ORIGINAL RESEARCH PAPER

Pathology

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SALIVARY DUCT CARCINOMA –A CASE SERIES

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ABSTRACT

Salivary duct carcinomas are aggressive, high grade salivary gland malignancies. It accounts for 1-3% among all salivary gland tumors. This tumor exhibits aggressive clinical behaviour with a tendency for early cervical lymphadenopathies and distant metastases to the lungs and bones, which proves that the prognosis is unfavourable. They histologically resemble ductal carcinoma of the breast. Here we review the clinical data of four patients with SDC in the parotid gland and discuss the relevant literature.

INTRODUCTION:

Salivary duct carcinomas (SDC) are aggressive, high grade salivary malignancies first described by Kleinsasser et al(1). Since then more than 100 cases have been reported. It has also been termed cribriform salivary carcinoma of excretory ducts(2) and infiltrating salivary carcinoma(3). The tumors are characterised by a histological resemblance to ductal carcinoma of the breast. The reported incidence of Salivary duct carcinoma is 1-3% among all salivary tumors(4). This tumor exhibits aggressive clinical behaviour with a tendency for early cervical lymphadenopathies and distant metastases to the lungs and bones and thus, the prognosis of Salivary duct carcinoma is highly unfavourable(5). Surgical resection followed by radiation is the treatment of choice, however locoregional recurrences and distant metastases have been frequently reported(6). The disease is rarely found in the parotid gland. The present case series review the clinical data of four patients with Salivary duct carcinoma in the parotid gland and discusses the relevant literature.

CASE REPORTS:

Case 1:

A 50 year old female presented with a moderate, painless swelling of the left parotid region that had been apparent for 6 months. The patient had no history of fever or other constitutional symptoms. Physical examination revealed a firm, mobile lump that was not fixed to the overlying skin. Radiographically, a large moderately enhancing soft tissue density lesion arising from left parotid region was noted. The specimen of left parotid with segmental mandible was received in the Department of Pathology, Karpaga Vinayaga Institute of Medical Sciences for histopathological examination. Grossly, the tumor was measuring 12x11x7cm with overlying ulcerated skin. The ulcer measures around 7x6cm. Cut surface of tumor shows gray white to gray yellow, focal calcified areas measuring 1x1cm and multiple cysts of varying size noted. The tumor appears to be like multiple tiny cystic lesions from which a yellow necrotic material is seen to ooze out. Deep surface of the tumor shows multiple matted lymphnodes and salivary gland which seems to be involved by the tumor. Tumor seems to involve the skin of the segmental mandible. Posterior condyle measuring 7cm in length is unremarkable.

Microscopically, the excised mass showed a malignant neoplasm arranged in sheets, nests and comedo pattern with central necrosis. The individual cells were round to oval and showed eosinophilic cytoplasm and pleomorphic hyperchromatic nuclei most of which were seen surrounding the central necrosis. The tumor was seen arising from the salivary gland parenchyma with extensive infiltration into the surrounding structures encroaching upto the lateral skin. The intervening stroma showed fibrosis, hyalinisation with focal spotty calcifications and perineural invasion. Deep and lateral margins showed tumor infiltration and four lymph nodes showed metastatic carcinomatous deposits. Final histopathological diagnosis was given as salivary duct carcinoma of left parotid.

Case 2:

A 65 year old female presented with an insidious onset of painful swelling in right parotid region for 4 months duration. Local examination revealed a firm to hard, tender swelling measuring 4x3cm. Facial nerve palsy was noted. CT scan showed malignant lesion in right parotid gland. Fine Needle Aspiration Cytology was done and reported as High Grade Malignant neoplasm of parotid gland probably Salivary duct carcinoma. Later Parotidectomy with radical neck dissection was done and sent for histopathological examination. Grossly, the specimen was measuring 14x10x2cm. Cut surface showed an infiltrating gray white growth measuring 4x3.5x2.5cm with an adjacent salivary gland measuring 1.5x1.5x1cm. Microscopically, section studied showed salivary gland parenchyma with an adjacent infiltrating high grade malignant neoplasm composed of large polyhedral cells with abundant eosinophilic granular cytoplasm, highly pleomorphic vesicular nuclei with a prominent nucleoli and multinucleation. The tumor cells were arranged predominantly in solid sheets, papillary, tubular, focal cribriform pattern and occasional areas exhibited comedo necrosis. At places, the tumor cells were separated by extensive desmoplastic stroma and dystrophic calcification. Increase in mitotic activity with atypical mitotic figures was noted. The tumor also exhibited perineural and lymphovascular invasion. From the radical neck dissection 38 lymph nodes were dissected, out of which 36 nodes showed metastatic carcinomatous deposits. Histopathological diagnosis

was confirmed to be Salivary duct carcinoma of Right parotid. Immunohistochemistry showed focal membrane positivity of Her2 Neu.

CYTOLOGY

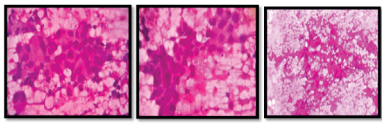


Fig 1A Fig 1B Fig 1C

1A(10x) Tumor cells are arranged in acinar configuration, monolayered sheets and papillaroid clusters
1B(40x) Attempted cribriform pattern
1C(40x) Cells are round to polygonal cells with abundant eosinophilic granular to clear vacuolated cytoplasm and highly pleomorphic vesicular nuclei with prominent nucleoli.

GROSS IMAGES

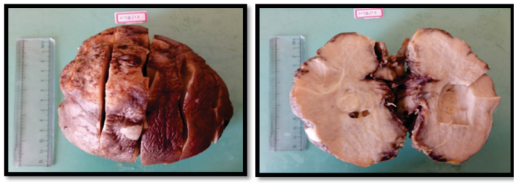


Fig 2A Fig 2B

2A Parotidectomy with radical neck dissection specimen altogether measuring 14x10x2cm
2B Cut surface shows grey white growth replacing the parotid gland measuring 4x3.5x2.4cm

HISTOPATHOLOGY IMAGES:

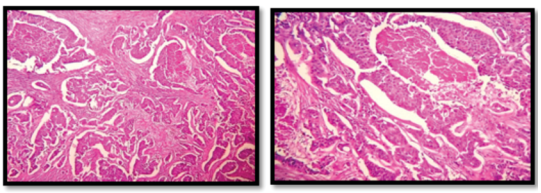


Fig 3A Fig 3B

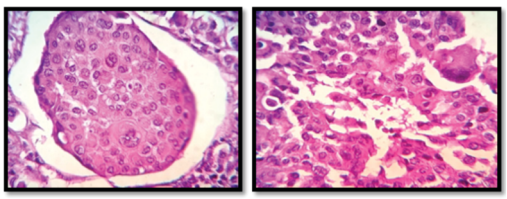
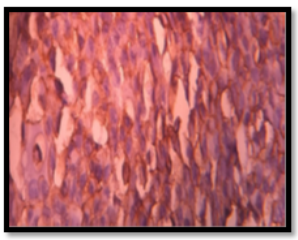


Fig 3C Fig 3D

3A(10x) Malignant neoplasm arranged in sheets and tubular pattern with areas of comedo necrosis
3B(10x) Tumor cells showing Comedo necrosis
3C(40x) Tumor cells are large polyhedral cells with abundant eosinophilic granular cytoplasm, highly pleomorphic vesicular nuclei with prominent nucleoli
3D(40x) Tumor giant cell with increased mitotic activity

IMMUNOHISTOCHEMISTRY:



Her 2 neu expression in salivary duct carcinoma – Membrane positivity.

Case 3:
A 58 year old male presented to the OPD with an ulcer over the right lower jaw for 3 months duration. Radiographically, there was bony erosion in the right retro molar region of mandible. Wide local excision with right neck dissection was done. The specimen was received in the department of Pathology for histopathological examination.

Grossly,the hemimandiblectomy specimen measured 7x4x3cm with attached single tooth in the socket and the mucosal aspect showed a nodular growth measuring 3x2x2cm. Cut surface of the growth was gray white and firm. Microscopically, an infiltrating malignant neoplasm arranged in solid sheets and clusters with many areas exhibiting central comedo necrosis were noted. The individual tumor cells were polyhedral in shape with moderate to abundant eosinophilic cytoplasm, highly pleomorphic hyperchromatic nuclei with an increased mitotic activity and tumor giant cells. Many areas showed lymphovascular invasion with tumor emboli. Radical neck dissection showed 13 lymph nodes, out of which 5 nodes showed metastatic carcinomatous deposits.

Case 4:
A 70 year old male presented with swelling over the right parotid region for 8 months which was painful. The patient presented with the complaints of difficulty in opening mouth and dysphagia for solid foods. Radical parotidectomy with neck dissection was done. The specimen was received in department of Pathology for histopathological examination. The specimen measured 17x10x6cm. The elliptical piece of skin measured 9x8x4cm. Cut surface through the elliptical skin showed an infiltrating gray white tumor which measured 10x2cm. Cut surface through the neck dissection showed group of matted lymph nodes measuring 7x5x3cm. On microscopy, multiple sections studied showed an ulcerated skin with an underlying tumor mass composed of round to polyhedral cells having a squamoid look. The tumor cells were arranged in small nests, sheets and islands having central comedo necrosis. The individual tumor cells showed moderate amount of eosinophilic cytoplasm and large pleomorphic nuclei with prominent nucleoli. The intervening stroma showed desmoplastic reaction with mononuclear cell inflammatory infiltrate. The tumor seemed to involve the skin, underlying subcutis and muscle. They also exhibited lymphovascular invasion. The circumferential margins were free of tumor. Out of twenty three lymph nodes that were dissected, twenty two showed metastatic carcinomatous deposits. Final histopathological diagnosis was given as High grade infiltrating salivary duct carcinoma of Parotid.

DISCUSSION:

Salivary duct carcinoma is a malignant condition that accounts for up to 2% of all primary salivary epithelial neoplasms. Most patients are over 50 years old and the male to female ratio is estimated to be 4:1. It mainly arises in the parotid gland, submandibular gland and occasionally in the minor glands(7,8).

Patients commonly present with a rapid growing firm mass around the facial nerve(7). They present with pain, swelling and facial paresis(9). Cervical adenopathies and lymphnode invasion are identified in 35 %(6) and 40-80% (10) of patients. In the present case series, all the four cases showed histopathological involvement of lymphnodes.

In 2005, Salivary duct carcinoma was defined as an independent entity by the world health organisation labelling it as an aggressive adenocarcinoma, which resembled high grade breast ductal carcinoma. It was previously divided into two categories; low grade and high grade Salivary duct carcinoma. The low grade Salivary duct carcinoma was recognised as a rare, cystic, proliferative carcinoma that resembled atypical ductal hyperplasia and micropapillary and cribriform low grade ductal carcinoma in situ(11). In the current definition of Salivary duct carcinoma, high grade Salivary duct carcinomas are tumors that consist of solid invasive cancer nests with polygonal cancer cells surrounding a comedo like necrosis.

Macroscopically, it is a yellowish or greyish white tumor that may

be nodular, multinodular, cystic or infiltrating surrounded by fibrosis with areas of haemorrhage, necrosis and cystic degeneration. It is usually a firm ill-defined mass.

Microscopically, the most peculiar feature is the similarity to ductal carcinoma of the breast. It is composed of an intraductal and invasive components. Intraductal component(carcinoma in situ) is cribriform, papillary, solid with comedo-like central necrosis. The infiltrative component is made of glands, cords of cells with desmoplastic reaction (12,7,13).
Salivary duct carcinoma is generally a hematoxylin and eosin stain based diagnosis, however specific immunohistochemical and staining techniques may confirm a diagnosis in certain cases, and immunomarkers may be beneficial for future therapeutic approaches. Immunohistochemically, Salivary duct carcinoma is positive for the expression of low molecular weight cytokeratins and epithelial membrane antigen(7). The overexpression of Her2 protein was identified in approximately 90% of cases(14).

Due to the infiltrative nature of Salivary duct carcinoma, radical surgery is the primary treatment; this includes the surgical removal of the tumor by parotidectomy with or without conservation of the facial nerve, followed by neck dissection to allow for ipsilateral lymph node excision. The rate of locoregional recurrence is high and the prognosis for survival is poor in case of insufficient resection margins, particularly in cases with lymph node invasion(10). Lymphatic embolism and perineural, extra-parotid and or lymphatic invasion are further indicators of a poor prognosis. Post operative radiation therapy is mandatory in advanced cases of Salivary duct carcinoma whereas chemoradiotherapy is reserved for metastatic forms of tumor.

CONCLUSION:

Salivary duct carcinoma is a rare and aggressive salivary gland malignancy. The histopathological features of Salivary duct carcinomas are distinctive and resemble in situ and invasive ductal carcinoma of the breast. The parotid gland is the most common site. Clinically, tumors are typically characterised by a rapidly growing parotid mass with pain, presence of cervical metastases and facial nerve involvement. Local recurrence rate associated with cervical node involvement and distant metastasis is considered a poor prognosis.

Treatment needs to be more aggressive including surgical removal of the primary site along with a neck dissection. Post operative radiotherapy should be recommended in all cases.

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