

# Malignant Myoepithelioma Arising from the Submandibular Salivary Gland: A Case Report

## Submandibular Tükrük Bezinde Gelişen Malign Miyoeptilyoma: Olgu Sunumu

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### ABSTRACT

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Myoepithelioma accounts for less than 1% of all salivary gland tumors. It is generally located in the parotid gland, less often in the minor salivary glands of the oral cavity and in the submandibular gland. This tumor can be classified as benign or malignant on the basis of clinical and histological findings. Malignant myoepithelioma is even more rare, representing 0.2-0.45% of all salivary gland tumors. Only 27 cases with malignant myoepithelioma arising from a major salivary glands have previously been reported in the English literature. Diagnosis is based on histological and immunohistochemical findings. Conservative surgery is the most accepted treatment choice. Radioterapy is only used when surgery is not considered feasible. In this study, a 61-year-old woman with submandibular gland malignant myoepithelioma was reported. Based on the English literature review, this case report represents the sixth case of malignant myoepithelioma of the submandibular salivary gland.

#### Keywords

*Myoepithelioma; carcinoma; submandibular gland*

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### ÖZET

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Miyoeptilyoma, tüm tükrük bezi tümörlerinin %1'inden azını oluşturur. Genellikle parotis bezinde, daha nadir olmak üzere oral kavitedeki minör tükrük bezleri ve submandibular tükrük bezinde lokalizedir. Klinik ve histolojik bulgular temelinde, tümör benign ve malign olarak sınıflandırılabilir. Malign miyoeptilyoma daha da nadirdir ve tüm tükrük bezi tümörlerinin %0.2-0.45'ine karşılık gelir. İngilizce literatürde, major tükrük bezinden kaynaklanan sadece 27 malign miyoeptilyoma olgusu daha önce rapor edilmiştir. Tanı histolojik ve immünohistokimyasal bulgular ile konur. Konservatif cerrahi en çok kabul gören tedavi seçeneğidir. Radyoterapi sadece cerrahinin uygun olmadığı durumlarda kullanılır. Bu çalışmada, submandibular bez malign miyoeptilyomalı 61 yaşında bir bayan tanımlanmıştır. İngilizce literatür gözden geçirildiğinde, sunulan bu olgu altıncı submandibular tükrük bezi malign miyoeptilyomasıdır.

#### Anahtar Sözcükler

*Miyoeptilyom; karsinom; submandibular bez*

Çalışmanın Dergiye Ulaştığı Tarih: 17.07.2009

Çalışmanın Basıma Kabul Edildiği Tarih: 28.12.2009

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## INTRODUCTION

Myoepithelioma of the salivary gland was first described by Sheldon in 1943.<sup>1</sup> Although it was initially considered as a subtype of pleomorphic adenoma, the World Health Organization classified it as a distinct entity in 1991.<sup>2</sup>

Myoepithelioma accounts for less than 1% of all salivary gland tumors. It is generally located in the parotid gland, less often in the minor salivary gland of the oral cavity and in the submandibular gland.<sup>2-4</sup> This tumor rarely progresses to malignant transformation.<sup>5</sup>

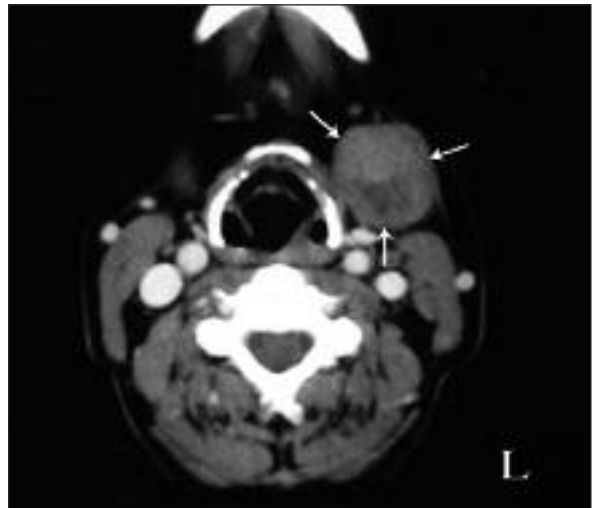
To the best of our knowledge, only five cases of malignant myoepithelioma of the submandibular gland have been previously reported in English literature,<sup>3,4,6,7</sup> and herein we reported the sixth case.

## CASE REPORT

A 61-year-old woman was admitted to our clinic with a 48 months history of a slow-growing mass in the right submandibular region. Physical examination on initial presentation revealed a 4 x 5 cm diametered hard, tender and semi-mobile mass involving the left submandibular region. The patient pointed out that the volume of the mass increased more rapidly in the last three months and that her pain became more apparent. The floor of the oral cavity and Wharton duct opening were normal. The remainder findings of the patient, including neurologic evaluation of the sensory and motor function, were within normal limits. Her past medical history was also unremarkable.

A preoperative fine needle aspiration cytology (FNAC) was performed. It showed class III cells (contained some cells with large and hyperchromatic nuclei that indicated possible malignancy), but no specific diagnosis was reported. Axial contrast-enhanced computed tomography (CT) scan demonstrated a 50 x 40 mm, solid, well-circumscribed mass with non-homogeneous enhancement in the left submandibular region, and the mandible was not involved (Figure 1).

The patient underwent surgery. It was seen that the tumor had invaded the surrounding normal submandibular gland and it was adherent to the neighboring structures. Salivary gland was resected with adjacent soft tissues and a few regional lymph nodes. Frozen sections revealed tumor-negative surgical margins.



**Figure 1.** Axial contrast-enhanced CT scan demonstrated a solid, well-circumscribed mass with non-homogeneous enhancement in the left submandibular region.

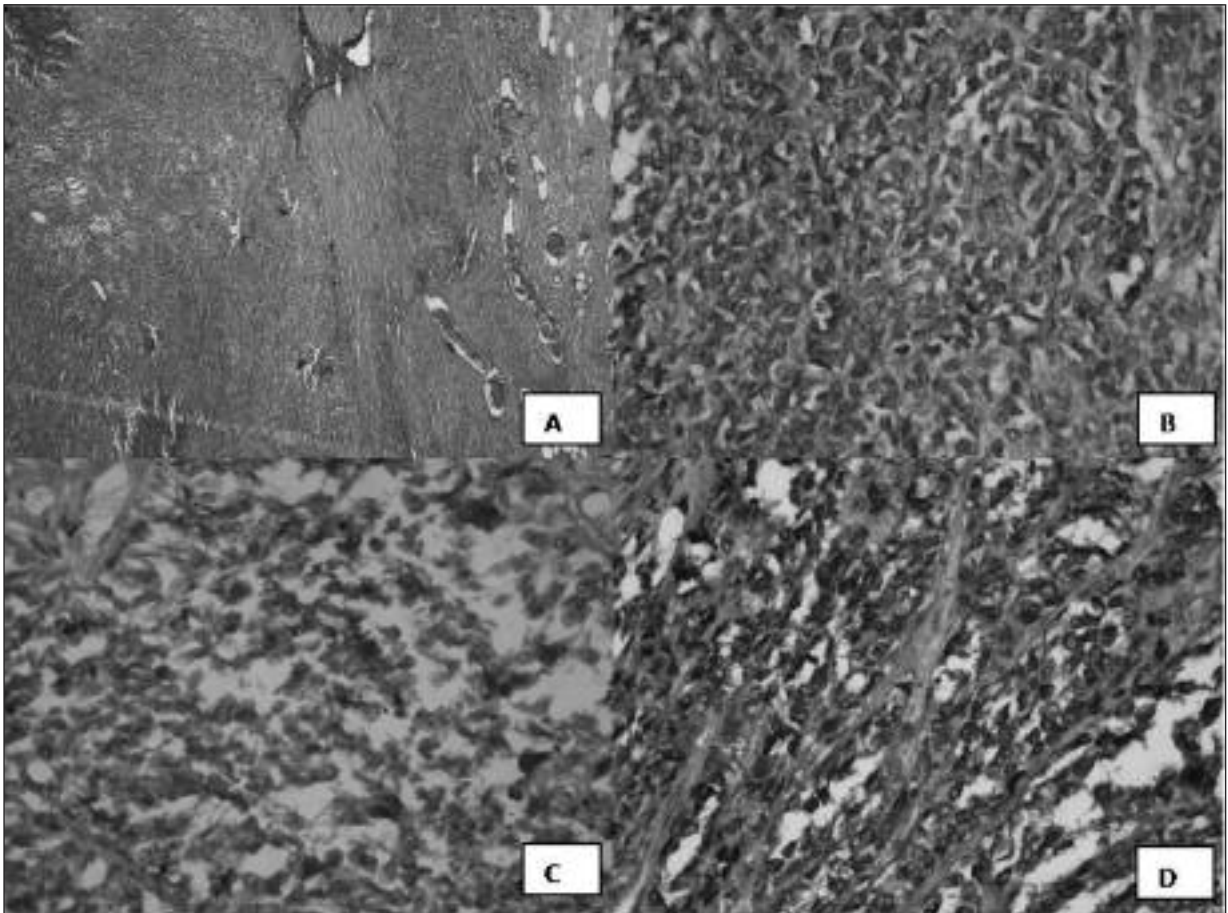
Histopathology revealed the mitotically active epithelioid and polygonal tumor cells with vesicular nuclei, distinct nucleoli, and eosinophilic cytoplasm. Meanwhile, some tumor cells had clear cytoplasm. An invasive growth pattern was seen through hematoxylin eosin stain (Figure 2 a, b). Tumor cells were immunohistochemically stained positively with Cytokeratin, Desmin, EMA (Figure 2c), and S-100 (Figure 2d). Histopathology confirmed the diagnosis of submandibular malignant myoepithelioma (MME) and there was not any lymph node metastasis.

The patient had an uneventful post-operative period. She was discharged from the clinic on the 7<sup>th</sup> post-operative day. No sign of disease was present during the follow-up examination performed 18 months after the operation.

## DISCUSSION

Myoepithelial cells are ectodermally derived contractile cells and exhibit a smooth muscle and epithelial phenotype.<sup>3,7</sup> Many normal tissues with a secretory function such as salivary glands, sweat glands, lacrimal glands, breasts and the prostate contain these cells.<sup>1,7</sup>

Although these cells are one of the most frequent components of many salivary gland tumors, pure myoepitheliomas are rare, accounting for less than 1% of all salivary gland tumors.<sup>1,7</sup> Myoepitheliomas can be classified as benign (BME) or malignant (MME) on the basis of clinical and histological findings.<sup>3</sup>



**Figure 2a.** Invasive growth pattern is seen (Hematoxylin Eosin [HE] x 100).

**Figure 2b.** Mitotically active epitheloid and polygonal tumour cells with vesicular nuclei, distinct nucleoli, and eosinophilic cytoplasm. Some tumor cells have clear cytoplasm (Hematoxylin Eosin [HE] x 400).

**Figure 2c.** Tumor cells are positively stained with EMA, (x 200).

**Figure 2d.** Tumor cells are positively stained with S-100, (x 200).

The tumor usually appears as an asymptomatic mass that slowly increases in size over a period of several months or years for BME.<sup>8</sup>

MME is even more rare, representing 0.2-0.45% of all salivary gland tumors. Approximately 55 MME cases have been reported in the English literature.<sup>3</sup> Only 27 cases of malignant myoepithelioma of the major salivary gland and five submandibular MME have been previously reported in the English literature.<sup>3,4,6,9</sup>

Although malignant myoepitheliomas are generally regarded as a low-grade malignant tumors, they sometimes show aggressive features.<sup>10</sup> Macroscopically, the lesion may invade the surrounding tissues and produce both local and distant metastases. Recurrence is frequent.<sup>8</sup> Microscopically, MME shows vascular and perineural invasion, marked cellular pleomorphism, im-

munoreactivity to p53, and high proliferative activity with a poor clinical outcome.<sup>3</sup>

MME is more commonly seen in women at the age of 60 (with a ratio 2:1).<sup>11</sup> The mean tumor size for MME was reported as 4.9 cm (range from 2.5-8 cm).<sup>3</sup> With regard to occurrence, the main primary site is the parotid gland and the most common intra-oral site is the hard palate.<sup>2,10,12</sup> They sometimes arise in the nasal cavity, nasopharynx, larynx and lung.<sup>12</sup>

Malignant myoepitheliomas may arise either “de novo” or develop in a pre-existing pleomorphic adenoma or BME.<sup>6,8</sup> The prognostic implication of the histogenesis of MME is controversial.<sup>10</sup> According to Nagao et al.,<sup>3</sup> there was no difference in prognosis in terms of the absence or the presence of a pre-existing pleomorphic adenoma. However, Di Palma and Guzzo<sup>13</sup>

suggested that “de novo” tumors tend to be larger with a more aggressive growth pattern and a shorter clinical history. If, “pleomorphic adenoma” is a pre-existing lesion, they are smaller in size, have an insidious onset, and lower malignancy rate. MME arising from a pre-existing BME displays an intermediate pattern. Usually, de novo MME and those which developed from pre-existing BME arise from the minor salivary glands.<sup>14</sup>

Based on the clinical course and the histologic features, we speculated that the MME of the presented case possibly arose from a pre-existing pleomorphic adenoma. For the other previously reported five cases in the literature, MME of the submandibular gland arose de novo in one, took origin from a pre-existing BME in one, and from a pleomorphic adenoma in two cases.<sup>3,6,9</sup>

Malignant myoepithelioma in the submandibular gland demonstrate a well-circumscribed mass with an internal lobulated pattern and an inhomogeneous density on contrast-enhanced CT as reported by Uemaetomari et al.<sup>9</sup> Adenoid cystic carcinoma, mucoepidermoid carcinoma and acinic cell carcinoma should be included in radiologic (CT) differential diagnosis.<sup>4</sup> In the presented case, axial contrast-enhanced CT scan analysis demonstrated a 50 x 40 mm solid, well-circumscribed mass with non-homogeneous enhancement in the left submandibular region.

Architecturally, myoepithelioma of salivary gland displayed either solid, myxoid, or reticular growth patterns. Histopathologically, cells of myoepithelioma may be plasmacytoid, spindle-shaped, epithelioid, clear or a combination of these.<sup>15</sup> Spindle-shaped types of myoepithelioma originates from the parotid gland, and the plasmacytoid types arise from minor salivary glands of the palate.<sup>4</sup> Our case showed a combined differentiation (plasmacytoid/epithelioid/spindle-shaped) and solid stroma.

Diagnosis is based on histological and immunohistochemical findings. S-100 protein and vimentin are not usually present in normal myoepithelium and are

non-specific, but very sensitive immunohistochemical markers of neoplastic myoepithelial cells.<sup>14</sup> The malignancy is supported by infiltrative growth, necrotic areas, cytologic atypia, high mitotic rate and cellular pleomorphism. Tumour cells were immunohistochemically positively stained for EMA, Cytokeratin, Desmin, and S-100 in our case. Malignant myoepithelioma was diagnosed histopathologically.

The major differential diagnosis of myoepithelioma is a pleomorphic adenoma. Myoepitheliomas are composed completely, or almost completely of myoepithelial cells, however the amount is variable in the pleomorphic adenoma, but may reach levels comparable to those in myoepithelioma.<sup>12</sup>

Regarding the treatment of MME, there is little information available at the present time. Due to the limited number of cases and the widespectrum of the neoplasm, published results tend to be conflicting.<sup>8</sup> But conservative surgery is the most accepted treatment choice.<sup>12</sup> If there are clinically apparent metastases in the cervical lymph nodes, therapeutic neck dissection is indicated.<sup>8</sup> Radioterapy is used only when surgery is not considered feasible.<sup>12</sup> According to the literature, MME which arises from a preexisting pleomorphic adenoma, like the case presented here, has the best clinical outcome, if treated properly.<sup>13,14</sup>

In our case, we resected the submandibular gland with adjacent soft tissues and a few regional lymph nodes. As there was no clinical and histological lymph node metastasis, neck dissection was not performed. During most recent follow-up examination performed 18 months after the operation, our patient was healthy and there was no sign of the disease.

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## CONCLUSION

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We advise early tumor removal and avoidance of incomplete removal for the prevention of the development of MME from a pre-existing pleomorphic adenoma. Long-term follow-up is also recommended.

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