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ORIGINAL ARTICLE

Outcome of Treatment in Verrucous Carcinoma of Oral Cavity: A Tertiary Rural Hospital Experience

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Abstract Verrucous carcinoma of oral cavity is a highly well differentiated variant of squamous cell carcinoma with a low potential for invasion and metastasis. It is prevalent in the tobacco quid chewing population in our region. In this observational study, we reviewed the medical case records of 58 patients treated for oral verrucous carcinoma staged T2 to T4a. All patients underwent wide excision of tumour which included marginal mandibulectomy in 22 and hemimandibulectomy in 23 patients along with neck dissection saving the accessory nerve and internal jugular vein. 5 patients were found to have bone involvement along the alveolar sockets. 11 patients had other associated premalignant lesions in oral cavity. Only 2 patients had lymph node metastasis without extra nodal spread in submandibular region. With a mean follow up of 6 years and minimum follow up of 1 year, 3 patients had local recurrence. All these 3 patients had bone involvement and 2 of them had lymph node metastasis on histopathological examination. 3 patients who had associated premalignant lesions developed second primary in oral cavity after 3 years. In our experience, verrucous carcinoma has good prognosis when treated by surgery. Bone involvement along alveolar sockets and associated oral premalignant lesions adversely affect the outcome. There was no difference in the outcome between selective and modified radical neck dissection. Therefore selective neck dissection (supraomohyoid) would be adequate in treating these patients. Adjuvant radiotherapy can be reserved for T4a lesions or for positive margins.

Keywords Verrucous carcinoma · Oral cavity · Outcome of surgery · Recurrence · Composite resection · Premalignant lesions · Bone erosion

Introduction

Head and neck cancers account for about 30% of all malignancies in the Indian subcontinent and 50% of them are oral cancers. The prevalence of oral cancer in India is 20 per 100,000 population. Verrucous carcinoma is a highly well differentiated variant of squamous cell carcinoma with low potential for invasion and metastasis. It was first described in 1948 by Lauren V. Ackermann. It is a slow growing exophytic malignancy with warty appearance and pushing margin. It is associated with addiction to chewable tobacco and betel nut as well as Human papilloma virus infection. The most common sites are oral cavity(buccal mucosa and lip). It is more common in 6th–7th decade of life with a male preponderance. Surgery is the treatment of choice. Radiotherapy is avoided as radiation induced anaplastic transformation has been reported. We performed an observational study to document the risk factors, behavior and aggressiveness and outcome of treatment on 58 patients with verrucous carcinoma of oral cavity.

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Aim

To document the outcome of treatment and clinical and histopathological factors affecting the outcome in verrucous carcinoma of oral cavity.

Objectives

- To document the impact of clinical variables like location of primary tumour and invasion of skin and bone on the outcome of verrucous carcinoma of oral cavity.
- To correlate lymph node metastasis with the stage and location of primary tumour.
- To document the impact of positive or close margins of resection and presence of other premalignant lesions or field cancerization on the outcome in verrucous carcinoma of oral cavity.

Materials and Methods

Source of data It is a retrospective observational study conducted at a tertiary rural hospital from 2001 to February 2018 on patients with Verrucous carcinoma of oral cavity. The Institutional Ethical committee clearance was obtained. Data was analysed from Medical case records by descriptive statistics.

58 patients with verrucous carcinoma of the oral cavity between the ages of 35 to 70 years and staged T2 to T4a were included in this study. Patients with Recurrent oral cancers or Second Primary cancers as well as patients who had received chemotherapy or radiation for any malignancies were excluded from the study. Majority of the patients (56%) were in the age group of 55- 65 years. There were 9 male patients and 49 female patients.

Majority of them were addicted to tobacco quid chewing, smoking, and alcohol. The most common site was buccal mucosa (65%). 32 patients were staged T2 (55%). 17 patients were T3 (29%) and 9 patients were T4a (16%) (Fig. 1). Seven patients had palpable lymph nodes in submandibular region at initial presentation. Associated Premalignant lesions like leukoplakia and Oral submucous fibrosis were found in 11 patients out of whom, field cancerization with condemned mucosa was noted in 9 patients. All the patients in this study were negative for human papilloma virus DNA.

All the patients had surgery as the primary treatment. 45 patients underwent composite resection which included marginal mandibulectomy in 22 (37%) and hemimandibulectomy in 23 patients (39%) (Fig. 2). 2 of these patients required upper alveolectomy also as part of composite resection (Fig. 3). 13 (22%) patients underwent only wide excision of primary tumour.

Modified radical neck dissections, and supra-omohyoid neck dissections (SOHND) were performed in 34 (58%) and 24 (41%) respectively.

Reconstruction was done with pectoralis major myocutaneous flap in 27 patients (47%), supraclavicular flap in 12 patients (20%), fore head flap in 10 patients (17%), skin grafting in 9 patients (16%).

Results

Histopathological examination confirmed verrucous carcinoma in all patients. One patient was found to have positive margin medially where the tumour was extending across the lower alveolus, floor of mouth and into lateral border of tongue. 5 patients were found to have bone involvement on histopathological examination and 6 patients had skin involvement. Among the 5 patients who had bone involvement, 3 had lower gingivo buccal sulcus tumours reaching the alveolar sockets, 1 had buccal mucosa tumour extending to gingiva of last 2 molars and retromolar trigone and in 1 patient the tumour was extending to upper alveolar sockets. Among these 5 patients, 3 recurred within the first year after surgery (Table 1). Among the 6 patients who had skin involvement, the primary tumour was extending minimally to the skin of angle of mouth or lower lip. 3 of them also had tumour involving the mandible.

2 patients had a single metastatic lymph node in submandibular region. Among these 2 patients, 1 had primary tumour involving the entire buccal mucosa and extending to upper alveolus and 1 patient had lower gingvo-buccal tumour extending to retromolar trigone involving the mandible. None of the patients had extra-capsular spread. 23 patients received post operative radiotherapy (39%).

Patients were followed up for a minimum of one year with a mean follow up of 6 years. 3 patients had local recurrence 6 months, 8 months and 9 months respectively after surgery. Among these 3 patients 2 were lower gingivo-buccal sulcus tumours staged T4a at presentation as they had skin and bone involvement and 1 patient was staged T3 with tumour extending into floor of mouth and lateral border of tongue and had positive margin on resection. All these 3 patients had associated premalignant conditions in oral cavity at the time of initial presentation (2 had leucoplakia and areas of submucous fibrosis and 1 patient had field cancerization in oral cavity) (Table 2). 2 patients were salvaged by wide excision of recurrent tumour and a local boost of radiotherapy with chemotherapy (Cisplatin). 3 patients developed second primary in

Fig. 1 Pre operative photographs of patients with oral verrucous carcinoma

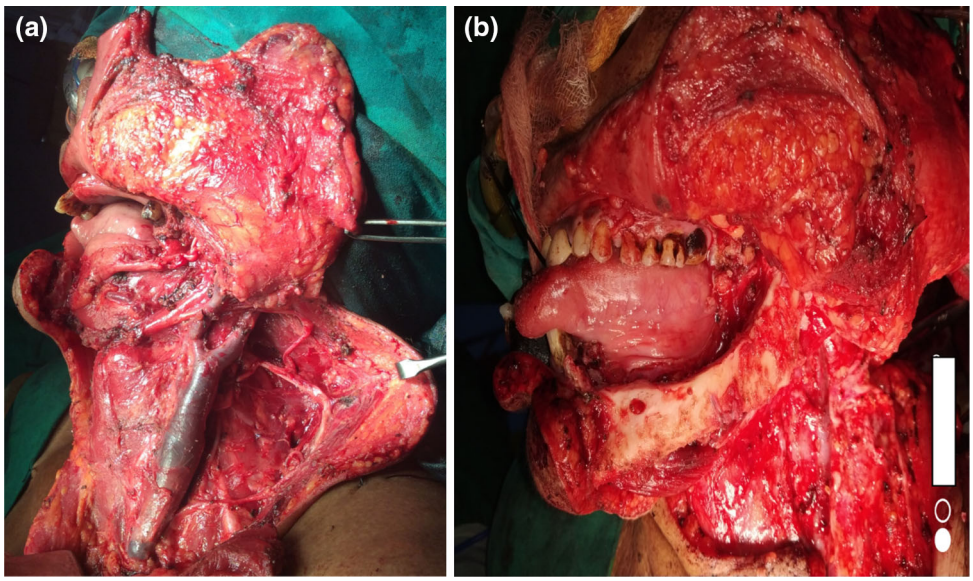

Fig. 2 Composite resection done for oral verrucous carcinoma [Hemimandibulectomy with upper alveolectomy (**a**) and Marginal mandibulectomy (**b**)]

oral cavity 3 years after surgery which was salvaged in 2 patients and 1 patient is alive with disease. All these 3 patients who developed second primary had premalignant lesions in oral cavity at initial presentation (2 submucous fibrosis and 1 leukoplakia). After a mean follow up of 6 years, 44 patients are alive and disease free. 2 patients died due to disease and 5 patients died due to other causes. 1 patient is alive with disease (local recurrence). 6 patients were lost to follow up after a period of 3 years.

Discussion

Oral cancer has high prevalence in India particularly among the lower socioeconomic population. It accounts for 29% of all cancers in our region [1]. Verrucous carcinoma of oral cavity is a slow growing variant of squamous cell carcinoma and has a favourable prognosis. The risk factors include addiction to chewable tobacco, betel nut and human papilloma virus. It is common in elderly male patients.

In our study, 84% of patients were females. This was in contrast to other studies on oral verrucous carcinoma which reported male preponderance. The most common age group was 55 to 65 years similar to other studies in India where average age group was 54 years [2, 3]. This was in contrast to other studies done in western countries on oral verrucous carcinoma in literature where the common age group was around 70 years [3–5]. The high prevalence among female patients and at a younger age may be due to the addiction to tobacco quid from early age among women in this region. Buccal mucosa was the most common site due to the habit of keeping tobacco quid in the cheek for long time. Similar observations were made in other Indian study involving 133 oral verrucous carcinoma patients [3]. However in a Chinese study lower lip was the most common site for verrucous carcinoma [4].

7 patients in this study had palpable lymph nodes in submandibular region out of which only 2 were found to have lymph node metastasis on histopathology. The reactive lymph nodes in submandibular region could be due to poor oral hygiene and dental infections among the patients

Fig. 3 Resected specimen of locally advanced verrucous carcinoma of oral cavity

in this region. Other studies in literature have also shown that cervical lymph node metastasis in verrucous carcinoma is not common and occurs only late in the disease [2, 5].

45% percent of patients in our study had locally advanced disease T3 and T4a which is due to lack of cancer awareness in this economically backward area. Nearly 20% of the patients had other pre-malignant conditions in oral cavity and in 9 patients field cancerization was seen in oral cavity and oropharynx. Among 9 patients staged T4a bone involvement was seen in 5 patients. All these 5 patients had tumours reaching the lower alveolar tooth sockets and the tumour had pushing margin. This was similar to the bone involvement in verrucous carcinoma reported in other studies. A small percentage of patients in this study (6 patients) had skin involvement. This was also late in the disease and in most of these patients the skin involvement was due to extension of the tumour across the angle of the mouth or across the vermilion. This was similar to the findings in other studies where verrucous carcinoma had low potential for deep invasion [2]. Inspite of 9 patients being T4a, only 3 recurred and 1 of them was found to have positive margin on histopathology. Other studies have also shown a favourable outcome in patients with verrucous carcinoma even when the disease is locally advanced [2, 6–8]. Similar to other studies and literature, in our study also positive margins and bone involvement and other premalignant lesions in oral cavity were factors predisposing to recurrence [2]. The case series reported from India and from South America have reported cervical lymph node metastasis and location of the tumour as factors predisposing to recurrence [2, 5]. In our series also, location of the primary tumour close to the alveolar sockets and involvement of retromolar trigone were poor prognostic factors. However, since only 2 patients had cervical lymph node metastasis without extra-nodal spread, the role

Table 1 Table showing time of recurrence in months in patients who had oral verrucous carcinoma with bone involvement (n = 5)

	Recurrence			
		R 6 months	R 8 months	R 9 months
Bone				
−	53	0	0	0
+	5	1	1	1
Total	58	1	1	1

Table 2 Table showing time of recurrence in months in patients who had associated premalignant conditions in oral cavity (n = 11). The 2 patients who recurred 8 and 9 months after surgery had localized areas of leucoplakia and submucous fibrosis in oral cavity

	Premalignant lesions		
	Field cancerisation	Leukoplakia	Submucous fibrosis
Rec			
No Rec	8	9	9
R 6 months	1	0	0
R 8 months	0	1	1
R 9 months	0	1	1
Total	9	11	11

of lymph node involvement on the outcome cannot be commented upon.

The first line of treatment for all patients in this series was surgery and the loco-regional control was good with only 3 patients with locally advanced disease recurring [6–8]. The mandible could be saved in 35 patients (22 marginal mandibulectomy and 13 transoral wide excision). This was similar to the treatment given in various other series. Among 11 patients who had premalignant conditions in oral cavity in addition to verrucous carcinoma at the time of initial presentation, 3 patients developed second primary cancers in the oral cavity after a period of 3 to 5 years.

In our series, only patients who had poor prognostic factors like positive or close margins, bone involvement or skin involvement on histopathological examination following surgery were subjected to adjuvant radiotherapy. Therefore, the possibility of transformation of verrucous carcinoma to poorly differentiated carcinoma following radiotherapy cannot be commented upon. A few authors have used radiotherapy as primary modality of treatment for oral verrucous carcinoma [9, 10]. However, we are of the opinion that surgery is the preferable modality of treatment in verrucous carcinoma particularly when the disease is advanced or depth of invasion is more than 3 mms [2, 6, 8].

There was no difference in regional outcome between patients who underwent supraomohyoid neck dissection and those who underwent modified radical neck dissection in our series. Similar outcome was quoted by studies done in Tata memorial hospital India [2]. The small number of patients who had lymph node metastasis had only first echelon (submandibular) lymph node involvement.

Conclusion

Verrucous carcinoma of oral cavity has a significant prevalence among people addicted to tobacco quid chewing. It has a good prognosis when treated by adequate surgical resection. Adjuvant radiotherapy can be reserved for locally advanced disease. Verrucous carcinoma does not invade deep into tissues and lymph node metastasis occurs late in the disease. Positive margins of resection, co-existing premalignant lesions in oral cavity and bone involvement along alveolar sockets predispose to recurrence.

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Compliance with Ethical Standards

Conflict of interest There is no conflict of interest among the authors.

Ethical Approval Institutional ethical approval and consent for publication: DMC/KLR/IEC/248/2018-2019.

Human and Animal Rights No animals or human experiments are done during the study.

Informed Consent Informed consent was taken from all the patients at the time of treatment and their attendants to include their clinical and histopathological findings in the study not revealing their identity.

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