Myofibroblastic Sarcoma of the Base of Tongue

Case Report and Review of the Literature

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Background: Mesenchymal malignancies with myofibroblastic differentiation exhibit a spectrum from low-grade myofibroblastic sarcoma mimicking fibromatosis to pleomorphic high-grade sarcoma. Low-grade myofibroblastic sarcoma shows a wide anatomic distribution with a predilection for the head-and-neck region; however, intermediate- and high-grade myofibroblastic sarcomas in this localization are exceptional.
Case Report: A 56-year-old woman with intermediate-grade myofibroblastic sarcoma of the base of tongue is presented. She was treated with surgical excision, but computed tomography proved local residual tumor. Reexcision and chemotherapy were refused by the patient. Irradiation was given to a total dose of 66 Gy.
Result: 50 months after completion of radiotherapy, the patient is in good health without any evidence of disease. According to the review of the literature, base of tongue as the primary site of myofibroblastic sarcoma has not been published so far.
Conclusion: Similarly to the low-grade form, intermediate- and high-grade myofibroblastic sarcomas may also occur in the head-and-neck region. In case of incomplete excision, radiotherapy may be an effective treatment.

Key Words: Myofibroblastic sarcoma · Base of tongue · Radiotherapy

Strahlenther Onkol 2009;185:198–201
DOI 10.1007/s00066-009-1925-8

Myofibroblastisches Sarkom des Zungengrundes. Fallbericht und Literaturübersicht

Hintergrund: Mesenchymale maligne Tumoren mit myofibroblastischer Differenzierung beinhalten ein Spektrum von niedrigmalignen myofibroblastischen Sarkomen, die einer Fibromatose ähneln, bis hin zu hochmalignen pleomorphen Sarkomen. Niedrigmaligne myofibroblastische Sarkome treten in allen Körperregionen auf, bevorzugt im Kopf-Hals-Bereich. Intermediär- und hochmaligne myofibroblastische Sarkome sind im Kopf-Hals-Bereich selten zu finden.
Fallbericht: Vorgestellt wird 56-jährige Patientin mit intermediärmalignem myofibroblastischem Sarkom des Zungengrundes. Nach Exzision fand sich in der CT-Untersuchung ein lokaler Residualtumor. Reexzision und adjuvante Chemotherapie wurden von der Patientin abgelehnt. Sie erhielt eine Radiatio mit einer Gesamtdosis von 66 Gy.
Ergebnis: 50 Monate nach Beendigung der Strahlentherapie ist die Patientin in gutem Allgemeinzustand und tumorfrei. Die Durchsicht der aktuellen Fachliteratur ergab, dass bisher noch kein primäres myofibroblastisches Sarkoms im Bereich des Zungengrundes beschrieben wurde.
Schlussfolgerung: Intermediär- und hochmaligne myofibroblastische Sarkome können ebenso wie die niedrigmalignen myofibroblastischen Sarkome im Kopf-Hals-Bereich auftreten. Eine postoperative Strahlentherapie nach inkompletter Resektion stellt eine effektive Behandlungsmethode dar.

Schlüsselwörter: Myofibroblastisches Sarkom · Zungengrund · Strahlentherapie

Introduction

More than 80% of malignant tumors of the head-and-neck region originate from squamous epithelium. The incidence of mesenchymal tumors is low, and among these, myofibroblastic sarcomas are extremely rare [14, 16, 22].

Myofibroblasts are mesenchymal spindle cells that share ultrastructural features of both fibroblasts and smooth muscle cells [22]. The presence of myofilaments in the cytoplasm of myofibroblasts bestows them with contractile properties. Gabiani et al. were the first to describe these cells in 1971 [7].

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Received: July 31, 2008; accepted: December 10, 2008

Histologically, myofibroblasts are spindle-shaped cells with ill-defined eosinophilic cytoplasm. The nucleus is fusiform containing a small central eosinophilic nucleolus [16]. Myofibroblastic cells or myofibroblastic differentiation are present in wound healing and in different reactive and neoplastic conditions (reactive stromal component in numerous neoplasms). Pseudosarcomatous proliferations, fasciitis, hypertrophic scar, superficial and deep fibromatoses generally also show myofibroblastic differentiation [16].

Tumors with myofibroblastic differentiation present with variable morphological and immunohistochemical characteristics due to the plasticity of the myofibroblasts [14]. Myofibroblastic sarcomas occur in almost every organ, more commonly in the superficial soft tissues, particularly in the head-and-neck region; however, until now base of tongue as the primary site of myofibroblastic sarcoma has not been published in the literature.

Here, we describe the case of a 56-year-old woman with an intermediate-grade myofibroblastic sarcoma of the base of tongue, who was treated with tumor excision and – because of the presence of residual tumor – postoperative radiotherapy.

Case Report

In December 2003, a 56-year-old woman presented with progressive swallowing difficulties and suffocation at the Department of Otorhinolaryngology, Szent Imre Hospital, Budapest, Hungary. The clinical history was unremarkable. She was smoking two packets of cigarettes per day.

During the examination, a round, pedunculated, livid mass measuring 4 cm in diameter and covered with fibrinoid fur was detected on the right side of the base of tongue protruding to the pharyngeal space, which fell on the larynx. Nevertheless, the structure of the larynx was normal and the glottis was duly wide. There was no clinical involvement of cervical lymph nodes.

The exophytic tumor was resected without delay. A computed tomography (CT) scan was requested after the surgical procedure. This showed the presence of a residual tumor mass at the base of the tongue (Figure 1).

Microscopic examination of the resected specimen showed an ulcerated tumor composed of spindle-shaped, elongated and stellate cells embedded in myxoid matrix (Figure 2a). Focally, the spindle-shaped cells formed short fascicles. Centrally, small hyalinized areas were also present. The neoplastic cells showed mild to moderate nuclear pleomorphism and high mitotic activity (1–5/1 high-power field [HPF]) with numerous atypical mitoses (Figure 2b). The amount of cytoplasm was variable showing pale eosinophilic to pale basophilic staining characteristics. Scattered multinucleated neoplastic giant cells also appeared. The spindle-shaped neoplastic cells were vimentin-positive and showed negative reactions with anti-h-caldesmon, anti-desmin, anti-S-100 and anti-AE/AE3 cytokeratin antibodies. Approximately 15% of the cells

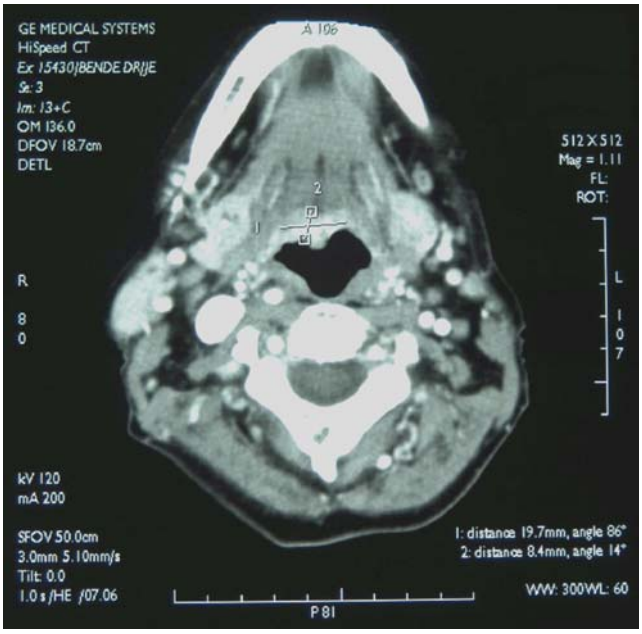


Figure 1. Postoperative computed tomography showed residual tumor (18 x 8 x 20 mm) at the base of tongue with inhomogeneous accumulation the radiopaque material.

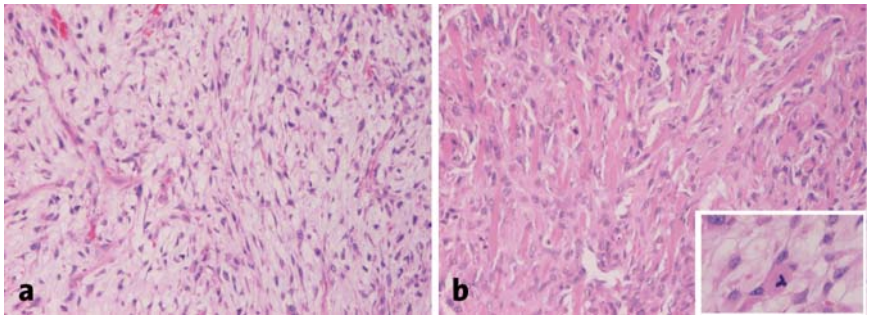
Abbildung 1. Die postoperative CT-Untersuchung zeigte einen Resttumor (18 x 8 x 20 mm) am Zungengrund mit inhomogener Kontrastmittelaufnahme.

reacted with smooth muscle α-actin. The histopathologic diagnosis was intermediate-grade myofibroblastic sarcoma.

The patient refused an extended reoperation, or chemotherapy. So irradiation was carried out with a dose of 66 Gy (2 Gy/day; five fractions/week) to the primary site and the upper neck using opposed lateral 6-MV photon beams. Dose was prescribed to the midline. The lower neck was also irradiated up to 50 Gy using an anteroposterior field. Dose prescription was at 3 cm depth. The spinal cord was shielded after 40 Gy. Electron beams (9 MeV) were used to supplement the posterior cervival lymph nodes up to 50 Gy. 2 months after irradiation, the control CT showed complete tumor regression. Since then, she has been followed with CT or magnetic resonance imaging (MRI) performed once a year (Figure 3). After a follow-up period of 50 months the patient is alive without any evidence of disease.

Discussion

Myofibroblasts are altered fibroblasts, which occur in the stroma of normal organs and in reactive processes, such as granulation tissue. A variety of benign and intermediate soft-tissue tumors show myofibroblastic differentiation. Malignant mesenchymal neoplasms showing evident and dominant myofibroblastic differentiation are described as myofibroblastic sarcoma, myofibrosarcoma, low-grade myofibroblastic sarcoma, low-grade spindle cell sarcoma consisting of myofibroblasts,



Figures 2a and 2b. a) Detail of myofibroblastic sarcoma. Atypical spindle-shaped and stellate myofibroblasts, embedded in myxoid matrix.
b) Foci of hyalinized collagen bundles with atypical myofibroblasts showing atypical mitosis (insert).

Abbildungen 2a und 2b. a) Myofibroblastisches Sarkom. Atypische spindelförmige und sternförmige Fibroblasten, die in einer myxoiden Matrix eingebettet sind.
b) Herde von hyalinen Kollagenbündeln mit atypischen Myofibroblasten, die atypische Mitosen (Insert) aufweisen.

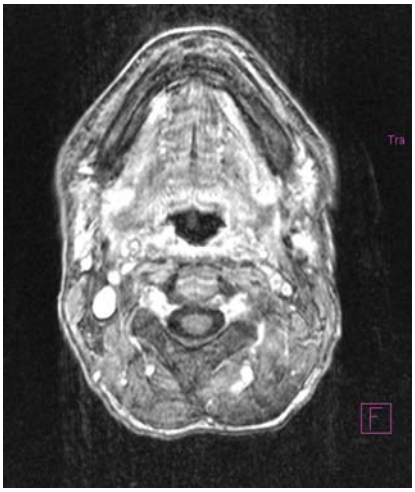


Figure 3. After 48 months, no residual tumor was detected on the MRI scan.

Abbildung 3. Die MRT-Untersuchung nach 48 Monaten ergab keinen Hinweis auf Tumorgewebe.

or myofibroblastic variant of leiomyosarcoma [4]. Myofibroblastic sarcomas are uncommon but have been described in different sites and organs such as breast, thyroid, pleura, thoracic wall, skin, tongue, and jaw [14, 16, 22].

In 1998, Mentzel et al. described a detailed analysis of low-grade myofibroblastic sarcoma [16], and in the World Health Organization classification of soft-tissue tumors, it is classified as a distinct entity [6]. Histologically, low-grade myofibroblastic sarcoma is composed of slender spindle cells arranged in interlacing fascicles. Tumor cells have a scanty to moderate amount of eosinophilic or amphophilic cytoplasm and fusiform nuclei which are either tapering and wavy or slightly plumper with small nucleoli, and usually characterized with mild nuclear pleomorphism and low mitotic rate (1–6/10 HPFs). Immunohistochemically, myofibroblastic sarcoma is positive for vimentin, smooth muscle actin, calponin and fibronectin, rarely positive for desmin, and negative for laminin and type IV collagen [16]. High-grade (pleomorphic) myofibroblastic sarcomas were described as pleomorphic sarcomas composed of atypical spindle, polygonal and giant cells showing ultrastructural evidence of myofibroblastic differentiation and numerous mitotic figures [5]. The reproducibility of diagnostic criteria of high-grade myofibroblastic sarcomas is weak, and these tumors are morphologically and clinically indistinguishable from pleomorphic undifferentiated sarcomas.

Using the modified National Cancer Institute three-step grading system, however, low-grade, intermediate-grade and high-grade myofibroblastic sarcoma can be distinguished. Intermediate-grade myofibroblastic sarcomas are characterized by ≥ 6 mitoses/10 HPFs without high nuclear pleomorphism [8, 22]. The presented case with its histological, cytological and immunohistochemical characteristics is consistent with the diagnosis of myofibroblastic sarcoma and, because of the high mitotic count, should be graded as intermediate.

Low-grade myofibroblastic sarcomas are considered to have a wide anatomic distribution with predilection for the head-and-neck region [12, 16, 18, 23]. Main presenting symptom usually is a painless, enlarging mass. The male/female ratio is 2.5/1.

In the literature, there are many articles on the therapy of head-and-neck cancers, but – due to their rarity – only few dealing with sarcomas [1–3, 9–11, 19–21, 25].

The treatment for myofibroblastic sarcoma as well as all other types of sarcomas is surgical excision with wide margins. Adjuvant therapies such as chemotherapy and radiotherapy have also been used in some cases [13, 15, 16, 24].

In the *American Journal of Surgical Pathology*, Mentzel et al. reported a series of 18 low-grade myofibroblastic sarcomas [16]. Five tumors arose in the oral cavity including four tongue lesions. Patients with tumors of the tongue complained of a painless swelling or an enlarging mass. The mean size of the tongue tumors was 1.8 cm (range, 1.4–2.5 cm). These patients were treated with excision only and were alive with no signs of recurrence ever since (mean follow-up time 27.5 months; range, 0–42 months).

Meng et al. presented six patients with low- or intermediate-grade myofibroblastic sarcoma of the nasal cavity and paranasal sinus. The mean size of the tumors was 4.2 cm (range, 3.0–6.5 cm). Three patients had positive margins after resection and three were resected with negative margins. All patients received radiotherapy to a total dose of 50 or 60 Gy, depending on the margin status. All of them died of local re-

currences during a mean follow-up time of 20 months (range, 12–27 months) [15].

Fisher published a study about the clinical behavior of myofibroblastic sarcoma [5]. Among 39 low-grade myofibroblastic sarcomas, recurrence occurred in 13 patients (33%) and metastasis in three (8%). Of 22 cases with high-grade myofibroblastic sarcoma, seven (32%) recurred and 15 (68%) metastasized. Low-grade myofibroblastic sarcoma showed frequent local recurrence and rare distant metastases. As the clinical behavior of high-grade myofibroblastic sarcomas was demonstrated to be similar to malignant fibrous histiocytoma and other pleomorphic sarcomas, they should be managed identically [17].

Our patient was treated with irradiation (66 Gy) after incomplete resection of myofibroblastic sarcoma at the base tongue and after a follow-up period of 50 months she is alive without evidence of disease.

Owing to the rarity of this type of sarcoma, its biological behavior and the treatment of choice are still unclear. This case report suggests that irradiation might be a curative treatment for intermediate-grade myofibroblastic sarcoma of the base of tongue.

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