Long Term Survival in Unresectable Stage IV Esophageal Squamous Cell Carcinoma Treated with Chemoradiation: A Case Report

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Abstract

Introduction: Esophageal squamous cell carcinoma is one of the most common gastrointestinal cancers in Iran. Development of para-aortic lymphadenopathy is classified as stage IV and long term survival is rare. We report a case of esophageal squamous cell carcinoma with paraaortic lymphadenopathies, who was treated with systemic and nonsurgical locoregional therapy.

Report of the Case: A 39-year-old female with squamous cell carcinoma of the distal esophagus and proximal stomach, that was unresectable on laparatomy, was referred to our center for palliative treatment. She received six cycles of chemotherapy (Paclitaxel / Cisplatin), and then concurrent chemotherapy and radiotherapy to the primary tumor and paraaortic region with a total dose of 5220 centigray (cGy). Six years later, she was still alive without any complaints or disease progression.

Conclusion: It seems that patients with locally advanced unresectable esophageal squamous sell sarcinoma can be treated radically with systemic and nonsurgical locoregional therapy, to achieve long term survival.

Key words: Esophageal squamous cell carcinoma, survival, treatment.

Introduction

Squamous Cell Carcinoma (SCC) of esophagus is one of the most common Gastro Intestinal (GI) cancers in Iran [(1)]. Most of the patients are diagnosed in advanced stages with lymph node involvement [(2)]. From 20% of patients, who are diagnosed in stage IV half are due to abdominal and paraaortic lymphadenopathies[(3)]. Patients with paraaortic lymphadenopathy are classified as stage IV and those with a good performance status are usually treated with systemic chemotherapy to improve their quality of life with a median survival of 8 -9 months at best [(4-6)].

High dose radiotherapy could be curative when the pathology is SCC. Administration of high dose radiotherapy to abdominal cavity is not justified due to the presence of several sensitive dose limiting organs in the vicinity of the tumor, such as kidneys and small bowels. Therefore, paraaortic lymphadenopathy is considered as stage IV in the AJCC staging system [(7)], and cure is almost always impossible. We report a case of stage IV esophageal SCC, due to huge paraaortic lymphadenopathies, who was treated with a combination of systemic and non surgical locoregional therapy and was still alive 6 years after treatment without progression.

Report of the case

A 39-year-old female was referred to our hospital to receive treatment for her advanced esophageal SCC in February 2006. She had a history of progressive dysphagia to solid foods since 5 months ago and to liquids recently. She also complained of epigastric pain and loss of appetite resulting in more than 6 Kg weight loss in the last 2 months. She had no history of active or passive smoking and her past medical history was insignificant. On physical examination, her performance status was 1 according to the Eastern Cooperative Oncology Group (ECOG) scale and was a little emaciated. There was also a healing laparatomy scar extending from the xiphoid to more than 5cm below the umbilicus.

Review of her documents revealed that she had an infiltrating ulcer in the distal esophagus, with

involvement of the cardia and proximal part of the stomach that obstructed more than 80 percent of the lumen on esophagogastroscopy. There was no history of imaging studies such as computed tomography or barium meal. A biopsy specimen taken during esophagogastroscopy confirmed moderately differentiated esophageal SCC (Figure 1).

She underwent laparatomy to resect her tumor. According to her operating summery sheet, she had a huge tumor involving the full thickness of distal esophagus and proximal stomach, with extension to the anterior aspect of the pancreas, porta hepatis and portal vein. The sheet also included a report on celiac lymphadenopathy and a paraaortic mass extending from the celiac to the infra renal region. The tumor was considered unresectable and after placing a feeding tube in the jejunum and suturing the abdominal wall, the patient was taken to the recovery room.

On admission to our hospital, laboratory data showed normal values for all blood parameters except for a low level of hemoglobin (10 mg/dl). Liver enzymes and bilirubin were in the normal range and renal function testes were also unremarkable. Chest and abdominopelvic spiral computed tomographic scanning demonstrated distal esophageal wall thickening encompassing the cardia circumferentially and proximal stomach. Huge lymphadenopathy was also demonstrated in the celiac and paraaortic region with extension to the infra renal level (Figure 2).

Computed tomographic scanning did not show any other visceral metastases. According to AJCC (6th edition), our patient was in stage IV (T4N1M1), and palliative chemotherapy was considered for her.

In March 2006, treatment started with chemotherapy including paclitaxel (200 mg/m2) and cisplatin (75 mg/m2) every 3 weeks. Cisplatin was administered with appropriate hydration and emesis prophylaxis during 1 hour followed by paclitaxel during 3 hours. Three cycles were prescribed without major toxicity and all cycles were administered on schedule.

After three cycles, the patient started oral feeding with mild dysphagia to solid foods. Spiral computed tomographic scanning showed more than 30% decrease in primary, celiac and paraaortic masses (Figure 3).

The jejunostomy tube was extirpated and treatment continued with three more cycles of chemotherapy with the same medications.

Again, there was no major toxicity and all courses were prescribed full dose and on planed dates. Dysphagia resolved completely but computed tomography showed no more reduction in the tumor size and no visceral metastases.

At this time, the patient was in good condition with performance status of zero according to the ECOG scoring system. After explaining the advantages and disadvantages of locoregional treatment using concurrent chemoradiation to the patient and her family, verbal consent was obtained from the patient and treatment continued with concurrent chemoradiation in July 2006.

Clinical Target Volume (CTV) consisted of the

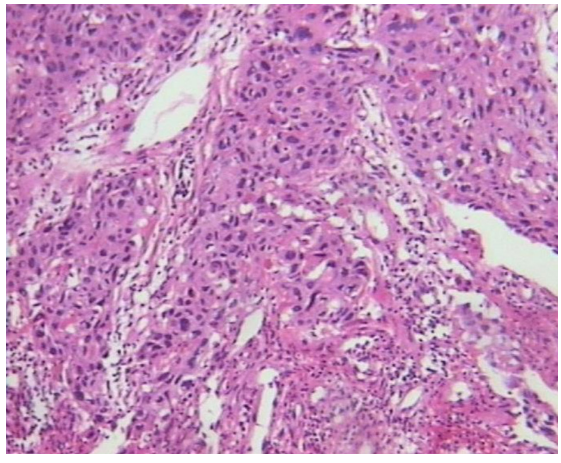

Figure 1: Biopsy specimen taken during esophagogastroscopy showing moderately differentiated esophageal SCC

distal esophagus and paraesophageal adipose tissues to 3cm above the proximal end of the tumor defined on pre chemotherapy computed tomography scanning. All of the stomach and lymphadenopathies in the celiac and paraaortic regions with about 1.5 cm margin were included in CTV. CTV was expanded 2cm more in all directions to define Planning Target Volume (PTV). Treatment was prescribed using two anteroposterior and posteroanterior portals with appropriate at-risk organs (kidneys, heart, lung and liver) shielded. The extent of the radiotherapy field to encompass PTV started from the 6th thoracic vertebra and ended at the 4th lumbar vertebra (more than 25 cm in length). The radiation dose was 4500 centigray (cGy) in 25 fractions using cobalt 60 treatment machine. After the last session of radiotherapy, since high energy linear accelerator was available in our center, we continued treatment with two more localized lateral portals to boost tumor volume plus 1 cm margin in all directions with 4 more 180 cGy fractions using 18 MV photons.

We planned to administer chemotherapy during the first and last four days of radiotherapy. During the first four days, chemotherapy consisted of cisplatin 75 mg/m2 on day 1 and 5Fu 750mg/m2 on days 1 to 4 with protracted continuous intravenous infusion. We could not administer chemotherapy in the last 4 days because of patient's refusal due to GI side effects. One month later, chest and abdominopelvic computed tomography scanning showed more decrease in the size of the paraaortic mass without new metastatic lesions. The patient received follow-up visits with yearly computed tomography scanning, blood cells count, and liver and renal function tests. After about 6 years, our patient was in good condition, had gained more than 15 Kg of weight and had no complaints of her previous disease or treatment related side effects.

Discussion

To our knowledge, there is no report of long term survival for esophageal SCC with bulky paraaortic lymphadenopathies.

Most esophageal cancers are SCC in our country[8]. SCC has a little different behavior in comparison with adenocarcinoma that is more prevalent in west countries. SCC usually extends locally and somehow in a stepwise manner so it first propagates to the lymphatic system and then to other distant visceral and non visceral sites through systemic circulation. Involvement of lymph nodes is a common finding at presentation for esophageal SCC [9-10], and increases the rate of distant metastases [11]. Therefore, a local approach alone for treating locally advanced SCC cannot guarantee cure because of the high risk of distant metastases [11-15]. Localized SCC of the esophagus, like most other SCCs such as head and neck SCC and anal canal SCC, could be sterilized by non surgical treatment using high dose radiotherapy in various combinations with chemotherapy [16-25]. Adding chemotherapy to radiotherapy can help to control SCC using lower doses and with fewer side effects [13, 26,27]. Hence, patients with locally advanced SCC need chemotherapy to control micro metastases

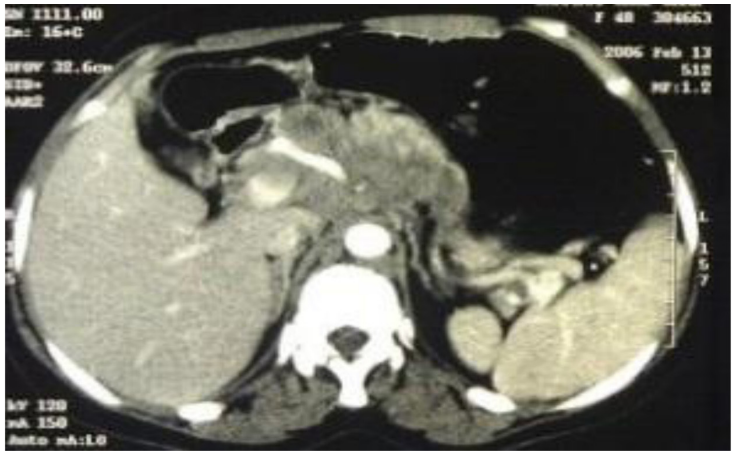

Figure 2: Huge lymphadenopathy in the celiac and paraaortic region with extension to the infra renal level.

and also to increase the effect of radiotherapy when indicated.

Our patient was in stage IV according to the 6th edition of AJCC staging system [7], so we started treatment with chemotherapy and achieved good subjective (disappearance of dysphagia and weight gain), and also reasonable objective responses (decrease in tumor size). She was young and in good condition without adverse events resulting from chemotherapy so continuation of chemotherapy was a reasonable option to control distant site micro metastases and maintain the patient's quality of life.

Local therapy in metastatic SCC is indicated to palliate patient's symptoms. Prescribing high dose radiotherapy to the lower esophagus and paraaortic region could raise the probability of acute and late side effects that can affect quality of life. We know that the probability of resistant clone to chemotherapy is higher in bulky tumors as compared to low volume tumors so there is increased risk of recurrence in bulky SCCs in comparison with low volume SCCs. Considering the partial response and residual tumor after 6 cycles of chemotherapy, the probability of recurrence was high as we know the best median survival rate in different studies for stage IV disease is 11–22 months [16, 28, 29]. Even in patients who achieve pathological complete response to chemotherapy, recurrence in the tumor bed and distant sites is usual [15-17], so adding local therapy to systemic treatment is reasonable.

Sueyama et al. treated a 60-year-old man who had SCC of the esophagus with paraaortic lymphadenopathies without distant metastases[30]. He received two cycles of cisplatin and 5 fluorouracil followed by concurrent chemoradiation and after one more cycle of chemotherapy, the patient underwent surgery because of recurrence suspicion. He achieved pathological complete response and was alive after 26 months. In comparison with our patient, he received high dose radiation to the primary tumor (70 Gy), and moderate dose radiation to the upper abdomen (48Gy) concurrent with chemotherapy. Our patient survived for 6 years after treatment; which can be regarded as cure and complete sterilization of the tumor mass using doses less than the dose administered in the aforementioned study.

It seems that doses ranging from 50 to 54 Gy concurrent with chemotherapy are reasonable for treating SCC of the esophagus with curative intent. With new advancements in radiation therapy, administration of such doses is more feasible nowadays. In patients with locally advanced SCC of the esophagus, the aim of treatment should be cure, especially when the patient is in good condition and young enough to tolerate multimodality treatments.

Conclusion

It seems that patients with locally advanced unresectable esophageal squamous cell carcinoma can be treated radically with systemic and nonsurgical locoregional therapy, to achieve long term survival.

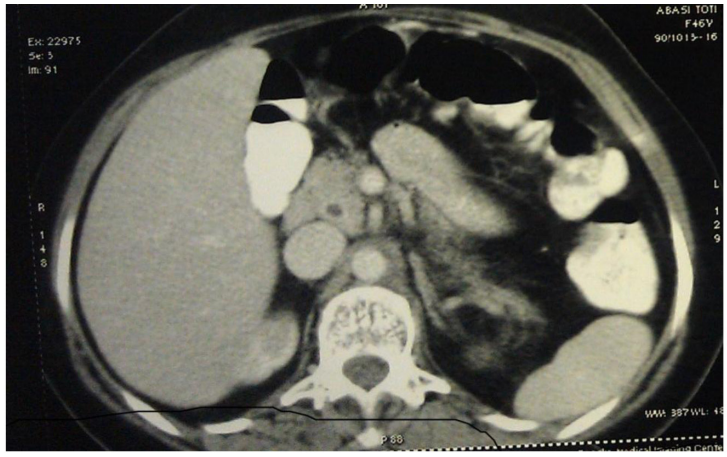

Figure 3: Spiral computed tomographic scanning shows more than 30% decrease in primary, celiac and paraaortic masses.

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