

High risk and poor prognostic features determining aggressiveness of disease in post operative locally advanced cases of oral cavity carcinoma: an institutional experience

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ABSTRACT

Locally advanced oral cavity cancer is managed in multidisciplinary setting including surgery followed by postoperative radiotherapy (PORT) and chemotherapy. We also follow the same protocol however during the active treatment only our patients had recurrence of disease. We enrolled 16 cases of locally advanced oral cavity cancer seen from September to November 2015 at our Radiation Oncology department. Most common presentation is age group of 31-40 years and 14 cases were males out of 16. The pattern of presentation included cases as 9 carcinoma tongue, 5 carcinoma buccal mucosa, 1 carcinoma angle of mouth and 1 carcinoma of lower alveolus. All these patients were operated and referred for PORT. The dose of PORT planned was 60 Gy/30# for 6 weeks along with concurrent cisplatin 30mg/m² weekly. All these patients by the mid of the treatment developed nodal recurrence confirmed on Biopsy. When the high risk factors were extrapolated it was found that depth was more than 1 cm, base of resection (BOR) was also close all being <0.5 cm and margins being very close the cut off being 0.3 cm. All these patients had their PORT started after 7 weeks of surgery. Age <45 years, depth >1 cm, BOR <0.5 cm and close margins with cut off 0.3 cm, perinodal extension or otherwise presence of perineural invasion were poor prognosis features determining aggressiveness of disease. This study gave an impetus to explore more in such type of poor prognosis patients and we look forward for more insight.

Keywords: High Risk, Poor Prognosis Features, Oral Cavity Carcinoma

Introduction

Head and neck cancers are commonest presentation with about nearly 40,000 new cases detected annually and most of these patients are in advanced stage at presentation only. Tobacco and alcohol overuse are major causative factors for head and neck carcinoma. [1,2] In India people are usually addicted with tobacco in various forms like chewing and smoking. Majority of cases present in very advanced stages with more than 70% of cases at presentation having either large primary or large nodes or both. Usually in such advanced cases if the disease is resectable surgery is done first followed by adjuvant therapy including radiation and chemotherapy according to the indications present. Postoperative radiotherapy is

given when the histopathology report shows tumor size more than T 2 stage, lymphovascular involvement, perineural involvement, surgical margin positivity, or close margins node positivity, perinodal extension and bone involvement. [3,4,5] In patients where multiple nodes are positive or close margins or positive margins status is there, they are additionally offered concurrent chemotherapy. We also follow this same protocol however in this study during the active postoperative radiotherapy and chemotherapy protocol only patients started developing recurrence of the disease. Thus we conducted this study to extrapolate in detail the high risk poor prognostic features responsible for early recurrence in these patients. We expect that with the results and experience from this study we can choose such high risk cases requiring immediate attention.

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Materials and methods

We have enrolled 16 cases of locally advanced oral cavity cancer cases seen from September 2015 to November 2015 at our department of Radiation

Oncology being referred for postoperative radiotherapy treatment. Males dominated in this study with total 14 cases out of 16 cases. Most common age presentation is age group of 31-40 years. The pattern of presentation included 9 carcinoma tongue cases, 5 carcinoma buccal mucosa cases, 1 carcinoma angle of mouth and 1 carcinoma of lower alveolus. All these patients were locally advanced and were taken for surgery first. For the 9 patients of carcinoma of tongue surgery done was ranging from partial to total glossectomy with bilateral modified neck dissection. 5 patients of carcinoma buccal mucosa were operated for Commando operation 1 patient of carcinoma of angle of mouth and one patient of carcinoma of lower alveolus were operated for wide local excision with marginal mandibulectomy with ipsilateral modified neck dissection. All these patients after surgery were referred to us for postoperative radiotherapy. These patients after proper dental evaluation were taken for postoperative radiotherapy according to the indications of adjuvant radiotherapy including advanced T stage (T3/T4), the presence of lymphovascular positivity, the presence of perineural positivity, positive or close surgical margins, lymph node positivity, extracapsular nodal extension and bone positivity. The dose of postoperative radiotherapy planned was 60Gy/30# with 2 dimensional radiotherapy techniques with conventional dose of 2 Gy/# for 6 weeks. Because of poor prognostic factors these patients were also offered concurrent cisplatin 30mg/m² weekly with post operative radiotherapy. Because of huge workload and being a busy regional cancer centre patient's number is huge. Thus all these patients after surgery and taking utmost measures of getting the patient undergo thorough dental evaluation and preparing proper immobilization masks including plaster of paris cast preparation these patients were started for their postoperative radiotherapy mostly after 7 weeks of surgery. On day of starting radiotherapy, planning was done and patient was thoroughly counseled for maintaining proper oral hygiene and ensured their adequate analgesia too. Hygiene is very important for causation of head and neck cancer and also for determining responsiveness of therapy. [6] During their postoperative radiotherapy treatment when patients used to come for regular checkups we observed recurrences. 5 of the 16 patients before they even complete their second week of postoperative radiotherapy developed nodal recurrence. When we observed this nodular swelling we got it biopsied and it turned out to be metastatic squamous cell carcinoma. We stopped the postoperative radiotherapy treatment and then referred the patient to medical outpatient department for starting palliative chemotherapy. All these patients had nodal recurrence

of more than 2 cm and hard ones which even surgical people found difficult to reoperate. Another 9 patients developed recurrence after in their third week of postoperative radiotherapy treatment but because of failure of any further surgical intervention postoperative radiotherapy was stopped and advised palliative chemotherapy after biopsy confirmation of recurrent metastatic node. One patient developed recurrence in fourth week and last patient developed recurrence in fifth week but despite nearing their completion of postoperative radiotherapy treatment the radiotherapy was stopped and started on palliative chemotherapy after histopathological confirmation. Two out of sixteen patients had Level IV nodal recurrence both of them with primary in carcinoma of tongue. One patients had level V nodal recurrence with primary from buccal mucosa rest all patients had level II nodal recurrence.

Result

We tried to extrapolate their histopathological findings and tried to study the biology of the disease as the recurrence was very quick keeping us also in astonishment and as a lesson to learn for future to concentrate more on these types of patients requiring immediate attention. All these patients had nodal recurrence confirmed on Biopsy. When the high risk factors were extrapolated it was found that depth more than 1 cm was the commonest finding amongst all these cases. All these patients had their postoperative radiotherapy treatment started after 6 weeks of surgery implying time factor being most important in determining prognosis of patients. Base of resection was also very close all being <0.5 cm and margins being very close the cut off being 0.3 cm were also determining mostly the early recurrence in these patients. All patients were young with age <45 years of age indicating at young age disease behaves more aggressively. Out of 16 cases 14 were males but this finding being coincidental as mostly oral cancers were found in males because of more use of tobacco.

Discussion

Head and neck cancers are the most common cancers in India with majority of cases being advanced in which surgery is offered first for resectable ones followed by adjuvant therapy according to the indications present. Postoperative Radiotherapy is standard care of treatment in such advanced cases. [3] Role of adjuvant chemotherapy was explored by Cooper *et al* [4] and Laramore *et al*. [7] The indications of postoperative radiotherapy include tumor

size more than T 2 stage, lymphovascular involvement, perineural involvement, surgical margin positivity, or close margins, node positivity, perinodal extension and bone involvement. Adjuvant chemotherapy is given in patients with multiple nodes positivity or close margins or with positive margins status.[8,9] We also did the same protocol however in this study during the active postoperative radiotherapy and chemotherapy protocol only patients started developing recurrence of the disease. When all the high risk features were spread out on a common sheet, many poor prognostic features were highlighted. The very obvious and first finding we could make out was the young age of presentation in this study indicating aggressiveness of disease as has been found in literature search too. [10,11] Other significant features like depth > 1 cm was also very important poor prognostic deterministic factor. All the 16 cases had depth more than 1 cm very importantly emphasizing depth more than 1 cm as detrimental factor. The tumor thickness is in turn related to nodal involvement thus leading directly or indirectly as guide for aggressiveness of disease. [12] Nodal positivity especially when multiple nodes are positive or having extra capsular extension also determines chances of early recurrence as seen in our study where 11 cases out of 16 had perinodal extension. This factor is also studied well by Greenberg et al [13] when he shared his experience of carcinoma tongue cases with perinodal extension as aggressiveness determining factor. In rest cases when it was not pericapsular extension then even perineural invasion as an alone factor was important in bringing out early recurrence. [14] Another common feature amongst all cases very obviously seen was that all patients had their postoperative radiotherapy started after 7 weeks of surgery determining timing being a very important issue to be addressed. Marshak et al [15] studied importance of starting postoperative radiotherapy treatment within 4-6 weeks of surgery. The logic behind this time factor game is the concept of tumor repopulation where the intention is to complete the treatment in as short time as possible.[16] Another way of dealing this time issue is to try different radiotherapy regimes like hyperfractionation or accelerated radiotherapy but these regimens ultimately lead to profound side effects especially when combined with concurrent chemotherapy eventually leading to treatment breaks and thereby delaying the treatment to be completed in stipulated time. [17] Base of resection was also very close all being <0.5 cm and margins being very close the cut off being 0.3 cm highlighting its importance as poor prognostic feature.

Conclusion

Thus after studying all above high risk and poor prognosis features it was very much clear that young patients fare badly as seen in our study with all patients being young than 45 years of age. Other poor prognostic features like tumor thickness more than 1cm, Base of resection <0.5 cm and close margins with cut off 0.3 cm, perinodal extension or otherwise presence of perineural invasion were also important in determining aggressiveness of disease. Time factor had also an important role to play concluding that it is better to start postoperative radiotherapy within in 4-6 weeks of surgery. This preliminary study gave an impetus to explore more in such type of poor prognosis patients by adding more options like adding targeted chemotherapy or trying some different radiotherapy regimens. We look forward for more insight in future for such cases.

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