CASE REPORT

Salivary duct carcinoma

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ABSTRACT
Salivary duct carcinoma (SDC) is a rare adenocarcinoma accounting for 0.5 to 6% of all the salivary gland neoplasms. Histologically, it has a striking resemblance to the intraductal and infiltrating ductal carcinomas of the breast. Though salivary duct carcinoma was first reported in 1968, it was not listed in the WHO classification of 1972. But later on, on account of its distinctive clinical and pathological characteristics it was recognized as a distinct entity in the WHO classification of 1991. Here we report a case of salivary duct carcinoma presenting as a palatal growth in a 55-year-old female along with the immunohistochemical findings.

Key words: Salivary duct carcinoma, Duct carcinoma.

INTRODUCTION
Salivary duct carcinoma (SDC) is an uncommon, high grade adenocarcinoma arising from the ductal epithelium. This nomenclature comes from the striking resemblance of this tumour histopathologically to the ductal carcinomas of breast. Because virtually all salivary gland neoplasms arise from salivary ducts, the term SDC has been criticized as being too vague and not conveying the inherent biologic aggressiveness associated with this tumour. SDC comprises of 0.5 to 6% of all salivary gland neoplasms (1). Intraoral SDCs account for less than 2% of all malignant salivary gland tumours of oral cavity (2). SDC have a predilection for older individuals over 50 years (3, 4), usually in 6th to 7th decades (1) with male to female ratio of 3:1. (1, 4) Clinically, SDC is characterized by aggressive behavior with an early and marked tendency towards metastasis especially to lungs, bones and liver, local recurrence, and a significant mortality rate. Here we report a case of salivary duct carcinoma occurring in a 55-year-old female presenting as a fast growing palatal growth, along with the immunohistochemical findings.

REVIEW OF LITERATURE
Kleinsasser and colleagues first described this entity and first used the term "salivary duct carcinoma" in 1968(4). It received recognition slowly in the literature. In several reviews of large series of the salivary gland neoplasms, the tumour has either not been identified or recognized or has been confused with other entities. Seifert and Caselitz (1989) allude to 37 SDCs in a review of 4068 salivary glands whereas Ellis et al (1991) mentioned 3 SDCs of a total of 13, 749 benign and malignant salivary gland neoplasms contained in Armed Forces Institute of Pathology (AFIP) salivary gland registry (3). Although salivary duct carcinoma was not listed in the WHO classification of 1972, it is included in the 1991 classification; as its separate categorization is justified because of its distinctive clinical and pathological characteristics(1). Very few cases of SDC arising from minor salivary glands have been reported of which are cases reported by Delgado (1993) and Jose et al (2000) (5).

CASE REPORT
A 5-year-old female patient was referred to the Government Dental College and hospital, Aurangabad, with a chief complaint of a growth on palate since 4 to 5 months. Detailed history revealed initial pain and mobility of maxillary left posterior teeth of which the second molar exfoliated subsequently. Fifteen to twenty days later, an exophytic growth developed in the same region. She also had nasal stuffiness, epiphora with left eye, and an altered voice.

Tissue abuse habits included a snuff dipping habit for 3 to 4 years duration with a frequency of 5 to 6 times a day. In medical history, there was history of hysterectomy and radiotherapy for carcinoma cervix 8 years back.

On extraoral examination, a firm, non-tender diffuse swelling measuring about 5cm x 5cm approximately was noticed in the left maxillary region. It extended from ala
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Fig. 1: A large pedunculated nodular growth on the palate.

Fig. 2: Contrast enhancing computed tomography showing an enhancing malignant mass involving the hard palate and maxillary sinus.

Fig. 3: Infiltrating duct, intraductal, and solid patterns of dysplastic cells along with areas of central necrosis. (H and E, X40)

Fig. 4: Cells with scanty cytoplasm, indistinct cell borders, vesicular nuclei having a stippled appearance and few nucleoli. (H and E, X400)

Fig. 5: Tumour tissue reactive for cytokeratin. (X400)

Fig. 6: Tumour tissue showing positivity for epithelial membrane antigen [EMA]. (X100)
of nose up to the zygomatic area anteroposteriorly and superoinferiorly from 1 cm below the infraorbital margin up to a line joining the corner of mouth to tragus of ear. The nasolabial fold was obliterated and the upper lip was incompetent. The left supraclavicular lymph nodes were palpable and non-tender on examination.

On intraoral examination, a firm to hard, pedunculated nodular growth which measured 4 cm x 4 cm approximately was observed in the palatal region. It extended from the gingivae of teeth # 24, 25, 26, 28 to cross the midline covering almost the entire hard palate. The teeth in the lesional area showed mobility (Fig. 1).

The computed tomography features were suggestive of a contrast enhancing malignant mass involving the hard palate and medial wall of left maxillary sinus with destruction of bone (Fig. 2).

Incisional biopsy was performed. The Hand Estained sections showed islands of basoid cells in a dense connective tissue stroma. The cells were round to oval with vesicular nuclei, few nucleoli, scanty cytoplasm, and indistinct cell borders. Some islands showed small cystic spaces forming a cribriform-like pattern. Areas of central necrosis (comedonecrosis) were seen in the tumor islands. The diagnosis of adenoid cystic carcinoma of solid or basoid type was made.

Later on, partial maxillectomy was done and tissue sent for histopathology. The gross specimen consisted of the maxillary bone along with the teeth. The maxillary sinus was completely filled with the tumour mass, which was firm to hard in consistency.

On histopathological examination, Hand Estained sections showed intraductal (in situ) or circumscribed nests of dysplastic ductal cells growing in solid, cribriform, and papillary patterns. The large tumor islands showed typical large central cystic spaces. Areas of central necrosis were seen in almost all islands. The tumor cells formed a rim, several cells thick around the cystic spaces. There was moderate to severe cellular pleomorphism, with few mitotic figures. The cells were round to polygonal with scanty cytoplasm, indistinct cell borders, vesicular nuclei showing stippled appearance, and having few nucleoli. In addition to intraductal component, the infiltrative tumour elements were seen composed of small clusters of tumour cells showing either lumina or cribriform arrangement or solid irregularly shaped aggregates. A diagnosis of salivary duct carcinoma originating from minor salivary glands of palate was made. But the cellular architecture on H and E sections, showed some features of neuroendocrine differentiation, and hence immunohistochemistry was done (Fig. 3, 4).

The tumour tissue was reactive for cytokeratin (Fig. 5) and epithelial membrane antigen (EMA) (Fig. 6) and non-reactive for synaptophysin, chromogranin, gross cystic disease fluid protein (GCDFP), and neuron-specific enolase (NSE).

**DISCUSSION**

Salivary duct carcinoma (SDC) is a rare salivary gland neoplasm accounting for 0.5 to 6% of all salivary gland carcinomas (1) and is regarded as a high grade malignancy in the current WHO classification of salivary gland neoplasms (5). The parotid gland has been the site of occurrence in 85% to 86% of cases, followed by submandibular gland (7%), and intraoral minor salivary glands (5%) (1). Histopathologically, it is characterized by the presence of an intraductal tumour along with infiltrative features, morphologically resembling in most cases intraductal and infiltrating ductal carcinomas of mammary gland (6). To diagnose SDC, one must first learn to recognize it histologically (3). WHO defines SDC as "an epithelial tumour of high malignancy with formation of relatively large cell aggregates resembling distended salivary ducts. The neoplastic epithelium presents a combination of cribiform, looping (Roman bridging) and solid growth patterns, often with central necrosis both in the primary lesions and lymph node metastases. This extremely rare carcinoma resembles comedocarcinoma of the breasts" (3). Because of its distinctive clinical and pathologic characteristics it was included as a separate entity in the WHO classification of 1991, separating it from the category of adenocarcinomas NOS (not otherwise specified) on account of its predictable aggressive behavior and dismal prognosis. Araujo et al (7) studied SDC ultrastructurally and the features of his study were consistent with the hypothesis of a ductal, striated, or excretory duct origin of the tumour cells.

The presenting features usually include a painful or painless, rapidly enlarging firm mass, frequently associated with facial nerve palsy or paralysis (1). Cervical nodal metastases at the time of diagnosis have been reported in 59 to 83% of the patients (1). In our case, the tumour followed the typical aggressive pattern with invasion of maxillary sinus as well as the nasal cavity. The left supraclavicular lymphnodes were enlarged, almost obliterating the supraclavicular space. Since SDC resembles the ductal carcinoma or comedocarcinoma of breasts, when SDC occurs in females, as in the present case, the possibility of metastasis from a primary breast carcinoma should be ruled out. But, the presence of foci of intraductal (in situ) carcinoma of course indicates it to be a primary neoplasm in that site (3). Although SDC has been regarded as a high grade carcinoma, Delgado et al has described 10 cases that were thought to represent the low grade counterpart of SDC (3). These tumours differed from high grade SDC in their bland cytomorphology and lack of comedonecrosis. According to Delgado et al's findings, the present case fits in the category of high grade.
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SDC, as there was moderate to severe cellular pleomorphism and central necrosis in many islands. Garland and co-workers required comedonecrosis for the diagnosis of SDC but others regard comedonecrosis as a characteristic but not a requisite for diagnosis of SDC (4).

Immunohistochemically SDCs are reactive for cytokeratin (AE1, AE3, and CAM 5.2) and EMA, and variably positive for carcinoembryonic antigen (3). Regarding S-100 protein, Simpson et al and Delgado et al observed 6 and 12 tumours respectively to be negative for S-100 protein whereas Brandwein et al found 9 of 9 tumours stained to be positive for this antibody (3). In this case, immunohistochemistry showed the tumour tissue to be reactive for cytokeratin and EMA and non-reactive for synaptophysin, chromogranin, NSE, and GCDFP. This ruled out the possibility of neuroendocrine features in the tumour. Laforga (2004) had reported a case of SDC with neuroendocrine features in which the tumour tissue showed predominantly solid and apocrine pattern with positivity for synaptophysin, chromogranin, and GCDFP-15 (8). GCDFP is seen to be positive in 76% of cases with SDC (9) but in present case it was negative.

The differential diagnoses for SDCs are those salivary gland neoplasms which show ductal and papillary configurations and cells with eosinophilic cytoplasm. Such tumours include acinic cell carcinoma, mucopidermoid carcinoma, papillary cystadenocarcinoma, oncocytic carcinoma, and polymorphous low grade adenocarcinoma (PLGA) (7). In addition to papillary cystic pattern, most acinic cell adenocarcinomas show other tumour growth configurations including microcystic, solid, and follicular patterns. Furthermore, a number of cell types, including acinar, intercalated duct, vacuolated, clear, and nonspecific glandular, are typically present in acinic cell carcinoma, which contrasts with one cell type observed in SDC. The presence of epidermoid and mucous cells distinguishes high grade mucopidermoid carcinoma from SDC. Lack of cribriform and papillary pattern, separates mucopidermoid carcinoma and papillary cystadenocarcinoma and oncocytic adenocarcinoma from SDC. PLGA as compared to SDC shows a bland cytologic picture and absence of central necrosis. In the present case, initially on incisional biopsy, the diagnosis of solid adenoid cystic carcinoma was made which was obvious since no other tumour pattern except cribriform and solid configuration was seen.

The most effective therapy is complete surgical excision followed by radiotherapy. Because of high incidence of regional metastasis during the course of the disease, treatment of cervical lymph nodes either by neck dissection or irradiation, should be accomplished even if the neck is clinically negative (3). Large series of cases indicate that over 50% to 60% of patients of SDC die of their disease within 5 months to 6 years after treatment (10, 11). This case was treated by surgical excision of lesion followed by radiotherapy for the cervical lymph nodes.

In summary, a case of high grade salivary duct carcinoma arising from minor salivary glands on the palate, on account of its relative rarity, distinct clinical, and pathologic features and a dismal prognosis is described.

REFERENCES


