

# A case report of metastasizing myoepithelial carcinoma of the parotid gland arising in a recurrent pleomorphic adenoma

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## Abstract

Myoepithelial carcinoma, arising in a recurrent or in a pre-existing pleomorphic adenoma of the parotid gland is an extremely rare cancer. We herein report the case of myoepithelial carcinoma occurring in a recurrent pleomorphic adenoma, which showed a high metastatic potential. A 53-year-old male, who had undergone a superficial parotidectomy of the pleomorphic adenoma 2 years previously, presented with recurrent parotid swelling and with multiple coin lesions in the lung. A total parotidectomy and a thoracoscopic biopsy of the lung lesion revealed both lesions to be myoepithelial carcinoma. The patient died about 12 months later despite undergoing intensive chemotherapy. © 2008 Elsevier Ireland Ltd. All rights reserved.

**Keywords:** Myoepithelial carcinoma; Pleomorphic adenoma; Hypercellularity; Myoepithelial cell; Carcinoma ex pleomorphic adenoma

## 1. Introduction

Pleomorphic adenoma is well known to be a benign salivary gland tumor which uncommonly undergoes malignant transformation. When a malignancy arises in pleomorphic adenoma, it is usually carcinoma. Myoepithelial carcinoma of the salivary gland is extremely rare and accounts for less than 1% of all salivary gland tumors. It may develop *de novo* or may appear in a pre-existing pleomorphic adenoma. We herein report the case of a myoepithelial carcinoma with a high grade of malignancy arising from a recurrent pleomorphic adenoma. The histological findings of both the initial and the recurrent neoplasm are described in detail.

## 2. Case report

A 53-year-old male with a swelling of the left parotid region visited our clinic in 2003. He had undergone a

superficial left parotidectomy in 2001 for the treatment of a pleomorphic adenoma. During the examination, a hard tumor measuring 6 cm in diameter was palpable. No facial nerve palsy was observed to be present. A computed tomographic (CT) study showed a large tumor in the left parotid gland [Fig. 1]. No lymph node enlargement was noted. A fine needle aspiration biopsy of the tumor showed the features of pleomorphic adenoma. A total parotidectomy was planned for what was thought to be a recurrent pleomorphic adenoma. However, multiple coin lesions were also found in the lungs on both chest X-ray films and computed tomography [Fig. 2].

A left total parotidectomy was therefore performed. In the parotid region, only a capsulized tumor which could be easily separated from the facial nerve was found. Stenson's duct was resected due to tumor infiltration. In frozen sections, the histopathological diagnosis was a recurrent pleomorphic adenoma with a proliferation of myoepithelial cells. Since there was no finding of malignancy, a partial lung resection biopsy under thoracoscopy was also performed. The histopathological examination revealed myoepithelial carcinoma of both the parotid gland tumor

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Fig. 1. An axial CT indicates the recurrent tumor. No enlarged lymph nodes are noted in the neck.

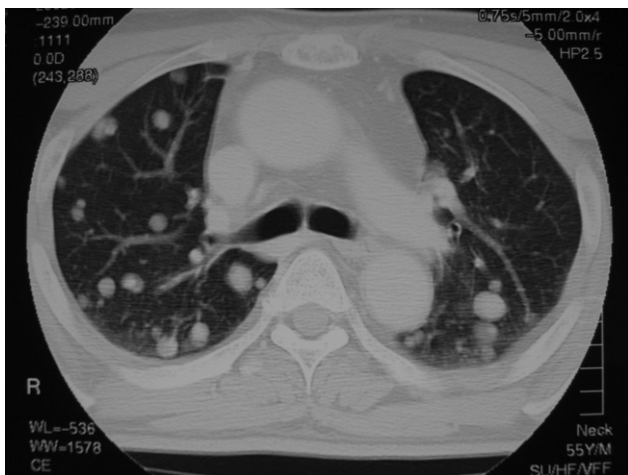


Fig. 2. Multiple coin lesions were revealed in the lung on computed tomography.

and the lung tumor, occurring simultaneously with the recurrent pleomorphic adenoma. Although the patient underwent chemotherapy using docetaxel and TS-1 (the oral chemotherapy including fluorouracil and tegafur), the parotid and lung tumors continued to develop further. As a result, the patient died 3 years after the initial operation.

### 3. Pathological findings

Both the initial tumor and the recurrent tumor were reviewed. The former showed a mixture of myxoid, solid, and chondroid stroma. Ductular formations of round cells were found [Fig. 3]. No cytological atypia, mitosis, or necrosis was seen. In a certain area, a hypercellularity of the myoepithelial tissue was found [Fig. 4]. Although the resection margin was free from the tumor, some tumor cells had invaded the capsule. Consequently, the neoplasm was

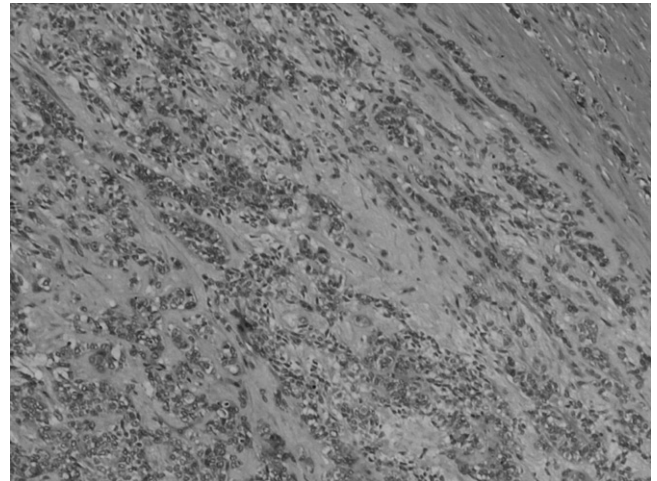


Fig. 3. A photograph of the initial tumor. The area of the typical pleomorphic adenoma composed of a myxochondroid stroma and ductal formations is shown (HE  $\times$  100).

diagnosed to be pleomorphic adenoma with a predominance of myoepithelial cells.

The recurrent tumor showed the monotonous growth of atypical epithelial round cells with any abundant mitosis, as well as neither necrosis nor hemorrhage [Fig. 5]. The parotid gland and the lung tumor were very similar except for the presence of tubular formations in the lung tumor, which consisted of myoepithelial cells [Fig. 6]. Some multinucleated cells were also present. The immunohistochemical markers were positive for anticytokeratin, partially positive for anti- $\alpha$  smooth muscle actin and anti vimentin, diffusely positive for anti s-100 protein, and negative for alcian-blue. These findings confirmed the diagnosis of myoepithelial carcinoma with a high grade of malignancy arising from a recurrent pleomorphic adenoma.

In the present case, we performed a total parotidectomy, thereby extracting the primary lesion, in spite of the

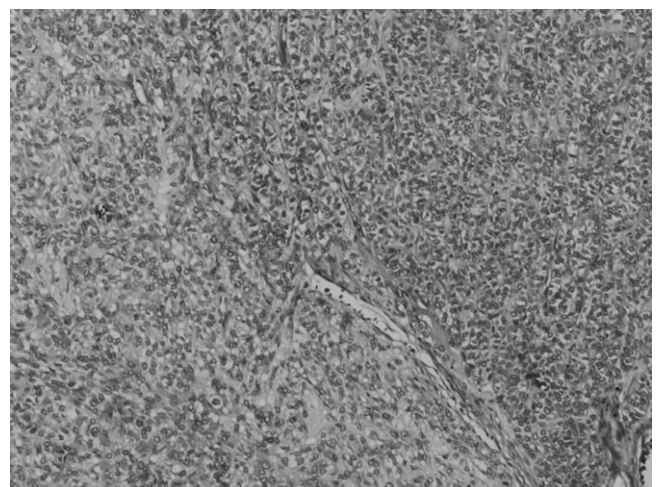


Fig. 4. A photograph of the first tumor. The area of a hypercellularity of the myoepithelial cells (HE  $\times$  100).

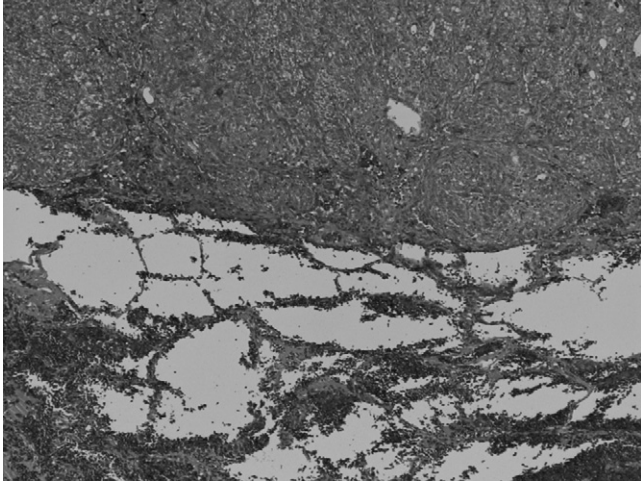


Fig. 5. A photograph of the recurrent tumor showing the monotonous growth of atypical epithelial round cells with abundant mitosis, necrosis, and hemorrhage (HE  $\times$  100).

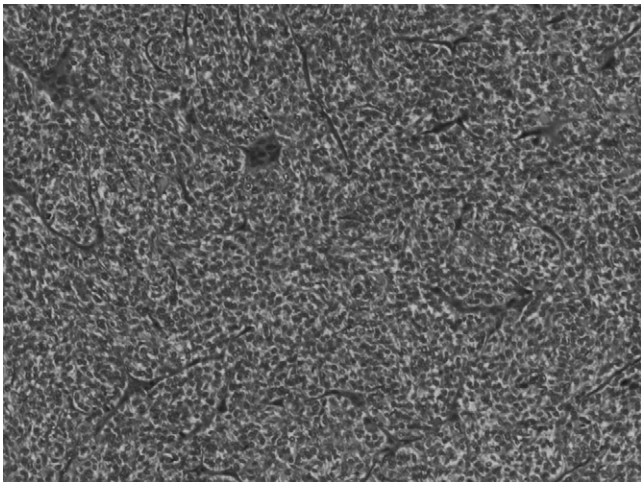


Fig. 6. A photograph of the lung tumor. Some multinucleated cells were present. Tubular formations, which were composed of myoepithelial cells, were found (HE  $\times$  100).

presence of multiple lung metastases. This operation, itself, for this case may be controversial due to the fact that the chest CT before the operation revealed multiple metastases, a metastatic pleomorphic adenoma, carcinoma ex pleomorphic adenoma, or other malignant tumors which also had to be considered. The patient requested the tumor extraction and a definite diagnosis. Furthermore, the histopathological diagnosis was necessary for us to perform appropriate additional therapy. In the end, a total parotidectomy was thus performed.

#### 4. Discussion

Myoepithelial carcinoma of the salivary gland is a very rare tumor, which comprises less than 1% of all salivary

gland tumors [1]. It is a new entity included in the updated classification of salivary gland neoplasm by the World Health Organization in 1991 [2,3]. The parotid gland is the primary site of occurrence [3]. This neoplasm may develop in two different ways; namely, it may appear *de novo* in a normal salivary gland or it may arise from a recurrent pleomorphic adenoma [1,2].

Based on previous reports, in which a *de novo* formation is an indication of a high-grade malignancy and a secondary formation from a pleomorphic adenoma is associated with a low grade of malignancy, the present case would therefore be expected to be a low-grade malignancy [4,5]. However, the actual clinical course of the present case, with distant metastasis and a 3-year survival from the initial operation, was considered to correspond to a high-grade malignancy. In addition, based on the pathological findings, this tumor was regarded as being a high-grade malignancy because of the extensive necrosis, hemorrhage, and mitotic activity which were found [6,7]. The prognostic implications of the histogenesis of the myoepithelial carcinoma therefore remain controversial.

Histopathologically, the first extracted tumor, which was diagnosed to be a pleomorphic adenoma, showed a special feature in the present case. It was different from common mixed tumors in that a hypercellularity of the myoepithelial cells was found in a certain area. The tumor infiltrated the capsule of the tumor, but not the extracapsular area, and it lacked cytological atypia, mitosis, and necrosis. As the tumor was thought to have been completely removed, no intensive follow up was done. Taking the progress and the pathological findings into consideration, the neoplasm, which was extracted in 2001, was therefore considered not to be a pure pleomorphic adenoma, but a mixed tumor with a malignant potential. In the literature, a myoepithelial proliferation has been identified as a possible predictor of an aggressive clinical behavior of the benign pleomorphic adenoma. Cresson et al. stated that aneuploidy in a DNA-flow cytometry of the cells from the tumor might reflect the malignant potential of a pleomorphic adenoma [8].

It remains controversial whether this neoplasm was classified as a myoepithelial carcinoma or a carcinoma ex pleomorphic adenoma in the classification by the WHO in 2005. Histopathologically, undifferentiated carcinoma, adenocarcinoma, and squamous cell carcinoma are mainly observed as the malignant components of a carcinoma ex pleomorphic adenoma [2,9]. A myoepithelial carcinoma as a malignant component is rare. In cases of carcinoma ex pleomorphic adenoma, both carcinoma and adenoma components were supposed to exist in the primary lesion. However it is often difficult to demonstrate a pre-existing pleomorphic adenoma because the malignant component may overgrow the other component [2]. In the present case, there was no evidence of the existence of adenoma in the recurrent tumor despite the examination of multiple sections. Nevertheless, the presence of tubular formations in the lung tumor might have been a vestige of the

pleomorphic adenoma. Namely the present neoplasm was supposed to be a “myoepithelial carcinoma ex pleomorphic adenoma.”

Regardless, the present myoepithelial carcinoma was expected to follow the ‘pleomorphic adenoma–carcinoma sequence.’ Moreover, it was considered that the initial pleomorphic adenoma had progressed to some extent in this sequence and that the first operation stimulated the tumor, and had some effect on the development of the neoplasm as previously described. Therefore, pleomorphic adenoma with a hypercellularity of the myoepithelial cells should therefore be treated as a pre-malignant neoplasm.

We herein present our findings of a rare case of a high-grade metastatic myoepithelial carcinoma arising from a recurrent pleomorphic adenoma with malignant and metastatic potential. The rarity of this case is that pleomorphic adenoma as a pre-malignancy was observed. In addition, it is rare that a metastatic lung tumor was also histopathologically identified. The biological properties of a myoepithelial carcinoma, even if it develops secondarily, may depend on the histopathological findings, such as atypia, hemorrhage, and mitosis. Although pathological reports showed negative surgical margins in the first operation in our case, the tumor recurred not only locally but also distantly, in the lung metastasis. It is therefore very important to intensively follow up patients presenting with pleomorphic adenoma showing this characterized pathological form, especially

when demonstrating hypercellularity of the myoepithelial cells.

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