its 'patternless' growth pattern lead Chan et al. to identify SFT as a true diagnostic dilemma, being potentially mistaken with a large number of both benign and malignant tumors (4). Mesenchymal neoplasms predominantly composed by spindle cells, in fact, include several distinct lines of differentiation, such as, fibroblasts, adipocytes, smooth and striated muscle cells, Schwann cells, endothelial cells, etc. These cells may give rise to tumors exhibiting at least focal morphological features that recapitulate those occurring in SFT. Therefore, it is not surprising that in the current series some tumors had been originally diagnosed as distinct entities, such as benign fibrous histiocytoma, or low-grade sarcoma, based on morphology alone.

Solitary fibrous tumor, in fact, displays unspecific clinical presentation, its morphological features might be equivocal, especially in small incisional biopsies and, nowadays, immunostains are mandatory to confirm the diagnosis, as suggested by Chan et al. (4) and Alawi et al. (18). SFT consistently manifests vimentin and CD34 immunoreactivity, along with variable bcl-2 and CD99 positivity, but lacks CD68, pan-cytokeratins, desmin, and S-100 protein immunoreactivity. As demonstrated in this study, the positivity for CD34, bcl-2, and CD99 is not uniformly distributed within SFT and the evaluation of immunostains should possibly rely on adequate and complete sampling of the tumor mass. Also, the differential diagnosis based on immunoprofiling should also take into account the lack of CD68, pan-cytokeratins, desmin, and S-100 protein positivity to possibly rule out histiocytic, muscular and Schwann cell-derived neoplasms.

Even when strict morphologic criteria are adopted and appropriate immunostains employed, the diagnosis of this neoplasm remains difficult, especially at extra-pleural sites, due to extreme intra-tumoral variability and close similarity of single parts of individual tumors with prognostically different benign and malignant soft tissue neoplasms.

On the bases of previous (18) and current analyses, it is evident that a significant number of SFTs were at first misdiagnosed as and that only at subsequent more-attentive re-evaluations a correct diagnosis was achieved.

As repeatedly put forward, most of the diagnostic problem resides in the 'patternless' growth pattern of SFT, in its intra-tumoral morphological variability and immunophenotypic dishomogeneity. Therefore, the authors wish to stress the opportunity of extensive multiple sampling of the mass or complete examination of the excised tumor whenever deemed possible. Based on the above considerations, in fact, it is possible that the examination of single histological preparations, especially if derived from incisional biopsies, may display equivocal histological features of highlight areas of the tumor devoid of the distinctive immunopositivity of this tumor.

Figure 1 Composite figure of a solitary fibrous tumor of the cheek. (a) Macroscopic appearance showing a focally ulcerated mass; (b) OPT showing absence of bone involvement; (c) well-encapsulated mass measuring 5 cm in maximum diameter; (d) microscopic appearance of SFT showing a richly vascular proliferation with focal hemangiopericytoma-like pattern (H&E, original magnification, ×150); (e) hypercellular areas close to a hypocellular area composed by bland-looking spindle cells (h&e, original magnification: ×150); (f) densely collagenized stroma (h&e, original magnification ×200); (g) consistent immunoreactivity for CD34 in the spindle cell component, with the exception of hypocellular areas (original magnification ×200); (h) moderate immunoreactivity for bcl-2 (original magnification ×200).

References

1. Wagner E. Das tuberkelahnliche Lymphadenom (der cytogene oder reticulirte Tuberkel). *Arch Heilk (Leipig)* 1870; **11**: 497.
2. Klemperer P, Rabin CB. Primary neoplasms of the pleura. *Arch Patol* 1931; **11**: 385–41.
3. England DM, Hockholzer L, Mccarthy MJ. Localized benign and malignant tumours of the pleura. A clinicopathologic review of 223 cases. *Am J Surg Pathol* 1989; **13**: 640–58.
4. Chan JKC. Solitary fibrous tumor – everywhere, and a diagnosis in vogue. *Histopathology* 1997; **31**: 568–76.
5. Briselli M, Mark EJ, Dikersin JR. Solitary fibrous tumor of the pleura: eight new cases and review of 360 cases in the literature. *Cancer* 1981; **47**: 2678–89.
6. De Perrot M, Fisher S, Brunder RA, Sekine Y, Keshavjee S. Solitary fibrous tumor of the pleura. *Ann Thorac Sur* 2002; **74**: 285–93.
7. Fletcher JA, Fletcher CDM, Mandahl N, Guillou L. Extrapleural solitary fibrous tumour and haemangio pericytoma. In: Fletcher CDM, Unni KK, Mertens F, eds. Pathology and genetics of tumours of soft tissue and bone. *World Health Organization classification of tumours*. Lyon: IARC Press, 2002; 86–90.
8. Robinson LA. Solitary fibrous tumor of the pleura. *Cancer Control* 2006; **13**: 264–9.
9. Witkin G, Rosai J. Solitary fibrous tumor of the mediastinum. *Am J Surg Pathol* 1989; **13**: 547–57.
10. Van De Rijn M, Lombard C, Rouse R. Expression of CD34 by solitary fibrous tumors of the pleura, mediastinum and lung. *Am J Surg Pathol* 1994; **18**: 814–20.
11. Brunnemann RB, Ro JY, Ordonez NG, et al. Extrapleural solitary fibrous tumor: a clinicopathologic study of 24 cases. *Mod Pathol* 1999; **12**: 1034–42.
12. Fukunaga M, Naganuma H, Nikaido T, Harada T, Ushigome S. Extrapleural solitary fibrous tumor: a report of seven cases. *Mod Pathol* 1997; **10**: 443–50.
13. Dotto JE, Ahrens W, Lesnik DJ, Kowalski D, Sasaki C, Flynn S. Solitary fibrous tumor of the larynx: a case report and a review of the literature. *Arch Pathol Lab Med* 2006; **130**: 213–6.
14. Dorfman DM, To K, Dickersin GR, Rosenberg AE, Pilch BZ. Solitary fibrous tumor of the orbit. *Am J Surg Pathol* 1994; **18**: 281–7.
15. Thompson M, Cheng LH, Stewart J, Marker A, Adlam DM. A paediatric case of a solitary fibrous tumour of the parotid gland. 6. *Int J Pediatr Otorhinolaryngol* 2004; **68**: 481–7.
16. Magro G, Bisceglia M, Michal M, Eusebi V. Spindle cell lipoma-like tumor, solitary fibrous tumor and myofibroblastoma of the breast: a clinico-pathological analysis of 13 cases in favor of a unifying histogenetic concept. *Virchows Arch* 2002; **440**: 249–60.
17. Cerda-Nicolas M, Lopez-Gines C, Gil-Benso R, et al. Solitary fibrous tumor of the orbit: morphological, cytogenetic and molecular features. *Neuropathology* 2006; **26**: 557–63.
18. Alawi F, Stratton D, Freedman P. Solitary fibrous tumor of the oral soft tissue: a clinicopathologic and immunohistochemical study of 16 cases. *Am J Surg Pathol* 2001; **25**: 900–10.
19. Gonzales-Garcia R, Gil Diez Usandizaga JL, Hyun Nam S, Rodriguez Campo FJ, Naval-Gias L. Solitary fibrous tumor of the oral cavity with the histological features of aggressiveness. *Br J Oral Maxillofac Surg* 2005; **44**: 543–5.
20. Shimoyama T, Horie N, Ide F. Solitary fibrous tumor of the palate: a case report and review of the literature. *J Oral Maxillofac Surg* 2004; **62**: 895–7.
21. Shnayder Y, Greenfield BJ, Oweity T, Delacure MD. Malignant solitary fibrous tumor of the tongue. *Am J Otolaryngol* 2003; **24**: 246–9.
22. Jordan RC, Regezi JA. Oral spindle cell neoplasms: a review of 307 cases. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 2003; **95**: 717–24.
23. Yamashita Y, Satoh T, Goto M. Solitary fibrous tumour of the tongue: a case report with immunohistochemical studies. *Int J Oral Maxillofac Surg* 2002; **31**: 681–3.
24. Harada T, Matsuda H, Maruyama R, Yoshimura Y. Solitary fibrous tumours of the lower gingiva: a case report. *Int J Oral Maxillofac Surg* 2002; **31**: 448–50.
25. Vargas PA, Alves FA, Lopes MA, *et al*. Solitary fibrous tumour of the mouth: report of two cases involving the tongue and cheek. *Oral Dis* 2002; **8**: 111–5.
26. Shine N, Nor Nurul Khasri M, Fitzgibbon J, O'leary G. Solitary fibrous tumor of the floor of the mouth: case report and review of the literature. *Ear Nose Throat J* 2006; **85**: 437–9.
27. Gonzalez-Garcia R, Gil-Diez Usandizaga JL, Hyun Nam S, Rodriguez Campo FJ, Naval-Gias L. Solitary fibrous tumour of the oral cavity with histological features of aggressiveness. *Br J Oral Maxillofac Surg* 2006; **44**: 543–5.
28. Eversole LR, Christensen R, Ficarra G, Pierleoni L, Sapp JP. Nodular fasciitis and solitary fibrous tumor of the oral region: tumors of fibroblast heterogeneity. *Oral Surg Oral Med Oral Pathol Oral Radiol Endod* 1999; **87**: 471–6.
29. Hanau CA, Miettinen M. Solitary fibrous tumor: histological and immunohistochemical spectrum of benign and malignant variants presenting at different sites. *Hum Pathol* 1995; **26**: 440–9.