UNVEILING THE MYSTERIOUS WORLD OF SALIVARY DUCT CARCINOMA OF THE PAROTID GLAND- A RARE CASE REPORT AND REVIEW OF THE LITERATURE.

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**Abstract:** Among many variants of salivary gland tumors, salivary duct carcinoma (SDC) of the parotid gland is a highly aggressive and rare malignant tumor which ranks among those with the worst prognosis and a significant mortality. These tumors got their name based on its microscopic resemblance and being analogous to similar schemes in the ductal carcinoma of the breast. The characteristic microscopic features of salivary duct carcinoma are composed of comedo necrosis, a cribriform and papillary pattern of intraductal growth and aggressive infiltration to adjacent structures. Majority of cases are typically treated with radical parotidectomy with or without neck dissection followed by adjuvant radiotherapy. We present a case of a 60 year old male patient who presented with progressive facial paralysis and right parotid swelling. FNAC was positive for malignancy. PET-CT showed a lesion in right superficial lobe of parotid with bilateral neck nodes. Patient underwent right total parotidectomy with right radical neck dissection and left modified neck dissection. Facial nerve was preserved. Microscopic examination reported it as a salivary duct carcinoma, positive for Her2/neu antibody with lymph node metastasis (22/23). Patient received adjuvant radiotherapy and 12 cycles of Transtuzumab. There were no recurrences or metastases within 12 months of follow-up.

**Introduction**
Salivary duct carcinoma is a rare clinicopathologically distinct primary malignancy of the salivary glands accounting for 1% to 3% of all primary salivary epithelial neoplasms.1 It was first described by Kleinsasser et al. in 1968.2 It was included in 1991 in the second version of the World Health Organization classification of tumors of salivary gland. Its main characteristics include an aggressive behavior, early metastasis, local recurrence and significant level of mortality. In approximately 85% of the cases, the primary site of occurrence is the parotid gland followed by the submandibular gland. The tumor has predilection for elderly patients mainly in the sixth to seventh decades of life. A large number of patients experience facial nerve palsy and pain, and have cervical lymphadenopathy at presentation.3
The prognostic factors of salivary duct carcinoma are not clearly identified because this tumor has a dismal prognosis and is relatively uncommon. The tumor size, histologic variants, and having arisen from a pleomorphic adenoma or de novo may be associated with the prognosis. We present a case of a 60 year old male who was diagnosed with salivary duct carcinoma and was treated with surgery, radiotherapy and trastuzumab and has no recurrence or metastases within 12 months of follow up.

**Case Presentation**

We present a case of a 60 year old male patient who presented with progressive facial paralysis and right parotid swelling. Physical examination revealed a, hard and non-compressible mass in the right parotid gland which was painless on palpation. There were no palpable cervical lymph nodes and no abnormalities within the oral cavity.

**Investigations**

Chest X-ray of the patient was normal. FNAC from the right parotid swelling was positive for malignancy. PET-CT showed a lesion in right superficial lobe of parotid with bilateral neck nodes. Patient underwent right total parotidectomy with right radical neck dissection and left modified neck dissection. Facial nerve was preserved. Histopathological examination revealed Adenocarcinoma, moderately differentiated with comedo necrosis pattern and features consistent with salivary Duct Carcinoma (Fig. 1). Twenty two out of twenty three lymph nodes involved by carcinoma (22/23). Tumor embolus identified. Immunohistochemical studies showed positive staining for EMA, Her2/neu, p63 and CK 7 (Fig. 2-5) and negative staining for progesterone receptor and CK 5/6 (Fig. 6-7).
Treatment

In view of the histopathology and IHC reports patient was planned for adjuvant radiotherapy and sequential Transtuzumab based chemotherapy. Patient received adjuvant radiotherapy by Intensity Modulated Radiotherapy technique (Fig 8) on a linear accelerator (CLINAC 2100) to a dose of 66 Gy in 33 fractions @ 2Gy per fraction over a period of six and a half weeks. Patient tolerated treatment well. Following this patient received 12 cycles of Transtuzumab with a loading dose of 4mg/kg followed by two weekly doses of 2mg/kg.
Differential Diagnosis
The histopathologic differential diagnosis of SDC\textsuperscript{7-8} includes

- Primary oncocytic, mucoepidermoid and myoepithelial carcinomas
- Metastatic melanoma
- Adenocarcinoma not otherwise specified (ADC-NOS)
- Warthin's tumor (WT) with nuclear atypia
- Acinic cell carcinoma squamous

Outcome and Follow-Up
Upon completion patient was put on close follow up with monthly follow up for a period of 6 months followed by two monthly follow up for a period of next six months. Follow up included clinical (general physical examination and local examination) and radiological investigations. Patient’s contrast enhanced MRI face and neck done 6 weeks after completion of treatment revealed “post op changes noted in the form of non visualization of the Right parotid gland, diffuse increased attenuation noted in the interfascial planes and adjacent planes and no definitive evidence of any focal or diffuse lesion showing abnormal signal intensity/ contrast enhancement to suggest any residual/recurrence”. PET scan done after six months of completion of treatment revealed “No FDG avid lesion noted in the scan as compared to the pre operative scan”. Patient was on scheduled follow up and a repeat PET scan done on completion of one year revealed no evidence of FDG avid lesion.

Discussion
Salivary duct carcinoma (SDC) is a very rare, high grade aggressive tumor which has pathomorphologic resemblance to ductal carcinoma of the female breast and has an estimated incidence rate of 1% to 3% of all malignant salivary gland tumors. Amongst salivary glands the parotid gland is the most commonly involved gland which often involves the extracranial part of the facial nerve with high propensity to metastasize through the temporal bone via perineural spread.\textsuperscript{9} In some very rare instances, submandibular glands and minor salivary glands are also involved. Low incidence of gingival metastases have also been documented in patients of SDC.\textsuperscript{10} In some cases Salivary duct carcinoma may develop in pre-existing pleomorphic adenoma.

SDC usually affects elderly males with a mean age ranging between 55 to 61 years. Its normal presentation can involve a rapidly growing mass, which develops aggressively with possibilities of local recurrence, early distant metastases and high degree of mortality. In 40% to 60% of cases facial paralysis is observed whereas lymphadenopathies are noted in 35% of cases.\textsuperscript{11} CT scan and MRI features are non-specific but are helpful in the diagnosis of malignancy and in their management. Positive diagnosis is based on histologic examination. A review by Jamal et al\textsuperscript{12} reported a male predominance of salivary duct carcinomas (average 71 %), and they most commonly occurred in the parotid gland (average 87%), with only a few cases having been reported in the submandibular and minor salivary glands. The age distribution of salivary duct carcinoma has a peak incidence in the sixth and seventh decades of life, and in Jamal et al.’s review, the mean age at diagnosis was 64 years. The local recurrence rate of salivary duct carcinoma was 32%, while 47% had lymph node metastasis and 44% had distant metastasis. Distant metastasis was the most common cause of death and was primarily to the lungs and bones.

The gross findings include a tumor of variable size, which is usually firm with a variable cystic component. An infiltration of the adjacent parenchyma is seen in most of the cases. The most peculiar feature microscopically is its similarity to ductal carcinoma of the breast. The
tumor mainly has an intraductal and invasive component as an essential feature. Intraductal component is mainly composed of cribriform, papillary and solid with comedo-like central necrosis whereas the infiltrative component is made of glands and cords of cells with desmoplastic reaction. Several variants such as sarcomatoid salivary duct carcinoma, low-grade neoplasm, and mucin-rich variants have also been described in various literatures.\textsuperscript{13}

Immunohistochemical findings are mostly not useful, but a constant overexpression of keratin, HER/2 neu, CEA, and c-erb-B2 works as an important parameter. Patients found to be HER/2 neu positive are principally treated with Transtuzumab.

Delgado et al\textsuperscript{14} based on the degree of intraductal or infiltrative component have classified SDC mainly into 3 subtypes: 1) Predominantly intra ductal: - In this subtype 90\% of the tumor is intra ductal 2) Predominantly infiltrative: - In this subtype less than 20\% of the tumor is intra ductal or 3) Infiltrative: - In this subtype the tumor is entirely infiltrative. The significance of this classification is not known however it has been seen that the predominantly infiltrative tumor has poor prognosis. Therapeutic approach seems to be non-consensual owing to the restricted knowledge because of the limited data but many authors recommend a total parotidectomy even in T1 tumors because local disease recurrence condition is often life-threatening.\textsuperscript{15} If facial paralysis is present, a radical parotidectomy is obligatory. In patients with involvement of the submandibular or minor salivary glands, tumor resection with wide margins of surrounding tissue is indicated to control local disease condition.

No consistent therapeutic approach and protocol exists for this rare tumor entity. Many authors recommend adjuvant radiotherapy based on the pathological stage, grade, resection margins, extraparotid extension, cervical lymph node metastasis, lymphatic embolus and perineural invasion. Recurrence was observed and reported in all the patients in literature with parotid SDC who have undergone parotidectomy but failed to undergo lymph nodal neck dissection.\textsuperscript{16}

Limaye S A et al\textsuperscript{17} treated 13 patients of salivary duct carcinoma and Her2/neu expression with Transtuzumab for a period of one year and concluded that Her2/neu positivity and treatment with trastuzumab correlated well with long-term survival and response. Based on this data, they proposed the examination of Her2/neu status routinely in all patients with salivary duct carcinomas and the treatment be directed accordingly in order to optimize the better treatment outcomes.

**Conclusion**

Rarity and complexity associated with diagnosis of salivary duct carcinoma makes it a challenging task for the clinician and the pathologist and hence high degree of clinical suspicion is required for correct diagnosis and appropriate management of these patients.

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**References**


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