Maxillary sinus carcinoma

Natural history and outcome

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ABSTRACT

Objective: To assess natural history, treatment outcome and pattern of relapse in patients with maxillary sinus carcinoma.

Methods: A review was conducted of the medical records of all adult patients with maxillary sinus carcinoma, who were treated at King Faisal Hospital and Research Centre, Riyadh, Kingdom of Saudi Arabia, between January 1990 and December 1999. A total of 60 patients were identified for analysis, 36 men and 24 women; the median age was 58-years (range 23-95). Major presenting symptoms were facial swelling 55%, facial pain 50%, and nasal obstruction 43.4%, with a median duration of 5-months (range 1-24). Histology was quamous cell carcinoma in 71.7% and adenoid cystic in 16.7%. They were restaged according to American Joint Committee on Cancer classification 1997 as II, III and IV in 1, 10 and 49. Thirty patients received treatment with curative intent (surgery in 4 patients, radiotherapy in 2, and combined modality in 24), 6 patients refused treatment and 24 were treated palliatively.

Results: With a median follow up of 50-months (range 2–128) in surviving patients treated with a curative intent, 12/30 failed locally, 4/30 in the regional neck nodes and 2/30 had systemic relapse. The actuarial 5-year overall survival (OS), relapse free survival (RFS) and local control rate (LC) were 55%, 39% and 51%. Treatment modality was the only significant prognostic factor for outcome, with 5 year OS, RFS and LC of 72%, 49% and 61%, for combined modality using surgery followed by radiotherapy compared to 0% for single approach (p=0.0003, p=0.0052 and p=0.0098)

Conclusion: This study indicates that the majority of our patients presented with advanced disease, resulting in poor outcome to conventional treatment modalities. Efforts should be directed to minimize the delay in diagnosis at the primary care level. Combined modality treatment should be offered to all patients with locally advanced disease. New approaches such as neoadjuvant or concurrent chemoradiotherapy with or without surgery need to be considered and evaluated in prospective studies.

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Cancer of the paranasal sinuses is a rare disease. It represents 3.9% of head and neck cancer and 0.3% of all malignancies diagnosed annually in the Kingdom of Saudi Arabia (KSA).[1] The optimal modality of management is still undefined. A wide variety of treatment options have been used such as radiation, surgery and chemotherapy in different combinations and sequences.[2-7] However, it is difficult to achieve satisfactory results mainly as of complicated anatomic structures. Several studies have indicated a dismal outcome and poor prognosis of this disease.[8-12] New advances in the last decade have resulted in survival improvement and have influenced other methods of treatment.[9-11] The

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purpose of this paper is to assess the natural history, treatment outcome, and pattern of relapse in patients with maxillary sinus carcinoma in KSA.

Methods. The King Faisal Specialist Hospital and Research Centre (KFSH&RC) is the main tertiary referral center for 186 public hospitals and numerous private clinics in the Kingdom of Saudi Arabia. Using the tumor registry, and head and neck cancer database, 60 adult patients consecutively presented with maxillary sinus carcinoma between January 1990 and December 1999, were identified and retrospectively reviewed. All patients were jointly evaluated at a multidisciplinary combined clinic by head and neck surgeons and radiation oncologists. They were restaged according to American Joint Committee on Cancer (AJCC) classification 1997, based on physical examination; routine laboratory tests, chest x-ray, and computerized tomography (CT) scan of the head and neck. Histological diagnosis was proven with biopsy. Relapse was defined based on clinical examination and pathological confirmation. Thirty patients were treated with curative intent, 4 underwent radical surgery (all stage III), 2 underwent radiation therapy (one stage II and the other is IV), and the remaining 24 patients underwent combined modality approach utilizing surgery and radiation. Six patients refused treatment and 24 received palliative treatment. Of the patients treated by surgery, partial maxillectomy was performed in 14 followed by radiation in 12 of them, total maxillectomy in 9 followed by radiation in 7, and total maxillectomy with orbital exenteration followed by radiation therapy in 5 patients. Radiation therapy was delivered using either Co60 or 6MV linear accelerator with a dose ranging from 50-66 Gy in conventional fractionations for patients treated with curative intent and 8-30 Gy in palliative cases. Radiation therapy started 3-5 weeks after surgery.

Statistical methods. The overall survival (OS) was calculated from the date of diagnosis to the date of last follow up or death from any cause, and relapse free survival (RFS) was measured from treatment completion date to the date of clinical recurrence or last follow up. The local control rate (LC) was measured from date of treatment completion to the date of local relapse or last follow up. Patients with residual local disease after completion of the treatment were considered having zero time of local control. Patients who died of other causes were censored on the date of death. Patients lost to follow up were included in all analyses, and were censored on the date of last follow up. Univariate analysis was performed to evaluate prognostic factors, and survival curves were plotted using the Kaplan Meier methods and

Table 1 - Patient characteristics.

Variable	n	(%)
Sex		
Male	36	(60)
Female	24	(40)
Age		
≤40	11	(18.3)
>40	49	(81.7)
Habit		
Smoker	13	(21.7)
Shamma	4	(6.3)
Pathology		
Squamous cell ca.	43	(71.7)
Adenoid cystic ca.	10	(16.7)
Undifferentiated ca.	5	(8.3)
Adenocarcinoma	2	(3.3)
Neck node		
-ve	46	(77)
+ve	14	(23)
Distance metastasis		
-ve	56	(93.7)
+ve	4	(6.7)
Stage		
II	1	(1.7)
III	10	(16.7)
IV	49	(81.6)
Treatment aim		
Curative	30	(50)
Palliative	24	(40)
Patients refused	6	(10)

- ve - negative, + ve - positive, ca.- carcinoma

Table 2 - Presenting symptoms.

Variable	n	(%)	Median duration (m)	Range (m)
Symptoms				
Facial swelling	33	(55)	5	1-12
Facial pain	30	(50)	4	1-12
Nasal obstruction	26	(43.4)	4	2-18
Nasal bleeding	12	(38.3)	3	1-24
Toothache	15	(25)	5	2-18
Mouth ulcer	14	(23.3)	5	1-24
Visual disturbance	14	(23.3)	5	1-24
Tooth mobility	13	(21.7)	4	1-12
Headache	11	(18.3)	8	3-24
Nasal discharge	4	(6.7)	7	3-12

Table 3 - Prognostic factors.

Variable	n	5y. OS	*P* value	5y. RFS	*P* value
Age					
<40	9	67		44	
>40	21	50	NS	43	NS
Sex					
Male	19	54		45	
Female	11	60	NS	30	NS
Smoking					
Yes	15	51		40	
No	15	61	NS	38	NS
Stage					
II	1	----*		----*	
III	10	56		44	
IV	19	52	NS	34	NS
Treatment modality					
Combined	24	72		49	
Single	6	0	0.0003	0	0.0052
Pathology					
Scca	18	50		45	
Adenoid cystic	7	56	NS	38	NS

* not reached, RFS - relapse free survival, OS - overall survival

compared using the log rank test. Differences were considered significant for p value ≤0.05. All P values were 2 tailed. Statistical program for social sciences (SPSS) version 10.0 computer program was used for all analyses.

Results. Patients details and presenting symptoms are listed in **Table 1 & 2**. The median age at diagnosis was 58-years (range 23-95), with a male to female ratio of 1.5:1. The majority of patients were older than 40-years (81.7%), and 13 patients were smokers. Squamous cell carcinoma was the main histological type representing 71.7% of all patients, and regional nodes were involved in 23% at time of presentation.

Survival. With a median follow up of 50-months for surviving patients who received curative treatment (range 2-128), data were available for all patients except 3 lost to follow up, 2 were free from disease at last evaluation. Fourteen patients died all from disease, apart from one from unrelated cause. The 5 year OS and RFS were 55% and 39%.

Local control and patterns of failure. Out of 30 patients who underwent radical treatment, 5 had persistent local disease, and 13 relapsed with a median time of 7-months (range 1-50). Fifty-four percent of relapsed cases were local, 31% in the regional neck lymph nodes and 15% had distant metastasis. Three patients were successfully salvaged after relapse; 2 of them after neck node recurrence, and one was a local failure. The 5-year LCR was 51%.

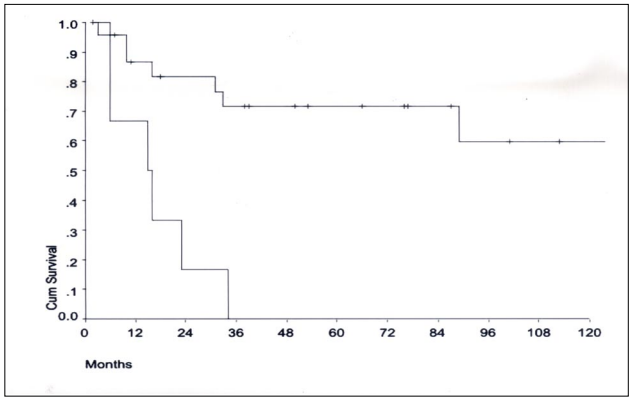

Figure 1 - Overall survival.

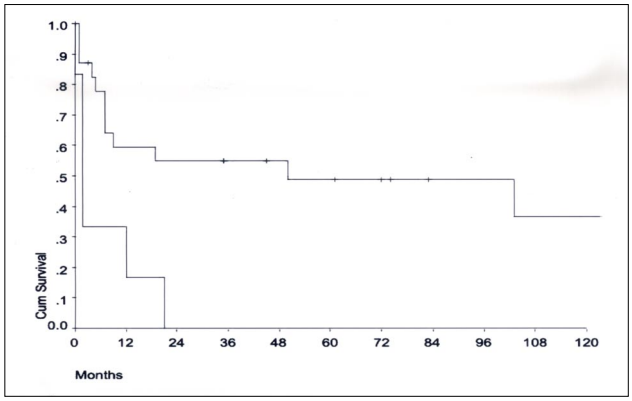

Figure 2 - Relapse free survival.

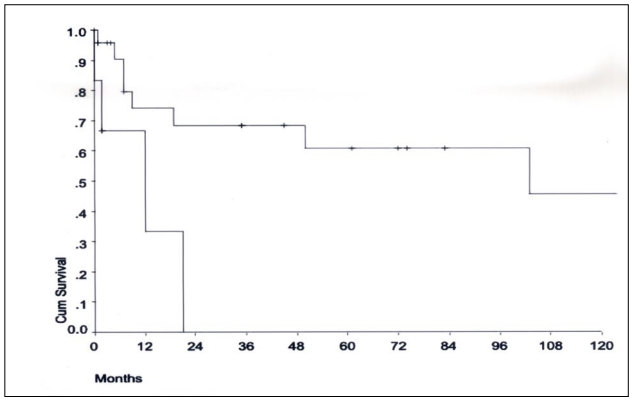

Figure 3 - Local control.

Prognostic factors analysis. Univariate analysis for the influence of patient, tumor and treatment related variables on relapse free and over all survival rates are presented in **Table 3**. Treatment modality was the only significant factor that predicted difference in outcome for OS, RFS and LCR in favor of combined approach over single modality using either surgery or radiotherapy. Patients underwent combined modality therapy had 5-year OS, RFS and LC of 72%, 49% and 61%, compared to 0% for single approach (p=0.0003, p=0.0052 and p=0.0098) **(Figures 1, 2 & 3)**.

Discussion. Maxillary sinus is a pyramid shaped cavity lined by ciliated epithelium and is bound by bony partitions. Tumors commonly arise from the epithelium, or the mucous gland, and invade underling bone in early course of the disease. Symptoms from tumor are usually vague and non-specific, particularly in early stages. It is not rare for patients to be misdiagnosed and treated as sinusitis prior to tumor progression. Ninety-eight percent of our patients presented with advanced disease at time of diagnosis. The dry desert atmosphere and frequent dust exposure in countries such as KSA could explain the delay in diagnosis. Most published reports from different countries indicated high percentage of locally advanced cases at presentation.[8-10] The incidence of regional neck nodes metastasis varies in the literatures ranging from 4-15%.[8-14] However, it was 23% in our patients indicating more advanced cases in this paper. The male predominance in this cohort of patients is in concordance with other series, which may be linked to more risk factors exposure. The 5-year OS and RFS for our patients were 55% and 39%. This is in keeping with other recently reported outcomes.[2,8,9] The prognostic factors analysis revealed that, combined modality treatment approach using surgery followed by postoperative radiation is the strongest predictor for both 5-year OS and RFS with a value of 72% and 49%. The patients treated by single modality failed to live more than 36 months, despite having early stage disease. The influence of multimodality treatment on the outcome of maxillary sinus carcinoma was also observed by several authors in a number of retrospective studies.[8-12,15,16] Our study failed to detect any significant influence regarding age, gender, habit or histological type on the clinical outcome; although Le et al[11] showed that gender and age were independent prognostic factors. The effect of age was also reported by Hayashi et al,[10] as patients younger than 60-years do better than older groups. This could be linked to more aggressive treatment for younger patients. Local disease extent is a well known prognostic factor with a strong association with outcome[11,13,14] however, only a trend for better outcome not reaching a statistical significant was observed in our series, mainly due to the small sample size. Failure at the primary site is the most frequent pattern of recurrence in this tumor, with a low salvage rate and dismal prognosis.[9-11] Our result indicated that combined modality therapy using surgery followed by radiotherapy improves the LC. Several authors have reported similar observation.[8-11] In order to improve the LC, additional modalities were used such as topical or intra-arterial chemotherapy, especially in Japanese literature but have not made a significant impact in the treatment of maxillary sinus cancer and could not be reproduced elsewhere.[9-12]

In conclusion, our study indicates that the majority of our patients presented with advanced disease, resulting in poor outcome to conventional treatment modalities. Efforts should be directed to minimize the delay in diagnosis at the primary care level. Preplanned combined modality treatment should be offered to all patients with locally advanced disease. New approaches such as neoadjuvant or concurrent chemoradiotherapy with or without surgery need to be considered and evaluated in prospective studies.

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