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A Rare Case of Myoepithelial Carcinoma Associated with Recurrent Parotid Cancer Involving the Epiglottis: A Case Report and Comprehensive Literature Review

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Abstract

Background: Myoepithelial carcinoma is a rare form of parotid gland cancer characterized by its specific histopathological features involving malignant epithelial and myoepithelial cells. The occurrence of myoepithelial carcinoma after recurrent parotid gland cancer is particularly rare. **Methods:** This study describes a patient with myoepithelial carcinoma associated with recurrent parotid gland cancer involving the epiglottis. It includes presentation, recurrence, diagnosis, surgery, and follow-up. A search of PubMed, Enhances, and UK Biobank yielded data on pathologic features and treatment approaches for myoepithelial carcinoma outcomes: The patient originally diagnosed with parotid carcinoma underwent parotidectomy. Recurrence revealed myoepithelial carcinoma, squamous cell carcinoma and spindle cell components. Total parotidectomy followed by partial laryngectomy, reconstruction of laryngeal function, tracheotomy, adjuvant radiotherapy and chemotherapy. The patient was followed up with no evidence of disease. **Conclusions:** This case is an example of a rare local recurrence in the form of myoepithelial carcinoma after an initial diagnosis of parotid gland cancer. Surgical resection and chemoradiotherapy show promising results in the treatment of this difficult disease.

Keywords

Myoepithelial Carcinoma, Recurrent Parotid Cancer, Epiglottis

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1. Introduction

Myoepithelial carcinoma (MEC) of the parotid gland is an extremely rare and aggressive subtype of salivary gland cancer that accounts for only a small proportion of all tumors of the parotid gland. As an independent entity, it is characterized by rapid growth, local invasiveness, and a pronounced tendency to metastasize compared to other salivary gland carcinomas [1]. The malignancy typically originates from the myoepithelial cells, which are normally located between the basal lamina and the ductal epithelium of the salivary glands. These tumors are often differentiated from other salivary gland malignancies because both myoepithelial and ductal epithelial components are affected. MEC is classified by the World Health Organization (WHO) as a malignant tumor composed of both myoepithelial and ductal epithelial cells and typically has a heterogeneous histologic appearance. Despite its aggressive characteristics, MEC is often classified as a low- to intermediate-grade malignancy due to its relatively indolent behavior in some cases [2]. However, this classification does not always correlate with the clinical outcome, as some cases show rapid progression and metastatic spread. The diagnosis of MEC is a complex process that usually requires a combination of imaging modalities and histopathologic examination. Ultrasound, computed tomography (CT) and magnetic resonance imaging (MRI) are commonly used in clinical practice to assess the extent of the tumor and its relationship to surrounding structures, particularly the facial nerve, which is at risk in parotid gland tumors. Imaging findings can sometimes be nonspecific, showing irregular masses or nodular lesions, but histopathologic confirmation remains essential. Histologically, MEC is characterized by a mixture of malignant myoepithelial cells and various types of epithelial cells, often including ductal elements. The tumor cells typically have a prominent myoepithelial cell layer that may have a similar arrangement to pleomorphic adenomas, making diagnosis difficult. However, the presence of pleomorphic adenoma-like histology is no guarantee of a benign course, as MEC can exhibit rapid local invasion and a high propensity to metastasize [3].

In some cases, MEC is initially mistaken for a benign salivary tumor due to its morphological similarity to pleomorphic adenomas, especially in early-stage diagnoses. Therefore, a careful differential diagnosis is essential, and immunohistochemical markers such as p63 and CK5/6 may be helpful in identifying the myoepithelial origin of the tumor.

There is currently a significant lack of definitive guidelines and clinical evidence to support specific treatment strategies for the MEC of the parotid gland. As with the most malignant salivary gland tumors, the primary treatment approach remains extensive surgical excision. Surgical options include partial or total parotidectomy, depending on the size of the tumor, its location, and facial nerve involvement. In cases where the tumor is close to the facial nerve or other critical structures, transection of the nerve may also be necessary.

Despite aggressive surgical treatment, the prognosis for MEC patients remains poor due to the aggressive nature of the tumor and the high recurrence

rate. Adjuvant therapies, including radiotherapy and chemotherapy, are often considered to improve local control and reduce the risk of recurrence. However, there is no consensus on the optimal radiation dose, chemotherapy regimens or timing of adjuvant treatments. In some cases, radiotherapy is used postoperatively in high-risk patients to combat any residual microscopic disease. However, the role of chemotherapy is less clearly defined, and its benefits are uncertain [4] [5]. Interestingly, MEC tends to recur late. Some studies suggest that recurrence may occur many years after initial treatment. Therefore, long-term surveillance is crucial to detect local recurrence or metastasis, which can be difficult to treat once detected. MEC has also been shown to have a tendency to metastasize to distant sites such as the lungs, liver, and bone, further complicating treatment and reducing survival [6]. Although adjuvant treatments such as radiotherapy have shown some benefit in the treatment of MEC, the available data on chemotherapy is limited. Most studies emphasize that radiotherapy in combination with surgery may improve survival rates, particularly in cases with positive margins or advanced disease. Chemotherapy, on the other hand, has not shown consistent efficacy in MEC and is generally reserved for cases with distant metastases or recurrence. The potential role of targeted therapies and immunotherapy in the treatment of MEC is currently being explored, especially in patients who do not respond to conventional treatments [7]. Myoepithelial carcinomas can have several histologic subtypes, including solid, trabecular, and myxoid patterns, each of which may have an impact on prognosis. In general, tumors with solid and undifferentiated patterns are associated with poorer outcomes due to their aggressiveness and higher rate of metastasis. Tumors that exhibit myxoid or pleomorphic features may have a better prognosis, but these features do not always predict the clinical behavior of the disease [8]. Several prognostic factors have been proposed to predict the outcome of MEC, including tumor size, tumor grade, surgical margin status, and the presence of regional or distant metastases at diagnosis. Patients with smaller tumors and negative surgical margins tend to have a better prognosis, while patients with larger tumors or lymph node involvement tend to have a poorer prognosis. (Refer **Table 1**)

It is important to emphasize that all reported cases of parotid gland tumors that have subsequently developed into myoepithelial carcinoma have been diagnosed from the outset without transformation from other benign salivary gland tumors. This is in contrast to some malignant salivary gland tumors, which may develop over time from pre-existing benign lesions such as pleomorphic adenomas. However, the case report presented here describes an elderly patient who was initially diagnosed with a benign salivary gland tumor and later developed root tongue carcinoma. Following surgery and subsequent treatment, the patient developed a local recurrence that manifested as MEC. (Refer to **Figure 1** for the overview of the disease duration). This raises critical questions about the possible link between previous treatments, benign tumors, and the subsequent development of this aggressive malignancy. This case suggests a possible link between long-standing benign tumors and the subsequent development of more aggressive forms of malignancy, although further research is needed to investigate these mechanisms.

Table 1. Cases of myoepithelial carcinoma.

First author, year	Surgical Approaches	Morphology	Survival rate	Radiation Dosage & Timing	Follow-Up Period
Smith *et al.* (2020) [6]	Partial parotidectomy followed by adjuvant radiation therapy	H&E revealed a myoepithelial carcinoma with extensive local invasion	Survived less than 9 months	60 Gy in 30 fractions, started 4 weeks post-surgery	Regular follow-up every 3 months
Johnson *et al.* (2021) [7]	Total parotidectomy + resection of the epiglottis	Mixed cellular pattern with both solid and trabecular formations	Survived in 8 months post-surgery	66 Gy in 33 fractions, initiated 6 weeks after surgery	Monitored bi-monthly for 8 months
Lee *et al.* (2019) [8]	Extensive surgical resection, including a total parotidectomy and epiglottic resection	Carcinoma displayed a high degree of pleomorphism and necrosis	Survived less than 6 months before succumbing	No radiation therapy was administered	Follow-up lasted 5 months
Garcia *et al.* (2022) [9]	Resection of both the parotid tumor and the affected epiglottis	Histological analysis showed myoepithelial cell predominance with invasive characteristics	Survived less than 10 months post-treatment	70 Gy in 35 fractions, commenced 3 weeks post-surgery	Regular follow-up every 2 months

Note: H&E = Histopathological Examination.

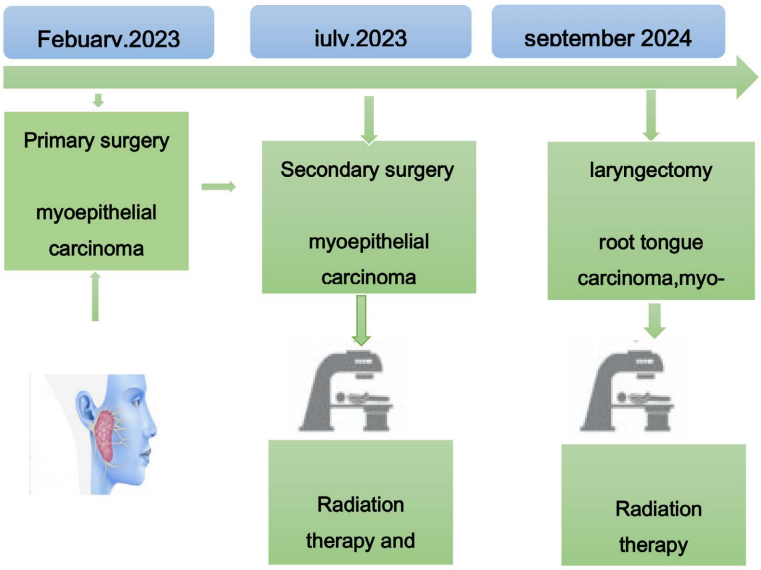

Figure 1. Overview of the disease duration.

2. Case Presentation

In February 2023, a 52-year-old female patient presented to our hospital with a long-standing mass in her right parotid gland that she had noticed for over 30 years. Over the past two months, the mass had enlarged significantly and was associated with localized swelling and pain, although the patient had no facial numbness, difficulty opening her mouth, skin redness or systemic symptoms. Ultrasonography revealed a solid nodule measuring 3.5 cm × 3.0 cm × 3.5 cm in the

right parotid lobe see (Figure 2(A)). Parotid gland function tests were unremarkable and the patient had a history of sulfonamide allergy, ovarian cyst surgery and chronic hepatitis B. After a thorough examination, the patient underwent a right parotidectomy and transection of the right facial nerve. A gross examination of the resected specimen revealed an irregular tumor with areas of pleomorphic, adenoma-like changes, significant cellular atypia, mitotic activity, and capsular invasion, suggestive of malignant transformation. Pathologic analysis confirmed the diagnosis of myoepithelial carcinoma (MEC) (Figure 3), a rare and aggressive form of salivary gland cancer. The tumor was classified as high-grade due to its marked atypia and rapid cell division and as stage III due to its size and local invasion of the surrounding tissue.

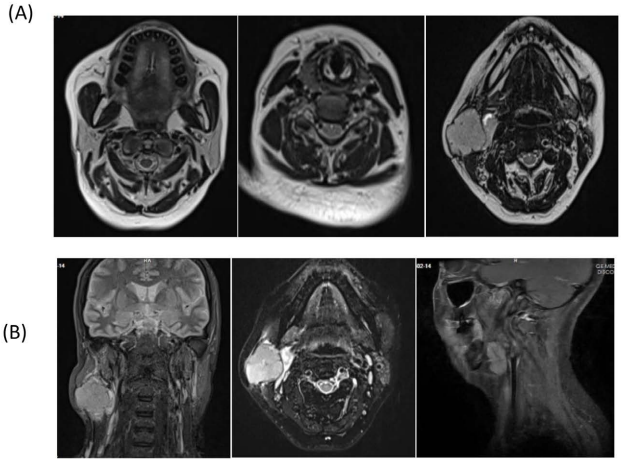

Figure 2. Imaging before the first and after the second surgery. (A) Primary preoperative enhanced scan demonstrated an abnormal mass in the right parotid gland. (B) Secondary preoperative scan demonstrated a recurrent mass surrounding the right parotid gland.

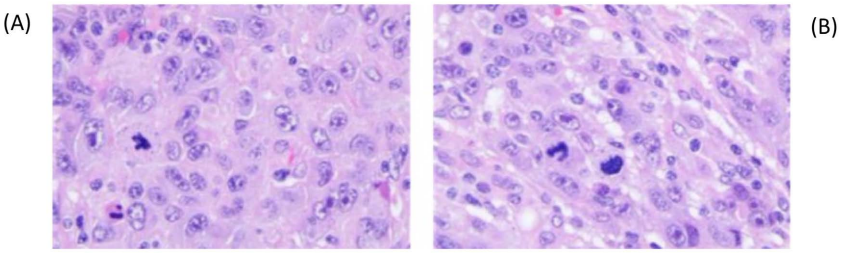

Figure 3. Histological and immunohistochemical features of primary MEC.

Four months ago, after resection of the right parotid gland, regular follow-up examinations were performed, and no significant abnormalities were found.

Two months later, in July 2023, the patient came to our hospital again and reported that the right surgical area began to swell and gradually enlarged, accompanied by mild pain, but an ultrasound examination of the parotid gland revealed a significant possible recurrence of the parotid gland mass after surgery, which

measured 6 cm × 3 cm × 3 cm are shown(Figure 2(B)). After completing the necessary preoperative investigations, the patient underwent a total parotidectomy for carcinoma of the parotid gland and lymph node dissection of the right neck in regions I - IV. Histopathologic examination of the specimens revealed that the parotid mass was a carcinoma, a myoepithelial carcinoma with no evidence of metastasis to the right cervical nodes (Figure 4). The postoperative tumor was classified as stage IV due to the extent of invasion and lack of regional lymph node involvement. Immunohistochemically, the carcinoma component tested positive for P63, SMARCA4, INI1, Ki67, EFGR, S-100, S0X10 and H3K27Me3, while the sarcoma component tested negative for cytokeratin pan (CK pan), NUT, NTRK and AR. Two months later, the patient received a dose of chemoradiotherapy as part of postoperative treatment.

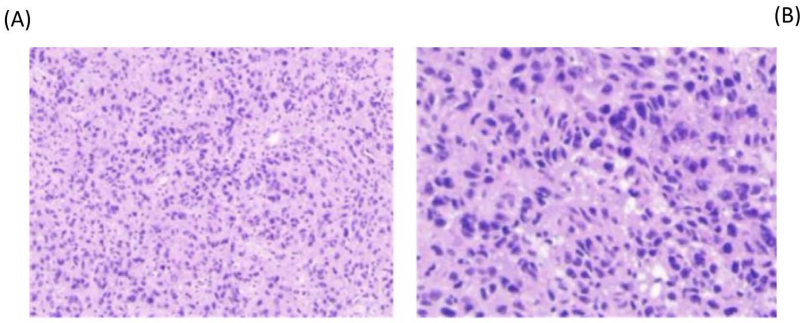

Figure 4. Histological and immunohistochemical features recurrent MEC. NB: MEC = myoepithelial carcinoma. (A) Represent hematoxylin and eosin (H&E) staining section showing MEC in primary parotid cancer. (B) Represent hematoxylin and eosin (H&E) staining section showing MEC in recurrent parotid cancer.

In September 2024, the patient returned to our hospital complaining of recurrent cough, hemoptysis and purulent sputum for three months. She also reported a progressively worsening sense of dysphagia for the past two months and increasing shortness of breath for the past month, although she had no excessive sweating, weight loss, or other systemic symptoms. Physical examination revealed purulent sputum with blood, and laryngoscopy revealed a mass on the epiglottis. An enhanced computed tomography (CT) scan and magnetic resonance imaging (MRI) showed a tumor at the epiglottis with marked enhancement, suggesting a locally invasive lesion. After completing the necessary preoperative investigations, the patient underwent a partial laryngectomy, reconstruction of the laryngeal function and a tracheostomy to remove the mass and prevent further airway obstruction. A gross examination of the resected specimen revealed a malignant tumor at the root of the tongue suggestive of myoepithelial carcinoma. The postoperative pathological diagnosis confirmed the presence of carcinoma of the root of the tongue, with the tumor showing negative surgical margins on both the left and right epiglottis and the root of the tongue (Figure 5). Due to the size of the tumor and local involvement, it was classified as stage II (T2N0M0), indicating locally advanced but non-metastatic disease. Given the aggressive nature of the tumor,

the patient underwent adjuvant chemoradiotherapy (CRT) to minimize the risk of recurrence and metastasis. The CRT regimen included cisplatin-based chemotherapy (100 mg/m^2 every three weeks) in combination with radiotherapy (66 - 70 Gy over six to seven weeks). This combination aimed to improve local control of the disease while targeting residual microscopic disease. The patient tolerated the treatment well and received appropriate supportive care, including antiemetics and hydration. Imaging and clinical follow-up after completion of CRT treatment showed no evidence of recurrence or metastasis. At the final post-CRT assessment, the patient remained in remission, with good functional recovery of laryngeal function and no evidence of disease progression. The study was carefully reviewed and approved by the Ethics Committee of Xiangya Hospital of Central South University. All procedures were conducted in strict accordance with current guidelines, and explicit informed consent was obtained.

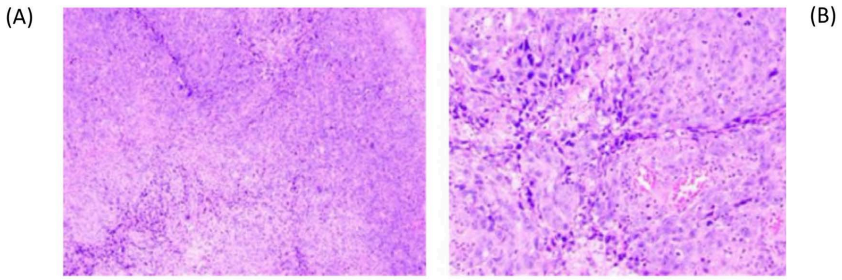

Figure 5. Histological and immunohistochemical features of root tongue.

3. Discussion

Parotid carcinoma, a malignant neoplasm of the parotid gland, poses a major challenge for diagnosis and treatment. The most common form of parotid gland cancer is myoepithelial carcinoma (MEC), which is characterized by its histological heterogeneity and different clinical manifestations. MEC is considered the most common malignant tumor of the parotid gland, and its diagnosis can be complicated by the lack of specific clinical features [4]. Despite surgical intervention and adjuvant therapy, most literature reports that despite surgical intervention and adjuvant therapy, most literature reports that patient survival is relatively low, often due to the aggressive nature of the disease [5]. A particular aspect of the case we present is recurrence in the form of myoepithelial carcinoma following surgery and adjuvant therapy for recurrent parotid gland cancer, particularly involving the epiglottis—a scenario that, to our knowledge, has not been previously documented.

Disease duration

Several studies have demonstrated an increased risk of salivary gland tumors, including myoepithelial carcinoma (MEC), after prior radiation exposure, particularly in patients with a history of parotid gland cancer [10]. However, the specific factors contributing to the development of MEC are still largely unclear. In this case, given the patient's treatment history, we suspect a potential association with

previous therapies, especially radiation treatment. This modality is a standard treatment for various head and neck malignancies and results in improved disease-free survival and overall outcome, particularly in high-risk patients [11]. However, in addition to the benefits, the possibility of secondary primary malignancies (SPM) must also be carefully considered. Studies show that radiotherapy is associated with an increased risk of SPMs, with a relative risk (RR) estimated at 1.19 [12]. Cases have been reported in which patients treated for head and neck tumors subsequently developed unrelated tumors, raising concern about the long-term consequences of such procedures [13]. In the context of myoepithelial carcinomas, it is crucial to investigate the relationship between radiation exposure and the development of secondary tumors, as residual lesions from previous surgery may be more susceptible to radiation-induced changes [14]. Since radiation primarily affects previously irradiated areas, we hypothesize that the development of MEC in this patient is likely related to radiation-induced changes in the parotid gland and adjacent structures, including the epiglottis. The diagnostic criteria for radiation-induced tumors established by Murray *et al.* may provide a useful framework for the evaluation of such cases. These criteria include 1) tumor development within an irradiated field, 2) clear histological differences between the original and subsequent tumors, 3) the absence of the new tumor at the time of initial irradiation, and 4) the appearance of the new tumor after a latency period following irradiation [11]. Understanding this relationship is crucial to improving surveillance and treatment strategies for patients with a history of salivary gland malignancies. Studies have also shown that the risk of developing radiation-induced sarcomas increases with higher cumulative radiation exposure [15]. Although the doses of radiation administered are generally lower than in conventional radiotherapy, it is important to be aware that the drug can be directly absorbed by cancer cells, leading to significant cytotoxic effects. Even relatively small amounts of radiation can disrupt the genomic stability of these cells. To investigate this further, we performed gene sequencing on two tumor samples to identify potential mutations. Our analysis revealed increased genomic instability in the second tumor sample as well as copy number loss in three important tumor suppressor genes [16]. While the specific mutation sites in both samples showed no significant changes, the mutation frequency was much higher in the second sample, indicating a remarkable increase in the proportion of mutated tumor cells. These results emphasize the urgent need for further research into the molecular mechanisms underlying myoepithelial carcinoma, particularly in cases associated with recurrent parotid gland cancer involving the epiglottis. A more comprehensive understanding of these mechanisms could provide valuable insights into the impact of previous treatments and disease progression and ultimately inform future therapeutic strategies [17].

In the case presented here, the patient remained permanently disease-free during follow-up after a total parotidectomy for parotid carcinoma, a right-sided cervical lymph node dissection, a laryngectomy, and subsequent chemoradiotherapy.

This finding emphasizes the crucial role of comprehensive investigation in deciding on the treatment of myoepithelial carcinoma associated with recurrent parotid gland cancer involving the epiglottis. It also suggests that the inclusion of chemoradiotherapy may provide significant benefits in the treatment of these complex cases. Continued surveillance and further research are essential to understand the long-term effects and outcomes associated with these treatment strategies.

4. Conclusion

Myoepithelial carcinoma (MEC) of the parotid gland is a rare and aggressive cancer that poses significant diagnostic and therapeutic challenges. Surgical resection is the primary treatment option. However, a comprehensive approach that includes chemotherapy and radiotherapy is crucial to improving outcomes and minimizing the risk of recurrence, particularly in cases involving epiglottis. A multidisciplinary approach, including collaboration between surgeons, oncologists, and radiologists, is essential for optimal treatment and decision-making. Given the rarity of MEC, further research is needed to refine treatment protocols, evaluate the efficacy of combination therapies, and establish standardized guidelines. In addition, molecular studies could identify specific genetic mutations or biomarkers that could lead to more targeted and personalized treatment strategies. Continued research and clinical trials are essential to better understand the pathogenesis of MEC, improve treatment options, and increase the long-term survival and quality of life of patients with this rare and complex malignancy.

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Ethics Approval

This study was approved by the Medical Ethics Committee of the Xiangya Hospital Central South University.

Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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