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A Rare Case of Clear Cell Carcinoma of the Parotid Gland in Iran

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Abstract

Introduction: Salivary gland tumors are rare head and neck lesions. The majority are benign, with only 20% of cases malignant. An epithelial-myoepithelial carcinoma is a rare low-grade malignant salivary and lacrimal gland tumor, which accounts for less than 1% of salivary gland tumors. It mostly involves the parotid gland and affects adults in their sixth and seventh decades. It is usually painless, unless the minor salivary glands are affected.

Case Presentation: We describe a rare case of a 35-year-old woman who presented with a 1-year-old unilateral painful parotid swelling in December 2014.

Conclusions: A complete immunohistochemical study should be considered in cases of malignant salivary gland tumors. To reduce the recurrence rate of these tumors, the optimum therapies are radiotherapy and chemotherapy.

Keywords: Adenocarcinoma, Clear Cell, Parotid Gland, Neoplasms

1. Introduction

Salivary gland tumors are rare head and neck lesions. The majority are benign, with only 20% of cases malignant (1). Malignant salivary gland tumors are divided into three groups: low, intermediate, and high grade (1). An epithelial-myoepithelial carcinoma is a low-grade biphasic malignant tumor (2, 3). Occasionally, a high-grade or dedifferentiated form may be observed (2, 3). This malignant tumor can occur in conjunction with hybrid salivary gland tumors, for example, in combination with adenoid cystic carcinomas and lymphoepithelial carcinomas (4, 5). This salivary gland tumor was first described by Donath et al. in 1972 and classified as a salivary gland tumor by the world health organization in 1991 (6, 7). Epithelial-myoepithelial carcinomas comprise less than 1% of salivary gland tumors, and they mostly affect the parotid gland of adults in their sixth and seventh decades (4). We describe a rare case of a young woman and the clinical, radiographic, and microscopic findings.

2. Case Presentation

A 35-year-old woman with a 1-year-old painful lesion near her ear presented to the department of oral and Maxillofacial surgery at Guilan University of Medical Sciences, Rasht, Iran in December 2014. She reported that the lesion had been small at first and had responded to analgesics. However, it had increased in size over time and had became so painful that it impaired normal functions, such as sleeping. The clinical examination revealed a 4-cm lesion, which was firm, tender on palpation and fixed to the surrounding tissue. The skin over the lesion was smooth and showed no change in color. Neither neck lymphadenopathy nor facial weakness was observed, and a review of the patient's medical records revealed nothing of note. MRI revealed a well-defined lobular and multi-septated mass, which measured $16 \times 13 \times 15$ cm on the lateral aspect of the right TMJ. It adhered to the deep lobe of the parotid gland but not to any musculoskeletal structures. (Figure 1) Superficial parotidectomy was subsequently performed under general anesthesia, and a well-circumscribed nodular mass, together with surrounding normal parotid gland tissue, was sent for a histopathological examination. Following wide surgical excision and reconstruction of the defect with an SCM muscle flap in a referral, general, governmental hospital, the patient was referred for radiotherapy and chemotherapy treatment.

The lesion comprised a piece of oval creamy colored soft tissue of $6.5 \times 4.5 \times 1$ cm, with a creamy colored surface on sectioning, and it was close to the surgical margins. Hematoxylin and eosin histological staining showed malignant neoplastic proliferation of epithelial and myoepithelial salivary gland cells in a sclerotic stroma, with a nodular arrangement and no fibro-connective capsule. In some areas, layers of polygonal cells with central nuclei, clear cytoplasm, and poorly defined margins were detected, and invasion of the surrounding nerve tissue was observed (Figure 2A). The findings suggested a differential diagnosis of myoepithelioma, clear cell carcinoma, or

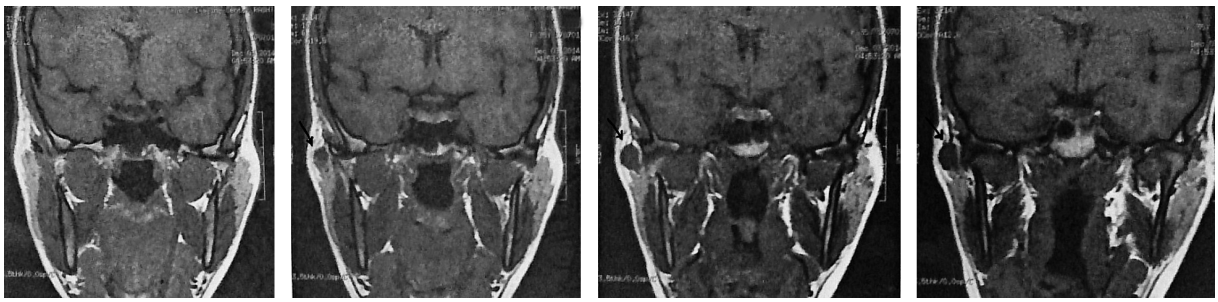

Figure 1. A well-defined, lobulated, multiseptated mass measuring about 16 × 13 × 15 mm within the lateral aspect of the right TMJ, adhering to the deep lobe of the parotid gland but unrelated to the bony structure, TMJ, or other muscles.

epithelial-myoepithelial carcinoma. Immunohistochemical staining was used for a definitive diagnosis. Cytokeratin markers were positive in epithelial duct-like structures, and S100 and smooth muscle actin (SMA) were positive in the myoepithelial part containing clear cytoplasm. Staining for the Ki-67 marker revealed that 15% of the cells were neoplastic. The immunohistochemical staining confirmed the diagnosis of an epithelial-myoepithelial carcinoma (Figure 2B). A 10-month-follow up showed no recurrence of the lesion.

3. Discussion

An epithelial-myoepithelial carcinoma is a low-grade malignant neoplasm of the salivary gland, and in rare cases, of the lacrimal gland (4, 6, 8). It is identified by its biphasic morphology, with a cuboid luminal population of cells and eosinphilic cytoplasm (4, 7). These cells are similar to intercalated duct cells and surrounded by large polygonal myoepithelial cells containing clear cytoplasm (4, 7). Epithelial-myoepithelial carcinomas mostly occur in adults in their 60s and 70s, with a female to male ratio of 2:1 (5, 6). Thus, the present case of a 35-year-old woman is very rare. The lesion in the present study was a lobular unilateral parotid mass, which measured 4 cm on palpation. Clinically, an epithelial-myoepithelial carcinoma occurs as a large lobular slow-growing mass, often unilaterally in the major salivary glands but mostly in the parotid gland, and the majority of cases are de novo (6, 7). However, they may also occur in submandibular and minor salivary glands (2). The large lobular growth of myoepithelial tumors, as opposed to an infiltrative growth pattern, is due to the low level of secretion of matrix-degrading proteinases and high level of secretion of proteinase inhibitors by myoepithelial cells (6). Epithelial-myoepithelial carcinomas are rarely associated with pain and facial weakness (4, 6, 7). According to various case reports (2, 4, 7, 9, 10), epithelial-myoepithelial carcinomas of the parotid glands are often painless, without any evidence of mucosal ulceration (4). Generally, rapid growth, pain, and facial weakness are rare and suggest a high-grade tumor. In the present study, the patient had progressive pain, which was the result of nerve invasion, as shown by the microscopic analysis of the lesion.

Various imaging techniques are used today for the assessment of parotid gland tumors (10). Ultrasound was the first technique to be used for parotid lesions because of its speed, repeatability, and noninvasive nature (10). However, as it cannot differentiate inflammatory lesions and some tumors, other methods, such as CT scans and MRI, are used today (7, 10). In studies that used ultrasound in initial assessments, MRI and CT scans were used for more accurate assessments (10). MRI and CT scans are used for comprehensive assessments of large tumors and to determine the possible relationship of lesions in parotid glands with surrounding vessels to enable grading, access for resection, and draw up a treatment plan for neck dissection (10, 11). The higher resolution and contrast of MRI make it more suitable than CT scans for the assessment of parotid tumors (10). However, to assess the presence or absence of calcification, MRI should be used in conjunction with a CT scan or other techniques. The differential diagnosis of salivary gland lesions is difficult using imaging techniques. However, the use of diffusion-weighted MR techniques promises to improve the differential diagnosis (1, 9, 10). In MRI assessments, malignant tumors of the parotid glands usually appear as medium to large (larger than 3 cm), with poorly defined margins and a heterogeneous internal pattern due to the presence of necrotic areas (9, 10). In the present study, the MRI assessment of the patient revealed a lobular lesion, with a well-circumscribed margin similar to that seen in soft tissue neoplasms. These findings were similar to an MRI image in a study by Piscioli et al. (10) but dissimilar to those descried by Tongeren et al. (9). In that study, an axial T1 assessment revealed a lesion

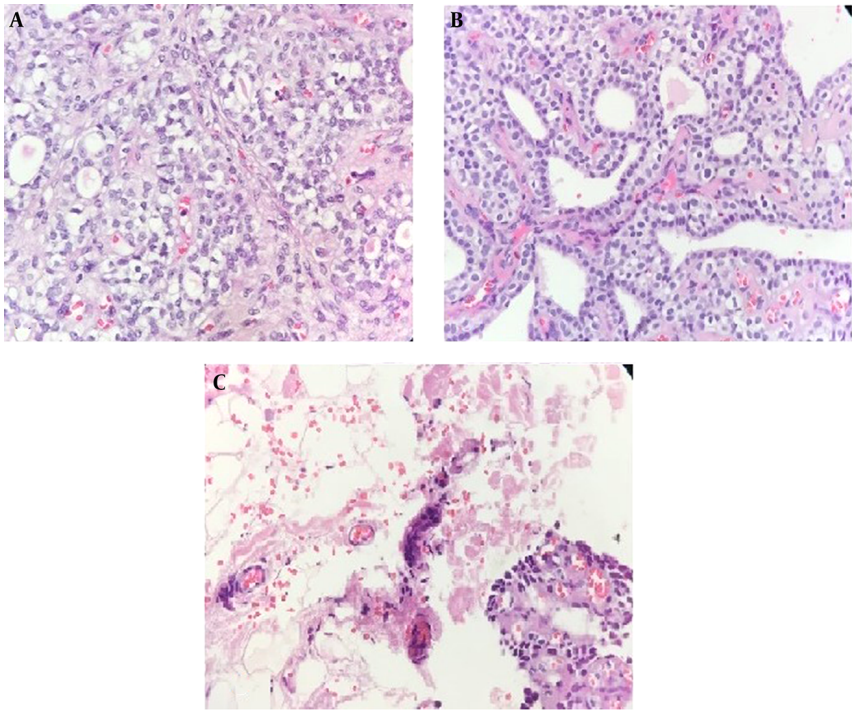

Figure 2. A, B Hematoxylin and eosin histological staining revealed malignant neoplastic proliferation of epithelial and myoepithelial salivary gland cells in a sclerotic stroma, with a nodular arrangement. An area of clear cells can also be seen (× 40). C. Vascular invasion (× 40).

Table 1. Patient's Clinical Data

Clinical Information	Data
Age	35
Gender	Female
Chief Complaint	1-year-old painful mass near the ear
Signs and Symptoms	Painful, fixed and firm lesion, without change of color and tender on palpation
Lymph-Adenopathy	None
Past Medical History	None
MRI Findings	Well-defined, lobular, and multi-septated mass adhered to the deep lobe of parotid
Treatment	Wide surgical excision and reconstruction of the defect with an SCM muscle flap
Final Diagnosis	Epithelial-myoepithelial carcinoma

with a poorly defined margin. Generally, on CT scans and MRI, epithelial-myoepithelial carcinomas cannot be differentiated from other parotid neoplasms (7).

Epithelial-myoepithelial carcinomas are considered low-grade malignant tumors of the salivary gland, with 81.8% 10-year survival (4, 8). Similar to breast and skin lesions, the diagnosis is based on the observation of a dual structure of cuboid epithelial cells with eosinophilic cytoplasm in the luminal layer and myoepithelial cells with surrounding clear cytoplasm, together with confirmation of the diagnosis by immunohistochemical staining (2, 4, 5). The observation of a solid growth pattern, nuclear atypia, aneuploid DNA, necrosis, a positive surgical margin, and high proliferative activity are indicative of local recurrence and metastasis of this tumor (4). In immunohistochemical staining of epithelial-myoepithelial carcinomas, epithelial markers, such as CK5, 6, 7, and 14 are used (4, 5). The epithelial component also stains positive

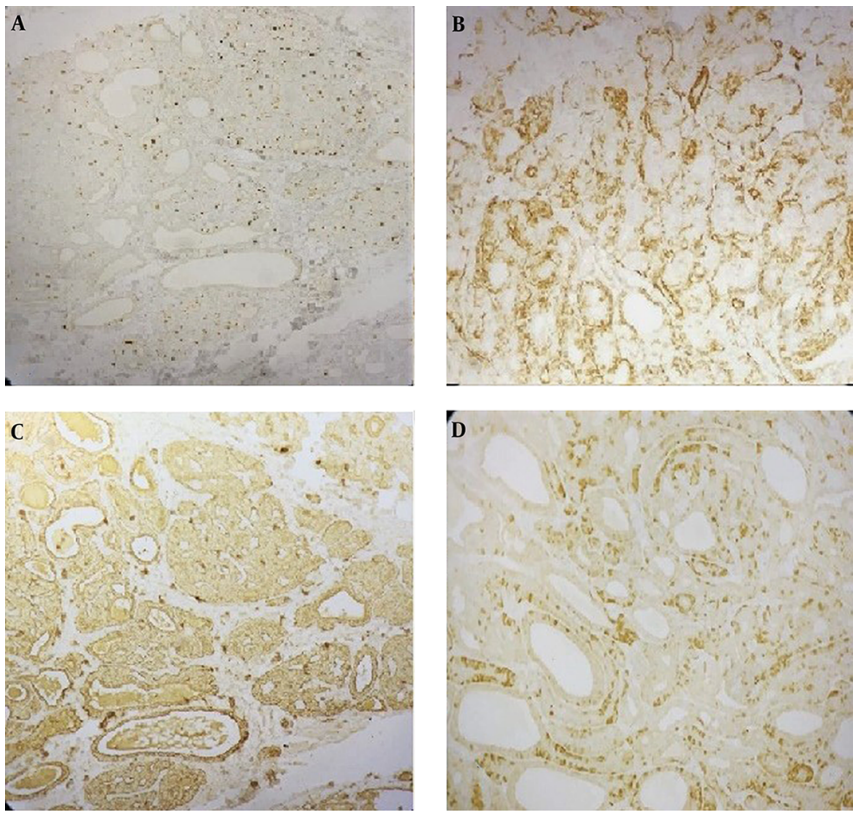

Figure 3. Ki-67 Immunostaining × 10, SMA immunostaining × 10, CK immunostaining × 10, and S100 immunostaining × 10.

with S100, EMA, and SMA markers (4, 5). In the present study, the epithelial component tested positive with the CK marker. Calponin, GFAP, SMA, P63, and CD10 are used for staining the myoepithelial component. Calponin is a smooth muscle-specific antibody used for staining myoepithelial cells in salivary gland tumors (5). It has moderate sensitivity and specificity (5). According to Savera et al., 75% of myoepithelial carcinoma cells were stained by calponin (12). In a study by Seethala et al., 59.1% of epithelial-myoepithelial carcinoma cells were positive using the calponin marker (13). In the present study, we used SMA to assess the presence of myoepithelial cells due to its availability and relatively high sensitivity and specificity, which turned positive, confirming the presence of these cells and therefore epithelial-myoepithelial carcinoma. S100 antibodies, vimentin, GFAP, and P63 are also used as nonspecific markers to assess myoepithelial cells (5). In the present study, the cells stained positive for S100, revealed the presence of a myoepithelial component. The Ki-67 staining (MIB-1 index) usually varies from 5% - 10% for epithelial-myoepithelial carcinomas (5). In the present study, it was 15%, which was higher than normal. As reported earlier, the MIB1 index, solid growth pattern, nerve invasion, and tumor size have no effect on the prognosis of a lesion (4). According to previous studies, only nuclear atypia in more than 20% of tumor cells can adversely affect the prognosis of a lesion (4, 14).

The recurrence rate of epithelial-myoepithelial carcinomas has been reported to be 35% - 50%,with metastasis in 8.1% - 25% of these cases (13). The 5-year and 10-year survival of patients following complete surgical excision were 93.5% and 81.8%, respectively, in a study by Seethala et al. and 87% and 67.5%, respectively, in a study by Maurer et al. (13, 15).

Footnote

Authors' Contribution: Bardia Vadiati Saberi participated in the execution, case report design, interpretation of the data, and drafting of the manuscript; Shirin Modabbernia participated in the execution of the immunohistochemical component of the study; Shirin Modabbernia also made the original diagnosis of the case, conceived the study design, participated in the analysis, data interpreta-

tion, and drafting of the manuscript; All the authors critically reviewed and approved the final manuscript.

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