Epithelial-myoeipithelial carcinoma of the lower alveolus

Epithelial-myoeipithelial carcinoma (EMC) is a biphasic tumor and classified as a low-grade tumor of the salivary glands. EMC commonly occurs in the parotids with a reported incidence of around 1% out of all neoplasms of the salivary glands and it is a rare tumor of the minor salivary glands in the oral cavity, especially on the lower alveolus. A 48-year-old male patient presented with a rapidly progressive ulcer-infiltrative growth on the lower alveolus with involvement of the overlying cheek skin in a short span of period. We describe here a case of locally advanced EMC of the lower alveolus, its diagnosis by histopathological examination and immunohistochemical staining, and management by surgery and local external beam radiotherapy (EBRT). In our limited experience in the treatment of EMC on the lower alveolus, wide local excision of the tumor, followed by EBRT had resulted in a good therapeutic outcome at the 3 years posttreatment follow-up. In conclusion, EMC of the lower alveolar mucosa is extremely rare, and patients should also be advised close follow-up for the detection of loco-regional recurrences after treatment.

Key words: Epithelial-myoeipithelial carcinoma, lower alveolus, minor salivary glands

INTRODUCTION

Epithelial-myoeipithelial carcinoma (EMC) is a biphasic tumor and classified as a low-grade tumor of the salivary glands. The tumor was first described by Donath et al. in 1972. EMC was recognized as early as 1956. EMC is commonly seen in the parotid gland. However, it also occurs in the minor salivary glands (MSGs) with a reported incidence of around 1% out of all neoplasms of the salivary glands. EMC has also been reported in extremely rare sites such as the base of the tongue. Histology of EMC is characterized by variable proportions of duct-forming eosinophilic cells and myoeipithelial differentiated clear cells surrounding the duct-forming cells. Immunohistochemical (IHC) staining is often needed for the confirmation of diagnosis. We describe here a case of locally advanced EMC on the lower alveolus and its management.

CASE REPORT

A 48-year-old male patient presented with the complaint of a progressive, painless ulcer on the left lower gum of 1-month duration and progressive blackish discoloration of the skin of left cheek region of 15 day’s duration. The patient was a smoker and tobacco chewer. On extra-oral examination, there was an area of 4 cm × 3.5 cm indurations of the skin on the left cheek region [Figure 1a]. A lymph node of 1 cm × 2 cm in size, hard, nontender and mobile was palpable on the left submandibular region (level IB). Intra-oral examination showed an ulcer-infiltrative growth on the left lower alveolus, adjacent lower gingival buccal sulcus and the buccal mucosa. Orthopantogram showed erosion of the underlying bone [Figure 1b]. Punch biopsy from the margin of ulcer-infiltrative growth for the 1st time revealed inflammatory granulation tissue lined by squamous epithelium and no evidence of malignancy. Second biopsy from a deeper tissue and the interdental tissue after the extraction of 34 and 35 teeth revealed malignancy of epithelial tumor showing glandular differentiation [Figure 2]. IHC was done for cytokeratin (CK), vimentin, S-100 protein and smooth muscle actin (SMA). IHC staining was positive for the expression of CK, S-100, SMA, and vimentin [Figure 3a-d]. The diagnosis of EMC was confirmed after histopathological examination (HPE) and IHC.
The patient was treated by surgery, followed by local radiotherapy. Wide local excision of the growth along with left segmental mandibulectomy and involved cheek skin was done with a margin of 1 cm normal tissue. Left sided modified radical neck dissection preserving the spinal accessory nerve, and the internal jugular vein was done for the lymphatic clearance. The defect was repaired by the ipsilateral pectoralis major myocutaneous flap. The resected specimen in was sent for the final HPE, which also revealed EMC as the final diagnosis. The examination of regional lymph nodes on the neck dissection specimen revealed 2 out of 21 nodes were involved without any perinodal spread. The patient further received 25 fractions/50 gray of external beam radiotherapy (EBRT) after 4 weeks from the date of surgery. On the follow-up, after 3 years following the treatment, the patient was disease free with grade 1 trismus [Figure 4].

**DISCUSSION**

Epithelial-myoeipithelial carcinoma is a rare tumor of the MSGs in the oral cavity, especially on the lower alveolus. MSGs are distributed throughout the mucosa of the oral cavity and nasopharynx. MSGs of the oral cavity are at the risk of developing malignancy and over 30 histologically distinct tumors may arise from it. Though this not the 1st case of oral EMC, but its presentation is unusual in many ways. In the oral cavity, EMC has been seen at the palate and buccal mucosa. EMC is also seen in extra oral sites such as the para-nasal sinuses, pharynx, and the bronchus. Epithelial myoeipithelial tumor rather than a carcinoma has been reported in the trachea. Angiero et al. in a series of oral EMCs have demonstrated that in males it is seen above 75 years of age, however in the present case the patient was of 48 years of age. EMC mostly presents as ulcer-proliferative growth in the oral cavity, however, in the present case it presented with an ulcer-infiltrative with involvement of the cheek skin in a short span of period according to the history of the patient, and thus, it mimicked a clinically aggressive malignancy of the mandibular alveolus. Biopsy had to be taken twice from the growth and a deeper tissue for biopsy after dental extraction was required to establish the definitive histological diagnosis, and it highlights the infiltrative nature, which was associated with the erosion of underlying mandibular erosion.

The origin of EMC is considered to be derived from the intercalated ducts of salivary glands. With the use of morphologic and immunphenotypic differentiation, the current concept of origin of EMCs is not specific to any cell of origin. The histological differential diagnoses of this rare tumor are myoeipithelial carcinoma,

![Figure 1](image1.png) (a) The external skin grossly involved by the lower alveolar growth, (b) Orthopantogram showing the involvement of mandible

![Figure 2](image2.png) Photomicrograph of (H and E, ×40) showing neoplastic tubules lined by 2 types of cells, central cuboidal with eosinophilic cytoplasm surrounded by cells with clear cytoplasm

![Figure 3](image3.png) Immunohistochemical staining (×40) showing the staining of (a) Cytokeratin, (b) S-100 (c) smooth muscle actin and (d) Vimentin

![Figure 4](image4.png) Follow-up intra-oral picture with grade 1 trismus and no evidence of disease
clear cell carcinoma, and pleomorphic adenoma. IHC is required to
differentiate this tumor from similar tumors such as pleomorphic
adenoma and adenoid cystic carcinoma.\textsuperscript{[10]} The histology of EMC
is characteristic, and in the present case classic biphasic tubular
histology of inner ductal cells with cuboidal epithelium and outer
clear myoepithelial cell layers was demonstrated on hematoxylin and
eosin stain. IHC confirmed the biphasic nature of this tumor. In the
present case, the IHC was positive for the expression of CK, which
revealed its epithelial component and IHC positivity for vimentin,
SMA and S-100 protein confirmed the myoepithelial component and
hence the diagnosis of EMC could be confirmed. Nuclear protein
p63 is a sensitive and specific marker for myoepithelial cells,\textsuperscript{[11]}
though it was not done in the present case.

Treatment of EMC of the palate has been reported with surgery,
followed by EBRT without recurrence at 2 years follow-up.\textsuperscript{[8] In the
present case of EMC in the lower alveolus, the patient was treated by
surgery, followed by EBRT and the surgery in the present case was
radical in view of the widespread involvement of the disease. The
response of the treatment was good as there was no local recurrence
or metastasis at the 3 years follow-up. Role of chemotherapy is not
clear in EMCs, and it has been shown to stabilize the disease in the
case of a metastatic EMC.\textsuperscript{[13]} Ren et al. have advocated the use of
chemotherapy only as an adjuvant therapy along with radiotherapy
and surgery as the prime modality of treatment.\textsuperscript{[14] In our limited
experience and considering the rarity of this entity, treatment
with surgery followed by EBRT without chemotherapy should be
considered as sufficient.

Seethala et al. in a series have shown the recurrence rate of 36.3% in
EMCs.\textsuperscript{[9]} In the present case, there was no loco-regional recurrence
after 3 years. Furthermore, in the present case the patient presented
with an aggressive ulcer-infiltrative growth of less than a month's
duration with considerable involvement of the cheek skin and
underlying bone and so, EMC as a low grade tumor in the present
situation is contrasting with that of the histopathological appearance.
Yu et al. have suggested that EMCs should be classified as high-grade
malignancies.\textsuperscript{[8]}

**CONCLUSION**

Epithelial-myoeoepithelial carcinoma of the lower alveolar mucosa is
extremely rare. However, there is a report of myoepithelial carcinoma
of the maxillary sinus arising from a pleomorphic adenoma.\textsuperscript{[14]} In
view of its aggressive clinical course, the patient should be offered
multi-modality treatment with wide local excision and EBRT. The
patients should also be advised close follow-up for the detection of
locoregional recurrences after treatment.

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