

Immunohistochemical Analysis in Salivary Duct Carcinoma of the Upper Labial Mucosa: A Rare Case Report

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ABSTRACT

Salivary Duct Carcinoma (SDC) is a rare typically high grade, aggressive malignancy arising from the ductal epithelium of salivary glands characterised by ductal formations and central necrosis having pathomorphological resemblance to ductal breast carcinoma. Parotid and submandibular salivary glands are the most commonly affected while very few cases involving the minor salivary glands of the palate, labial mucosa, floor of mouth have been reported. This high grade malignancy must be treated aggressively by complete local excision with radical neck dissection and postoperative radiation therapy seems to offer maximum benefit for the patients. This article highlights a case of a 80-year-old male patient having an intraoral ulcer over a swelling which was since five years on the left side of upper lip with left submandibular lymph nodes enlargement is reported. An immunohistochemical analysis of the biopsy specimen was carried out which concluded a SDC. The swelling was surgically excised followed by postoperative radiotherapy and adjuvant chemotherapy. The patient was on a regular follow-up for two and a half years without any local recurrence or distant metastasis.

Keywords: Adenocarcinoma, Comedonecrosis, Minor salivary gland

CASE REPORT

A 80-year-old male patient was relatively asymptomatic before five years when he noticed a small pea sized swelling in the upper lip region which was gradually increasing in size but patient did not consult any doctor for the same. However, patient got concern when he noticed an ulceration over the same swelling since last 20 days. There was no pain or paraesthesia without any history of bleeding or pus discharge from the same. Then he consulted private hospital where Computed Tomography (CT) scan of head and neck region was done and patient was referred to a tertiary health care centre. Patient had no past medical history and family history. Patient was having a habit of bidi smoking 5-7 per day and Khaini (form of tobacco) placement in lower labial vestibule for 2-3 minutes for 8-10 times a day since 10 years.

On inspection a single ill-defined swelling of size approximately 2×2 cm was present extraorally over the left side of upper lip. Intra orally a single well defined ulcerative lesion having greyish white floor with well-defined white margins was present over the swelling of left labial mucosa [Table/Fig-1]. On palpation, swelling was well defined, smooth, lobular, and freely mobile with an overlying ulceration [Table/Fig-2]. Ulcer was having a nodular base, firm consistency, non tender without any fixity to the underlying structure or any bleeding/discharge. Left submandibular lymph nodes were palpable, enlarged, firm in consistency and mobile. In addition to this, patient had smoker's melanosis, nicotina stomatitis and homogenous leukoplakia. Clinically, there were diffuse melanin pigmentation in the oral cavity, blanching of the palate, inflamed minor salivary glands of palate and homogenous white patches in relation to bilateral buccal mucosa and alveolar ridges. Clinically, minor salivary gland neoplasm, squamous cell carcinoma and tuberculous ulcer were suspected.

Chest X-ray of the patient was normal. Contrast CT scan of the head and neck region revealed 29×25×19 mm sized heterogeneously enhancing solid nature lesion in upper lip on the left side with internal vessels [Table/Fig-3]. Also, few enlarged lymph nodes were noted in left submandibular region largest measuring 25×18 mm in size. After performing incisional biopsy the sample was send to Oral Pathology Department. Histopathological examination revealed a

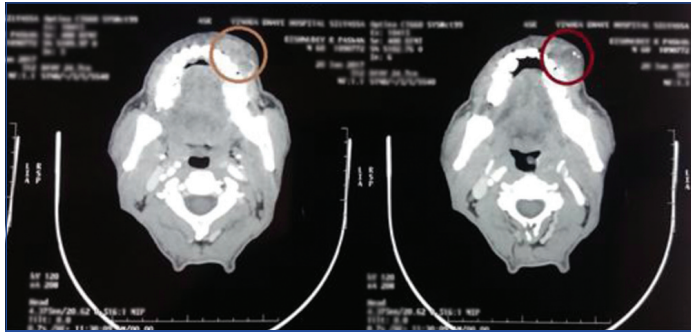


[Table/Fig-1]: Intraoral picture showing an ulcerated swelling on the left side of upper lip.

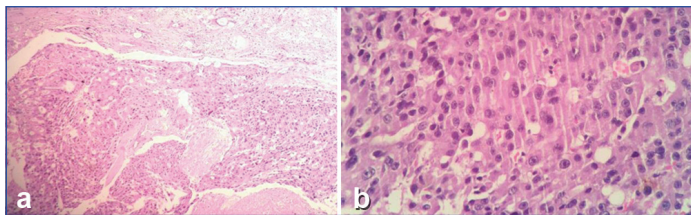


[Table/Fig-2]: Extraoral picture showing a swelling on the left side of upper lip.

poorly differentiated carcinoma favouring squamous cell carcinoma. Few areas of glandular structures and comedonecrosis were seen which was suggestive of adenocarcinoma [Table/Fig-4a,b]. Hence, Immunohistochemistry (IHC) was done which showed GCDFFP-15, PR (focal weak positive 4-5%), Carcinoembryonic Antigen (CEA) and CK7 (creatine kinase) markers positive and P63 negative which concluded SDC.



[Table/Fig-3]: Contrast CT scan shows heterogeneously enhancing solid lesion in labial mucosa.



[Table/Fig-4]: a) A 10X magnification H&E section shows atypical ductal epithelial cells, cribriform growth pattern and b) 40X magnification H&E section shows polygonal shaped cells with nuclei.

In present case of SDC of upper labial mucosa staging of lesion was done T2 N1 M0 i.e., stage 3 was reported. The lesion was surgically excised with radical neck dissection followed by postoperative radiotherapy with adjuvant chemotherapy. Radiotherapy was given for four weeks and carboplatin 100 mg/m² weekly. Patient was disease free and on regular follow-up since two and a half years [Table/Fig-5].



[Table/Fig-5]: Postoperative intraoral view showing complete surgical excision and extraoral view showing radical neck dissection of left side.

DISCUSSION

The SDC is a rare aggressive malignancy arising from the ductal epithelium of salivary glands characterised by ductal formations and central necrosis described by Kleinsasser O et al., in 1968 representing 1-3% of all malignant salivary gland tumour [1,2]. It was officially defined as a distinct clinicopathologic entity in the revised histologic classification of salivary gland neoplasms by the World Health Organisation (WHO) in 1990 [3,4]. It is also a type of rare adenocarcinoma showing cribriform pattern and comedonecrosis as seen in ductal carcinoma of breast [5].

Tumours of the minor oral salivary glands are generally stated to account for about 15% of all salivary gland neoplasms [6]. SDC predominantly affects male >50 years of age. Similarly the present case was of a 80-year-old male patient. Usually, patients notice

a slow growing painless mass initially and in advanced stages complain of pain, paraesthesia, pressure etc., due to facial nerve involvement in cases of parotid gland involvement. In the present case, patient had a complaint of a slow growing painless mass since 5 years. Also, there was an ulceration over the swelling located in the upper lip on the left side. There was no pain or paraesthesia without any history of bleeding or pus discharge from the same. The appearance of the ulcer was completely different from a usual squamous cell carcinomatous ulcer in which there are multiple red papillary projections, indurated base and borders with bleeding on slightest provocation and rapidly spreading in nature [5,7].

The asymptomatic slow growing swelling and the long duration (5 years) was most likely to be suggestive of a benign tumour. However, submandibular lymph node enlargement led us to the suspicion of conversion of a benign tumour into a malignancy [7]. Histologically, the poor differentiation of the lesion was suggestive of a poorly differentiated malignancy. Few areas of glandular structures and comedonecrosis led us for an immunohistochemical analysis [8].

The SDCs are immunoreactive for low and high molecular cytokeratin and markers such as CEA, LeuM1, and Epithelial Membraneantigen (EMA). Strong nuclear reactivity for Androgen Receptors (AR) is reported in all SDC. SDC cells are focally positive for apocrine marker GCDFFP-15 and Mitochondrialantigen (MIA), and typically negative for S-100 protein, myoepithelial markers, and oestrogen and Progesterone Receptors (PR). P63 marker shows positivity for squamous cell carcinoma and is generally used in poorly differentiated carcinomas. P63 negative values helped to rule out squamous cell carcinoma. PR was weakly positive which ruled out breast carcinoma. Gross Cystic Disease Fluid Protein 15 (GCDFFP-15), Carcinoma embryonic antigen and CK7 were positive which confirmed SDC [9,10].

The differential diagnosis of SDC spans a range of low-grade and high-grade salivary gland malignant neoplasms, the most common ones of which include papillary cystadenocarcinoma, papillary cystic acinic cell carcinoma, high grade mucoepidermoid carcinoma and metastatic carcinoma of breast. Breast adenocarcinoma is among the most common adenocarcinomas to metastasise to the parotid gland. It has been suggested that negative oestrogen receptor together with diffuse intense staining for CEA favour a diagnosis of SDC over breast carcinoma. SDC should also be differentiated from high grade mucoepidermoid carcinoma. The presence of squamoid or intermediate basaloid cells and intracellular mucin characterises the latter [5,11].

It is more aggressive than the more common salivary malignancies with five year overall survival ranging from 42% (stage 1) to 23% (stage 4). The lesion was surgically excised with radical neck dissection followed by radiotherapy and carboplatin weekly due to the aggressive nature of the lesion. SDC in the present case might have arisen from a carcinoma expleomorphic adenoma taking into consideration the long duration and clinical appearance of the lesion [12,13].

CONCLUSION(S)

In the present case, according to TNM staging T2N1M0, it was a stage 3 cancer. A complete surgical excision of the swelling with radical neck dissection on the left side followed by postoperative radiotherapy with adjuvant chemotherapy gave us a disease free survival of two and a half years. Hence, although SDCs are aggressive in nature associated with metastasis and low survival rate, an early diagnosis and appropriate management improves the survival rates.

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