

Original Research Article

Patterns of recurrences in carcinoma of alveolus**Dr Kunal Goutam¹, Dr Pramod Chandra Pathy², Dr Padmalaya Devi³, Dr Mohan lal Khadia⁴**¹Asst professor, Dept. of surgical oncology, AHRCC, Cuttack²Associate Professor, Dept of Head & Neck oncology, AHRCC, Cuttack³Prof &HOD, Dept of Surgical oncology, AHRCC, Cuttack⁴SR, Dept of Surgical oncology, AHRCC, Cuttack***Corresponding author**

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Abstract: In India Khaini and tobacco consumption is very high. Health awareness would certainly decrease the advanced presentation of the oral cancers to the clinicians which would help in better control of the disease. A prospective study was carried out in 60 patients of inferior alveolar carcinoma. Preoperative staging evaluation was done with physical examination including indirect laryngoscopy, laboratory studies, OPG, chest x-ray. Patients were evaluated with history and clinical examination at every visit and imaging studies and biopsy were used in case of any suspicious findings at every 2months for 1st year, every 3 months in 2nd year and 4months in 3rd year. The recurrence pattern and the factors affecting the recurrence were observed.

Keywords: alveolar carcinoma, laryngoscopy, laboratory studies, OPG, chest x-ray

INTRODUCTION

Oral cancer is the most common cancer among males and third most common cancer in female in India. Death rate in oral cavity cancer is third in males and fourth in females. The suffering, disfigurement and death due to this disease are easily avoidable, since the risk factors have long been identified. High prevalence of alveolar cancer in India is attributed to the widely prevalent habit of placing a quid containing tobacco in gingivobuccal (GB) sulcus. Alveolar cancer has the ability to invade the bone by direct extension, necessitating mandibular resection. In addition to lymph node metastasis, survival is related to the stage of the primary tumor, lymphovascular invasion, status of resection of margins and the number and anatomical level of positive nodes and the presence and extent of extra capsular spread. These pathological features are important indicators of tumor behaviour and should be incorporated into protocols for assay of prognosis. In HNSCC overall 19% developed loco-regional recurrence and 8% developed distant failure. Although, locoregional failure for oral cavity squamous cell carcinoma decreased due to use of multimodal therapy (surgery and radiotherapy), it still remains the most common site of failure. Distant failure has decreased as

improved locoregional control may have allowed time for recognition of distant metastases.

MATERIALS AND METHODS

A total of 60 patients from February 2014 to June 2016, with a biopsy proven diagnosis of inferior alveolus squamous cell carcinoma were prospectively included in the study.

Inclusion criteria

1. Squamous cell carcinoma of inferior alveolus only.
2. Performance status on European Cooperative Oncology Group (ECOG) Scale less than or equal to 2.
3. Tumor T-status ranging from cT1 to cT4a (as per American Joint Committee on cancer (AJCC) 7th edition).
4. No extension into upper alveolus, buccal mucosa, tongue or floor of mouth.
5. Nodal status ranging from cN0 to cN2
6. No evidence of distant metastasis (cM0)

Exclusion criteria

1. Other histologic types apart from squamous cell carcinoma
2. Poor performance status
3. Tumor status cT4b
4. Nodal status cN3
5. Any evidence of distant metastasis
6. Previous surgery or radiotherapy to the primary or the neck and any history of chemotherapy in the past

Preoperative staging evaluation was done with physical examination including indirect laryngoscopy, laboratory studies (blood biochemistry), OPG, chest radiograph.

Surgical Technique

For mandible: Marginal mandibulectomy was done in cases with no bone invasion clinically and on OPG. Segmental mandibulectomy was done in cases with evidence of bone invasion on OPG and hemimandibulectomy in cases with extensive bone invasion on OPG.

For neck

Selective neck dissection (Levels I, II and III) was done in clinically N0 neck irrespective of T- status. Modified radical neck dissection was done in clinically node positive cases without any evidence of extracapsular spread intraoperatively or in cases requiring pectoralis major myocutaneous flap for

reconstruction irrespective of nodal status. Radical neck dissection was done in clinically node positive patients with suspicion of extracapsular spread intraoperatively.

Reconstruction: Primary closure was done in cases wherever possible. Where primary closure was not possible, tongue flap or pectoralis major myocutaneous flap was used.

Pathological Analysis

The resected specimens were analysed by routine hematoxylin and eosin staining.

Adjuvant Treatment

In cases which were pT1-2, N0, M0, only follow up was done. In pT3-4, N+, M0 cases EBRT (60 Gy in 30 Fractions) and in margin positive cases EBRT (66 Gy in 33 fractions) was used for adjuvant treatment. In ECS positive cases, concurrent CT-RT was used with Cisplatin 50mg/m2 weekly with EBRT.

Follow Up

Patients were evaluated with history and clinical examination at every visit and imaging studies and biopsy were used in case of any suspicious findings. The visits were schedule at schedule at every 2 months in first year, every 3 months in second year and 4 months in third year. Continuous data were expressed as mean ± standard deviation. Statistical analysis was performed using SPSS version 14.0, Student T test, Fishers exact test and chi square test.

OBSERVATION

Table-1: Relation of sex with recurrences

Sex	No of patients	Recurrence	%
Male	41	6	14.5%
Female	19	2	10.5%

Table-2: Relation of age with recurrence

Age	Male	Female	Recurrence
4th decade	1	1	0
5 th decade	14	3	1
6 th decade	11	10	5
7 th decade	12	3	2
8 th decade	3	2	0

Table-3: Relation of addiction with recurrences

Addiction	No of patients	Recurrence	%
Tobacco/alcohol	54	8	14.8%
No tobacco/alcohol	6	0	0

Table-4: Relation of T-status with recurrence

T-status	No of Patients	Recurrence	%
T1	3	0	0
T2	6	0	0
T3	28	2	7.14
T4	23	6	26

Table-5: Relation of N-status with recurrence

N-status	No of patients	Recurrence	%
N0	42	3	7.14
N1	14	2	14.28
N2	4	3	75
N3	0	0	0

Table-6: Type of neck dissection with recurrence

Neck dissection	No of patients	Regional recurrence	%
SND	36	1	2.7
MRND	18	1	5.5
RND	6	1	16.6

Table-7: Relation of mandibular resection type with recurrence

Mandibulectomy type	No of patients	Recurrence	%
Marginal (MM)	17	1	5.8
Segmental(SM)	33	2	6.0
Hemi(HM)	10	3	30

Table-8: Relation of pT-status with recurrence

pT-status	No of patients	Recurrence	%
T1	2	0	0
T2	5	0	0
T3	12	1	8.3
T4	41	7	17

Table-9: Relation of margin status with recurrence

Margin status	No of patients	Recurrence	%
Margin negative	56	5	8.9
Margin positive	4	3	75

Table 10: Relation of tumor differentiation with recurrence

Tumor differentiation	No of patients	Recurrence	%
Well differentiation	14	1	7.14
Moderately differ	38	3	7.89
Poor differentiation	8	4	50

Table 11: Relation of vascular, neural and bone invasion with recurrences

Invasion	No of patients	Recurrences	%
Vascular	6	4	66.67
Neural	4	2	50
Bone	39	7	7.9

Table 12: Relation

Nodal status	No of patients	Recurrences	%
N0	32	0	0
N1	22	2	9.1
N2	6	1	16.6
N3	0	0	0

Table 13: Number of positive nodes with recurrences

Positive nodes	No of patients	Recurrences	%
1-2 nodes	19	1	5.2
3-4 nodes	7	2	28.5
5 or more	0	0	0

Table 14: Adjuvant treatment with recurrence

Adjuvant Tt	No of patients	Recurrence	%
Observ(pT1/T2N0M0)	6	0	0
Adj.RT(pT3/T4N+, M+)	50	7	14
Conc CT-RT	3	1	33.3

DISCUSSION

The study was a prospective study of 60 patients of squamous cell carcinoma of lower alveolus and was observed for the factors affecting recurrence. The mean age of disease was 5th and 6th decade and male: female ratio 3:2 differs from other reports of M: F ratio 3to4:1. This might be explained by the increasing consumption of tobacco and paan by females in this part of world.

In early cases (T1 and T2), the ability of the OPG to detect mandibular invasion is 75%. This study compares favourably with other reported studies which range from 68-75% [1, 2]. The OPG's lack of sensitivity i.e. the ability to detect early stages of bone invasion allows for a high incidence of false negative interpretations [2, 3]. This study compares favourably with 25% false negative interpretations. The 2 specimens for which the OPG failed to detect a mandibular bone defect were found to be at early stages of bone invasion and were limited to the mandibular cortex. O' Brien et al examined the sensitivity of the OPG in detecting mandibular bone invasion when the tumor was restricted to the periosteum and mandibular cortex and found a false negative rate of 44%. In advanced cases (T3 and T4) the sensitivity of detection of bone invasion is higher as given by O' Brien and Browne et al (90- 98%). This study compares favourably with 98% sensitivity. OPG is a useful initial assay of mandibular invasion and due to lack of sensitivity allows relatively high incidence of false negative interpretations.

Recurrence pattern in various age groups shows maximum recurrences in the 6th decade where maximum numbers of patients were present. Out of 41 male's patients, 6 recurred (14.6%) and out of 19 females 2 recurred (10.5%). As tobacco consumption is higher in males in this part of the world, we get more squamous cell carcinoma in males. Sex is not significant in determining the survival. 60 patients in this study had exposure to tobacco and alcohol. The recurrence rate was higher in these populations. None recurred in the other group with any exposure to tobacco and alcohol. The relation of tobacco and alcohol with oral cavity cancers is three fold.

1. As a causative agent- Review of studies worldwide indicates a strong causal relationship between smoking and HNSCC. Smoking was an independent risk factor in 80-90% of patients [5].
2. Affects treatment outcome- Use of these substances has been associated with immunosuppression, malnutrition and impaired tissue oxygenation resulting in hypoxic radio-resistance.
3. Field cancerization.

McGregor and Mac Donald pointed out that when the tumor originates in the gingival ridge mucosa, the vascular channels in the tooth roots in the alveolar bone permit early invasion of the bone. 30-50% of alveolar cancer patients have mandibular invasion demonstrated radiographically or histologically. Dubner and Heller reported that tumor invading deeply into the bone requires segmental mandibulectomy. Superficially invasive cancer and cancers arising close to the bone may sometimes be treated with marginal mandibulectomy. On studying the recurrence, 19% had

recurrence following marginal mandibulectomy, 6% following segmental mandibulectomy. Here we found 5.8% (1/17) recurrence following marginal mandibulectomy, 12.1% (4/33) following segmental mandibulectomy and 30% (3/10) following hemi mandibulectomy. All the recurrences developed were within the soft tissue. Marginal mandibulectomy should never be followed when mandibular bone has been invaded even superficially. These results compared favourably with Eugene N Myers and Munoz, Geren and Ord *et al.*; all showing recurrence rate of around 5% following marginal mandibulectomy.

On nodal evaluation, out of 43 cN0 (71.6%), 34 were pN0, but 9 were pN1 on histopathology. Out of 13 cN1 cases (21.6%), 11 were pN1 and remaining 2 were pN2 on final histopathology. 4cN2 patients (6.66%) were confirmed to have pN2 disease on final histopathology. Van den Brekel *et al* have shown that the early identification of nonpalpable metastatic HNSCC through USG and FNAC followed by neck dissection can result in overall higher rate of nodal evaluation. Most contemporary head and neck onchologists maintain that the cervical lymphatics to be included in the treatment strategy in the same manner even when the neck is without metastasis but when the chance of occult metastasis is 20% or more. Arguably, this is a subjective and arbitrary matter, a point which is made by Weiss *et al* in their paper on dissection on N0 neck.

Out of 60 cases in this study, 2 patients were staged T1, 5 cases were T2, 12 were T3 and 41 were T4. As per the above results most of the cases were in advanced stage. Out of 41 T4 cases, 7 recurred (17.1%), one T3 case recurred (8.3%). No local or regional recurrences were noted in T1 and T2 lesions. This association was however not significant. Out of 8 poorly differentiated cases, all 8 had bone invasion, 4 recurred. Out of 38 moderately differentiated cases, 29 had bone invasion and 3 recurred. Out of 14 well differentiated cases, 4 had bone invasion and 1 recurred. This association was however not significant. Oral carcinoma that invades the mandible, high grade invasion pattern increases the rate of mandibular margin positivity and local recurrence and results a fourfold increased risk of death with disease in multivariate analysis.

Lee *et al.*; reported that 5% of all oral cavity carcinomas had margin positivity. In this study margin positivity rate is 4/60 (6.6%). With the possible exception of the larynx, most studies of head and neck squamous cell cancers indicate that 50-80% of patients

with positive surgical margins will develop local recurrence. Conversely 15-30% of patients with margins that are judged to be pathologically adequate or free develop recurrence. This may be due to remote satellite tumor, field cancerization and lymphovascular or perineural infiltration. In this study, 3/54 patients with negative margins developed local recurrence (5.5%).

Perineural invasion has been reported in 5-52% cases of HNSCC. This wide variation results from a tendency to identify PNI only when larged named nerves are involved. In this study, PNI was seen in 4/60(6.6%) cases. Out of 4 PNI cases 2 recurred and out of 56 patients without PNI 6 recurred (10.7%). This association was however not significant. Perineural invasion by squamous cell cancers correlates with an increased incidence of local recurrence and regional lymph node metastasis. Vascular invasion was found in 6/60 patients. Out of 6 vascular invasions 4 recurred (66.6%) and 4 recurred in 54 cases with no vascular invasion (7.4%). This association was however not significant. Presence of vascular invasion in the primary tumor had been noted to increase the risk for subsequent loco-regional recurrence in oral cavity cancers. In alveolar carcinoma nodal metastases are seen in 30% of cases. In this study nodal metastases were seen in 26/60 cases (43.33%), as most of the cases were of advanced T stage. Most investigators have found that the number of positive lymph node correlates to some extent with prognosis as well as regional recurrence and distal metastases.

Out of 19 patients with 1-2 positive lymph nodes, recurrence was seen in 4 patients (local-3, regional-1). 7 patients with 3-4 nodes positive, recurrence were seen in 4 patients (local-2, regional with distant-1, local with regional and distant-1). None of the 34 patients with pathologically negative lymph nodes had any evidence of recurrences. This association was however not significant. Extracapsular spread has been seen in upto 60% of cases of oral cavity squamous cell carcinoma [12]. In this study it has been 11.5% (3/26). This discrepancy might be due to low rate of nodal metastases seen in alveolar carcinoma in comparison to other oral cavity cancers. As the size increases, ECS positivity increases. Other studies indicate that ECS occurs in 15-25% of lymph nodes in N1 and 75% in N2 cases. In this study, pN1 cases were 0/20 (i.e. no ECS), pN2 cases were 3/6 (i.e. ECS in 50% of N2 patients). Distinction is essential between extracapsular spread that is microscopic versus macroscopic because the latter is associated with a 10 fold greater risk of neck

recurrence than the microscopic one. In this study out of 3 ECS recurrence was with 1 macroscopic patient.

Out of 60 patients, 50 were given adjuvant RT. Delay in initiation of RT occurred in 8 cases. The dose of radiation used was 60Gy in margin negative cases and 66Gy in margin positive cases, divided over 30-33 fractions. One important factor influencing local control in patients with positive margins is dose of postoperative radiotherapy, as Zelefsky *et al.*; noted a 7 year local control rate in 92% of patients who received ≥ 60 Gy compared with 44% in patients receiving ≤ 60 Gy. Out of 4 margin positive cases in this study who were given 66Gy, 3 recurred (75%), but this was not significant. Efficacy of post operative radiotherapy in improving locoregional control has never been directly validated in randomised control trials; the role is well accepted in selected circumstances based on good retrospective data. Concurrent CT-RT was used in ECS positive cases (3 cases). CT was given with weekly injections of 50mg of Cisplatin as per Institute Protocol. There are less data available regarding the adjuvant application of CT-RT.

In our study mean time of follow up was 12.78 months. Things needed for early detection are

- Categorization of patients with bad prognostic features who need aggressive follow up
- Compliance of the patient
- Good clinical examination is needed as a sequelae of previous treatment may make early detection of recurrence challenging with tumor often growing unnoticed deep into surrounding tissues

All our recurrences were detected by local examination and proved by biopsy. In this study 6/60 (10%) patients developed local recurrence, all within 6 months and soft- tissue recurrences. Out of 6, 4 had margin positive disease. Distant metastasis is rare in tumor of alveolar ridge and is reported at a rate of approximately 4%. Distant metastases by hematogenous spread to visceral sites from a head and neck squamous cell cancer most commonly includes spread to the lungs(66%), bone(22%), liver(9.5%). Presence of distant metastases is an ominous sign because almost 90% of patients died within 2 years of detection of first metastases. In this study, distant metastases were seen in 2/60 (3.3%). Both the distant recurrences occurred in the lungs, first at 10 months and second at 14 months. Both the patients died within 1year of their detection of metastases. There was no case with isolated distant metastases. Longer follow up would help in detecting more distant recurrences.

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