Low Grade Myofibroblastic Sarcoma of Tongue: a Case Report

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Summary

A case of a 24-year-old woman with a 6 weeks lasting nodule of the right margin of the tongue is described. The nodule was 20 mm in diameter and showed surface ulceration. The diagnosis of low grade myofibroblastic sarcoma was supported by histological, immunohistochemical and electronmicroscopic examination. Although the tumor resection was not complete, the patient is free of disease 1 year after operation. The differential diagnostics of low grade myofibroblastic sarcoma is discussed.

Key words: tumor – oral cavity – tongue – low grade myofibroblastic sarcoma

Souhrn

Low grade myofibroblastický sarkom: kazuistika

Autoři prezentují případ 24leté ženy se šestiměsíční anamnézou nádoru pravé hrany jazyka. Nádor byl povrchově exulcerovaný a měřil 20 mm v průměru. Na základě histologického, imunohistochemického a elektronmikroskopického vyšetření byla stanovena diagnóza low grade myofibroblastický sarkom. Ačkoli nádor nebyl odstraněn úplně, pacientka je 1 rok po operaci bez klinických známek lokální recidivy či generalizace nádoru. V článku je diskutována diferenciální diagnostika této méně časté léze.

Klíčová slova: nádory – dutina ústní – jazyk – low grade myofibroblastický sarkom

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Low grade myofibroblastic sarcoma (LGMS) is a distinct myofibroblastic malignancy with predilection for the head and neck region which occurs predominantly in adult patients with slight male predominance. Although LGMS shows a wide anatomic distribution, oral cavity and tongue seem to be preferred locations (12). Histologically, LGMS is an infiltrative lesion composed of spindle-shaped cells with eosinophilic cytoplasm and fusiform nuclei. The immunophenotype of tumor cells is variable: actin positive/desmin positive, actin positive/desmin negative and actin negative/desmin negative. Ultrastructurally, the tumor cells are consistent with myofibroblasts.

The differential diagnostics of myofibroblastic lesions is very difficult and based mainly on careful examination of slides stained with hematoxylin- eosin. The electronmicroscopic examination can support the origin of tumor cells.

Case report

A 24-year-old woman presented a painless lesion of the right margin of the tongue lasting for 6 weeks. Clinical examination showed a firm, ulcerated nodule of 20 mm in diameter (Fig. 1). The remaining mucosa of the oral cavity showed no abnormality; there was no regional lymphadenopathy.

Except for smoking 5 cigarets per day, the personal history of the patient was negative.

A resection of the lesion was performed and material was sent for histological examination.

Although the tumor was not removed completly, the patient is free of disease 1 year after operation.

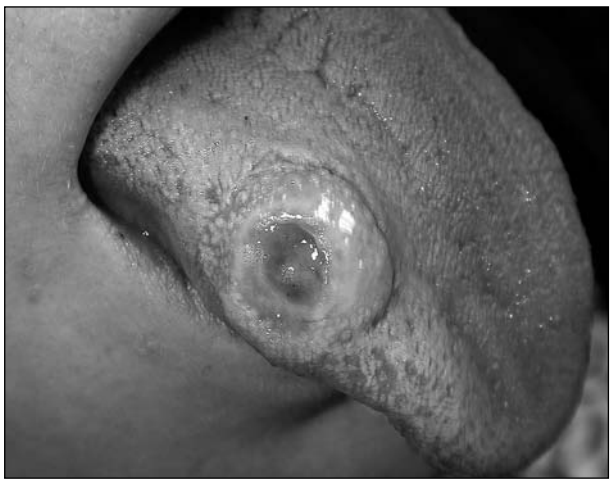

Fig. 1. An ulcerated nodule at the right margin of the tongue

Material and Methods

The specimen was immediately fixed in 10% formalin, embedded in paraffin and routinely stained. Immunohistochemistry was performed using monoclonal antibodies listed in Table 1. For visualization EnVision+ Dual Link System Peroxidase (DakoCytomation) was used with diaminobenzidine as chromogene.

Tab. 1. Primary antibodies used for immunohistochemical examination

	Clone	Dilution	Source
Vimentin	V9	1:50	DakoCytomation
Smooth muscle actin	1A4	1:200	DakoCytomation
Cytokeratins	AE1/AE3	1:150	DakoCytomation
Sarcomeric actin	Alpha-Sr-1	1:40	DakoCytomation
Desmin	D33	1:200	DakoCytomation
Calponin	CALP	1:100	DakoCytomation
S-100 protein	4C4.9	1:4000	Neomarkers
Melanosome	HMB 45	1:400	DakoCytomation
CD 34	QBEnd 10	1:50	Novocastra
CD 117	polyclonal	1:50	DakoCytomation
Ki-67	MIB-1	1:30	DakoCytomation

For electron microscopy, the tissue from paraffin block was used, postfixed in 1% osmium tetraoxide and embedded in epoxy resin (Ducupan-Epon). Sections were stained with uranyl acetate and lead citrate and examined under electron microscope Phillips 208.

Results

The resection specimen measured 30 x 20 x 20 mm and showed surface ulceration 10 mm in diameter. A firm, yellow-white coloured tumor with ill defined margins measuring 20 mm in diameter was present on sectioning. No regressive changes (e.g. necrosis) were grossly identified.

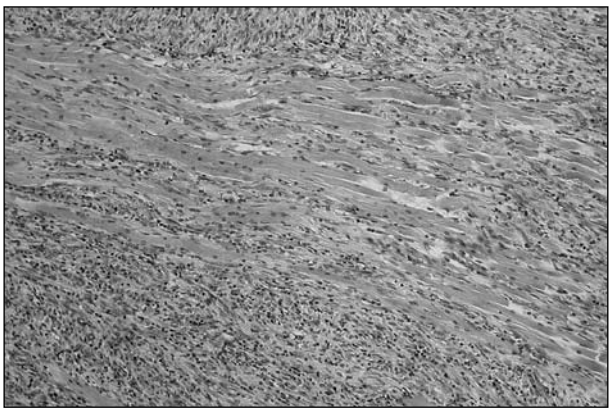

Fig. 2. Infiltrative growth of the tumor cells into the striated muscle (HE, 400x)

Histologically, the tumor cells infiltrated the striated muscle fibres of a tongue (Fig. 2). A smaller, „satellite“ tumor nodules around the “main” tumor mass were also present (Fig. 3). The tumor grew in fascicular or storiform pattern. The spindle-shaped tumor cells have ill defined cell borders, pale cytoplasm and slightly anisomorphic nuclei with distinct nucleoli. The mitotic count was 2–3 per hpf; no mitoses were atypical. The tumor was slightly infiltrated by mixed inflammatory cells.

Immunohistochemically, the tumor cells showed diffuse and strong positivity for vimentin and smooth muscle actin. Proliferating marker Ki-67 was positive in less than 5% cells. The immunohistochemical detection of desmin, calponin, cytokeratins, sarcomeric actin (SCMA), S-100 protein, HMB 45, CD 34, CD 99 and CD 117 was negative.

Electronmicroscopic examination of the tumor cells showed indentation of nucleus and pe-

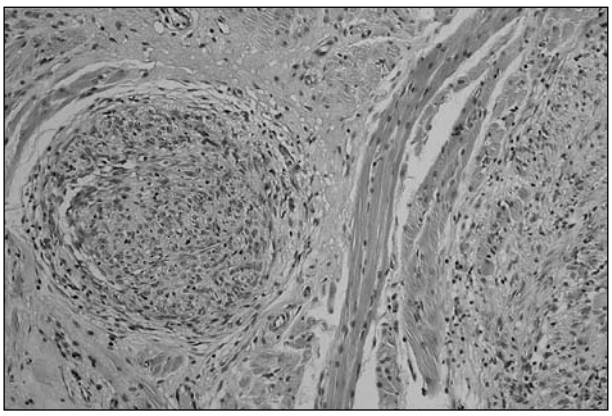

Fig. 3. Smaller, “satellite” tumor nodule in vicinity of the main tumor mass. (HE, 400x)

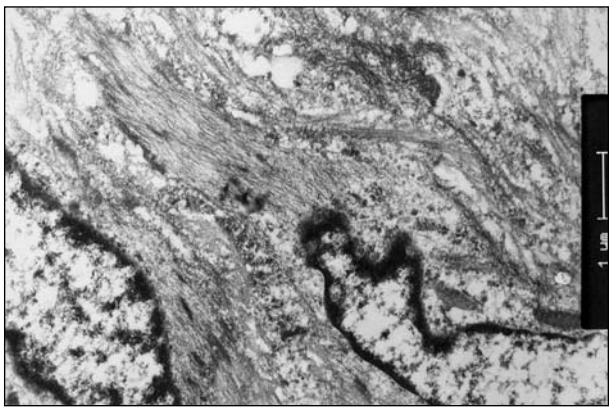

Fig. 4. Myofibroblastic characteristics of the tumor cells: indentation of the nucleus and "stress fibres" (6000x)

ripheral bundles of thin cytoplasmic filaments ("stress fibres") (Fig. 4).

Discussion

Myofibroblasts are modified fibroblasts, which can occur in normal tissues (e.g. periodontal ligaments), in reparative granulation tissue and in reactive soft-tissue lesions (11). They are, however, also a principal cell type in benign and malignant soft-tissue tumors.

Myofibroblasts are spindle-shaped or stellate cells with ovoid pale nucleus and distinct nucleolus. The cytoplasm is usually amphophilic and there are indistinct cell borders. Ultrastructurally, myofibroblasts can be distinguished from fibroblasts and smooth muscle cells by the findings of indentation of nucleus, presence of peripheral or subplasmalemmal bundles of thin cytoplasmic filaments, termed stress fibres, and a distinctive cell-stromal attachment termed fibronexus (7).

Low grade myofibroblastic sarcoma (LGMS) is a well defined malignant tumor composed of myofibroblasts. It can occur at any age (range 9-75 years, mean 40 years) with slight male predominance; the tumor size varies from 1.5 cm to 17 cm (12). LGMS can arise in soft tissues of various anatomic sites, including extremities, trunk (e.g. retroperitoneum, breast and heart) and genital tract, but there is a predilection for the head and neck region. Oral cavity (especially tongue, cheek and gingiva), nasal cavity, salivary glands and bones (e.g. maxilla and mandible) can be affected (1–3, 6, 8 10, 13, 15–17, 19–21, 23, 25–30).

Grossly, most cases were described as firm, gray-white coloured tumors with ill-defined margins. Histologically, the tumor cells show diffuse fascicular or storiform growth pattern and they infiltrate surrounding tissues (e.g. skeletal muscle). The cytological and ultrastructural characteristics of neoplastic cells are consistent with myofibroblasts (described above). Increased mitotic activity of tumor cells and tumor necrosis is associated with more aggressive behaviour of LGMS.

Tumor cells in LGMS show a variable immunophenotype: actin positive/desmin negative, actin negative/desmin positive, and actin positive/desmin positive cases (21). In addition, neoplastic cells can express fibronectin, calponin, CD 34, CD 99 and CD 117, whereas S-100 protein, epithelial markers and h-caldesmon are negative (9, 21). LGMS is usually a tumor of low grade malignancy, prone to local recurrency (about 30% in general) (21), even after many years. However, metastases to lungs have been also reported (17, 30). Therefore, close clinical follow-up of the patient is mandatory.

Differential diagnosis of LGMS includes reactive myofibroblastic lesions, benign myofibroblastic lesions and other myofibroblastic sarcomas. In these cases, immunohistochemistry is not helpful and the differential diagnosis is based on careful examination of the slides stained with hematoxylin-eosin. On the other hand, many histogenetically different spindle-cell tumors can be distinguished from LGMS using immunohistochemistry.

Nodular fasciitis is a rapidly growing lesion, histologically with variable cellularity and myxoid stroma. It is less cellular and uniform than LGMS. Although mitoses can be present, the cells lack nuclear atypia, which is usually present in LGMS (24). Fibromatoses are composed of uniform, collagen-producing myofibroblasts without nuclear pleomorphism. Inflammatory myofibroblastic tumor (IMT) is histologically characterized by fasciitis-like, fascicular and sclerosing areas with a prominent chronic inflammatory infiltrate with numerous plasma cells. In addition, anaplastic lymphoma kinase (ALK) can be immunohistochemically detected in 30–40% of IMTs (5, 18). The inflammatory infiltration in the presented case of LGMS was, however, due to tumor ulceration. Infantile fibrosarcoma (IF) is a tumor of borderline malignancy, which occurs mostly in the first 4 years of life. It is composed of a mixture of fibroblasts and myofibroblasts. Histologically, IF consists of herringbone fascicles of spindle cells without nuclear atypia. High grade myofibroblastic sarcoma (HGMS) (also called MFH-like) is often difficult to distinguish from other high grade sarcomas. This diagnosis should be established in that cases, where the presence of myofibroblasts is confirmed by electronmicroscopy (4, 22). A case of HGMS as a complication of radiotherapy was also described (14).

Histogenetically different spindle-cell tumors can be distinguished from LGMS using immuno-

histochemistry. Spindle-cell carcinoma shows positivity for cytokeratins, fibrosarcoma is SMA negative, leiomyosarcoma has a different microscopic appearance and shows desmin and h-caldesmon positivity. Spindle-cell rhabdomyosarcoma shows SCMA positivity, angiosarcoma shows positivity for endothelial markers (e.g. F VIII, CD 31 and CD 34) and malignant peripheral nerve sheath tumor shows at least focal positivity for S-100 protein. Synovial sarcoma in a classical biphasic variant shows positivity for cytokeratins, epithelial membrane antigen and vimentin.

In summary, LGMS is a well-defined myofibroblastic malignancy with predilection for head and neck region, which is prone to local recurrency, rather than metastasing. For the diagnosis, a careful examination of routinely stained slides is crucial. Immunohistochemistry can be useful in differential diagnosis from some other spindle-cell lesions and tumors. Electronmicroscopic examination can support the diagnosis of LGMS by proving the origin of tumor cells.

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