Adenoid Cystic Carcinoma of the Buccal Mucosa with Rare Delayed Frontal Bone Metastasis: A Case Report

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Abstract
Adenoid cystic carcinoma (AdCC) is a malignant neoplasm, which accounts for 5-10% of all salivary gland tumors (1). About 50% of these tumors originate from intraoral minor salivary glands usually in the hard palate (1). Three clinically obvious characteristics of AdCC include slow growth rate, perineural invasion and high incidence of distant metastasis (1). The most commonly-affected sites of distant metastasis are bone, liver and brain, followed by lungs (2). Lymph node metastases are rare; The most common sites involved by hematogenous spread are lungs (2). This is a report about a patient with a rare form of AdCC on buccal mucosa with an unusual metastasis to the frontal region after a two-year follow up.

Key words: adenoid cystic carcinoma, buccal mucosa, frontal metastasis.

Introduction
Adenoid cystic carcinoma (AdCC) is a rare type of salivary gland tumor (3). This tumor occurs most often in the minor salivary glands of the oral cavity rather than in major salivary glands (1, 2, 3). About 50% of these tumors arise in the minor salivary glands of hard palate (4). It has also been reported in other organs such as lungs, uterine cervix, breast, skin and the upper digestive tract (5). AdCC is characterized by a number of clinical features including slow growth rate, perineural invasion, local recurrence, delayed onset of distant metastasis and prolonged clinical course (1, 2, 4, 5 ). AdCC has a poor prognosis especially in minor salivary glands compared to major salivary glands (2).
In the present case, AdCC was located in a rare region of the oral cavity, the buccal mucosa, with a subsequent metastasis in an unusual region after a two-year follow-up (i.e., the frontal area). We emphasize that the early diagnosis of malignant tumors in the oral cavity can facilitate patients’ treatment and help prevent worsening prognosis in patients with malignant tumors.

**Case Report**

A 47-year-old male referred to the Department of Oral Medicine, School of Dentistry, Mashhad, Iran. With the chief complaint of a mass on the right buccal mucosa (Fig. 1). The patient reported that the lesion first appeared three years before, initially observed as a small swelling in the right buccal vestibule of maxilla, interfering with proper fitting of denture. The swelling progressively increased up to its present size during the previous five months. He also reported slight pain while eating and tenderness on palpation.

**Clinical examination**

An intraoral examination revealed a swelling on the right buccal mucosa, which was about 3 cm in the maximum dimension, extending superiorly from the tuberosity and inferiorly to the inferior border of the mandibular angle (Fig. 2a). On palpation, the swelling was firm in consistency with an irregular and well-circumscribed border (Fig. 2b). The overlying mucosa was normal in color and its surface was smooth except for a granular area of 1 cm. Moreover, leukoedema was observed on the right buccal mucosa. The color of the overlying skin was normal and no regional lymph nodes were palpable. Since the swelling was located anterior to the parotid gland, salivary secretion was not altered and there was no evidence of facial nerve dysfunction. There was also no relevant medical history. The patient underwent sonographic examination and computed tomography (CT) scan. The sonographic image showed an infiltrative solid mass on the right buccal mucosa. The CT image revealed an infiltrative solid mass on the right buccal mucosa adjacent to the lateral wall of the right maxillary sinus and the dento alveolar process. The tubular structure of the lesion was suggestive of hyper vascularity and vascular malformation. The adjacent bones were normal in the CT image. Based on the history and clinical examination, provisional diagnoses of salivary gland tumors and mesenchymal tumors were given.

An incisional biopsy was taken under local anesthesia. Histologically, the lesion was composed of isomorphic hyperchromatic basaloid tumor cells arranged in a cribriform pattern with pseudocystic structures. The tumor cells were small and cuboidal in shape. The tumor cells also invaded the peripheral skeletal muscle and fat tissue. In addition, superficial ulceration was observed. The histological features were suggestive of AdCC (Fig. 3). As tumoral invasion was not detected in the histological examination of the six submandibular lymph nodes, the diagnosis of stage I (T₂N₀M₀) was established. The absence of metastases was confirmed by CT and bone scan. Surgical excision of the lesion with skin grafting was carried out (Fig. 4).

The patient received 35 cycles of chemotherapy and radiotherapy. For chemotherapy regimen, cisplatin and 5-fluorouracil were applied. Two years later, the patient referred to our department with the chief complaint of a firm mass (1.5 cm) on the right side of his frontal region which had appeared since 2 months before (Fig. 5). The overlying skin was normal and the diagnosis of AdCC was made following an incisional biopsy (Fig. 6). The patient was referred to an oncologist for chemotherapy and further assessment. After performing CT-Scan, lung metastasis was also detected. Therefore stage IV was identified for the patient.

Three cycles of cisplatin and 5-fluorouracil was started for the patient. As no change was observed in the size of the frontal tumor, the chemotherapy was continued with Taxol and carboplatin for 3 cycles. The patient is now under the supervision of oncologists.
Discussion

Head and neck malignancies of the salivary glands are relatively rare, constituting 7% of all neoplasms in this area (3). AdCC, which was previously referred to
as cylindroma, accounts for 10 % of these malignancies (3). However 30-50% of primary tumors of buccal mucosa are malignant; however, it is a rare area for AdCC occurrence (2). To the best of our knowledge, our case is the sixth case with involvement of this region. Five studies performed in India have reported AdCC on the buccal mucosa (1, 2, 4, 5, 6) (Table 1). In the present case, the patient referred to our department two years later with a mass on his frontal region. As the distant metastasis of AdCC to the lung and bone is more frequent than metastasis to the head and neck area, the current lesion could not certainly be diagnosed as a metastatic form of AdCC in the frontal region and may simply be a second primary tumor. AdCC is the second most common malignancy of salivary glands preceded by mucoepidermoid carcinoma, occurring predominantly in the fifth and sixth decades of life with a slight female predilection (2, 7). Nailk et al. and Sanji et al., reported AdCC in male patients, whereas other authors have mainly reported this tumor in female patients (1, 2, 4, 5, 6). Our case also occurred in a 47-year-old male. Approximately 25-50% of AdCCs metastasize distantly, especially to the lungs and bones. In addition, lymph node metastasis is relatively rare (4, 8). It should be noted that in this study, we are the first to report a case of AdCC metastasis from the buccal mucosa. AdCC is characteristically associated with small size and slow, progressive growth (2, 4, 5, 9). Our patient also complained of a slow-growing swelling for about three years. Furthermore, the tumor has a propensity for perineural invasion, which may cause pain in patients with AdCC (2, 4, 5, 9). Pain resulting from the AdCC of buccal mucosa was detected in the studies by and the solid pattern (4, 10). AdCC is classified as grade I (with cribriform or tubular patterns), grade II (with less than 30% solid pattern) or grade III (greater than 30% solid pattern) (11). In the present case, the cribriform pattern of AdCC was dominant.

### Table 1. Cases of Adenoid cystic carcinoma occurred on the buccal mucosa

<table>
<thead>
<tr>
<th>Authors</th>
<th>Year published</th>
<th>Country</th>
<th>Age &amp; Gender</th>
<th>Tumor location</th>
<th>Symptom</th>
<th>Follow up</th>
<th>Metastasis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Singh S</td>
<td>2010</td>
<td>India</td>
<td>50-year-old male</td>
<td>Right buccal mucosa</td>
<td>Slight pain</td>
<td>3 years</td>
<td>-</td>
</tr>
<tr>
<td>Ajila V</td>
<td>2012</td>
<td>India</td>
<td>48-year-old female</td>
<td>Left buccal mucosa</td>
<td>Painful</td>
<td>3 years</td>
<td>-</td>
</tr>
<tr>
<td>Nailk LR K</td>
<td>2013</td>
<td>India</td>
<td>48-year-old male</td>
<td>Right buccal mucosa</td>
<td>Painful</td>
<td>10 years</td>
<td>-</td>
</tr>
<tr>
<td>Kumar AN</td>
<td>2013</td>
<td>India</td>
<td>26-year-old female</td>
<td>Right buccal mucosa</td>
<td>Painful on palpation</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>VIDYALAKSHMI S</td>
<td>2014</td>
<td>India</td>
<td>34-year-old female</td>
<td>Left buccal mucosa</td>
<td>-</td>
<td>6 months</td>
<td>-</td>
</tr>
<tr>
<td>Dalirsani Z</td>
<td>2016</td>
<td>Mashhad</td>
<td>47-year-old male</td>
<td>Right buccal mucosa</td>
<td>Painful on palpation</td>
<td>2 years</td>
<td>Metastasis to the frontal region</td>
</tr>
</tbody>
</table>

### Prognosis and treatment

Surgery, radiotherapy, chemotherapy and combined therapy are therapeutic modalities for AdCC. Surgery with free margins is the treatment of choice. Surgery followed by radiotherapy consists of 5 daily treatments per week, for a period of approximately 6 weeks (3). It is noted that neutron therapy can achieve more reasonable local control as the primary mode of treatment compared to photon therapy. Stereotactic body radiation therapy such as Novalis, Cyber knife and TomoTherapy are used for destroying tumour cells (3). Chemotherapeutic regimens for AdCC include Palitaxel, Doxorubicin, Vincristin, Epirubicin, Mitoxanthrone, 5-Fluorouracil and Cisplatin. Molecular Targeted Therapy is also a promising approach in cancer treatment. It uses certain drugs such as Imatinib (against CD117), Gefitinib (against EGFR), Lapatinib and Cetoximabm in treating AdCC. The role
of immunotherapy, gene therapy and hormonal treatment for AdCC are still undergoing clinical trials. For the present case, surgery, radiotherapy and chemotherapy were performed (3, 12, 13).

Clinical stage, perineural invasion, observed histologic variable, surgical margin status, tumor site and cervical metastasis are the main factors determining AdCC prognosis (14). Distant metastasis is a significant characteristic of this tumor even in cases with sufficient local surgery (3). AdCC is associated with poor long-term prognosis with better prognosis in major salivary glands compared to minor types (2). In the reported case, metastasis to the frontal region was noted after two years. In other studies reporting AdCC on the buccal mucosa, no recurrence of metastasis was observed.

References

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