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Maxillary Sinus Squamous Cell Carcinoma in a Tertiary Hospital in the Philippines

ABSTRACT

Objective: To establish preliminary demographic and clinicopathologic data on Maxillary Sinus Squamous Cell Carcinoma (SCC) in the Philippine General Hospital

Methods:

Design: Retrospective Case Series

Setting: Tertiary National University Hospital

Participants: Socio-demographic and clinical data from records of 22 patients admitted at the Department of Otorhinolaryngology of the Philippine General Hospital from 2013-2016 and histopathologically confirmed to have Maxillary Sinus SCC were collected and described using means and proportions.

Results: There were 15 males and 7 females with a mean age of 50 years old (range 24 to 77 years old). Maxillary mass/swelling was the most common chief complaint. The mean gap between initial symptoms and consult was 6.77 months. Initial biopsies were obtained from the maxillary sinus in 16 patients, with 1 patient noted to have undergone malignant transformation from a prior intranasal squamous papilloma. Staging was advanced (Stage IVA in 16, IVB in 4, and III in 2) with no patients with Stage I or II disease. Sixteen (16) patients underwent surgery and radiotherapy while 6 patients received radiotherapy (RT) with or without chemotherapy. Regional and distant metastases were uncommon.

Conclusion: In this series, maxillary sinus SCC occurs more in males with a maxillary mass as the most common chief complaint. Delay in treatment is common with a mean gap of 6 months between initial symptoms and consult. Neck node metastasis is uncommon and most patients undergo surgery with radiotherapy as treatment.

Keywords: *maxillary sinus cancer; paranasal sinus cancer; squamous cell carcinoma*

Maxillary sinus squamous cell carcinoma (SCC) is a rare cancer, comprising about 0.2-0.8% of all malignant neoplasms^{1,2} and 3% of all head and neck malignancies.¹ It is the most common histopathologic type among maxillary cancers.^{1,3,4} This disease is extremely rare in children with those between the ages of 55 to 65 years old usually affected.¹ It usually presents in advanced stages in patients who are often treated for benign conditions before malignancy is diagnosed and the overall 5-year survival is at 42%.¹

There have been reports of varying clinical behavior among Maxillary SCC in various regions worldwide through the years. Aggressive presentation and rapid onset of maxillary carcinomas are rarely seen in western Europe⁵ while prevalence of cervical metastasis at initial presentation has been observed in India.^{3,6} Survival has improved through the years but conflicting results depending on the modality of treatment have also been reported.^{3,7-9}

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The authors declare that this represents original material, that the manuscript has been read and approved by all the authors, that the requirements for authorship have been met by each author, and that each author believes that the manuscript represents honest work.

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Local studies tend to focus more on head and neck malignancies in general and a literature search of MEDLINE (PubMed) and HERDIN using the search terms Maxillary Sinus Cancer (MeSH Term) AND Squamous Cell Carcinoma (MeSH Term) AND Philippines (All Fields) did not yield specific studies on maxillary sinus SCC. The rarity of this disease, along with varying findings in the literature necessitates the establishment of baseline data for maxillary sinus SCC. This paper aims to establish preliminary sociodemographic and clinicopathologic data on maxillary sinus SCC in our institution.

METHODS

With institutional review board approval, this retrospective case series considered for inclusion the records of patients admitted at the Philippine General Hospital Department of Otorhinolaryngology public ward from January 1, 2013 – December 31, 2016 who were diagnosed with histopathologically-confirmed maxillary sinus SCC. Records of patients diagnosed with other cancers of the maxillary sinus, residual or recurrent maxillary sinus SCC, and those with incomplete records were excluded.

We reviewed the patient database of the Department of Otorhinolaryngology to determine eligible patients for this study. Patient records were coded and de-identified socio-demographic data such as age, sex, location, past medical history, family medical history, personal social history, as well as clinical data including chief complaint, time between symptom onset and initial consult, signs/symptoms, staging (T, N, M), biopsy approach, histopathologic diagnosis/grading, intraoperative anatomic involvement, regional metastasis and distant metastasis were extracted from patient records. Data were written in data collection sheets and subsequently encoded in a Microsoft Excel Office 365 database. Data were checked for accuracy of encoding. Data analysis utilized Microsoft Excel version 1903 (Microsoft Corp. Redmond, WA, USA) to generate descriptive analysis. Means and proportions were used to describe the study variables.

RESULTS

Out of 25 patient records identified, 22 patients (15 males, 7 females) with ages 24 to 77 years old (mean age 50 years old) were included. Excluded were one record for incompleteness and 2 for non-SCC biopsy results. Twenty (20) patients were from Luzon, 2 from Visayas, none from Mindanao. Nineteen (19) of the 22 patients consulted within 6 months of initial symptoms with a chief complaint of mass or swelling in 21 and nasal obstruction in 1. Eleven (11) patients had a history of smoking, 15 had a history of alcohol ingestion and 11 had a history of both. Only three (3) patients had a history of Schedule 1 (high abuse potential) drug use. Nine (9) patients had comorbidities but only one (1) patient had a prior intranasal (not maxillary) mass while two (2) patients had prior intranasal (not maxillary) surgeries. The employment of patients varied, 3 were

carpenters/construction workers, 3 were jeepney drivers/dispatchers, 2 each were security guards, fishermen farmers, housewives, or retired, 1 each was a seamstress, animator, cashier, and mechanic, and 2 listed no occupation.

Initial biopsies were mostly taken from the maxillary sinus (n=16) and resulted in a diagnosis of squamous cell carcinoma for all patients with 1 patient noted to have undergone malignant transformation from a prior intranasal squamous papilloma. Staging was advanced in all (Stage IVA in 16, IVB in 4, and III in 2) with no patients staged I or II in this series. Sixteen (16) patients underwent surgery with radiotherapy, the rest were advised radiotherapy with or without chemotherapy. Eleven (11) patients with advanced staging underwent maxillectomy with orbital exenteration.

The most common signs/symptoms are enumerated in *Figure 1*. Apart from cheek fullness/maxillary swelling, patients also frequently presented with a palatal bulge (n=20). Other pertinent signs/symptoms included are hyposmia (n=3), bleeding mass (n=3), septal deviation (n=3), and skin changes (n=3).

Areas often grossly involved intraoperatively include the oral cavity (n=19; usually the palate and the gingiva), the nasal cavity (n=17; from an intranasal extension of the maxillary mass), and the orbit (n=13; usually through lysis of the orbital floor).

Nine (9) patients presented with clinically palpable neck nodes. Of the nine (9), only five (5) underwent neck dissection and had available post-operative histopathologic results. Three (3) of the five (5) patients

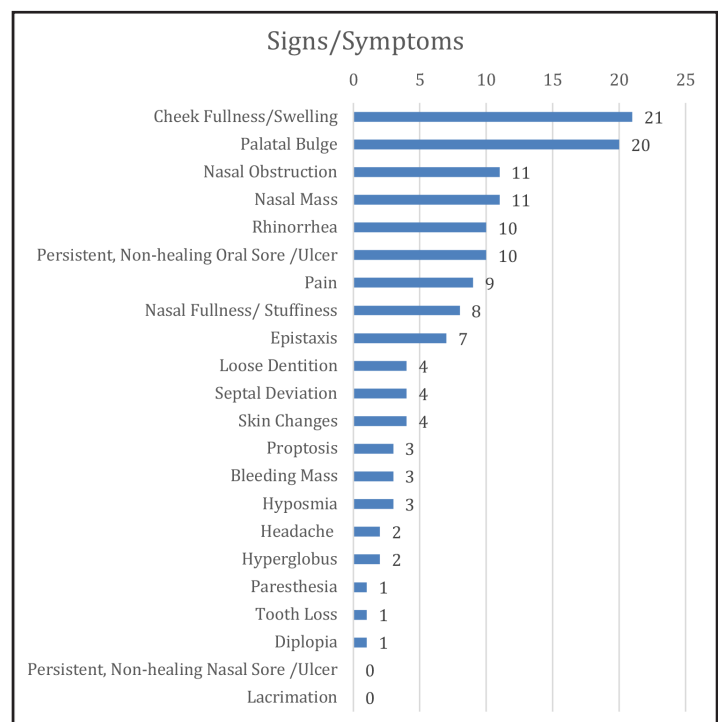


Figure 1. Most Common Signs/Symptoms

Table 1. Comparison of Maxillary Sinus Cancer Data

Origin (Authors, Year Published)	USA (St. Pierre & Baker, 1983)	Netherlands (Tiwari, et al. 1999)	Brazil (Santos, et al. 2014)	Japan (Kondo, et al. 2016)	India (Qureshi, et al. 2006)	Philippines (Hernandez & Cabungcal, 2019)*
Number of Patients	66 patients (1964-1975)	43 squamous cell carcinoma patients (1975-1994)	58 patients (more adenocarcinomas than squamous cell carcinomas)	26 patients (2002-2008)	73 patients (1994-1999)	22 patients (2013-2016)
Gender Distribution, Age	42 Male, 24 Female Average age at 60 years	28 Male, 15 Female Age range at 32-90 years	35 Male, 23 Female Median age of 59 years	18 Male, 8 Female Average age at 64.2 years (50-84 years)	39 Male, 23 Female Median age 55 years	15 Male, 7 Female Average age at 50 years (24-77 years)
Stage Distribution	1 Stage I, 8 Stage II, 21 Stage III, 36 Stage IV	7 Stage II, 20 Stage III, 16 Stage IV	5 Stage I or II, 53 Stage III or IV	4 with T2, 13 with T3, 9 with T4a	61 Presented with T3/T4 Disease	0 Stage I/II, 2 Stage III, 16 Stage IVA, 4 Stage IVB
Percentage of Lymph Node Metastasis	10.6% of patients had lymph node metastasis		17.2% of patients had regional metastasis	8 patients had lymph node metastasis (30.8%)	6 presented with lymph node metastasis	3 patients had lymph node metastasis
Treatment	Surgery + RT	Surgery + RT, Chemotherapy + RT	Surgery +RT, Chemotherapy + RT	Chemotherapy + RT	Surgery + RT, Chemotherapy, Radiotherapy	Surgery + RT, RT +/- Chemotherapy
Outcomes	5-year survival 75% for T2, 28.5% T3, 19.4% T4	5-year disease-free survival 64% for Surgery+RT 2-year survival of 37% for Chemo+RT	Overall 5-year survival rate of 17.7%	Overall 5-year survival rate of 71.3%	Overall 5-year survival after Surgery + RT of 43%	

*data from the present series

yielded positive regional metastasis to the cervical lymph nodes.

Diagnostics for distant metastases were normal for most patients including liver ultrasound (n=18), chest x-ray (n=16), Aspartate Aminotransferase (n=16), Alanine Aminotransferase (n=12) and Alkaline Phosphatase (n=14). Four (4) patients had remarkable liver ultrasound findings -- 2 had benign findings (hepatic cyst and parenchymal disease), 1 had a hepatic focus measuring 1.8cm, and another had non-specific calcifications. Biopsy was not obtained from any of the masses identified. Four (4) patients had significant x-ray findings suggestive of infection (pneumonia in 1, pulmonary tuberculosis in 3).

DISCUSSION

The general demographic and clinicopathologic profile of patients with maxillary SCC in this series is similar with findings in our literature review from the region. (Table 1) Common symptoms include pain, nasal discharge, epistaxis and obstruction, commonly affecting males more than females at a ratio of 1.5:1.¹ Other symptoms include: (1) nasal fullness, stuffiness or obstruction, (2) pain, (3) cheek paresthesia, (4) cheek fullness or swelling, (5) palatal bulge, (6) persistent, non-healing nasal/oral sore or ulcer, (7) nasal mass, (8) proptosis, diplopia or lacrimation.¹ Similar to existing literature, our study revealed male

predominance in this disease – with a male: female ratio of 2.1:1. The presence of a maxillary mass was the most common chief complaint identified.

The development of maxillary sinus cancer appears to be influenced by several factors such as: exposure to (1) nickel, (2) chlorophenols, (3) textile dust, (4) Thorotrast instillation, (5) smoking, (6) formaldehyde, (7) wood, (8) concurrence of sinonasal (Schneiderian) papilloma, and (9) Human Papilloma Virus.^{1,7} However, due to methodological limitations of this study, we were unable to identify these factors in our sample. Smoking and alcohol ingestion were observed in at least half of the patients and were more frequently noted than Schedule 1 drug use. Employment as a construction worker or jeepney driver was more common among the patients in our series. Risk for exposure may be inferred, at best, from the patients’ residence or employment.

The dilemma with diagnosing Maxillary Sinus SCC is that tumor growth is usually indolent. Delay in consultation may range from a month to even years, with some patients in this series first consulting ophthalmologists for eye symptoms or dentists for dental symptoms, only to discover that the problem was in the maxillary sinus. Many patients in our series presented in advanced stages, in contrast to the rarity of aggressively presenting maxillary carcinomas among patients



in western Europe.⁵ Since the maxillary sinus is an area surrounded by bone, significant bony involvement usually occurs prior to clinically apparent symptoms such as a cheek bulge which usually prompts medical consult. Patients may initially be diagnosed with some areas as unresectable, profoundly affecting prognosis.

The usual treatment for maxillary sinus SCC in our institution was surgery with radiotherapy. Radiotherapy with or without chemotherapy was usually advised for patients who were poor surgical candidates.

It has been established in the literature that histopathologic diagnosis is a strong factor for nodal metastasis with a primary SCC or undifferentiated carcinoma being the most likely to result in neck node metastasis.¹¹ The grading of differentiation (well-differentiated, moderately-differentiated, and poorly-differentiated) has been found to have no significant difference in the likelihood for nodal metastasis.¹¹ Only three (3) patients (2 well-differentiated SCC, 1 poorly differentiated SCC) out of the 22 patients in our study presented with positive cervical metastasis, relatively low compared to the high (46%) incidence (69 out of 148 patients) noted in India.^{3,5} This is consistent with findings in literature that nodal metastasis is uncommon in tumors without extensive lymphatic involvement, as is the case for the maxillary sinus.¹¹ Studies such as by Le *et al.*, found an overall incidence of 15.5% for neck node metastases in patients with Maxillary SCC.¹² Due to this low rate of neck node metastasis, elective neck dissection is not routinely done for patients with maxillary sinus SCC in our institution. Fine needle aspiration biopsy (FNAB) is likewise not done for clinically palpable neck nodes among patients with maxillary sinus SCC as these patients are treated with an additional neck dissection. Our results may underestimate the incidence of neck node metastases in our institution. However, FNAB may be explored as an option to determine neck node metastasis among patients who are not good candidates for surgical management.

There have been conflicting reports regarding factors influencing nodal metastasis, with some studies citing that extension of tumor outside of the maxillary sinus was closely related to the risk of cervical lymphadenopathy for maxillary sinus SCC.^{12,13} Another study reports that staging (T2 in particular) confers a higher risk for nodal metastasis than T3 or T4 tumors.⁴ A study by Ahn *et al.* found that the increase in risk begins with T2 tumors and progresses to T3 and T4 tumors as well.¹⁵ All three patients who presented with positive cervical metastasis were staged as T4a tumors and 2 of the 3 patients were positive for tumor at the area of the pterygoid plates. These findings may be worth investigating in future research.

There are several limitations to this study. First, the limited sample size precludes the generalizability of our findings. Our series was also limited to the patients of one department (otorhinolaryngology) in our hospital and does not reflect the general surgery census of the same hospital. It is recommended that more patients with maxillary sinus SCC be included in future studies to gain more insight from trends observed in the data. The inclusion of imaging findings and post-treatment follow-

up in the analysis will make the data more robust. Second, no association between the variables and the diagnosis of maxillary sinus SCC may be drawn from this series due to the limited number of patients included. The authors aimed to establish preliminary data for this condition and such associations may better be evaluated using other methods of statistical analysis in future studies with a larger sample size. A longer study period can also allow us to evaluate outcomes. Third, review of patient records limits the kind of data available. Clinicians usually do not ask about (or write down) technical risk factors such as exposure to substances and these may only be implied based on employment. In retrospect, broader inclusion criteria—including all types of maxillary sinus cancers— might have resulted in more patients and may have provided a more comprehensive understanding of the clinical behavior and outcomes of various maxillary sinus malignancies in our institution.

In conclusion, our series found that maxillary sinus SCC occurs more in males, with a maxillary mass as the most common chief complaint. Delays in treatment are usual, with a mean gap of 6 months between initial symptoms and consult. Neck node metastasis is uncommon and most patients undergo surgery with radiotherapy as treatment.

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