Epithelial-myoepithelial carcinoma is a biphasic low grade malignant tumor, which represents approximately 1% of all salivary gland tumors. This tumor occurs mostly in parotid gland, followed by submandibular gland and minor salivary glands. Women, mostly fifth to eighth decade of life, are commonly affected. Histopathologically, epithelial-myoepithelial carcinoma is composed of inner single layer of eosinophilic cuboidal ductal cells and outer single or multiple layers of clear myoepithelial cells. We present a case of a 69 years old man who had a scar on lower lip for 10 years and voice annoyance for 3 months. The biopsy for lower lip was reported “infiltrative clear cell epitheloid neoplasm” and vocal cord biopsy result was “verrucous carcinoma”. After cordectomy and wedge resection of lower lip, histopathology revealed Epithelial-Myoepithelial Carcinoma for lower lip and microinvasive verrucous carcinoma for left vocal cord. Our case has very uncommon location and presentation for EMC. The tumor location was minor salivary glands of lower lip and the clinical presentation was quite different. Coexistence with microinvasive verrucous carcinoma of vocal cord is the other unique part of our case.

Keywords: Epithelial myoepithelial carcinoma; microinvasive; minor salivary glands; verrucous carcinoma.
CASE REPORT

A 69 year-old male patient, former smoker (40 package-year), submitted to our out-patient clinic for a lower lip mass with a one year-duration growth. Mass was located on the skin 0.5 cm below the lower lip vermilion border in the median line. The lesion measured approximately 2x1.5 cm. The lesion was continuous through the oral mucosa. It was non-tender, non-compressible nodular mass without any pulsation on skin side. However, in the oral mucosal side, lesion was ulcerative centrally (Fig. 1A, B). There was no palpable cervical lymph node. Skin lesion was the reason for the admission and the patient was unaware of oral mucosal involvement. MR showed a lesion with periferic contrast in submental area and its size was approximately 27x17 mm. A biopsy was taken from there and histopathologically it was an infiltrative clear cell epitheloid neoplasm. The differential diagnosis was including tumors of salivary glands and adnexal tumors. The patient also had voice annoyance for 3 months. He had a vocal cord biopsy from another hospital. The pathology report was compatible with verrucous carcinoma. Upon this, the patient underwent cordectomy for verrucous carcinoma and wedge resection of lower lip for the ulcerated lesion.

On gross examination of wedge resection of lower lip, there was a ulceroinfiltrative tumoral lesion on skin. Its size was 2x2x1.5 cm. Histopathologically, the tumor, under the ulcerated epithelium, had an invasive growth pattern to the dermis, resulting multiple tumor nodules between the sclerotic stroma. The tumor showed bicellular architecture, clear polygonal myoepithelial cells and cells forming duct with round central nuclei (Fig. 2) Mild atypia was seen, there were no atypical mitoses and perineural invasion.

Immunohistochemically, epithelial cells forming duct were positive for EMA (Fig. 3), Pan-CK, CK7 , the myoepithelial cells were positive for p63, p40 (Fig. 4), HM-WCK (Fig. 5), CK5/6. Ki-67 index was %5 (Fig. 6) and p53 had wild type expression.

In two vocal cords, there were verrucous carcinoma (Fig. 7). The tumor size was 1.5 cm in left vocal cord and
0.9 cm in right vocal cord. In left vocal cord, microinvasion was seen (Fig. 8). There was no lymphovascular invasion or perineural invasion.

**DISCUSSION**

EMC is a low-grade malignancy, rarely transforms to high-grade or dedifferentiated EMC [4]. It is mostly arise in the major salivary glands, the rate of involving minor salivary glands is 5.1%; only one case involved the buccal mucosa [7].

Histopathologically, EMC is characterized by a glandular structure consisting of inner epithelial cells and outer myoepithelial cells. The inner layer is composed of cuboid or low columnar ductal epithelial cells with eosinophilic cytoplasm and round central nuclei. The outer layer consists of polygonal large myoepithelial cells with eccentric nuclei and the cytoplasm is pale or clear [3]. The external basement membrane underlies the myoepithelial cells. The stroma consists of almost acellular collagen. Rarely, tumors may invade the blood vessels or perineurium. Mitotic figures and nuclear pleomorphism are rarely present [1]. Immunohistochemical staining
is essential to identify the double layer cell morphology in this tumor. The inner-layer cells are positive for cytokeratin, EMA, and carcinoembryonic antigen, and the outer-layer cells are positive for SMA, p-63, S-100, and vimentin [1, 4]. In the present case, the double structure was recognized by CK7, EMA, p40 positivity.

Myoepitheliomas, myoepithelial carcinomas, clear cell oncocytomas, clear cell carcinomas, acinic cell carcinomas, mucoepidermoid carcinomas, and metastatic clear cell tumors are the clear cell dominated tumors which are in the differential diagnosis of EMC [1].

Epithelial-myoepithelial carcinoma has the double layer of inner cuboidal epithelial cells and outer clear myoepithelial cells. Myoepithelioma and myoepithelial carcinoma are composed of only myoepithelial cell layer. Immunohistochemistry can help to separate the two layers when they are histopathologically indistinct [8]. Oncocytoma may be sometimes dominated by clear cells, but mostly typical oncocyes are present. The clear cells often have pale granular cytoplasm with PAS positive granules in oncocytoma [9]. Clear cell carcinoma is seen in minor salivary glands and the tumor cells do not express S-100 for myoepithelial differentiation [10]. The clear cells in acinic cell carcinoma are not generally true clear cells. They represent as a fixation artefact. The characteristic secretory granules of normal acinic cell carcinoma can be seen with a careful search [11]. The clear cells of mucoepidermoid carcinoma contain PAS positive neutral mucin and squamous differentiation. Clear cells in a salivary gland tumor can originate from a metastatic carcinoma.

The immunohistochemical profile of renal carcinoma is different from salivary gland, and has not the biphasic pattern of epithelial-myoepithelial carcinoma [12].

Local recurrence of EMC found 23% to 50% of cases, lymph node metastases found 17% to 23%, and distant metastases to lung, kidney and brain found 8–10% of cases [13, 14]. EMC is characterized by a relatively good prognosis. If tumor size is 4 cm or more, solid tumors predominantly clear cells, forming nests and sheaths, the prognosis is worse [15].

Our case is located in minor salivary gland in oral buccal area and macroscopically caused ulceration on lower lip cutaneous side. Verrucous carcinoma on the vocal cord is detected synchronously in this patient. Morphologically, there were two separate lesions and no similarity between EMC and microinvasive verrucous carcinoma.

In conclusion, EMC of minor salivary glands is very rare and its ulceration effect on the skin hasn’t reported in any study. EMC can be found with other salivary gland tumors [16]. There is no data about the coexistence of EMC and the tumor of different anatomic site in the literature. The present case is unique for its location, clinical presentation, coexistence with microinvasive verrucous carcinoma of vocal cord. EMC in minor salivary glands and its involvement of other sites deserves wider recognition.

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