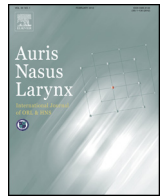




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A retrospective study of treatment for curative synchronous double primary cancers of the head and neck and the esophagus

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ABSTRACT

Objective: Curative synchronous double primary cancers of the head and neck and the esophagus (CSC-HE) are frequently detected, but a standard treatment remains to be established. We studied the clinical course to explore appropriate treatment strategies.

Methods: We retrospectively studied consecutive 33 patients who had CSC-HE. The disease stage was classified into 4 groups: group A, early head and neck cancer (HNC) and early esophageal cancer (EC); group B, early HNC and advanced EC; group C, advanced HNC and early EC; and group D, advanced HNC and advanced EC. As induction chemotherapy, the patients received 3 courses of TPF therapy (docetaxel 75 mg/m² on day 1, cisplatin 75 mg/m² on day 1, and 5-fluorouracil 750 mg/m² on days 1–5) at 3-week intervals. The clinical courses and treatment outcomes were studied according to the disease stage of CSC-HE.

Results: The disease stage of CSC-HE was group A in 1 patient (3%), group B in 9 patients (27.3%), group C in 3 patients (9.1%), and group D in 20 patients (60.6%). The median follow-up was 26 months, and the 2-year overall survival rate was 67.4%. In groups A, B, and C, the 2-year overall survival rate was 83.3%. In group D, the 2-year overall survival rate was 62.6%. Ten of 20 patients in group D received induction chemotherapy with TPF, and 6 patients were alive and disease free at the time of this writing.

Conclusion: The treatment outcomes of patients with CSC-HE were relatively good. TPF induction chemotherapy might be an effective treatment for patients with advanced HNC and advanced EC.

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1. Introduction

Double primary cancers are frequently detected in the head and neck and the esophagus [1–3]. Recent progress in endoscopic imaging has increased the frequency of detecting early double cancers [4–9]. Because curative synchronous double primary cancers of head and neck and the esophagus (CSC-HE) are associated with diverse tumor locations and disease stages, standard treatment strategies have yet to be established [10–13]. Therefore, multidisciplinary treatment policies are often planned on a case-by-case basis after consultation with medical oncologists, radiation oncologists, surgeons, and endoscopists, based on their clinical experience. We retrospectively studied the clinical courses and treatment outcomes in patients with CSC-HE to explore appropriate treatment strategies.

2. Patients and methods

From January 2010 through December 2014, esophageal squamous-cell carcinoma was diagnosed in 674 patients. Among the 674 patients with esophageal cancer, we retrospectively studied 33 consecutive patients who had CSC-HE. Clinical courses and treatment outcomes were studied according to the disease stage of CSC-HE.

In our study, synchronous double cancers were defined as untreated double cancers that were concurrently detected at the time of initial therapy. Intramucosal cancer of the esophagus is associated with a low incidence of lymph-node metastasis and good treatment outcomes [14]. As for disease stage, early esophageal cancer was defined as cancer localized to the mucosa without metastasis. Advanced esophageal cancer was defined as cancer that invaded the submucosa or deeper or cancer with metastasis.

In head and neck cancer, superficial cancer localized to the subepithelium has good treatment outcomes [15]. As for disease stage, early head and neck cancer was defined as cancer localized to the subepithelium without metastasis. Advanced head and neck cancer was defined as cancer that invaded the muscularis propria or deeper or as cancer with metastasis.

The disease stage of synchronous double cancers was classified into the following 4 groups: group A, early head and neck cancer (HNC) and early esophageal cancer (EC); group B, early HNC and advanced EC; group C, advanced HNC and early EC; and group D, advanced HNC and advanced EC.

The treatment policy was determined according to the physician's choice based on discussions with medical oncologists, radiation oncologists, surgeons, and endoscopists. Induction chemotherapy comprised 3 courses of TPF therapy (docetaxel 75 mg/m² on day 1, cisplatin 75 mg/m² on day 1, and 5-fluorouracil 750 mg/m² on days 1 to 5) at 3-week intervals [16–18].

Adverse events of TPF chemotherapy and of chemoradiotherapy (CRT) were evaluated according to the National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE), Version 4.0. Adverse events of CRT were divided into acute phase and late phase. The acute phase was

defined as within 90 days from the start of CRT, and the late phase was defined as more than 90 days after the start of CRT.

The Kaplan–Meier method was used to analyze overall survival rates. This retrospective study was approved by our institutional review board.

3. Results

The demographic characteristics of the 33 patients with CSC-HE are shown in Table 1. The study group comprised 26 men and 7 women with a median age of 67 years (range 39–83). The primary tumor of HNC was located in the oropharynx in 2 patients (lateral wall in 1, anterior wall in 1) the hypopharynx in 25 patients (piriform sinus in 13, posterior wall in 7, postericoid in 5), and the larynx in 6 patients (arytenoid in 3, epiglottis in 2, and vocal cords in 1). The primary tumor of EC was located in the cervical esophagus in 4 patients, the upper thoracic esophagus in 5 patients, the middle thoracic esophagus in 17 patients, and the lower thoracic esophagus in 7 patients. The clinical stage of HNC was I in 11 patients, II in 12 patients, III in 7 patients, and IV in 3 patients. The clinical stage of EC was I in 13 patients, II in 5 patients, III in 10 patients, and IV in 5 patients. The disease stage of CSC-HE was group A in 1 patient (3%), group B in 9 patients (27.3%), group C in 3 patients (9.1%), and group D in 20 patients (60.6%).

The clinical course of the 1 patient in group A is shown in Fig. 1. Treatment for early HNC and early EC was concurrently started. The patient concurrently underwent endoscopic resection was alive and disease free.

Table 1

Patient characteristics of 33 patients with synchronous double primary cancers of the head and neck and the esophagus.

Sex (male/female)	26/7
Median age (years) (range)	67 (39–83)
Tumor location	
Head and neck cancer	
Oropharynx	2
Hypopharynx	25
Larynx	6
Esophageal cancer	
Cervical esophagus	4
Upper thoracic esophagus	5
Middle thoracic esophagus	17
Lower thoracic esophagus	7
Clinical stage	
Head and neck cancer	
I	11
II	12
III	7
IV	3
Esophageal cancer	
I	13
II	5
III	10
IV	5
Disease stage of the synchronous double primary cancers ^a	
A (early HNC and early EC)	1
B (early HNC and advanced EC)	9
C (advanced HNC and early EC)	3
D (advanced HNC and advanced EC)	20

^a HNC: Head and neck cancer, EC: Esophageal cancer.

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