Retrospective Study

Retrospective analysis of survival of patients with squamous cell carcinoma of the maxilla after primary resection and elective bilateral neck dissection: An institutional experience

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Balakrishnan Ramalingam, Vijay Ebenezer
Department of Oral and Maxillofacial Surgery, Sree Balaji Dental College and Hospital, Pallikaranai, Chennai, India

Address for correspondence:
Dr. Balakrishnan Ramalingam, Department of Oral and Maxillofacial Surgery, Sree Balaji Dental College and Hospital, Pallikaranai, Chennai, India.
E-mail: bala4_us@yahoo.com

ABSTRACT

Background: A retrospective analysis of the 5-year survival rates of patients who underwent treatment for oral squamous cell carcinoma (OSCC) of the maxillary region was performed to analyse the prognostic factors for patient's survival. **Materials and Methods:** Twenty-four patients with SCC of the maxillary region, who underwent treatment at our hospital between 1999 and 2009 were included in the study. The patients underwent primary surgical resection and elective bilateral neck dissection. The patients with tumor positive margins were referred for chemo-radiotherapy after surgery. **Results:** The overall 5-year survival rate was 25%. The patients who had recurrence had presented with T3 or T4 lesions only. Of the patients who died, 14 out of the 18 were those who had tumor-positive margins and had undergone radiotherapy following surgery. **Conclusions:** Primary surgical treatment of SCCs of the maxillary region along with elective bilateral neck dissection yielded some improvement in survival rates, and can therefore be seen as a valuable strategy. Tumor-free resection margins and early detection of the lesion are the most important indicators for favorable prognosis.

Keywords: Maxillectomy, squamous cell carcinoma, survival

INTRODUCTION

With an increase in the abuse of smokeless tobacco, there has been an increase in the incidence of oral malignancies, the most common of them being squamous cell carcinomas (SCC; >90%).[1] The current estimates of age-standardized incidence and mortality associated with oral SCC (OSCC) are 6.6/100,000 and 3.1/100,000 in men and 2.9/100,000 and 1.4/100,000 in women, respectively.[2] A recent study on site prevalence of OSCC conducted in the western Uttar Pradesh has ranked the most prevalent sites as buccal mucosa (63.75%), followed by retromolar area (15%), floor of the mouth (11.25%), lateral border of the tongue (3.75%), labial mucosa (3.75%) and palate (2.5%).[3] Survival in patients with SCC of either the hard palate or maxillary alveolus is significantly influenced by T-stage and cervical nodal metastases.[4] The routine therapy usually consists of three strategies: radiotherapy, chemotherapy and radical surgical resection of the tumor including the lymph node levels involved according to the TNM staging. The three strategies are used in different ways and combinations and many concepts are described in the literature.[5-7]

Indications for postoperative radiotherapy (PORT) included Stage III or IV OSCC according to the 2002 criteria of the American Joint Committee on Cancer, the presence of perineural invasion or lymphatic invasion, the depth of tumor invasion or a close surgical margin. In a recent study by Fan *et al*, the 3-year overall and recurrence-free survival rates of OSCC

patients treated with PORT were estimated to be 73% and 70%, respectively. Univariate analysis revealed that differentiation, perineural invasion, lymphatic invasion, bone invasion, location (hard palate and retro-molar trigone), invasion depths > or =10 mm, and margin distances < or =4 mm were significant prognostic factors. The presence of multiple significant factors of univariate analysis correlated with disease recurrence. The 3-year recurrence-free survival rates were 82%, 76% and 45% for patients with no risk factors, one or two risk factors, and three or more risk factors, respectively.[8] In an another study by Lin *et al*, it has been found that the primary tumor site and neck stage are the prognostic predictors in advanced-stage oral cancer patients who received radical radiotherapy. The primary tumor extension and radiotherapy technique did not influence survival.[9]

However, surgery is considered a better treatment strategy than concurrent chemoradiation therapy for achieving positive survival outcomes. Wang *et al*, after a 10-year review of cases in a tertiary care referral center found a higher surgical salvage rate in patients with hard palatal cancer who had local recurrence or neck relapse. Soft palate or infratemporal fossa involvement had poor outcomes. Ulcerative tumor features, tumor volumes larger than 10 ml and local recurrent tumors that could not undergo salvage surgery also had poorer survival outcomes. Surgical management is still the first choice for patients with hard palate or alveolus SCCs even when patients had local or regional recurrence.[10]

In this retrospective study at our hospital we evaluated the treatment of SCC of the maxilla and the paranasal sinuses primarily by surgical means and to identify risk factors for the patients' survival.

MATERIAL AND METHODS

Twenty-four patients with SCC of the maxillary alveolus, hard palate and/or soft palate confirmed by incisional biopsy, who were treated at the Department of Oral and Maxillofacial Surgery at our hospital between 1999 and 2009 with a minimum of 5-year follow-up were retrospectively analyzed and included in the study. All patients underwent surgical resection of the tumor along with elective bilateral lymph node resection without preoperative radiotherapy or chemotherapy as per decisions taken by the tumor board. TNM staging was determined as per the clinical and radiological findings. The tumor was graded after histopathological examination of the biopsy specimen. The patient data was obtained from case sheets and the medical records [Tables 1-4]. The surgical procedure was based on the TNM staging and the location of the tumor. The lesions were excised along with a minimum of 1 cm symptom-free margin after obtaining due consent from the patients. However, in some cases tumor-free margins could not be ascertained due to the position of the tumors. Approach was determined by the size and the location of the tumor. Intraoral approach was used for small lesions, large lesions required Weber Fergusson approach. Midline lesions were removed by midfacial degloving [Figures 1-9]. In cases where the tumor extension was beyond the ethmoid or the orbit, the incisions were modified accordingly. Care was taken to preserve palpabrae and conjunctiva for orbital prosthesis. The reconstruction of the defect after resection was decided according to the size and staging. Most defects could be closed by local flaps, the buccal fat pad or pedicled temporal flap immediately after resection. Some cases with large defects were referred for free microvascular flaps. An obturator prosthesis was applied to facilitate closure of the defect. After resection, the specimens were sent for histopathological examination to ascertain tumor-free margins.

Table 1: TNM Staging

T1	3	N1	3	M1	0
T2	0	N2a	2		
T3	9	N2b	1		
T4	12	N2c	1		
		N3	0		

Table 2: Grading

G1	6
G2	11
G3	7

Table 3: Tumor localization

		Survival
Alveolus	4	2
Hard palate	3	1
Soft palate	3	0
Alveolus and hard palate	3	1
Hard palate and soft palate	2	1
Palate and pterygoids	1	0
Alveolus, hard and soft palate	3	0
Palate and maxillary sinus	2	1
Palate, maxillary sinus and orbit	1	0
Palate, maxillary sinus, ethmoids	1	0
Palate, maxillary sinus, orbit, ethmoids and skull base	1	0

Table 4: Survival rates

Parameter	No. of patients	No. of patients who survived disease free for 5 years	5-year survival %
Age (yrs) <50	6	2	33.3
Age (yrs) ≥50	18	4	22.2
Female gender	9	3	33.3
Male gender	15	3	20.0
T1	3	3	100.0
T2	0	0	0.0
T3	9	2	22.2
T4	12	1	8.3
N- 0	17	5	29.4
N 1–2	7	1	14.3
Grade 1	6	3	50.0
Grade 2	11	2	18.2
Grade 3	7	1	14.3
Perineural invasion + ve	2	0	0.0
Lymphatic invasion + ve	12	2	16.7
Bone invasion + ve	10	1	10.0
Invasion depth > 10 mm	7	1	14.3
Resection margin > 1.5 cm	6	6	100.0
Surgery alone	9	5	55.6
Surgery and RT	15	1	6.7
Overall duration of RT ≤50	10	1	10.0
Overall duration of RT >50	5	0	0.0
Overall dosage of RT <65 gy	9	1	11.1
Overall dosage of RT ≥65	6	0	0.0

Figure 1: (a, b) Preoperative appearance of the tumor

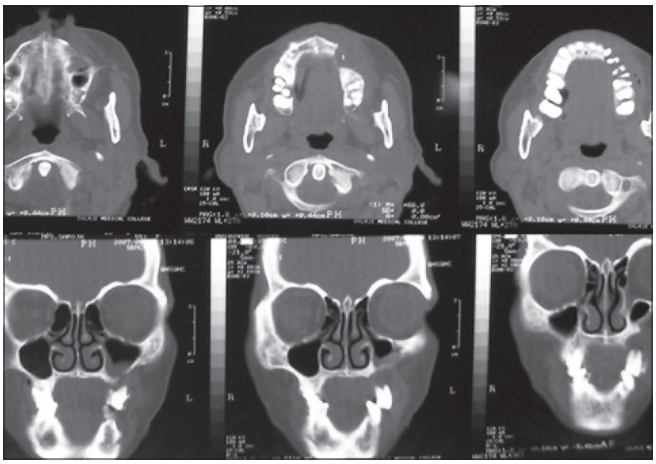

Figure 2: Preoperative CT

Figure 3: Weber Fergusson incision

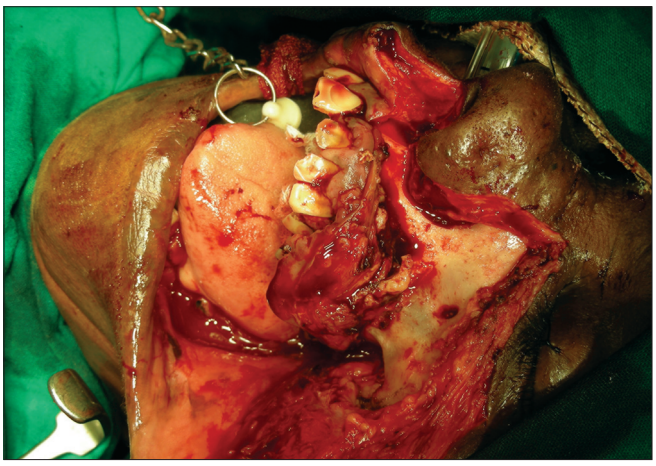

Figure 4a: Exposure

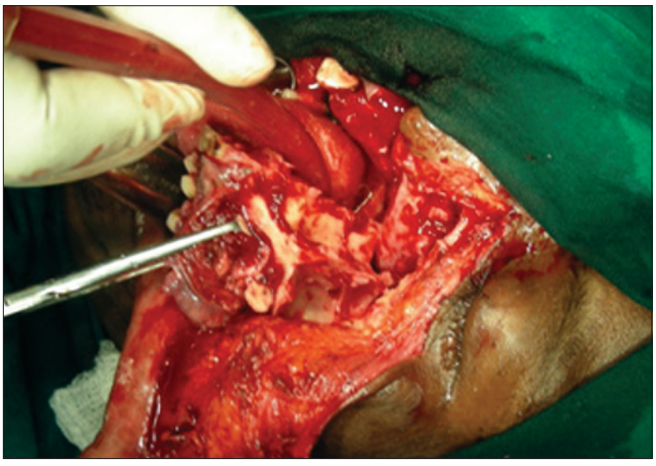

Figure 4b: Resection

RESULTS

All patients underwent surgical removal of their tumors. Bilateral neck dissection was performed simultaneously. Sixteen patients were reconstructed using local flaps and eight patients were referred for microvascular reconstruction and were provided a temporary prosthetic obturator. Eighteen patients succumbed to the tumor in the 5-year follow-up. Of them, four had undergone

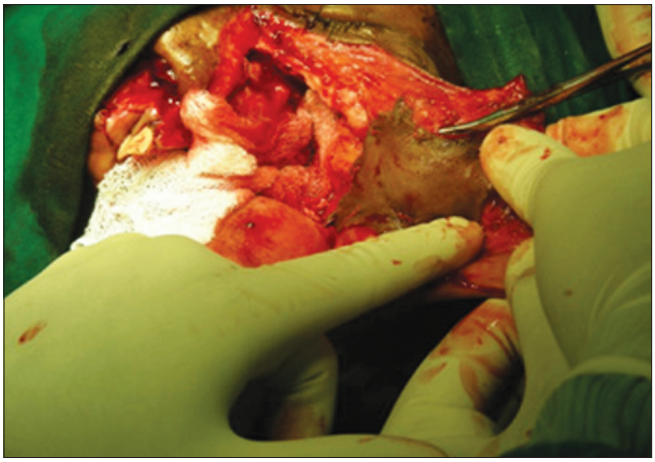

Figure 5: Closure of the defect using split skin graft harvested from the inner aspect of the thigh

Figure 6: Immediate postoperative appearance with temporary prosthesis

Figure 7: Healing of skin graft

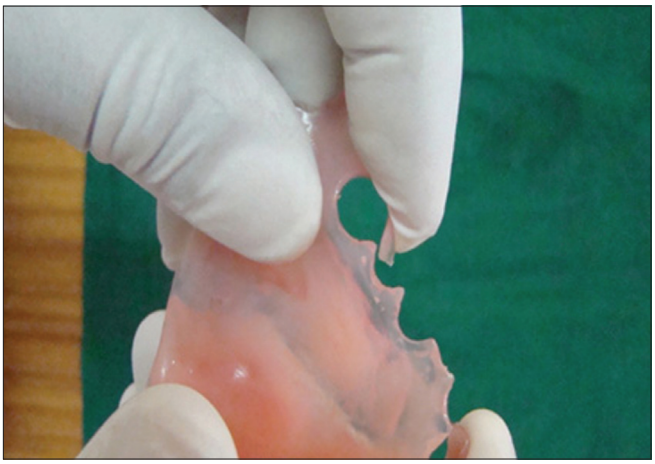

Figure 8: Flexible obturator replacing the temporary one

Figure 9: (a) Postoperative appearance, (b) Postoperative occlusion, (c) Postoperative smile

surgical resection alone and 14 had undergone surgery followed by Radiotherapy.

In six patients, the tumor could not be resected with a clear 1-cm border due to its extensive spread, where resection would involve damage to vital organs. In nine patients, the margins were tumor positive microscopically. All these 15 cases were referred to the chemo-radiotherapy team for management. While only seven cases exhibited nodal involvement, 12 of the resected lymph nodes exhibited metastasis. Fifteen patients survived for

24 months and were able to live a life of acceptable quality. The radiation doses for patients who received postoperative radiotherapy was between 46 and 76 Gy. Chemotherapeutic agents used were cisplatin and 5-fluorouracil. The survival rates were tabulated and compared. The survival rate of patients who exhibited perineural spread (0%), bone invasion (10%), lymphatic invasion (16.7%) and those with tumor thickness more than 10 mm (14.3%) exhibited a lower rate of survival.

DISCUSSION

SCC of the maxilla and paranasal sinuses occur less frequently than that of the buccal mucosa, floor of the mouth or lip. However, these tumors are noticed much later by the patients themselves due to their asymptomatic nature. The invasion of the maxillary sinus or the retromaxillary region manifests much later than that of the buccal region.[11] Eighty-seven percent of the 24 cases that were chosen for primary surgical intervention to the Oral and Maxillofacial Department were T3 and T4-sized lesions.

The tumor board has three primary options of treatments to choose from – surgery, radiotherapy and chemotherapy. While multimodal treatment is currently followed widely, the primary treatment is often the one that determines the prognosis and the quality of life of the patient. Choice of surgery as the primary treatment choice has been very successful at our hospital with 2-year survival of 62.5%. Patients with extensive spread beyond the maxilla, into the orbit, the ethmoids and skull base required an adjuvant radiotherapy when tumor-free margins could not be ascertained.

However, the role of postoperative radiotherapy is questionable. In his comparative study of 85 patients with SCC of the maxillary sinus who received all of their treatment at The University of Texas M.D. Anderson Cancer Center between the years 1971 and 1986, Stern *et al*.,[12] conclude that they found no statistical difference between patients who were treated surgically alone and patients who received a postoperative radiotherapy after tumor resection. The overall 5-year survival rate in his study was about 50%. Therefore chemotherapy or radiotherapy are avoided due to the adjuvant complications of osteoradionecrosis, blindness[13] limitations in mouth opening, stomatitis, nausea, xerostomia, pneumonia and hemogram changes with leucopenia or pancytopenia, etc. Surgical therapy after radiation has also been avoided due to the protraction of the treatment and the reduction of blood supply to the maxilla postradiation. Prolonged overall radiation time has been associated with poorer survival and local control. Late severe toxicity from chemo-radiation treatment of tumors has been assessed to be a significant problem in long-term survivors.[14]

However, in some cases where the surgery could be debilitating and deforming, and the prognosis is poor, in order to preserve the quality of life, the extension of the resection is limited and adjuvant therapies are given priority. Especially in cases where extension of the tumor involves the orbit, it is essential to weigh the cons of facial deformity. Since it has also been observed that even after exenteration of the orbit, the prognosis is often poor and therefore some authors suggest the preservation of the orbit to improve the patient's quality of life without compromising survival.[15,16] However, in our cases, we were able to provide the patient with a satisfactory prosthesis and a survival of more than 4 years by choosing surgery as the primary treatment and chemo-radiation as secondary treatment.

Similar conclusions are drawn by Dulguerov *et al*, in a systematic review of 220 patients.[17] They conclude that patients who underwent exenteration of the eye had a longer survival than those who opted not to. Similarly, those who underwent surgery had the highest survival rate, (79%) followed by those who had surgery and radiation (66%). Those who had radiation alone had the lowest survival rates (57%). In cases where tumor-negative resection margins could not be achieved because of the invasion of the tumor, primary surgery and postsurgical radiotherapy were advised. The achievement of negative resection margins has been a crucial prognostic factor.[14] In our study, 15 patients had positive resection margins and 14 of them (93.3%) died due to disease recurrence and spread.

The presence of positive lymph nodes is quite rare in cases of maxillary SCC compared with other subsites in the oral cavity.[18] In our series, only seven patients (29.4%) showed metastases at the time of operation but all received therapeutic neck dissection. Chiu *et al*, performed a chart review on all patients undergoing primary surgery and elective bilateral neck dissection for supraglottic carcinoma between 1989 and 2000 and found that the 2-year survival increased from 72% to 82.6%.[19] Simental *et al* also recommended elective neck dissection because of the better functional outcome compared with radical neck dissection.[20] SCC has a predilection for cervical metastasis and since occult metastasis cannot be entirely ruled out, it was decided that elective neck dissection be performed in a single stage than to wait for the tumor to recur. All cases where complete tumor resection could be ascertained, primary closure of the defect was done. In cases where the tumor clearance could not be ascertained, the patients were provided with a temporary prosthesis and reconstruction advised after radiotherapy.

A retrospective analysis of 62 patients diagnosed with SCC of the maxillary sinus treated with curative intent between 1994 and 1999 revealed a 3- and 5-year overall survival of 38% and 35% and a disease free survival of 29% and 26%, respectively. Patients with metastases in the cervical nodes fared adversely and died between 4 and 22 months of treatment. Pattern of failure in the series revealed that 45% of patients failed at the primary site. Isolated local failure occurred in 38.7% of the patients and was the most common pattern of recurrence.[21]

CONCLUSION

Our treatment protocol of primary surgical excision and elective neck dissection followed by radiation for cases with tumor-positive margins has yielded a survival rate of 25%. Since recurrence occurred only in T3, T4 patients and more often in patients with tumor-positive margins, we conclude that the complete excision of the tumor and its early detection are the prognostic factors for disease control. Lymphatic spread, thickness of the tumor, bone invasion and perineural invasion are also prognostic factors of importance.

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