

Management of Complications Following Chemoradiation in Carcinoma of Head and Neck: A Hospital Based Study

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ABSTRACT

Introduction: Head and neck cancers are becoming more and more common and a definite protocol should be followed for its management. Different types of complications are generally seen during the treatment period related with both chemoradiation and surgery. We present a study of our experience in the management of out-patient department presenting with different types of post chemo-radiation and surgical complications. Present research was done to study the management different types of post chemoradiation and surgical complications.

Material and methods: A total of 213 patients were studied during the study period (Jun 14 – Oct 15) in the, Department of Otolaryngology and Head and Neck Surgery, Assam Medical College, Dibrugarh, Assam. The same patients were treated in the study period. Different approaches like surgery, chemotherapy, radiotherapy and chemoradiation were used.

Results: Head and neck carcinoma can present with a varied way of complications both before and after treatment. Complications due to chemoradiation can be very distressing and painful. Different lines of treatment should always be prepared beforehand.

Conclusion: Complications of chemoradiation should be previously expected and pre-formed management protocol should be used for different complications of head and neck carcinoma.

Keywords: Management of Complications, Chemoradiation in Carcinoma, Head and Neck

INTRODUCTION

Cancer is characterized by the development of abnormal cells that divide uncontrollably and infiltrate and destroy normal body tissue. The sixth most common cancer globally is the oral cavity cancer. The incidence of oral cancer is strongly associated with social and economic deprivation. Important risk factors in the development of the disease are tobacco, betel quid, alcohol, age, gender, sunlight, candida and the human papillomavirus (HPV) infection. Nasopharyngeal carcinoma is a rare disease all over the world. It has often been less evaluated, misdiagnosed, partially treated, most commonly recurred and prognostically poor carcinoma. It has a bimodal peak with occurrence in the late second decades and in the fifth decades. Presently the incidence of nasopharyngeal carcinoma is low in most parts of the world. The rates are twice as high in males as in females.¹ Small cell neuroendocrine carcinoma which is an unusual laryngeal carcinoma accounts for slightly less than 0.5% of carcinomas. Patients usually complain of hoarseness and this tumor is biologically aggressive with at least 73% of patients dying with widespread tumor metastases. Two- and 5-year survivals are 16% and 5%, respectively. Chemoradiation offer the best hope of survival.² The association of small cell carcinoma with squamous cell carcinoma both in the larynx and hypopharynx is reported.³ The clinical management of sinonasal

cancer has improved owing to advances in imaging techniques, endoscopic surgical approaches, and precision radiotherapy.⁴ Fibrosarcoma (FS) is a malignant mesenchymal neoplasm of the fibroblasts that rarely affects the oral cavity. Fibrosarcoma (FS) is a malignant neoplasm of fibroblastic origin and may either arise in the soft tissue or be of primary intraosseous origin (20% of all cases).^{5,6} The latter origin has been debated since 1940, when Ewing established the initial entity, and is now generally accepted.⁷ It accounts for approximately 5% of all malignant intraosseous tumors⁸⁻¹⁰, and especially affects the long bones. Its occurrence in the head and neck is about 10% of cases, of these the mandible being the commonest site. Basosquamous carcinoma (BSC) is a rare epithelial neoplasm.^{11,12} It is a newer identity. BSC is most commonly seen on the head and neck, mainly involving the central face, and has a significant predominance in male Caucasians.¹³ The present treatment is primarily Chemoradiation. The objective of the study was to highlight the management of complications after chemoradiation in cancers of head and neck region.

MATERIAL AND METHODS

A total of 213 patients were studied and treated during the study period (Jun 14 – Oct 15) in Assam Medical College and Hospital, Dibrugarh. Different approaches like surgery followed by chemoradiation, chemotherapy, radiotherapy and chemoradiation were used.

The study was a retrospective study. Although the study period was short but it was important and a note should be taken about the actual scenario that is trending. In some of the cases special anaesthetic care has to be taken.

Inclusion criteria: All primary head and neck cancers presenting to OPD or being admitted in emergency during the study period.

Exclusion criteria: All secondary head and neck cancers.

Investigations

All the cases of sinonasal and nasopharyngeal cancers were diagnosed first by diagnostic nasal endoscopies and then by radiological investigations mainly CT and MRI. In figure 1-2. we can see that a heterogenous post-contrast enhancement is

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How to cite this article: Debajit Sarma, Projnan Saikia, Pradip Kumar Tiwari, Ranu Shukla, Neelam Jain, Arnav Das. Management of complications following chemoradiation in carcinoma of head and neck: a hospital based study. International Journal of Contemporary Medical Research 2016;3(9):2541-2545.

noted in the posterior nasopharynx involving the torus tubaris, fossa of Rosenmuller, prevertebral muscles. Superiorly erosion of left greater wing of sphenoid, left clinoid process, left petrous apex and infiltrating into the left cavernous sinus.

Routine blood examinations and other systemic laboratory examinations for the chemotherapy and radiotherapy were also performed in every case. Histopathological examination report in sino-nasal carcinomas showed them to be well differentiated squamous cell carcinoma. In cases with nasopharyngeal carcinoma histopathologically (Figure-3) the malignant cells were arranged in small groups and syncytial sheets were seen. Large numbers of lymphocytes and eosinophils leukocytes were also present. In cases with fibromyxoid sarcoma. HPE from the tissue revealed clusters of atypical spindle shaped cells embedded in myxoidmatrix. HPE from the neuroendocrine carcinoma of larynx showed undifferentiated small tumor cells with scant indistinct cytoplasm and nuclei with fine stippled chromatin and generally inconspicuous nucleoli.

STATISTICAL ANALYSIS

Statistical analysis was done with the help of descriptive statistics like mean and percentages using Microsoft office 2007.

RESULTS

Epidemiology: Out of all the diagnosed cases of head and neck neoplasms 213 cases (table-1) were admitted and planned for surgery, chemoradiation or both.

Environment: All the districts from where patients reported were generally same as far as environment was concerned and all have a specific period of dry, hot and dusty weather during similar period of a year. Communities with populated households and ill-ventilated houses and practicing of salted food- habits were having a rise in incidence. Also important risk factors in the development of the disease were tobacco, betel

Disease	No. of patients
Sinonasal	9
Nasopharyngeal	18
Posterior pharyngeal wall	1
Tonsillar	7
Vallecula and tongue	15
Floor of mouth	2
Buccal mucosa	16
Hard palate	4
Gingivobuccal sulcus	11
Retromolar trigone	2
Lip	3
Mandibular	5
Submandibular	1
Hypopharyngeal	3
Aryepiglottic fold	69
Epiglottic	2
Post-cricoid	2
Subglottic	3
Supraglottic	2
Thyroid	9
Esophageal	29
Total	213

Table-1: Location of tumor

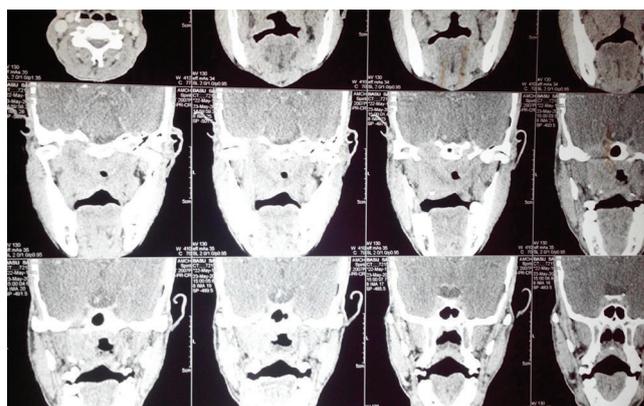


Figure-1: CT scan of head and neck region

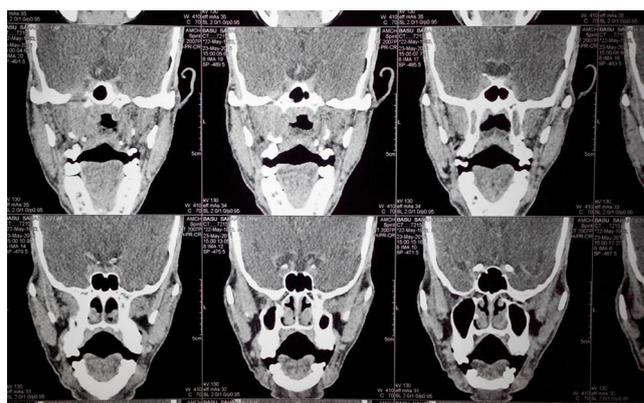


Figure-2: CT scan of head and neck region

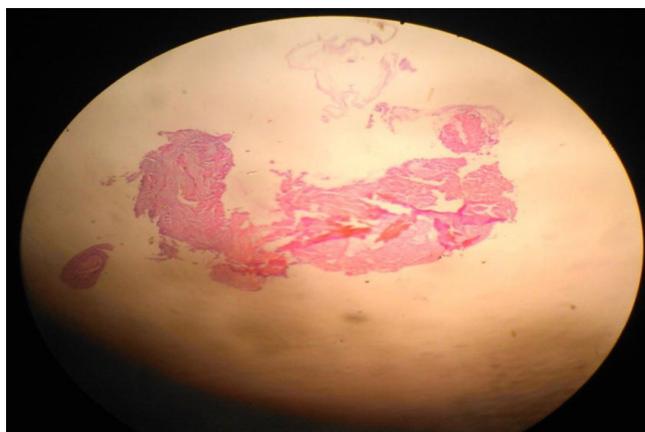


Figure-3: Microscopic images of nasopharyngeal carcinoma (10x)

quid, alcohol, age, gender, sunlight, candida and the human papillomavirus (HPV) infection.

Treatment modalities: All the cases were treated by chemoradiation primarily. Cisplatin based chemotherapy in a dose of 100mg/m² IV in 1 hour Radiation in a dose of 66 Gy -72 Gy on weekdays for six weeks was given.

Post treatment complications: It was mainly due to radiotherapy and was very distressing. Bone marrow dysfunction seemed to be the most common complications along with

- Decrease in cell count
- Feeling sick and lethargy
- Diarrhea
- Sore mouth and mouth ulcers
- Hair loss or thinning

- Feeling tired and run down
- Respiratory distress
- Bleeding from the cancerous tissue
- Fibrosis of underlying structures
- Post-radiation fistulous tract
- Xerostomia
- Mucositis
- Erythema and desquamation
- Trismus
- Ear discharges
- Cartilage necrosis

Management of complications

Dietary support, feeding gastrostomy, nasogastric intubation, steroids, colony stimulating factors, antibiotics, emergency tracheostomy and treatment of other endocrinal disorders caused due to chemoradiation were the main concern during the treatment of complications.

Mucositis was treated with the help of topical steroid like triamcinolone and i.v. steroid like methylprednisolone along with proton pump inhibitors like pantoprazole.

Dysphagia and immediate post treatment oedema was again treated with the help of i.v. steroids and enzymes like rutoside and bromelin. Ryles tube intubation and feeding gastrostomy were done in most of the cases with increasing difficulties of deglutition.

Oropharyngeal candidiasis was treated with fluconazole 50-100 mg daily has been associated with clinical recovery in 80 percent of patients within 10 days, or within five days with 200 mg daily.

Xerostomia was treated by frequent sips of water and pilocarpine in some cases. Immediate post-treatment respiratory distress was treated with emergency tracheostomy. Prophylactic tracheostomy was done in some cases.

Post treatment tracheo-esophageal fistula were treated accordingly with collaboration with the CTVS department. In cases with severe complications like perichondritis with holding of chemoradiation was done.

Blood counts were done for all the cases and patients with increased total count and respiratory tract infection were treated with antibiotics. Patients with decreased count were treated with colony stimulating factors like G-CSF and GM-CSF. Lower platelet counts were treated with platelet transfusion and decrease in other blood components were treated as per requirements. Routine blood counts were done every 10 days.

Other complications of chemotherapy like diarrhea, nausea vomiting and GI upset were treated accordingly. Ear discharge due to infections and post treatment complications were treated with care. Otitis media with effusion was treated with grommet insertion.

Osteoradionecrosis was seen in some of the cases. Wherever possible prerequisites for radiotherapy basically low teeth were removed, involvements of bony and cartilaginous structures were ruled out. Further cases with osteoradionecrosis were not recommended for further chemoradiation.

Post-operative radiotherapy given to various plastic and flap-surgical patients. In some of the cases there was necrosis of the marginal areas and these were treated by secondary surgical debridement and re-dressing of the skin surfaces.

Radiotherapy failure cases were defined as when even after

aggressive treatment there were documentation of metastasis in CT –scans. Cases with hypothyroidism and other endocrinal complications were treated with thyroxine and other conservative necessary treatments.

There were 3 reported deaths of cases undergoing treatment.

DISCUSSION

The dentist caring for a head and neck cancer patient should have clearly defined goals of dental management during the three phases of treatment.¹⁴⁻²⁰

1. Pretreatment goals

- eliminate potential sources of infection;
- counsel patient about short- and long-term complications of cancer therapy;
- provide preventive care.

2. Goals during cancer therapy

- provide supportive care for oral mucositis;
- provide treatment of oral candidiasis;
- manage xerostomia;
- prevent trismus.

3. Long-term, post-treatment goals

- manage xerostomia;
- prevent and minimize trismus;
- prevent and treat dental caries;
- prevent postradiation osteonecrosis (ORN);
- detect tumor recurrence

IMRT can be considered as the standard of care for head and neck cancer. Salivary gland-sparing IMRT helps in improved quality of life.²¹⁻²³ Residual salivary flow can be stimulated by sialogogues such as pilocarpine or cevimeline, and/or use of sugarless gum and buffered citric acid tablets. Salivary substitutes provide transient symptomatic relief.²⁴⁻²⁹ Patients who have heavily restored teeth may benefit from the use of silicone mucosal guards worn during RT to reduce the severity of mucositis associated with scatter of radiation off metal restorations.³⁰⁻³² Fluconazole 50-100 mg daily has been associated with clinical recovery in 80 percent of patients within 10 days, or within five days with 200 mg daily. Complete mycologic cure is difficult to achieve. Resistance to fluconazole is associated with non-albicans yeast such as *Candida glabrata* and *C.krusei*.³³ Oral hygiene must be maintained because of the lowered biological potential for healing of the periodontium after radiation therapy. The risk for developing ORN is reduced in patients who receive topical fluoride applications and maintain good oral hygiene because they are less likely to develop caries, periodontal disease and their sequelae.³⁴⁻³⁶ Sulaiman et al³⁶ extracted at least two weeks before RT whenever possible. They used neutral NaF 1.1 percent in a 5,000-ppm dentifrice toothpaste. In patients with small, early (T1N0 and T2N0) recurrences or new primaries in previously irradiated oropharynx, interstitial brachytherapy alone (60Gy) can result in a five-year local control rate of 69-80%, with a five-year overall survival of 30%, most deaths being due to causes other than the cancer. Local control is significantly better if the radiotherapy dose for re-irradiation is >50Gy. Radiotherapy delivered postoperatively to selected patients at high risk of locoregional recurrence may improve locoregional control and survival. Trismus can be a significant side effect of RT, especially if the lateral pterygoid muscles are in the field.

CONCLUSION

Oncology treatment decisions require an understanding of the staging of the patient's cancer and prognosis for survival, the types of therapy planned, timing of therapy, patient's motivation and ability to cooperate, and anticipated complications of treatment. Oral evaluation including periodontal examination before the patient begins cancer treatment should be done. This evaluation will help to prevent or mitigate oral complications associated with radiation and chemotherapy, and systemic sequelae of oral infection. Many of the complications of cancer therapy can be prevented by prior measures.

REFERENCES

- Hirayama T. Descriptive and analytical epidemiology of nasopharyngeal cancer. In: *Nasopharyngeal Carcinoma: Etiology and Control*. Eds. G. de The and Y. Ito. IARC Scientific Pub. 1978;20:167.
- Gnepp D.R. Small Cell Neuroendocrine Carcinoma of the Larynx: A Critical Review of the Literature, *ORL J Otorhinolaryngol Relat Spec*. 1991;53:210-219
- Ferlito A, Caruso G, Nicolai P, Recher G, Silvestri F. Primary Small Cell ('Oat Cell') Carcinoma of the Larynx and Hypopharynx: A Clinico-Pathological Study of 8 Cases with a Review of the Literature, *ORL*. 1981;43:43-49.
- Llorente JL, López F, Suárez C, Hermsen MA, Sinonasal carcinoma: clinical, pathological, genetic and therapeutic advances. *Nat Rev Clin Oncol*. 2014;11:460-72.
- Wanebo HJ, Konesh JR, MacFarlane JK, Elber FR, Byers RM, Elias G and Spiro RH: Head and neck sarcoma: report of the head and neck sarcoma registry. *Head Neck Surg*. 1992;14:1-7.
- Tran LM, Mark R, Meier R, Calcaterra TC and Parker R: Sarcomas of the head and neck. Prognostic factors and treatment strategies. *Cancer*. 1992;70:169-177.
- Ewing J: *Neoplastic Disease. A Treatise on Tumors*. Philadelphia, W.B. Saunders, 1940.
- Huvos AG and Higinbotham NL: Primary fibrosarcoma of bone. A clinicopathologic study of 130 patients. *Cancer*. 1975;35:837-847.
- Pritchard DJ, Sim FH and Ivins JC: Fibrosarcoma of bone and soft tissues of the trunk and extremities. *OrthopClin North Amer*. 1977;8:869-881.
- Taconis WK and Van Rijssel TG: Fibrosarcoma of long bones. A study of the significance of areas of malignant fibrous histiocytoma. *J Bone Joint Surg (Br)*. 1985;67:111-116.
- deFaria JL. Basal cell carcinoma of the skin with areas of squamous cell carcinoma: A basosquamous cell carcinoma? *J Clin Pathol*. 1985;38:1273-7.
- Weedon D. *Skin pathology*. London: Churchill Livingstone; 2002. p. 1158.
- Leibovitch I, Huilgol SC, Selva D, Richards S, Paver R. Basosquamous carcinoma: Treatment with Mohs micrographic surgery. *Cancer*. 2005;104:170-5.
- Eisbruch A, Ten Haken RK, Kim HM, Marsh LH, Ship JA. Dose, volume, and function relationships in parotid salivary glands following conformal and intensitymodulated irradiation of head and neck cancer. *Int J RadiatOncolBiolPhys*. 1999;45:577-87.
- Malouf JG, Aragon C, Henson BS, Eisbruch A, Ship JA. Influence of parotidsparing radiotherapy on xerostomia in head and neck cancer patients. *Cancer Detect Prev*. 2003;27:305-10.
- Henson BS, Eisbruch A, D'Hondt E, Ship JA. Two-year longitudinal study of parotid salivary flow rates in head and neck cancer patients receiving unilateral neck parotid-sparing radiotherapy treatment. *Oral Oncol*. 1999;35:234-41.
- Henson BS, Inglehart MR, Eisbruch A, Ship JA. Preserved salivary output and xerostomia-related quality of life in head and neck cancer patients receiving parotidsparing radiotherapy. *Oral Oncol*. 2001;37:84-93.
- Mell LK, Mehrotra AK, Mundt AJ. Intensity-modulated radiation therapy use in the U.S., 2004. *Cancer*. 2005;104:1296-303.
- Murdoch-Kinch CA, Kim HM, Vineberg KA, Ship JA, Eisbruch A. Dose-effect relationships for the submandibular salivary glands and implications for their sparingby intensity modulated radiotherapy. *Int J Radiat Oncol Biol Phys*. 2008;72:373-82.
- Jabbari S, Kim HM, Feng M, et al. Matched case-control study of quality of life and xerostomia after intensity-modulated radiotherapy or standard radiotherapy for head-and-neck cancer: initial report. *Int J Radiat Oncol Biol Phys*. 2005;63:725-31.
- Chao KS, Majhail N, Huang CJ, et al. Intensity-modulated radiation therapy reduces late salivary toxicity without compromising tumor control in patients with oropharyngeal carcinoma: a comparison with conventional techniques. *RadiotherOncol*. 2001;61:275-80.
- Chao KS. Protection of salivary function by intensity-modulated radiation therapy in patients with head and neck cancer. *SeminRadiatOncol*. 2002;12:20-5.
- Johnson JT, Ferretti GA, Nethery WJ, et al. Oral pilocarpine for post-irradiation xerostomia in patients with head and neck cancer. *N Engl J Med* 1993;329:390-5.
- Gorsky M, Epstein JB, Parry J, Epstein MS, Le ND, Silverman S, Jr. The efficacy of pilocarpine and bethanechol upon saliva production in cancer patients with hyposalivation following radiation therapy. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod*. 2004;97:190-5.
- Axelsson P, Larsson UB. Saliva stimulating effect of SST. A clinical long-term study. *Tandlakartidningen*. 1991;83:698-9.
- Epstein JB, Schubert MM. Synergistic effect of sialagogues in management of xerostomia after radiation therapy. *Oral Surg Oral Med Oral Pathol*. 1987;64:179-82.
- Epstein JB, Emerton S, Le ND, Stevenson-Moore P. A double-blind crossover trial of Oral Balance gel and Biotene toothpaste versus placebo in patients with xerostomia following radiation therapy. *Oral Oncol*. 1999;35:132-7.
- Momm F, Volegova-Neher NJ, Schulte-Monting J, Guttenberger R. Different saliva substitutes for treatment of xerostomia following radiotherapy. A prospective crossover study. *StrahlentherOnkol*. 2005;181:231-6.
- Rhodus NL, Bereuter J. Clinical evaluation of a commercially available oral moisturizer in relieving signs and symptoms of xerostomia in postirradiation head and neck cancer patients and patients with Sjogren's syndrome. *J Otolaryngol*. 2000;29:28-34.
- Kaanders JH, Fleming TJ, Ang KK, Maor MH, Peters LJ. Devices valuable in head and neck radiotherapy. *Int J RadiatOncolBiolPhys*. 1992;23:639-45.
- Reitemeier B, Reitemeier G, Schmidt A, et al. Evaluation of a device for attenuation of electron release from dental restorations in a therapeutic radiation field. *J Prosthet Dent*. 2002;87:323-7.

32. Ben-David MA, Diamante M, Radawski JD, et al. Lack of osteoradionecrosis of the mandible after intensity-modulated radiotherapy for head and neck cancer: likely contributions of both dental care and improved dose distributions. *Int J RadiatOncolBiolPhys.* 2007;68:396-402.
33. Groll AH, Piscitelli SC, Walsh TJ. Clinical pharmacology of systemic antifungal agents: a comprehensive review of agents in clinical use, current investigational compounds, and putative targets for antifungal drug development. *AdvPharmacol.* 1998;44:343-500.
34. Epstein JB, van der Meij EH, Lunn R, Stevenson-Moore P. Effects of compliance with fluoride gel application on caries and caries risk in patients after radiation Murdoch-KinchZwetchkenbaum therapy for head and neck cancer. *Oral Surg Oral Med Oral Pathol Oral RadiolEndod.* 1996;82:268-75.
35. Epstein JB, Stevenson-Moore P. Periodontal disease and periodontal management in patients with cancer. *Oral Oncol.* 2001;37:613-9.
36. Sulaiman F, Huryn JM, Zlotolow IM. Dental extractions in the irradiated head and neck patient: a retrospective analysis of Memorial Sloan-Kettering Cancer Center protocols, criteria, and end results. *J Oral MaxillofacSurg.* 2003;61:1123-31.

Source of Support: Nil; **Conflict of Interest:** None

Submitted: 15-07-2016; **Published online:** 20-08-2016