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CASE REPORT

Optimum Treatment of Carcinoma Esophagus in Geriatric Age with Multiple Comorbidities- A Case Report with Review of Literature

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ABSTRACT

Introduction: Standard management of concurrent chemo radiotherapy (CCRT) in upper and middle 1/3rd of cancer esophagus may be challenging to practice in the geriatric age group with multiple comorbid conditions. The treatment may lead to life threatening side effects while compromised treatment may lead to failure of the case. The present case reports the treatment of cancer esophagus patient in geriatric age group with multiple comorbidities treated with standard regimen of concurrent chemoradiation.

Case History: Sixty years old male with several comorbid conditions presented to our OPD with complaints of difficulty in swallowing in the past 6 months. Upper gastrointestinal endoscopy revealed ulcerated mass whose biopsy was suggestive of moderately differentiated squamous cell carcinoma. Positron emission tomography- computed tomography whole body scan revealed localized well-defined lesion in upper one third of the esophagus.

Echocardiography (2D Echo) showed cardiac comorbidity for which medications were prescribed and close monitoring was done by cardiologist. Diabetes was monitored by general physician and proper diet by nutritionist.

Patient was treated with standard CCRT protocol. There were no significant toxicities related to radiotherapy and chemotherapy. After 1-month of treatment upper gastrointestinal endoscopy revealed normal benign esopheagal mucosa. Follow up PET CT was done after 3 months which showed significant decrease with no new lesion. After 1-year follow up patient has no complaints of dysphagia.

Conclusion: Geriatric patients of upper or middle 1/3rd esophagus can be treated with standard chemo radiotherapy regimes by radiation oncologist in association with team of other physicians with regular monitoring of the comorbid conditions.

Keywords: Cancer esophagus, Chemoradiotherapy, Comorbidity, Geriatric.

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INTRODUCTION

Esophagus carcinoma is eighth most common cancer worldwide and sixth leading cause of death from cancer.[1] The management in geriatric age group may pose several challenges due to comorbidities and physiological changes associated with aging. This may lead to reluctance to treat with standard treatment protocols by clinicians.

The Radiation Therapy Oncology Group (RTOG) trial 85–01 established the superiority of CCRT compared with radiotherapy alone in esophageal cancer patients. However, the acute toxicity of this regimen was substantial- sixty-four percent of patients treated with CCRT experienced severe or life-threatening side effects.[2]

CCRT is considered the standard treatment for upper and middle one third esophageal cancers, but in patients of geriatric age group the use of concurrent chemotherapy has limited evidence in literature and not routinely practiced.[3] The present case was treated with CCRT for cancer upper 1/3rd esophagus in geriatric age group with multiple co morbid conditions under consultation with multidisciplinary team of clinicians.

CASE REPORT

Sixty years old male with a known history of diabetes mellitus and coronary artery disease (Percutaneous transluminal coronary angioplasty) presented to our OPD with complaints of difficulty in swallowing in the past 6 months. The dysphagia was more for solid foods and not associated with regurgitation of food. On examination there was no cervical lymphadenopathy. Upper gastrointestinal endoscopy revealed nodular soft tissue mass in esophagus just distal to upper esophageal sphincter which was ulcerated, fragile and bleeding on touch (Figure 1). Biopsy was suggestive of moderately differentiated squamous cell carcinoma.

In metastatic work up, Positron emission tomography-computed tomography (PET CT) whole body scan showed localized well defined discrete fluoro deoxy glucose

Figure 1: Upper GI endoscopy showing growth present in Upper 1/3rd Esophagus

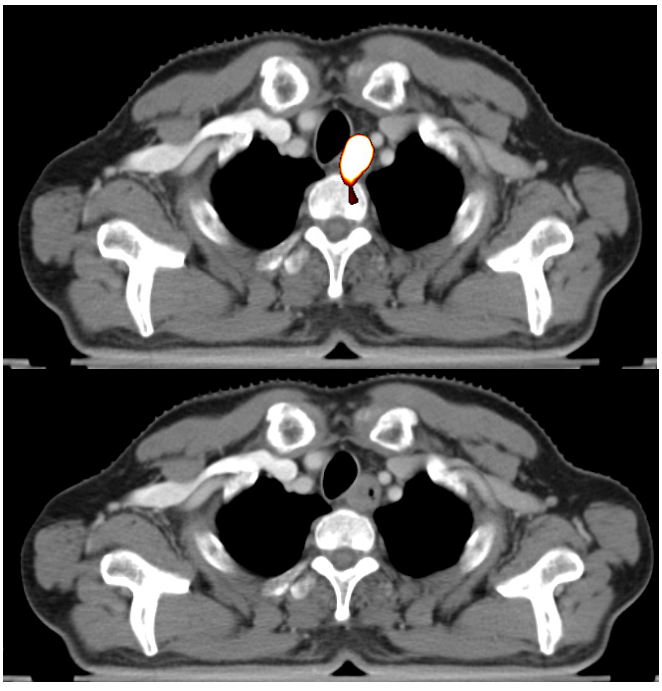

Figure 2: PET-CT scan showing FDG avid lesion in Upper 1/3rd Esophagus

(FDG) avid lesion in upper 1/3rd of the esophagus (SUV max- 20.61) along with FDG avid pretracheal lymph nodes (SUV max-8.85) (Figure 2).

Echocardiography (2D Echo) was done which showed regional wall motion abnormality in right coronary artery (RCA), Territory Hypokinetic with left ventricular ejection fraction (LVEF) 40%. On cardiologist consultation, furosemide pre and post chemotherapy along with low salt diet was advised, besides routine cardiac medications. Close monitoring by cardiologist was done on weekly basis.

Patient was referred to general physician for control of diabetes mellitus, where he was prescribed oral hypoglycaemias and was again in continuous consultation with the physician during the entire treatment. The patient was also under regular consultation with

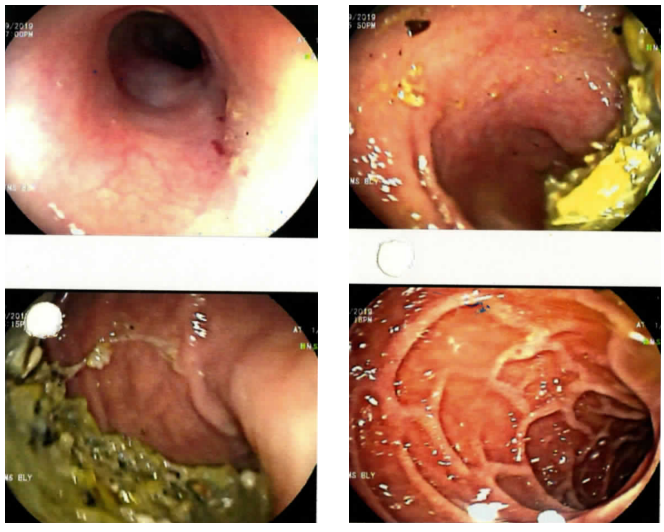

Figure 3: Upper GI Endoscopy showing normal benign esophageal mucosa after 1 month of treatment

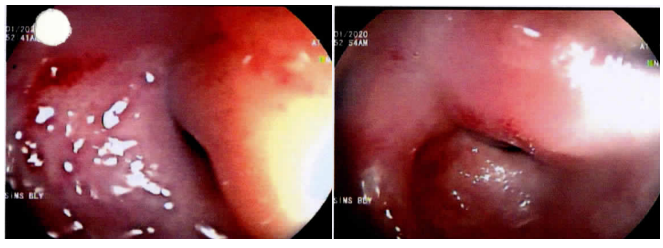

Figure 4: Endoscopy showing stricture after 6 months of follow up

nutritionist. He was regularly monitored for the diabetic diet and optimum calories so that he could tolerate the treatment well.

Patient was treated with standard CCRT protocol. He was delivered radiotherapy with a total dose of 50.4 Gy in 28 fractions at 1.8 Gy per fraction in $5^{1/2}$ weeks along with six cycles of concurrent chemotherapy (Cisplatin and 5FU). The patient had Grade I haematological toxicity and few episodes of vomiting and nausea. There were no significant toxicities related to radiotherapy and chemotherapy. After 1-month of treatment, upper gastrointestinal endoscopy showed normal benign esopheagal mucosa (Figure 3). Follow up PET CT was done after 3 months which showed significant decrease in metabolism, thickness and extent of esophageal wall thickening with decrease in metabolism of few mediastinal lymph nodes. No new lesion was seen. The patient developed stricture after 6 months and was treated by intermittent dilatation (Figure 4). After 1-year of follow up, patient has no complaints of dysphagia.

DISCUSSION

With the prolongation of average life-span, the number of elderly esophageal cancer patients is increasing year by year. The challenge in this elderly group is the decision making of optimum treatment. Elderly patients have multiple comorbidities and physiological

changes associated with aging which may restrict the use chemotherapy drugs, there by compromising the standard treatment. Furthermore, the data is limited on the use and toxicity of combined- modality treatments in these geriatric patient populations.

Most of the data suggest that older patients are at increased risk for cardiovascular and pulmonary complications.[4-7] A large SEER-medicare database review of esophagectomy outcomes showed that operative mortality increases with age, up to 13.4% in patients 70–79 years, and 19.9% in patients over the age of 80 years.[8] Given the potentially high morbidity and mortality rate and the high risk of recurrence when patients have lymph node-positive disease, the role of esophagectomy needs to be carefully considered in an older patient.[9,10]

The most common complications in older patients undergoing chemotherapy include myelosuppression, gastrointestinal toxicity, renal toxicity, and neurotoxicity. Chemotherapy can also affect cognition, function, and mood.[11] Combination of these issues can increase the risk of delirium, falls, and loss of independence. With age, renal glomerular filtration rate (GFR) decreases, resulting in the delayed elimination of many chemotherapy drugs like oxaliplatin, cisplatin, and capecitabine. Dose adjustment to the GFR should be considered for these drugs to decrease systemic toxicity and a careful review of home medications needs to be undertaken given polypharmacy in older patients with multiple comorbidities. In our patient we used cisplatin and 5 fluorouracil as weekly concurrent chemotherapy. Before each cycle complete blood count, liver function tests and kidney function tests are reviewed to check for any biochemical and hematological toxicity. The patient was also reviewed clinically by a physician weekly for the development of abnormal early signs and symptoms. The patient tolerated the chemotherapy drugs along with radiotherapy, mainly due to the supportive therapy and monitoring by a team of physicians and nutritionists.

Based on several clinical trials, CCRT has been the standard treatment for locally advanced esophageal cancer and is superior to RT alone.[3] However, very few studies have investigated CCRT in elderly patients.[12-15] The efficacy and toxicity of CCRT compared with RT alone for elderly patients have not been well documented.

Tougeron *et al.* reviewed 109 patients aged 70 years and above (mean age 74 years, range 70–88years) who received radiation with cisplatin-based chemotherapy.[12] Clinical complete response (CCR) was seen in 58% of patients, with a 2-years survival of 36%. Grade 3 or greater toxicity was seen in 24% of patients, and one death from febrile neutropenia was reported.

Similar rates of efficacy were reported by Anderson *et al.* in a study of 25 patients older than 65 years of age treated with CCRT using 5-fluorouracil and mitomycin.[13] In this small study, the CCR rate was 68%, with a 2-years survival of 64% and 36% experiencing significant toxicity.

On the contrary, the findings reported by Takeuchi *et al.*,[16] in a study of older patients (mean age 71) had worse survival and higher toxicity compared with younger patients treated with cisplatin and 5-FU (CF regimen) and radiation. Despite their poorer outcomes, the median survival of the older population was still 14.7 months (compared with 35.1 months in younger patients), with a 3-years survival of 29% (compared with 49% for younger patients), which is consistent with rates seen in the other studies. In our case, the patient had already completed a 13 months follow-up with no signs and symptoms of the disease. The treatment in the geriatric group of patients has to be individualized. The comorbidities have to be strictly controlled and monitored, which otherwise may lead to non-compliance and thus treatment failure.

Another small prospective study of 22 elderly patients aged more than 75 years were treated with CCRT (total dose of 50Gy with cisplatin).[17] The mean age was 79 years, histopathology was squamous carcinoma in 68% and the mean Charlson index score was one. CCR was seen in 64% with 2-years survival of 62 and 18% had complete remission at a follow-up of 26 months to 5.5 years. Eastern Cooperative Oncology Group performance status was initially stable but then worsened slightly during the last 2 weeks of treatment. Moreover, 22% had grade 2 vomiting, but no nephrotoxicity or toxicity-related death was seen. This study guides that aggressive CCRT can be adopted for elderly cancer esophagus patients. There are can be expectations of long term survival, the chance which should not be missed by compromising the standard treatment by the mere thought of the patient being elderly.

Patients of esophagus cancer usually have poor nutrition status. Further, standard treatment of CCRT, raises concern regarding enhancement and maintenance of nutrition status to tolerate the treatment. Malnutrition has been associated with reduced response to treatment and survival, affecting the quality of life severely and increasing health care costs.

In one large study of 348 patients of age more than 70 years, poor nutritional status is a predictor of early death who were treated with first-line chemotherapy.[18] Another study showed strong correlation between baseline nutritional status and overall survival after definitive chemo-radiotherapy, with patients who had signs of poor nutrition had much poor outcomes.[19,20] Nutrition, unlike many other geriatric risk factors, is an area that can be improved through various interventions. Despite the high rate of gastrointestinal issues of anorexia, dysphagia, and weight loss in our patient population, nutritional

interventions are not commonly used in oncology.[21] In the present case, high consideration was given to the patient's nutritional status. The cancer management included the nutritionist in the team for continuous monitoring of the nutritional status and making necessary interventions timely.

The limited literature supports chemoradiation in elderly patients with upper and middle 1/3rd esophageal cancers, demonstrating that older patients can tolerate and benefit from combined-modality treatment. However, it is important to note the limitations regarding these data and their applicability to all elderly patients with esophageal cancer. The studies are small and predominantly retrospective in nature. The fact that these older patients were selected by their physicians to undergo chemo-radiotherapy suggests that the decision-making is to be individualized and cannot be applicable.

CONCLUSION

Geriatric patients with cancer esophagus can be treated with standard chemo-radiotherapy regimes if a team of several clinicians are present in the institute, which may take care of comorbid conditions. The role of clinicians other than oncologists should be more emphasized during the treatment, and regular monitoring should be assured.

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