Case Report

Neoadjuvant Chemotherapy in Locally Advanced Cancers of Oral Cavity

Abstract

Oral cancers constitute a major burden of cancer in northeastern part of India. This can be attributed to the increased consumption of tobacco in various forms such as chewing, snuffing, powder or paste and smoking along with betel nut and areca nut. The majority of patients with oral cavity cancer present in an advanced stage which carries a poor prognosis. We present here a case of locally advanced (T4b) oral cavity cancer where 5-fluorouracil (5FU) and methotrexate (MTX) were used as neoadjuvant chemotherapy to attain a surgically resectable stage. The objective of this case report is to show the efficacy and impact of 5FU and MTX as induction chemotherapy in advanced oral cancers.

Keywords: *Locally advanced, neoadjuvant chemotherapy, oral cavity cancers, unresectable*

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Introduction

Cancer of the oral cavity is a common cancer in India, as 4 out of 10 cancers in the country are oral cancers.[1] In India, 60%–80% of patients with oral cancer present with advanced stage disease compared to 40% in the developed countries.[2] Squamous cell carcinoma is the most common histological variant of oral cancers.[3] Buccal mucosa and lower gingivobuccal sulcus are the most common subsites of oral cavity cancers. Surgery alone or in combination with postoperative radiotherapy is the treatment of choice for advanced cancers of the oral cavity.[4] Because of the close proximity of the infratemporal space and masticator space (MS) with oral cavity, these spaces are frequently involved by the cancers from the oral cavity.[5] When the tumor invades the MS, pterygoid plates, skull base, encases the internal carotid artery, and when there is extensive soft tissue involvement up to the hyoid bone and zygoma, these oral cavity cancers are regarded as unresectable. The American Joint Committee on Cancer classification has staged these cancers as T4b.[6] The locoregional recurrence is the common pattern of treatment failure in cancers of the oral cavity.[7] Recent advances in reconstruction techniques have enabled the possibility of wider resections with limited morbidity and to achieve complete (R0) surgical resection.[8] Induction chemotherapy to downstage the tumor plays an important role preoperatively, as close margin or margin positivity carries a poor prognosis.[9] Conventionally, T4b or unresectable oral cavity cancers are treated by chemoradiation with a palliative intent. The result of chemoradiation or radical radiation alone in advanced (T4b) oral cavity cancers is not satisfactory. The 1-year disease-free survival has been shown to range from 10% to 40% with radiotherapy and without chemotherapy.[10] With the advance in the reconstructive surgical techniques and induction chemotherapy, unresectable locally advanced oral cancers have been amenable to surgery. This is followed by adjuvant therapy with radiation and chemotherapy depending on the postoperative histopathological examination risk factors. The rationale of proposing neoadjuvant chemotherapy (NACT) in locally advanced oral cancers is to improve the overall outcome by reducing the tumor burden before radiation, facilitate possible resection following tumor shrinkage, and to prevent distant metastasis. Cisplatin and 5-fluorouracil (5FU) regimen have shown significant result in reducing the tumor size with lesser toxicity. At present, platinum-based doublet chemotherapy regimen remains the standard regimen of choice in view of its better response and increased symptom-free duration. We report a case of locally advanced oral cavity cancer which responded well to

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5FU and methotrexate (MTX), which was used as NACT. The patient was further treated by surgery and adjuvant chemoradiation.

Case Report

A 30-year-old female presented in the Outpatient Department of Head and Neck Oncology with the history of ulcer in the left side the oral cavity of 4-month duration. The ulcer had a history of rapid growth of 1 month and was also associated with mild pain. She was a tobacco and betel nut chewer. She had no other comorbid conditions. On examination, there was an ulceroproliferative growth of 5.0 cm × 6.0 cm size in the left lower alveolus extending to buccal mucosa with an area of skin involvement of 7.0 cm × 6.0 cm. There was no trismus. A hard, nontender, and mobile neck node of 3.0 cm × 2.0 cm size was palpable in the left level Ib region.

Computed tomography scan of the oral cavity revealed a soft tissue enhancing lesion in the left side of the lower alveolus with bone destruction and extensive soft tissue involvement and with an enlarged cervical lymph node in level Ib. Biopsy from the growth revealed well-differentiated squamous cell carcinoma [Figure 1]. Clinically and radiologically, the oral cavity growth was T4b. Metastatic workout for distant metastasis was normal. The final staging was T4bN1M0 (Stage IV).

Because of the widespread soft tissue involvement and borderline respectability, the patient was treated by upfront NACT with 5FU (500 mg) and MTX (50 mg) intravenous on weekly regimen for three cycles. Apart from grade I nausea and fatigue, she tolerated the chemotherapy well without any grade III/IV toxicities.

After three cycles of NACT, there was considerable reduction in the size of the growth with near-total response of the skin involvement. The patient further underwent wide excision with left segmental mandibulectomy and left modified radical neck dissection type II and repair was done with bipaddled pectoralis major myocutaneous flap. This was followed by postoperative chemoradiation. On follow-up at 6 months, following completion of treatment, she did not have any evidence of locoregional disease. The patient is presently under regular follow-up.

Discussion

According to the Indian Council for Medical Research, in India, nearly 70%–80% of patients with oral cavity cancers present in a locally advanced stage and the majority are treated with a palliative intent.[11] Because of the high consumption rate of tobacco and betel nut, there is a rise in the oral cavity cancers in the country compared to the western countries.[12] In our case also, the patient was a tobacco and betel nut chewer. Ramchandra stated that the most common age group of patients with oral cancer is 31–40 years (38.5%) and is followed by the younger age group of 21–30 years (35.2%).[13] Our case was a

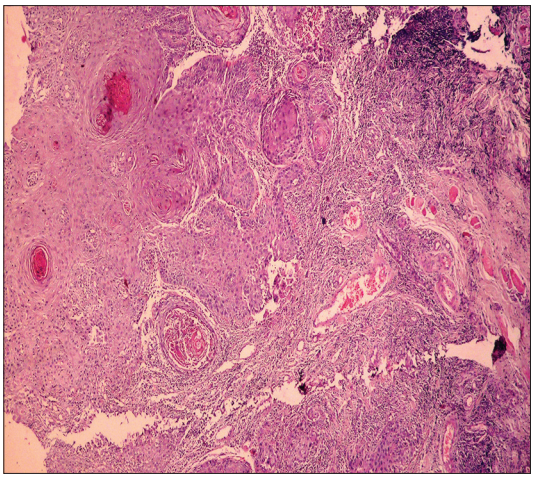

Figure 1: Sections of squamous epithelium displaying a tumor arranged in sheets, clusters in single with hyperchromatic irregular nuclei, and variable eosinophilic cytoplasm (H and E, ×10)

30-year-old female, who was relatively young. The majority of the patients present in the late stage in India, which was same in our case. The histopathology of the present case was suggestive of squamous cell carcinoma which is the predominant histology in oral cavity cancers. Concurrent chemoradiation, radical radiation, palliative radiation, and best supportive care are the different treatment strategies for T4b oral cavity cancers. However, the results of chemoradiation or radical radiation alone in T4b oral cavity cancers are not satisfactory with a disease-free survival of 1 year.[7] Moreover, surgical excision is the mainstay of treatment for cancers of the oral cavity,[14] and nonsurgical methods rarely achieve a lasting cure. The two-drug regimen with cisplatin-fluorouracil combination has been the regimen of choice for two decades, but in recent years, it has been superseded by a triple drug combination of cisplatin, fluorouracil, and a taxane (TPF). The role of induction chemotherapy in unresectable locally advanced head and neck cancers had been highlighted by two large landmark trials, the TAX 323 and TAX 324. In both the trials, the use of three-drug regimens led to response rates of around 68% which was superior to two-drug combination. However, oral cavity cancer patients included in these trials were <15%.

Patil *et al*. documented the effectiveness of NACT with TPF or TP in downstaging tumors and making them amenable for radical surgery with 2 years survival comparable to primary surgery. The response rate with the three-drug and two-drug regimens was 32.00% and 27.37%, respectively.[15] The estimated median overall survival was 12.7 months in comparison to 8 months in the nonsurgical category.[15] Joshi *et al*. assessed the efficacy and impact of NACT in T4b oral cavity cancers with MS involvement,[16] and they found that none of the patients achieved complete response, but resectability was achieved in 30.9% thus improving the outcome.[16] However, in our case, we used 5FU and MTX in the dose of 500 and 50 mg, respectively,

weekly for three cycles. There was a significant response making the tumor amenable to radical surgery. The patient underwent radical surgery followed by postoperative chemoradiation. Moreover, cancers in the advanced stages have higher degree of locoregional recurrences, so these patients need to have longer follow-up.

Conclusion

The use of 5FU and MTX in the form of induction chemotherapy in the locally advanced cancers of the oral cavity leads to good response, especially in patients with extensive soft tissue involvement. However, to establish the benefits of MTX-based doublet approach in unresectable oral cavity cancers, further prospective trials will be needed.

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Conflicts of interest

There are no conflicts of interest.

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