Management of unresectable head and neck cancers - a retrospective analysis at a rural medical college of India

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Abstract

Objective To study the natural course of disease in patients of advanced squamous cell carcinoma of head and neck (SCCHN) admitted in a rural tertiary hospital and to formulate an acceptable protocol of management and their prognosis.

Study design A 5-year retrospective analysis of patients of advanced SCCHN attended in the department of Radiotherapy and admitted at department of ENT at B. S. Medical College, Bankura, West Bengal were analyzed for the present study.

Setting B. S. Medical College, Bankura at West Bengal, which is a rural medical college and act as tertiary referral, center for three district of West Bengal namely Midnapur, Purulia, Bankura, part of Burdwan and adjoining area of Jharkhand state.

Patients We investigated 100 patients in our hospital who presented with advanced and in-operable stage of SCCHN.

Eligibility criteria Biopsy proved cases of SCCHN in stage III, stage IVA and stage IVB which is surgically unresectable and without any past history of radiotherapy and chemotherapy were included in this study.

Key demographic features Eighty-nine men and 11 female with advanced SCCHN were included in this study. Their median age was 48 years (36–78 years) with a median weight of 44 kg and median Karnofsky score 70.

Interventions Different types of palliative surgical intervention like Ryles' tube insertion (16%), feeding jejunostomy (11%), tracheostomy (60%) and arterial ligation (2%) was done to relieve the symptoms. Forty-three patients received chemoradiation and 22 patients received only radiotherapy. Best supportive care was provided to 35 patients.

Outcome Twenty-nine percent of patients had partial response in terms of disease control and none had complete response.

Conclusion Symptomatic relief of respiratory obstruction, dysphagia and pain constitute the mainstay of treatment in the present study. A short course of radiotherapy is found to be effective in control of symptoms and helps to improve the quality-of-life. Complete response to therapy in advanced head and neck squamous cell carcinoma with a poor nutritional status is very difficult to achieve.

Keywords Squamous cell carcinoma · Head and neck cancer · Terminal care of cancer · Palliation

Introduction

Squamous cell carcinoma of the head and neck (SCCHN) is one of the commonest cancers seen in developing countries including India, constituting up to 25% of the overall cancer burden [1]. About 75% of cancer patients in India present with advanced disease and are considered incurable [2]. Surgery, radiotherapy and or chemotherapy fail to produce any cure of these patients. From the IARC registry it is estimated that about 6,75,000 people diagnosed to have head and neck cancer are from developing world and 60% of this group are from low and middle-income group [3]. Advanced SCCHN carries a poor prognosis and patients usually die of uncontrolled loco-regional disease. The 5-year survival is <20% with a median survival of around 12 months even with best possible aggressive treatment [4]. Several critical organs

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or tissues like salivary glands, spinal cord, mandible, major blood vessels and nerves, thyroid gland falls within the vicinity of treatment volume of head and neck cancers which not only impair treatment delivery by radiation or surgery but also impairs function of speech, deglutition, hearing and respiration. Common symptoms of SCCHN are pain, dysphagia, odynophagia, otalgia, hoarseness, cough, dryness of mouth and respiratory distress. A retrospective analysis of 100 consecutive cases of advanced, unresectable head and neck cancer patients registered at department of Radiotherapy and admitted at Department of ENT we tried to follow the natural course of disease and optimize a protocol of management that is feasible at a rural tertiary hospital.

Materials and methods

In our multidisciplinary joint clinic of B. S. Medical College, treatment record of the last 100 consecutive cases of advanced unresectable, previously untreated patients of head and neck cancers were analyzed. The eligibility criteria for analysis were:

- No previous history of radiotherapy or chemotherapy
- Biopsy proved cases of SCCHN
- No recurrent disease
- Stage III or stage IVA disease with poor performance status
- Stage IVB disease that is surgically unresectable due to disease extension, carotid invasion, pre-vertebral fascia invasion, etc. or fixed or fungating neck node mass
- No past history of cancer.

The primary endpoints were symptom relief with detailed assessment of symptomatology. Secondary end points were disease progression to end of life.

Pretreatment evaluation and symptoms – all symptoms were recorded at initial presentation and pain assessment were done by visual analog scale (VAS) [5] and faces pain scale [6]. The patients were asked to grade the severity of their most distressing symptom on a pragmatic scale of mild, moderate and severe. Staging of the tumor was done after proper clinical examination and radiological investigation in the form CT scan. Routine hematological assessment, baseline biochemical estimation of liver function test, renal function and chest radiograph were done in all cases.

Symptom relief after course of different modality of treatment that had been offered was recorded and as the percentage of symptom relief compared to baseline was assessed. Type of concomitant medications that the patients had taken with dose, type and period of medication were recorded.

Treatment plan

All patients were prescribed medications for symptomatic relief either in the form of oral or parenteral route. Tracheostomy was done for relief of respiratory distress. Nutritional support and maintenance of body fluid electrolyte balance done and were recorded. For this purpose a few patients had Ryles' tube insertion or feeding jejunostomy. Antiseptic dressing and care of external wounds were done as and when required. Palliative radiotherapy was delivered to some patients and dose, duration, response to radiation and toxicity were recorded. Initial planned dose of radiotherapy was 30 Gy in 10 fractions over 2 weeks to the gross primary tumor with 1.5–2.0 cm margin and prophylactic neck node irradiation not done in any case. Those with neck node involvement at presentation neck gland were also included with the primary treatment portals. All patients were treated by Tele cobalt machine with appropriate immobilization using bilateral or anterolateral wedged field once daily for 5 days a week.

Patients who had been treated by chemotherapy were also analyzed with the course of adjuvant, neoadjuvant or concomitant set up and objective response were analyzed. Cisplatin was the main drug used as adjuvant therapy. Besides cisplatin, 5-fluorouracil bleomycin, mitomycin-C was also tried in some cases. The drug induced side-effects as recorded in the case sheet were analyzed in this study. Symptom relief after chemotherapy, radiation and oral medication was compared.

Result

The demographic data of the 100 patients are shown in the Table 1. Eighty-nine patients were male and median age at presentation was 48 years.

The major complaint as on the first visit was pain 100%, swallowing difficulty 75%, respiratory difficulty 66%, fungating wound 65%, speech problem 80%, mucosal ulceration and salivation 22% (Table 2). As evidence from Tables 3 and 4, larynx and laryngopharynx constitute 51% of the primary site. Sixty-four percent of the patients presented at the T4 stage and 61% had bilateral nodal metastasis. Twenty-seven percent of the patients needed

Table 1 Patients' demographic characteristics

Gender	
Male	89
Female	11
Median age in years (range)	48 (36–78)
Median Karnofsky score	70 (50–90)
Median weight	44 (30–62)

Table 2 Severity of most common symptoms at presentation

	Mild	Moderate	Severe
Respiratory difficulty	11	35	20
Pain	16	24	60
Dysphagia	37	35	3
Disfigurement of face	8	9	17
Foul smelling fungating wound	5 (≤2 cm)	35 (2–5cm)	25 (>5cm)
Hemorrhage	2	2	3

Table 3 Primary site at presentation

Primary site	
Oral cavity	16
Oropharynx	20
Larynx/SG larynx	21
Laryngopharynx	32
Parotid and other salivary glands	1
Nasopharynx	3
Max. antrum	7

Table 4 T and N stage in the present series

T Stage	
T2	2
T3	33
T4	65
N Stage	
N0	10
N1	Nil
N2	61
N3	29

either Ryles' tube insertion or feeding jejunostomy for their nutritional support and 60% of patients required tracheostomy during their therapy period to overcome respiratory difficulty (Table 5). For control of pain oral medication with paracetamol, NSAID, dexopropoxyphene or narcotic analgesics like tramadol or morphine were used as single agent or in combination (Table 6). None of the patients achieved complete response to treatment (CR) with radiotherapy or chemotherapy. A handful of patients (15%) partially responded (PR) to radiotherapy or chemoradiotherapy and that too lasts only for short duration (Table 7).

Those patients who had been treated for palliation of symptoms by cytotoxic combination of chemotherapy (Table 8) and/or radiotherapy had complications of

Table 5 Palliative procedure/surgical intervention in the present series

Procedure	No. of patients	Percentage
Ryles' tube insertion	16	16%
Feeding jejunostomy	11	11%
Tracheostomy	60	60%
Arterial ligation	2	2%

Table 6 Analgesics used for control of pain

Only paracetamol (PCM)	Nil
PCM + diclofenac (DCF)	5%
PCM + DCF + dexopropoxyphene	20%
PCM + DCF + tramadol	7%
PCM + DCF + morphine tablet	20%
Tramadol + tricyclic antidepressant	25%
Injection pentazocin + tricyclic antidepressant	23%

Table 7 Modality of treatment

Modality of treatment	No. of patients	Response	
		CR	PR
Radiotherapy only	22	Nil	7
Radiotherapy + chemotherapy	43	Nil	8
Surgery	0	0	0
Best supportive care	35	0	14

Table 8 Chemotherapy schedule

Chemotherapy used	No. of patients
Weekly cisplatin (CIS-DDP)	5
CIS-DDP + 5-fluorouracil (5-FU)	29
CIS-DDP + bleomycin + methotrexate	9

treatment like mucositis 75%, xerostomia 56%, massive hemorrhage 2%, aspiration 40%. Patients who had undergone both chemotherapy and radiotherapy developed more complications (98%) than those who had only single modality of treatment (65%).

From the record sheet it revealed that 65% of the total patients died. Principal cause of death was aspiration and pulmonary infection 50%, massive hemorrhage 6%, poor nutritional status (asthenia) and inter-current infection in 85% cases.

Discussion

Head and neck cancers have a profound impact on quality-of-life as they so often interfere with the most fundamental

aspects of self-identity and daily life: facial appearance, communication, breathing, eating and drinking. Many patients with head and neck cancer smoke and drink heavily and are from socially deprived area. The present study population belongs to the backward district of West Bengal and most of them presented with advanced disease.

In the developing world approximately 75% of patients with head and neck malignancies present with locally advanced disease [7]. When patients with stage III or stage IV disease are treated with conventional treatment-like definitive surgery and/or radiotherapy local recurrence and distant metastasis lead to poor long-term result [8]. Survival benefit associated with the use of chemotherapy compared to best supportive care in advanced SCCHN has not been well studied. Although a selected group of patients may derive apparent significant prolongation in survival but on an average survival improvements appears small at best. Mortan et al. had shown only a 2-month median survival benefit with cisplatin and/or bleomycin compared to no treatment [9]. Cisplatin and carboplatin has been used extensively in advanced head and neck cancers, carboplatin is more bone marrow suppressive and less active than cisplatin [10, 11]. In our observation also we find very little benefit with or without use of chemotherapy for this advanced staged disease. Neither paclitaxel nor docetaxel has been found superior to methotrexate with regard to survival as primary endpoint [12]. Meta-analysis report for combination chemotherapy showed cisplatin and infusion 5-FU compared to single agent therapy: higher response rate, increased toxicity and survival benefit <1 month [13]. Palliative radiotherapy provides an effective symptom relief and improvement in quality-of-life - as has been evidenced by large, randomized, meta-analysis report [14, 15]. In other study it has been observed that “best supportive care” alone is associated with a median survival of 3–6 months in advanced SCCHN [16, 17]. It has been argued that palliative radiotherapy neither improves survival nor positively impacts on quality-of-life of patients with SCCHN [18].

There is no level I evidence regarding the use of palliative head and neck radiotherapy but several retrospective series [19–21] case control studies [22, 23] single arm prospective trial [24–28] affirm that its use is associated with an improvement in outcome.

Erkol et al. used to practice palliative radiotherapy of similar cohort patients as ours with a dose of 30 Gy/10#/2 weeks or 20 Gy/2#/1 week interfraction interval and they achieved a good 1 year response rate 77% and 48%, respectively and symptomatic response rate 68% and 38%, respectively [19]. Tata Memorial Hospital (TMH) study of palliative radiotherapy in head and neck cancer evidenced-based review also concluded that a short course of fractionated regimen (20 Gy/5#) or (30 Gy/10#) or cyclical treatment (not practiced in our hospital) are effective modality of palliation [29].

To optimize protocol of management in advanced SCCHN best supportive care is the most effective modality of treatment in our study. Jassem et al. defined best supportive care (BSC) as “treatment administered with the intent to maximize quality-of-life without a specific antineoplastic regimen,” which included “antibiotics, analgesics, antiemetics, thoracentesis, pleurodesis, blood transfusions, nutritional support and focal external-beam radiation for control of pain, cough, dyspnea or hemoptysis [30].” In the present study tracheotomy, jejunostomy, wound management and arterial ligation were also included in best supportive care.

For the treatment of mild pain aspirin, acetaminophen or NSAIDs are generally recommended. The NSAIDs have been shown to be effective analgesics or co-analgesics when there is evidence of bone involvement. Patients with severe pain should be treated with an opioid. Corticosteroids, especially dexamethasone and methylprednisolone, have several uses as adjuvants. They provide an initial euphoric effect, tend to stimulate appetite are anti-inflammatory and ameliorate hypercalcemia. Tricyclic anti-depressants, especially amitriptyline, have an analgesic effect independent of their antidepressant activity. The concomitant antidepressant effects and improved sleep may all enhance the patient’s feeling of well being. Effective pain management in the present series by morphine tablet was possible only in a small group of patients. Other analgesic medicines are not effective as much as morphine tablet but patients had to satisfy with alternative non-narcotic analgesics because of scarcity of supply of morphine tablets. Forty-eight percent patients in the present series received tricyclic antidepressants which gave them a sense of well being.

The onset of tracheal obstruction may be slow if due to tumor growth, but acute if precipitated by hemorrhage or infection. In the present set up tracheostomy is the only option to relieve the respiratory obstruction and to save the patients life. Sixty percent patients in the present series underwent tracheostomy.

Multimodality treatments for patients with SCCHN often produce significant mucositis and dysphagia, mandating enteral nutritional support. In advanced SCCHN the primary presentation may be dysphagia or aspiration. Seventy-five percent of patients in this series presented with dysphagia. Swallowing disorder is usually always associated with aspiration of oropharyngeal or gastric contents into the larynx and lower respiratory tract. In presence of aspiration, it is important to maintain a good oral hygiene in order to reduce the bacterial colonization. Antiseptic mouthwash usually maintains good oral hygiene. Specific swallowing strategies include feeding patient at an upright position, dividing the food into small boluses, feeding slowly, etc. In patients with immobile hemipharynx it is helpful to tilt or turn the head towards the paralyzed side to open the contralateral normally functioning lateral food channel. For those with reduced tongue control, the postural compensation

techniques or exercises may be helpful. Sometimes artificial feeding via a fine-bore nasogastric tube or percutaneous endoscopic gastrostomy (PEG) tube has to be considered in appropriate cases. Patient preference has resulted in the increasing use of PEG tubes rather than nasogastric tubes. However, PEG tube was required for longer periods of time and was associated with more persistent dysphagia and an increased need for pharyngoesophageal dilatation [31].

There is a higher risk of massive arterial bleeding in patients with eroding tumors close to carotid arteries. Unconsciousness and death may occur rapidly before sedation is allowed. If time allows, patient should be sedated with midazolam or diazepam intravenously or intramuscularly.

Wounds in advanced SCCHN may be characterized by excessive purulent discharge, odor and infection and sometimes maggot infestation in neglected cases. In assessment, one should look for presence of: (1) adherent necrotic tissue; (2) exudate; (3) bleeding due to traumatic dressing change and relationship of the wound with major vessels; (4) pain with dressing; (5) surrounding skin condition; (6) odor; (7) infection; and (8) impact on patient. The aim of treatment is to control pain and odor, to reduce discharge, and to provide psychological support. Odor and discharge can be reduced by antibiotic (e.g. metronidazole) either topically or systemically, adequate ventilation, and the use of special dressing materials. Local radiotherapy may have a hemostatic effect for wound with bleeding.

Conclusion

A great extent of patients is reported in advanced stage in the rural-based medical college hospital of West Bengal where palliation with “best supportive care” is only option of treatment. Side-effects of chemotherapy and conventional radiotherapy are severe. Palliative radiotherapy not only avoids delay in treatment delivery but also produce much less treatment related toxicities. So a short course of radiotherapy, judicious use of analgesics, nutritional support and optimized multidisciplinary approach of management are the goal to get best therapeutic benefit.

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