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Original Article

MAXILLARY SINUS CARCINOMA: TREATMENT OUTCOME

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ABSTRACT

Introduction: Treatment of cancers of paranasal sinuses poses important challenges to the head and neck surgeons, radiation and medical oncologists. This study presents treatment outcome in 33 patients, who were retrospectively treated between 2000 and 2007.

Materials and Methods: The records of 33 patients (17 men and 16 women) with maxillary sinus squamous or adenocarcinoma treated with curative intent at Clinical Oncology and Nuclear Medicine Department, Mansoura University were analyzed. Patient›s age ranged from 24 to 85 years (median 50 years). Most tumors were locally advanced at presentation. All patients underwent conventional radiotherapy (RT), combined with surgery in 89% and 58%, received chemotherapy.

Results: The majority of patients presented with locally advanced disease (27 patients, 82%); nodal involvement was observed in 2 patients (6%). The most common site of recurrence was at the primary site, which was observed in 14 patients (42%) and regional failures occurred in 6 (18%). The 3 and 5-year overall survival was 36% and 33% and the disease free survival was 36% and 27%, respectively.

Conclusion: The majority of patients present with advanced disease resulting in poor outcome to conventional treatment modalities. Locoregional tumor progression and recurrence remain a significant pattern of failure. New approaches such as neoadjuvant or concomitant chemoradiotherapy with aggressive surgery need to be considered and evaluated in prospective studies.

Key Words: Squamous, adenocarcinoma, maxillary sinus, radiotherapy, chemotherapy, recurrence.

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INTRODUCTION

Cancers of the paranasal sinuses (PNSs) are uncommon, account about 3% of aerodigestive malignancies[1]. Their treatment poses important challenges to the head and neck surgeons, radiation and medical oncologists[2-5]. They are associated with suboptimal outcomes and significant tumor and treatment – associated morbidity[4-11]. PNSs often present in advanced stages. The complex anatomy and the close proximity of critical structures compromise effectual surgical excision and radiation deliverance[2,12,13]. Substantial uncertainty surrounds their fundamental aspects of treatment, hence the optimal therapy remains to be defined[14].

The purpose of this paper is to present the experience in the management of patients with maxillary sinus carcinoma treated with curative intent at Clinical Oncology and Nuclear Medicine Department, Mansoura University.

MATERIALS AND METHODS

The medical records of 33 patients with the diagnosis of maxillary sinus carcinoma treated with curative intent between 2000 to 2008 were reviewed.

There were 17 males and 16 females. The median age was 50 years (range 24-85 years). The most common presenting symptom was facial swelling (61%), followed by pain (39%), nasal obstruction (27%), epistaxis (15%) and crainial nerve neuropathy (12%). Facial edema and symptoms of sinusitis, each was present in 1 (3%) patient.

The diagnostic evaluation at presentation included a complete physical examination and CT/or MRI of the sinuses and brain. All patients were restaged retrospectively according to the 2002 American Joint Committee on Cancer Staging System (AJCC) for maxillary sinus tumors[15]. The majority of patients presented with advanced stage (III and IV, 82%). Nodal disease at presentation was seen in 2 patients. One patient had N1 and the other had N2 disease. No patient had distant metastases at time of diagnosis.

All patients had biopsy-proven squamous cell (79%) or adenocarcinoma (21%) of maxillary sinus. Differentiation of histologic subtypes was available in 23 of 33 patients; the tumor was well differentiated in 5 patients, moderately differentiated in 7 patients and poorly differentiated in 11 patients. Table (1) shows the general characteristics of patients.

Table 1: Patient characteristics.

Parameter	No. of patients (N=33)	%
Age (years)		
Mean ± SD	50.39 ± 13	
Median	50	
Range	24 – 85	
Sex		
Male	17	51.5
Female	16	48.5
Sex ratio (male: female)	1: 0.9	
Symptoms		
Mass	20	61
Pain	13	39
Nasal obstruction	9	27
Epistaxis	5	15
Cranial neuropathy	4	12
Facial edema	1	3
Sinusitis	1	3
Tumor stage (AJCC)		
I	2	6
II	4	12
III	20	61
IV	7	21
Histological Type		
Squamous cell carcinoma	26	79
Adenocarcinoma	7	21
Grade		
Well differentiated	5	15
Moderately differentiated	7	21
Poorly differentiated	11	33
Unknown	10	31

All the 33 patients were treated with a curative intent. Twenty-nine (88%) patients were treated with surgery followed by postoperative radiotherapy. The surgical extent ranged from radical maxillectomy in 2 (6%) patients, to total maxillectomy in 20 (61%), partial maxillectomy in 7 (21%) and 4 (12%) patients underwent biopsy only. Negative resection margins were achieved in 3 (9%) patients and 6 (18%) had positive margin, while margin status was unknown in 24 (73%) patients in postoperative microscopic examination. Two (6%) patients underwent a neck dissection. Nineteen (77%) patients received chemotherapy, of them 10 (30%) underwent adjuvant therapy, while 9 (27%) received concurrent radiotherapy and chemotherapy. The agents used included cisplatinum and 5-flurouracil. Radical RT alone was offered in 4 (12%) patients (Table 2). All patients underwent radiotherapy using 60Co -rays or 6-MV X-rays. Patients were treated using either a two- or three field, wedge pair arrangement. The median dose to the primary site for patients receiving postoperative RT was 5000 cGy; for those receiving RT alone and concurrent CT and RT it was 6000 cGy. The regional nodes were only treated in patients with neck node involvement.

Table 2: Treatment characteristics.

Parameter	No. of patients (N=33)	%
Surgery, primary tumor Procedure		
Radical maxillectomy	2	6
Total maxillectomy	20	61
Partial maxillectomy	7	21
Biopsy	4	12
Margin Status		
Negative	3	9
Positive	6	18
Unknown	24	73
Neck dissection		
Yes	2	6
No	31	94
Chemotherapy		
Yes	19	58
No	14	42
Timing		
Adjuvant	10	30
Concurrent	9	27
Radiotherapy		
PORT + CT	19	58
PORT	10	30
RT alone	4	12

Statistical Analysis:

Overall survival and disease free survival were calculated using the Kaplan – Meier method. These end points were determined from the date of diagnosis until the event of death for survival and local or regional failure for disease free survival.

RESULTS

After a median follow up of 18 months (range 4-90), 11 (33%) patients were alive at time of analysis; of these 9 (27%) had no clinical evidence of disease. Twenty two patients (67%) had died during the evaluation period, 14 (42%) as a result of recurrent or persistent primary tumor, 4 (12%) of treatment complications, 3 (9%) of other causes without evidence of disease. The cause of death was unknown in 1 (3%) patient. The majority of recurrences were within 1 year of diagnosis.

Out of the 33 patients, 16 (48%) relapsed. Fourteen (42%) patients experienced local recurrence, while 6 (18%) had regional recurrence. Isolated local and neck relapse were demonstrated in 10 and 2 patients, respectively. Isolated local failure was the most common pattern of recurrence (Table 3).

Recurrence was demonstrated in 13 out of 26 (50%) patients with SCC and in 3 out of 7 (43%) patients with adenocarcinoma histopathology.

Surgery was done in 29 patients. Fifty three percent of patients who received PORT + CT failed treatment while 20% of those received PORT only experienced relapse. All patients who received RRT relapsed (Table 3).

Table 3: Patterns of recurrence in relation to treatment modality.

Treatment (no.)	Local	Regional	Locoregional	%
PORT + CT (19)	9	1	-	53
PORT (10)	-	1	1	20
RRT (4)	1	-	3	100

Radiotherapy-related complications occurred in 7 patients (21%) and included brain necrosis, conjunctivitis, oromaxillary fistula, persistent mucositis, trismus and blindness (Table 4).

Table 4: Treatment Complications.

Complication	No. of patients (N = 33)	%
Brain necrosis	1	3
Conjunctivitis	1	3
Oromaxillary fistula	1	3
Persistant mucositis	1	3
Trismus	1	3
Blindness	2	6

The 3 and 5-year overall survival of the 33 patients was 36% and 33%, respectively (Figure 1). The 3 and 5-year disease free survival was 36% and 27%, respectively (Figure 2).

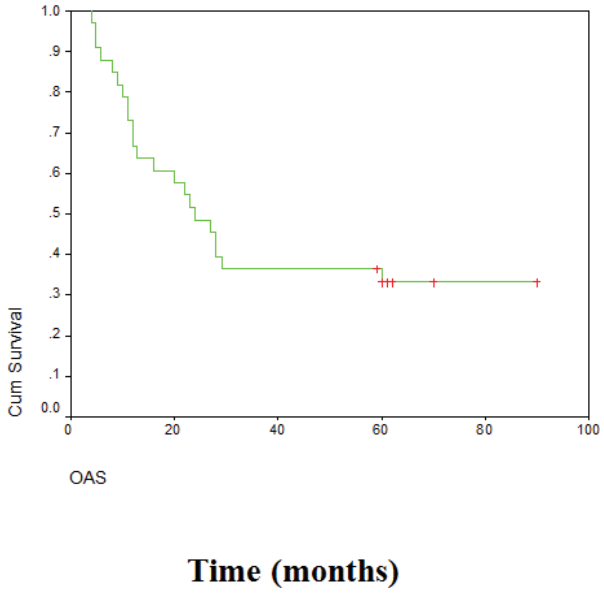

Figure 1: 5- year Overall survival.

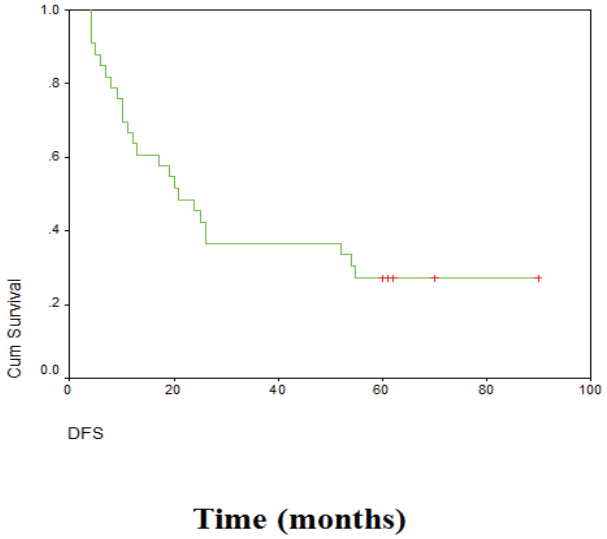

Figure 2: 5- year Disease free survival.

DISCUSSION

The patient distribution in the present study was consistent with other publications ; males are more commonly affected than females, most patients present with locally advanced tumors; 82% of our patients presented with T3 or T4 disease.

The presenting signs and symptoms result from invasion of the surrounding critical structures. In a series of 106 patients, Blanco et al.[3] described pain in 43%, nasal obstruction in 36%, cranial neuropathy in 26%, epistaxis in 24% and sinusitis in 14% of the cases. The presentation was similar in our patients with mass (61%) pain (39%), nasal obstruction (27%), epistaxis (15%) and crainial neuropathy (12%) as the most common presenting clinical features. Clinically positive cervical metastases were present in 6% of patients in the present series. This is in keeping with the 4-15% incidence of adenopathy noted in the literature[11,16-20].

The majority of literature supports the contention that surgery and radiotherapy in combination is the most significant mode of treatment of maxillary sinus carcinoma because this approach has demonstrated superior outcomes. This was evident in this study.

Blanco et al.[3] in 106 patients noted a statistically significant improvement in the disease free survival in the patients receiving combined modality treatment compared to those receiving radiotherapy alone (35% VS 29%; P<0.05). Qureshi et al.[16] reported 5-year overall survival of 42% after combined modality therapy (CMT). Hoppe[21] reported 5-year DFS and OS of 55% and 67%, respectively in 85 patients with PNS cancers treated with post-op RT (62% treated with IMRT or 3-D-CRT, rest with 2D). Daly et al.[22] reported on 36 patients with PNS cancers, 32 after gross total resection. They were treated with IMRT. The 5-year local control, DFS and OS rates were 58%, 55% and 45%, respectively.

Dirix et al.[23] reported actuarial 5-year OS and DFS rates of 54% and 37%, respectively for 127 patients with cancer of the PNSs or nasal cavity who were treated with preoperative or postoperative primary RT, using conventional or 3D-CRT. However Dulguerov et al.[24] demonstrated a progressive improvement in outcomes for all treatment modalities (surgery, surgery + radiotherapy and radiotherapy) during the past 4 decades.

Local failure remains the dominant cause of poor outcome in this tumor[2,12,13]. Pattern of failure in the present series revealed that 42% of patients failed at the primary site. Although our treatment outcomes lie within the published range for maxillary sinus carcinoma treated with surgery and conventional RT[2-4,16,25], strategies for improving local control are needed for the management of this disease. Tiwari et al.[18] have recommended a mandibulotomy for better clearance of the infratemporal fossa. Although, long-term results are awaited, the clearance with this approach seems to be encouraging.

The addition of neoadjuvant CT has been advocated for locally advanced PNSs carcinoma and has been shown to be beneficial in a selected number of patients. In one series 92% DFS was reported at a follow-up of 55 months following neoadjuvant chemotherapy[26]. Similarly, use of preoperative radiotherapy with concomitant intra-arterial chemotherapy has been reported[27].

Samant[27] treated 18 patients (84% T4 lesions) with preoperative high dose intra-arterial cisplatin + IV thiosulfate with concurrent RT (50Gy). Surgery was planned 8 wks post RT (organ sparing, if possible). A 2-yr OS of 68% and 5-yr OS of 53% were reported. However larger studies are needed to confirm these results[2,12,28,29].

In this study 6 out of 33 patients had disease failure in the cervical lymph nodes. The role of elective neck treatment is also debatable. Some authors recommend prophylactic ipsilateral neck irradiation based on their findings of more than 25% incidence of neck failure and high risk distant metastases and poor survival[4,11,20]. Other authors do not favor ipsilateral neck treatment[14,18].

In this study histological type had no influence on the clinical outcome. This was reported by others[30].

Treatment of PNSs cancer is often associated with significant late toxicity. Two of our patients (6%) developed unilateral blindness. Other investigators[31-33] have reported higher rates of unilateral and bilateral blindness, exceeding 60% and 10%, respectively, suggesting an increased incidence of late complications with long-term evaluation. In light of such high incidence of late sequelae, attempts to minimize toxicity with conformal RT21 or IMRT[21,22] techniques seem reasonable. Weber[34] reported acceptable ophthalmologic complications using accelerated fractionated RT for advanced sinonasal malignancies employing photons/ protons. Other treatment complications experienced by patients in this study were brain necrosis (3%), conjunctivitis (3%) oromaxillary fistula (3%), persistent mucositis (3%) and trismus (3%). The incidence rates were higher than that reported by Blanco et al.[3]. This may be attributed to that 11% of their patients were treated with 3D-CRT or IMRT.

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That this is a retrospective study with all of the potential inherent biases associated with this type of review mainly retrospective staging and non randomized treatment selection. But considering the lack of prospective, multi-institutional studies almost all the previous studies have also been based on retrospective studies. Although our long-term outcomes lie within the published range, the high proportion of locoregional failures and overall survival were disappointing and suggest a need for improved local treatment.

CONCLUSION

The present study indicates that the majority of our patients presented with advanced disease, resulting in poor outcomes to conventional treatment modalities. Locoregional disease progression remains a significant pattern of failure. New approaches such as neoadjuvant or concomitant chemoradiotherapy with aggressive surgery need to be considered and evaluated in prospective studies.

REFERENCES

1. Schantz SP, Harrison LB, Forastiere AA. Tumors of the nasal cavity and paranasal sinuses, nasopharynx, oral cavity and oropharynx. In: Devita VT, Hellman S, Rosenberg SA, editors. Cancer: Principles and practice of oncology. 6th ed. philadelphia: Lippincott Williams and Wilkins.; 2000.
2. Le QT, Fu KK, Kaplan M, Terris DJ, Fee WE, and Goffinet DR. Treatment of maxillary sinus carcinoma: A comparison of the 1997 and 1977 American Joint Committee on cancer staging systems. Cancer 1999 Nov 1;86(9):1700-11.
3. Blanco AI, Chao KS, Ozyigit G, Adli M, Thorstad WL, Simpson JR, et al. Carcinoma of paranasal sinuses: Long-term outcomes with radiotherapy. Int.J.Radiat.Oncol. Biol.Phys. 2004 May 1;59(1):51-8.
4. Jiang GL, Ang KK, Peters LJ, Wendt CD, Oswald MJ, and Goepfert H. Maxillary sinus carcinomas: Natural history and results of postoperative radiotherapy. Radiother. Oncol. 1991 Jul;21(3):193-200.
5. St Pierre S and Baker SR. Squamous cell carcinoma of the maxillary sinus: Analysis of 66 cases. Head Neck Surg. 1983 Jul-Aug;5(6):508-13.
6. Jiang GL, Morrison WH, Garden AS, Geara F, Callender D, Goepfert H, et al. Ethmoid sinus carcinomas: Natural

history and treatment results. Radiother.Oncol. 1998 Oct;49(1):21-7.
7. Amendola BE, Eisert D, Hazra TA, and King ER. Carcinoma of the maxillary antrum: Surgery of radiation therapy? Int.J.Radiat.Oncol.Biol.Phys. 1981 Jun; 7(6):743-6.
8. Grau C, Jakobsen MH, Harbo G, Svane Knudsen V, Wedervang K, Larsen SK, et al. Sino-nasal cancer in Denmark 1982-1991--a nationwide survey. Acta Oncol. 2001;40(1):19-23.
9. Hordijk GJ and Brons EN. Carcinomas of the maxillary sinus: A retrospective study. Clin.Otolaryngol.Allied Sci. 1985 Oct;10(5):285-8.
10. Tsujii H, Kamada T, Arimoto T, Mizoe J, Shirato H, Matsuoka Y, et al. The role of radiotherapy in the management of maxillary sinus carcinoma. Cancer 1986 Jun 15;57(12):2261-6.
11. Paulino AC, Fisher SG, and Marks JE. Is prophylactic neck irradiation indicated in patients with squamous cell carcinoma of the maxillary sinus? Int.J.Radiat.Oncol.Biol. Phys. 1997 Sep 1;39(2):283-9.
12. Paulino AC, Marks JE, Bricker P, Melian E, Reddy SP, and Emami B. Results of treatment of patients with maxillary sinus carcinoma. Cancer 1998 Aug 1;83(3):457-65.
13. Stern SJ, Goepfert H, Clayman G, Byers R, Ang KK, El Naggar AK, et al. Squamous cell carcinoma of the maxillary sinus. Arch.Otolaryngol.Head.Neck.Surg. 1993 Sep;119(9):964-9.
14. Waldron JN, O'Sullivan B, Gullane P, Witterick IJ, Liu FF, Payne D, et al. Carcinoma of the maxillary antrum: A retrospective analysis of 110 cases. Radiother.Oncol. 2000 Nov;57(2):167-73.
15. Page DL, Fleming ID, Fritz A, Balch CM, Haller DG, Morrow M. Nasal cavity and paranasal sinuses. In: Greene FL, editor. AJCC Cancer Staging Manual. 6th ed. New York: Springer; 2002.
16. Qureshi SS, Chaukar DA, Talole SD, and D'Cruz AK. Squamous cell carcinoma of the maxillary sinus: A Tata Memorial Hospital experience. Indian J.Cancer 2006 Jan-Mar;43(1):26-9.
17. Giri SP, Reddy EK, Gemer LS, Krishnan L, Smalley SR and Evans RG. Management of advanced squamous cell carcinomas of the maxillary sinus. Cancer 1992 Feb 1;69(3):657-61.
18. Tiwari R, Hardillo JA, Mehta D, Slotman B, Tobi H, Croonenburg E, et al. Squamous cell carcinoma of maxillary sinus. Head Neck 2000 Mar;22(2):164-9.
19. Nishino H, Miyata M, Morita M, Ishikawa K, Kanazawa T, and Ichimura K. Combined therapy with conservative surgery, radiotherapy and regional chemotherapy for maxillary sinus carcinoma. Cancer 2000 Nov 1;89(9):1925-32.
20. Le QT, Fu KK, Kaplan MJ, Terris DJ, Fee WE, and Goffinet DR. Lymph node metastasis in maxillary sinus carcinoma. Int.J.Radiat.Oncol.Biol.Phys. 2000 Feb 1;46(3):541-9.
21. Hoppe BS, Stegman LD, Zelefsky MJ, Rosenzweig KE, Wolden SL, Patel SG, et al. Treatment of nasal cavity and paranasal sinus cancer with modern radiotherapy techniques in the postoperative setting-the MSKCC experience. Int.J.Radiat.Oncol.Biol.Phys. 2007;67(3):691-702.
22. Daly ME, Chen AM, Bucci MK, El Sayed I, Xia P, Kaplan MJ, et al. Intensity-modulated radiation therapy for malignancies of the nasal cavity and paranasal sinuses. Int.J.Radiat.Oncol.Biol.Phys. 2007 Jan 1;67(1):151-7.
23. Dirix P, Nuyts S, Geussens Y, Jorissen M, Vander Poorten V, Fossion E, et al. Malignancies of the nasal cavity and paranasal sinuses: Long-term outcome with conventional or three-dimensional conformal radiotherapy. Int.J.Radiat. Oncol.Biol.Phys. 2007;69(4):1042-50.
24. Dulguerov P, Jacobsen MS, Allal AS, Lehmann W, and Calcaterra T. Nasal and paranasal sinus carcinoma: Are we making progress? A series of 220 patients and a systematic review. Cancer 2001 Dec 15;92(12):3012-29.
25. Bristol IJ, Ahamad A, Oswald MJ, Nguyen L, and Ang K. Post-operative radiation for maxillary sinus carcinoma: Does elective nodal irradiation affect regional control? Int.J.Radiat.Oncol.Biol.Phys. 2005;63(1 Suppl.):S75-6.
26. Rosen A, Vokes EE, Scher N, Haraf D, Weichselbaum RR, and Panje WR. Locoregionally advanced paranasal sinus carcinoma. Favorable survival with multimodality therapy. Arch. Otolaryngol. Head. Neck. Surg. 1993 Jul; 119(7):743-6.
27. Samant S, Robbins KT, Vang M, Wan J, and Robertson J. Intra-arterial cisplatin and concomitant radiation therapy followed by surgery for advanced paranasal sinus cancer. Arch.Otolaryngol.Head.Neck.Surg. 2004;130(8):948-55.
28. Hayashi T, Nonaka S, Bandoh N, Kobayashi Y, Imada M, and Harabuchi Y. Treatment outcome of maxillary sinus squamous cell carcinoma. Cancer 2001 Sep 15;92(6):1495-503.
29. Nibu K, Sugasawa M, Asai M, Ichimura K, Mochiki M, Terahara A, et al. Results of multimodality therapy for squamous cell carcinoma of maxillary sinus. Cancer 2002 Mar 1;94(5):1476-82.
30. Al Jhani AS, Al Rajhi NM, El Sebaie MM, Nooh NS, Mahasen ZZ, Al Amro AS, et al. Maxillary sinus carcinoma. Natural history and outcome. Saudi Med.J. 2004 Jul;25(7):929-33.
31. Parsons JT, Bova FJ, Fitzgerald CR, Mendenhall WM, and Million RR. Radiation optic neuropathy after megavoltage external-beam irradiation: Analysis of time-dose factors. Int.J.Radiat.Oncol.Biol.Phys. 1994 Nov 15;30(4):755-63.
32. Parsons JT, Mendenhall WM, Mancuso AA, Cassisi NJ, and Million RR. Malignant tumors of the nasal cavity and ethmoid and sphenoid sinuses. Int.J.Radiat.Oncol.Biol. Phys. 1988 Jan;14(1):11-22.
33. Sakai S, Kubo T, Mori N, Itoh M, Miyaguchi M, Kitaoku S, et al. A study of the late effects of radiotherapy and operation on patients with maxillary cancer. A survey more than 10 years after initial treatment. Cancer 1988 Nov 15;62(10):2114-7.
34. Weber DC, Chan AW, Lessell S, McIntyre JF, Goldberg SI, Bussiere MR, et al. Visual outcome of accelerated fractionated radiation for advanced sinonasal malignancies employing photons/protons. Radiother.Oncol. 2006 Dec;81(3):243-9.