A Case of Salivary Duct Carcinoma*

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ABSTRACT

Salivary Duct Carcinoma (SDC) is a rare type of aggressive cancer that arises from the salivary glands. It is predominantly seen in men and, generally, has a poor prognosis. Other highgrade carcinomas can mimic SDC. About 40-60% of SDC arise in pleomorphic adenomas. Most, if not all, SDCs express androgen receptor by immunohistochemistry. Therapeutically relevant genetic alterations include ERBB2/Her2 amplification PIK3CA and/or HRAS mutations. (Barnes et al.,2005). There are only 200 reportable cases worldwide (Gilbert, 2004). This is a case of a 63- year-old male, who presented with a two-month history of a pre-auricular mass, left associated with pain upon movement of the head from left to right, vice versa. Patient was diagnosed with parotid mass, left, to consider malignancy and underwent total parotidectomy, left with facial nerve sparring. Histopathology results reveal a Salivary Duct Carcinoma. The patient underwent eight cycles of chemotherapy using Cisplatin 50mg and Nimotuzumab 200mg with 32 days of concurrent radiotherapy using a total tumor dose per region 66Gy-post-op bed+(gross neck node level V + 0.5cm CTV margin), PTV 66Gy, No. of Fx: 33, Dose/Fx: 200cGy. At present, the patient is on regular follow up. No definite treatment protocols are published for Salivary Duct Carcinoma due to the lack of reported cases. More cases should be reported so that more definitive future studies will be made regarding this disease entity.

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INTRODUCTION

Salivary gland tumors are uncommon and only accounts to 2% of all head and neck neoplasms. Out of 2% from the said population, 85% arises from the parotid gland (Brunicardi et.al, 2015). According to the recent list of Cancer facts and figures 2017 and Philippine Cancer facts 2015, salivary duct carcinomas are not among the common cancers seen in both men and women. According to studies, majority of parotid gland mass are benign. Most of the tumors which are malignant in nature came from the minor salivary gland.

Salivary Duct Carcinoma is an aggressive and rare adenocarcinoma which resembles high-grade breast ductal carcinoma. It represents 9% of salivary malignancies. The male to female ratio is at least 4:1. Most patients present after age of 50 years. The parotid is most commonly involved, but submandibular, sublingual, minor salivary gland, maxillary and laryngeal tumors have been reported (Barnes, et.al 2005).

GENERAL OBJECTIVE

To present a case of Salivary Duct Carcinoma in a 60-year old patient.

SPECIFIC OBJECTIVES

1. To review the treatment options for Salivary Duct Carcinoma.
2. To be able to present a possible diagnostic method to diagnose such a neoplasm.
3. To emphasize the importance of multi-disciplinary approach to its management. (Head and Neck Surgery, Surgery Oncology, Pathology, Radiology, Medical Oncology, Radiation Oncology and Rehabilitation)

CASE REPORT

R.M. 63 years old, Male, Roman Catholic, Married, who came in with a chief complaint of a pre-auricular mass on the left side.

History of present illness started three months prior to admission when the patient noticed a firm, palpable, non-movable, non-tender pre-auricular mass approximately 2.0 cm in size on the left side. This is associated with pain upon moving the neck and not associated with facial asymmetry. The patient sought consult from a private physician, and was advised to undergo fine needle aspiration biopsy (FNAB) which revealed atypical cells of the parotid gland, left. The patient was also advised for CT scan with contrast of the head and neck which revealed 3.4x2.9 cm heterogeneously enhancing mass at left parotid gland. Laboratory tests and imaging were done and the patient was advised to undergo total parotidectomy, left.

The patient's past medical history includes hypertension for 20 years, anaphylactic shock in 1993, and underwent appendectomy in 1997.

The patient's family medical history includes hypertension, colon cancer, basal cell carcinoma and cerebrovascular disease on maternal side.

He is a government employee, 20 pack year smoker, and alcoholic beverage drinker.

On systems review, patient had no weight loss, blurring of vision, hearing loss, difficulty of breathing, chest pain, palpitations, dysuria, bloated sensation, diarrhea, constipation, melena or hematochezia. Pain at the left side of the preauricular area was noted.

Upon admission, patient was conscious, coherent, not in distress; Glasgow Coma Scale Score of 15 (E4V5M6). Vital signs were as follows: blood pressure of 140/100 mmHg, heart rate of 82 beats per minute, respiratory rate of 18 cycles per minute and the temperature is 36.5 degrees. A mass measuring 3.0 cm, movable, firm, non-tender mass at pre-auricular area, left was noted.

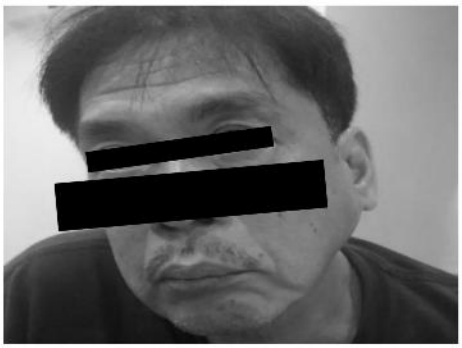

Figure 1: Pre-auricular mass, left

Head and Neck CT scan revealed a 3.4 x 2.9cm heterogeneously enhancing mass noted in the left parotid gland with its epicenter in the superficial lobe with signs of extension to the deep lobe with no definite encasement of retromandibular vein (figure 2). No signs of infiltration to the adjacent muscular and soft tissue planes were noted. Sub-centimeter level III lymph node was noted on the left side. The oral and nasopharynx appeared intact. The right lobe of the thyroid was slightly enlarged with a 1.5 cm hypodense nodule. The impression was a heterogeneously enhancing mass in the left parotid gland as described likely from a new growth. Tissue correlation was suggested. Sub-centimeter level III lymph node, left as described. Enlarged right lobe of the thyroid with a hypodense nodule as described.

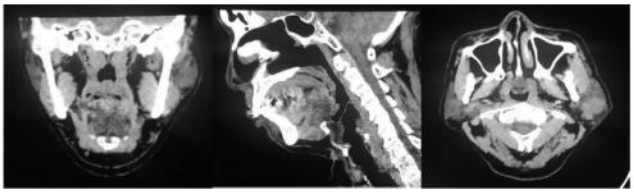

Figure 2: Head and Neck CT Scan without contrast

Figure 3: Head and Neck CT Scan with IV contrast

ADMITTING DIAGNOSIS

Mass, Pre-auricular area, Left, To Consider Malignancy.

COURSE IN THE WARD

Upon admission, patient was awake, alert, not in distress, no difficulty of breathing or shortness of breath with the following vital signs of blood pressure (BP) of 140/100mmHg, heart rate (HR) of 82bpm, respiratory rate (RR) of 18 cpm and with an oxygen saturation of 97%. Patient was placed on a low salt, low fat diet and was hooked to plain NSS 1L to run for 27gtts/min.

On the 1st hospital day, patient underwent Total Parotidectomy, Left with Facial Nerve Sparing. Patient was immediately transferred to Recovery Room and was eventually transferred to his room once his elevated BP normalized. Patient was noted to have asymmetry of the face, more on the left, patient can't close his left eyes, can't close his mouth full, can't elevated his left eyebrows.

On the 2nd hospital day, patient's Glasgow Coma Scale of 15, BP 140/100, HR 75, RR 18, afebrile, noted mildly soaked dressing at surgical site. Patient also complains of pain, inability to eat normally due to difficulty in closing the mouth full, inability to sleep due to difficulty in closing his left eye. Patient was given with pain meds, HTN meds, eye patch applied to left eye, and change of dressing done twice a day. The 3rd and 4th hospital days are unremarkable.

On the 5th hospital day, patient had dry surgical wound, afebrile, can tolerate pain at surgical site, still with asymmetrical face. Patient was referred to Rehabilitation Medicine service for co-management of stimulation of facial nerve. Patient was subsequently discharged and was sent home.

Post-operative, patient had weekly check-up at Rehabilitation Medicine, Quezon City General Hospital (QCGH). The patient underwent eight cycles of adjuvant chemotherapy at QCGH on his second post-operative month and radiotherapy at the University of Santo Tomas Hospital on his third post-operative month. Patient had repeat head and neck CT-scan with IV contrast, complete blood count and liver ultrasound every six months for surveillance.

OPERATIVE FINDINGS

Noted a mass on the parotid area, left measuring approximately 5.0 cm in widest diameter, hard movable adherent to facial nerve extending to the deep lobe, (Figure 4).

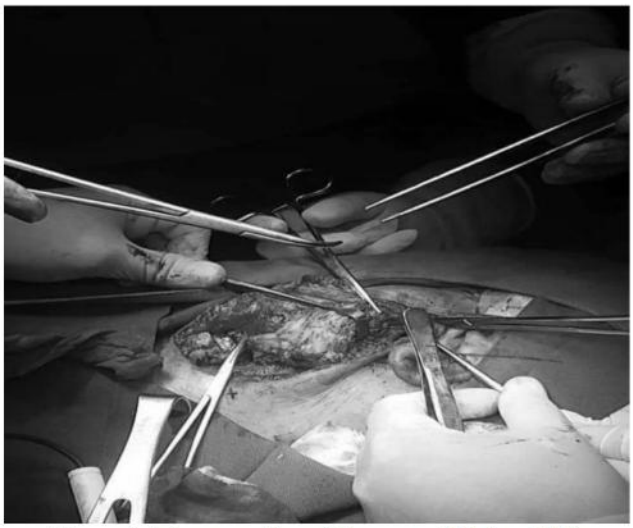

Figure 4: Intraoperative picture, parotid gland, left

POST-OPERATIVE DIAGNOSIS

Salivary Duct Carcinoma, Parotid, Left; s/p Facial Nerve Sparing, Total Parotidectomy, Left (11/27/2017).

HISTOPATHOLOGIC DESCRIPTION

GROSS DESCRIPTION: Specimen received in formalin labeled "parotid gland, left" measures 5 x 4 x 2 cm. It is light tan to gray, irregularly ovoid with firm to rubbery consistency. The surface of the specimen is light tan to yellow and has a slightly granular texture. Cut sections of the specimen reveal a whitish to gray solid parenchyma slightly blending into the adjacent fatty tissue. Specimen received in formalin labeled "deep lobe, parotid" consists of multiple, dark tan tissue fragments with irregular shapes and dull granular surfaces whose measurements range from 1.2 cm to 0.5 cm in diameter. Specimen received in formalin labeled "lymph nodes" measures 4.0 x 2.8 x 1.1 cm. It is gray, irregularly ovoid with firm to rubbery consistency. The surface of the specimen is gray to brown with a granular surface. Cut sections of the specimen reveal a gray to brown solid parenchyma with multiple serrations.

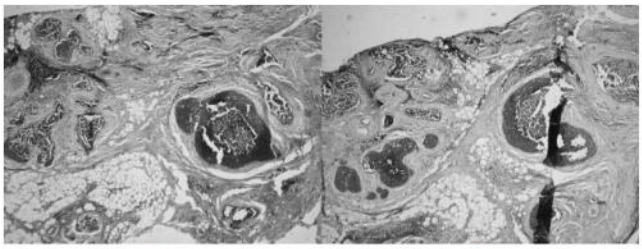

Figure 5. Microscopic image of parotid gland, left

MICROSCOPIC DESCRIPTION

Microsections show cells with hyperchromatic and pleomorphic nuclei with adequate cytoplasm arranged in small cluster and discohesive sheets with an infiltrative pattern. Some show comedonecrosis, (Figure 5).

HER-2-NEU RESULT

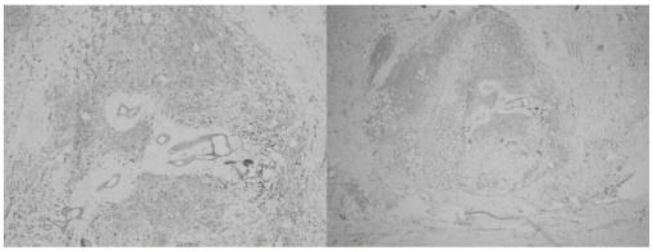

Figure 6. Microscopic image of parotid left with HER-2-NEU

Complete membrane staining with weak to moderate intensity in more than 20% of tumor cells, (Figure 6).

FINAL DIAGNOSIS

Salivary duct carcinoma with a background of sialadenitis; negative for tumor: surgical margins and all six (6/6); lymph nodes examined, lymphoepithelial cyst and focus of Warthin tumor; s/p Facial Nerve Sparing, Total Parotidectomy, Left (11/27/2017).

DISCUSSION

Tumors of the salivary gland are relatively uncommon and represent less than 2% of all the head and neck neoplasms. The major salivary glands are the parotid, submandibular, and

sublingual glands. Minor salivary glands are found throughout the submucosa of the upper aerodigestive tract. The majority of these neoplasms are benign, with the most common histology being pleomorphic adenoma (benign mixed tumor). In contrast, approximately 50% of tumors arising in the submandibular and sublingual glands are malignant. Tumors arising from minor salivary gland tissue carry an even higher risk for malignancy (75%). Salivary gland tumors are usually slow growing and well circumscribed. Patients with a mass and findings of rapid growth, pain, paresthesia, and facial nerve weakness are at increased risk of harboring a malignancy. The facial nerve, which separates the superficial and deep lobes of the parotid, may be directly involved by tumors in 10% to 15% of patients. Additional findings ominous for malignancy include skin invasion and fixation to the mastoid tip. Trismus suggests invasion of the masseter or pterygoid muscles. About 85% of salivary gland neoplasms arise within the parotid gland.

The incidence of metastatic spread to cervical lymphatics is variable and depends on the histology, primary site, and stage of the tumor. Parotid gland malignancies can metastasize to the intra and periglandular nodes. The next echelon of lymphatics for the parotid is the upper jugular nodal chain. Although the risk of lymphatic metastasis is low for most salivary gland malignancies, lesions that are considered high grade or that demonstrate perineural invasion have a higher propensity for regional spread.

Tumors arising in patients of advanced age also tend to have more aggressive behavior. Initial nodal drainage for the submandibular gland is the level Ia and Ib lymph nodes and submental nodes followed by the upper and mid-jugular nodes. Extraglandular extension of tumor and lymph node metastases are adverse prognostic factors for submandibular gland tumors.

Diagnostic imaging is standard for the evaluation of salivary gland tumors. MRI is the most sensitive study to determine soft-tissue extension and involvement of adjacent structures. Unfortunately, imaging studies lack the specificity for differentiating benign and malignant neoplasms.

Diagnosis of salivary gland tumors is frequently aided by the use of FNA. In the hands of an experienced cytologist familiar with salivary gland pathology, FNA can provide an accuratepreoperative diagnosis in 70% to 80% of cases. This can help the operative surgeon with treatment planning and patient counseling, but should be viewed in the context that a more extensive procedure may be ultimately required.

The final histopathologic diagnosis is confirmed by surgical excision. Benign and malignant tumors of the salivary glands are divided into epithelial, nonepithelial, and metastatic neoplasms. Benign epithelial tumors include pleomorphic adenoma (80%), monomorphic adenoma, Warthin's tumor, oncocytoma, or sebaceous neoplasm.

Nonepithelial benign lesions include hemangioma, neural sheath tumor, and lipoma. Treatment of benign neoplasms is surgical excision of the affected gland or, in the case of the parotid, excision of the superficial lobe with facial nerve dissection and preservation.

The minimal surgical procedure for neoplasms of the parotid is superficial parotidectomy with preservation of the facial nerve. Enucleation of the tumor mass is not recommended because of the risk of incomplete excision and tumor spillage. Tumor spillage of a pleomorphic adenoma during removal can lead to problematic recurrences.

Salivary duct carcinoma closely resembles ductal carcinoma of the breast, both macroscopically and microscopically, due to its abundance of very firm, fibrous, often ill-defined matrix. Comedo-type necrosis and calcification are seen microscopically, with cystic changes on macroscopic inspection. The majority (80%) of salivary duct carcinoma arises de novo, although in approximately 20 per cent of cases it arises within a pre-existing pleomorphic adenoma.

Survival is better if the tumour proportion is less than 50 per cent, if capsular invasion beyond the mixed tumour extends less than 15 mm, and if cervical nodal disease is absent. A pure, in situ form of salivary duct carcinoma has been described; this

is considered rare and is classified as intraductal carcinoma, but its existence is controversial.

Pure, in situ salivary duct carcinoma has not been recognized as an entity by the WHO classification system. The proportion of intraductal and extraductal growth in reported specimens is variable and has prognostic significance. Although the majority of salivary duct carcinoma behaves in a high-grade fashion, cases which have a predominant intraductal component of greater than 90% and which are minimally invasive (i.e. less than 8.0 mm) are reported to have a good prognosis. The intraductal component may represent the pre-invasive phase of invasive salivary duct carcinoma, which by itself is non-metastasizing and associated with an excellent prognosis. Macroscopically, salivary duct carcinoma is unencapsulated, poorly circumscribed and typically multi-nodular. Comedo-type necrosis, calcification and cystic change may also be seen. Reported tumor sizes range between 1.0 and 10.0 cm.

Microscopically, salivary duct carcinoma arises from the larger intralobular and extralobular ducts, and is characterized by intraductal and infiltrating components similar to the intraductal and infiltrative ductal carcinoma of the breast. Comedo necrosis is evident within the ducts, with 'Roman bridge formation', and evidence of an intraductal cribriform pattern is typically seen. Perineural invasion has been reported in 60 percent of cases, and around 30 percent show lymphovascular invasion.

Most cases of salivary duct carcinoma (SDC) are diagnosed on a hematoxylin and eosin slide preparation. Special stains are at present mainly confirmatory, although some immunohistochemical markers may in future be considered of therapeutic importance.

Three cases were reviewed, and revealed that the patients are male, on their 50s and 60s and presented with a pre-auricular mass. Imaging like CT scan was done and underwent total parotidectomy and neck dissection. Specimens after confirming the diagnosis of SDC were sent for immunohistochemistry. Human epidermal growth factor 2 (HER-2), high molecular weight cytokeratin (CK-H), CK8/CK18, p63, calponin, the estrogen receptor (ER) and the progesterone receptor (PR) are the requested panel. Chemotherapy and Radiotherapy were done to previous cases and resulted free of cancer for 3 years. In this case, the patient only underwent Her2neu immuno-histochemistry, underwent eight cycles of chemotherapy using Cisplatin 50mg and Nimotuzumab 200mg with 32 days of concurrent radiotherapy using a total tumor dose per region 66Gy-post-op bed+(gross neck node level V + 0.5cm CTV margin), PTV 66Gy, No. of Fx: 33, Dose/Fx: 200cGy. After the chemoradiotherapy session, the patient is advised to follow up at regular intervals to monitor for tumor recurrence.

CONCLUSION

Salivary duct carcinoma is one of the most aggressive of the salivary gland carcinomas, and phenotypically resembles high-grade ductal breast carcinoma. The parotid gland is the most common site. Clinically, tumors are typically characterized by a rapidly growing parotid mass with pain, the presence of cervical metastases, and early facial nerve involvement.

Following conventional treatment which comprises of surgery with or without radiotherapy, the local recurrence rate is high, associated with both cervical nodal involvement and distant metastasis, resulting in a poor prognosis.

Treatment needs to be more aggressive, including total surgical removal of the primary site together with a neck dissection. Post-operative radiotherapy should be recommended in all cases. Traditionally, chemotherapy has only been offered for clinically recurrent, disseminated disease. However, evidence suggests that improved disease control could be achieved by employing adjuvant chemotherapy in combination with post-operative radiotherapy.

Advances in immunocytochemistry have identified tyrosine kinase receptors and hormone receptors in salivary duct carcinoma. Certain specific histologic types carry promising immunophenotypic profiles, which should be exploited to identify patients suitable for innovative treatment options, administered within prospective clinical trials.

RECOMMENDATION

This case is recommended to be reported and documented in our hospital, in our country, and in the world since there are only 200 cases reported worldwide and no reportable case in our country. With this, it will increase awareness regarding the said disease, hence better diagnostics and proper attack in the management of the said disease. Immunohistochemical staining for Her2neu will help in the histopathologic diagnosis of such tumors and it also has possible therapeutic implications. Further studies on the presence of Her2neu in these tumors are recommended as there is still no definite criteria to determine the positivity Her2neu in these tumors as of this writing.

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