COMPARISON OF SURVIVAL PERIODS AND RESPONSE IN THREE MODES OF TREATMENT FOR Ca ESOPHAGUS AT CENAR QUETTA

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Background: Esophageal cancer is a fatal disease, with mortality matching the incidence. Balochistan province and Afghanistan happen to fall in the "Esophageal Cancer Belt". This study was designed to compare survival periods and response in three different modes of treatment for cancer of esophagus at CENAR Quetta i.e Radiotherapy plus Surgery, Radiotherapy plus Surgery plus single agent chemotherapy and Radiotherapy plus Surgery plus combined chemotherapy. **Methods:** During 1997, 59 patients with histopathological evidence of Ca esophagus were referred to CENAR from primary health care centers in Balochistan and Afghanistan. These 59 patients were divided into three groups. Group:I (n=22) treated by local irradiation plus surgery. Group:II (n=20) treated by local irradiation plus surgery plus Single agent chemotherapy i.e 5 florouracil. Group:III (n=17) treated by local irradiation plus surgery plus combination chemotherapy i.e Cis-Platinum and 5-florouracil. All patients were evaluated by endoscopic examination at 2 month intervals. **Results:** This study of 59 patients (mean age 55±13 years and male to female ratio of 1:3), shows that 2 year survival is 29% and median survival period is 9 month for all the patients. For group 1, median survival period = 5 month, 2 year survival =18% and complete response =17%. For group II, Median survival period = 9 months, 2 year survival =30% and complete response =20%. For group III, Median survival period = 11 month, 2 year survival = 41% and complete response = 22%.**Conclusion:** This study shows that overall survival is poor in cancer of esophagus and combined chemotherapy along with surgery and radiotherapy gives better results as compared to other two groups. Also single agent chemotherapy plus surgery plus radiotherapy give better results than radiotherapy plus surgery.

Keywords: Ca Esophagus, Chemotherapy, Radiation therapy

INTRODUCTION

Esophageal cancer is the 9th most common cancer in the world. It is the disease of mid and late adulthood (40-70%).[1] The incidence of the cancer varies around the world but is particularly high in regions of Iran, Northern China, and States of Central Asia, near the Caspian Sea, the native population of South Africa and Northern Italy. In most countries, this cancer is 2 to 4 times more frequent in men than women. In Iran, Northern China, Afghanistan, Esophageal cancer belt regions, this cancer is almost as frequent in women as in men. Approximately 9000 new cases occur annually in U.S.A and about 8500 fatalities are reported yearly.[2] It is a poor prognostic disease with only 8% of patients surviving 5 years or more.

Etiological factors associated with esophageal cancer are malnutrition, vitamins deficiency, anemia, poor oral hygiene, previous gastric surgery, specific carcinogens like hot tea, alcoholic beverages, tobacco, iradiation, esophagitis, zinc, nitrosamines, metallic compounds and

fungal toxins.[3] There are also some associated disorders like achalasia, Plummer-Vinson syndrome, Tylosis, esophageal diverticula, reflux esophagitis, hiatus hernia, Barrette's esophageal leukoplakias and ectopic gastric mucosa.[4] In China the country with highest mortality, rates have been decreasing since 1970s, probably as a consequence of diet with higher contents of food rich in proteins, Vitamin C, E and riboflavin.[5]

It has been seen that 15-30% of the tumors arises in upper one third of the esophagus, 40-50% in the middle one third and about 10% in lower one third. Cancer of upper two third of esophagus is invariably squamous cell carcinoma. In the lower third, squamous Cell Carcinoma is still more common. [6] But one third of the cases involving lower third of esophagus present with Adenocarcinoma arising from Barrette's esophagus.[7] Tumor spread within esophagus both longitudinally and eventually circumferentially resulting in complete esophageal obstruction. Invasion through the deeper layers of esophageal wall will result in spread to the surrounding mediastinal structures such as trachea, main bronchi, pleura, lungs, vertebrae and great vessels. Tumors of the upper third will spread to the deep cervical and supra clavicular lymph nodes. Those of the middle one third to the mediastinum paratracheal and subcarinal nodes and those of lower one third to the nodes of coeliac axis below diaphragm. Liver is the most common site of distant metastasis although lungs and skeleton may also be involved. [4,6]

Dysphagia and weight loss are the most common features, others are hoarseness, cough, aspiration pneumonia, pleural effusion, hematemesis, hemoptosis, maleena, Superior vena cava obstruction and Horner's syndrome etc.[8] Standard initial diagnostic work up comprises history, physical examination, esophagogram, pen-endoscopy with biopsy and brushings, CT scan and MRI of chest and upper abdomen, X-ray, biochemistry profile, complete blood picture with differential electrolytes, BUN examination, endoscipic U/S.[9,10] This work up demonstrates whether the disease is limited to the esophagus or is advanced. Limited disease is then proceeded by evaluating lymph nodes when indicating via thoracoscopy, mediastinoscopy, and laparoscopy and if still found limited to the esophagus definite therapy is given. Advanced disease on initial work up are further evaluated on bone scan, if indicated, CT scan of lower abdomen or brain scan, if indicated, then palliative therapy is given.

Because the majority of patients present with locally advanced (T3, T4) or nodes positive disease as esophagus is expansile organ, having rich and complex lymphatic drainage and no serosal layer, multi modality therapeutic strategy is essential. Reference institute involved in esophageal cancer treatment must have a multi disciplinary team trained in different modalities necessary to develop combined therapies.[11]

This study was designed to compare response and survival periods in three different modes of treatment for cancer of esophagus at CENAR. Quetta i,e Radiotherapy plus surgery, Radiotherapy plus surgery plus single agent chemotherapy and Radiotherapy plus surgery plus combined chemotherapy.

MATERIAL AND METHODS

During the year of 1997, 71 patients of cancer of Esophagus were referred to CENAR from primary health care centers of Balochistan and Afghanistan for histopathological evidence. Only those

patients were included in this study whose primary site of origin was esophagus. 59 patients (mean age 55±13 year) completed their treatment within two years follow up. These fifty nine patients fell into three groups.

Group No. 1: 22 patients were treated by local irradiation (i.e 50-60 Gy conventional tumor dose from Co. 60 Tele Therapy unit) plus surgery.

Group No. 2: 20 patients were treated by local irradiation i.e 40 Gy/20 fx from Co. 60 Tele Therapy unit plus Surgery Plus Single agent chemotherapy i.e 5 florouracil 600 mg/m^2 I/V Push, wkly x 4 wk.

Group No. 3: 17 patients were treated by local irradiation i.e 40 Gy/20 fx from Co. 60 Tele Therapy unit plus surgery plus combination chemotherapy i.e Cis- Platinum 60 mg/m^2 I/V infusion, 3 wkly x 4 doses. 5 florouracil 500 mg/m^2 I/V push wkly x 12 wks.

The patients in these three groups with complete esopohageal obstruction were surgically supported by esophageal prosthetic intubation for nutrition. All patients were evaluated by endoscopic examination at 2 month intervals to know the response to different modes of treatment given to these three groups. Mathematical percentages and median survival periods were used to compare the results obtained during two year study.

RESULTS

Among these 59 patients (mean age 55±13 year), male to female ration was 1:3 and 60% of the cases belonged to Balochistan and 40% of the patients were referred from Afghanistan. After 2 years follow up of these 59 cases, 2 years survival and median survival for all patients and their subgroups is shown in table1.

Table 1: Two-year survival

Category	Patients	2- year survival	Median Survival (months)
GROUP 1	22	4 (18%)	5
GROUP 2	20	6 (30%)	9
GROUP 3	17	7 (41%)	11
Total	59	17 (29%)	9

Response of patients to different treatment was categorized as partial, complete, stationary and progressive as show in table –2

DISCUSSIONS

Our study shows that cancer of esophagus is more common tumor in male with Male to female ratio of 1:3 which is comparable to the in western data, where males are affected five to six times more commonly[12].

In this small study population 60 and 40 % cases were referred from Balochistan and Afghanistan respectively. Both these territories share borders with the high incidence belt region for Ca. Esophagus, extending from Iran to China.[11] Most of the outlying rural hospitals do not have resources to do the histological studies and they choose to use traditional medical therapies, therefore they are not referred to tertiary care centers like CENAR. Registered cases at CENAR are clearly under representation of actual prevalence in Balochistan and Afghanistan.

This study shows that most of patients present in later age (mean age 55±13 year). This data about age of the patients at the time of presentation may indicate the fact that it is difficult to reach an early diagnosis due to vague symptoms in early stages and lack of standard health care system in this region, developing with slower pace.

Table 2: Response to therapy in three groups

CATEGORY	TOTAL PATIENT s	COMPLETE RESPONSE	PARTIAL RESPONSE	STATIONARY DISEASE	PROGRESSIVE DISEASE
GROUP 1	22	3 (14%0	6 (27%)	0 (0%)	13 (59%)
GROUP 2	20	3 (15%)	6 (30%)	1 (5%)	10 (50%)
GROUP 3	17	4 (24%0	7 (41%)	0 (0%)	6 (35%)

Our study shows poor overall survival, as 2 years survival is 29 % and median survival period is 9 months only for all the patients. Ca esophagus has a poor prognosis, as it is an expansible, deeply seated organ so the diagnosis is usually late. It has a complex lymphatic drainage, so early lymphatic micrometastasis is more frequent. It has no serosal layer to limit local infiltration of the disease to surrounding structures for sometime.[3] The results of treatment even in USA have not been favorable, as most series showing five years survival rates of only 5-11 %. In one particular series only 5 out of 600 patients survived 5 years.[13,14]

Our study shows that combined chemotherapy along with surgery and radiotherapy gives better results (median survival time of 11 month, 2 years survival of 41% and complete response in 22%) as compared to other two groups. Also single chemotherapy plus surgery plus radiotherapy gives better results than radiotherapy plus surgery (median survival period of 9 Vs 5 month respectively and complete response in 20 versus 17 % respectively). Kelson and Wilson[14] have also reported that combined chemotherapy gives better results than single agent chemotherapy but the better survival in group 3 may also be attributed to the small number of patients in group 3 versus other two groups. Therefore further evaluation of the above mentioned treatment on large scale and for longer follow up periods is required.

CONCLUSIONS

Ca. Esophagus is a fatal tumor and over all prognoses is poor. Combined chemotherapy with surgery and local radiation therapy has encouraging results as compared to other modes of treatment. The number of patients and follow up periods are small in this study but it provides a guideline for other investigators in future. And the registered cases seem to rise further, as more

health care and diagnostic facilities would become available in this less developed territory in future. Screening programs may help in early detection and survival.

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