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Original Article

Risk factors for recurrent pneumonia in post-irradiated patients with nasopharyngeal carcinoma

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Abstract

Background: Nasopharyngeal carcinoma (NPC) is a common cancer in eastern Asia. Chemoradiotherapy is the main treatment modality for NPC. Dysphagia and aspiration is not uncommon in post-irradiated NPC patients. The purpose of this study was to investigate the risk factors for recurrent pneumonia and the prognosis.

Methods: A retrospective chart review was conducted from January 2004 to December 2014. NPC patients who had been hospitalized for pneumonia in the study hospital were enrolled. The diagnosis of pneumonia was based on radiological evidence of chest inflammation and clinical symptoms. Patients' characteristics including demographic data, the hospital course, and the outcome of pneumonia were collected and analyzed.

Results: A total of 113 NPC patients were enrolled in this study. Among them, 96 NPC patients had pneumonia after radiotherapy: 43 had pneumonia twice, and 18 had multiple episodes of pneumonia. Forty-nine patients had tube feeding. The 30-day mortality rate was 51%. The mortality rate was significantly associated with metastatic nasopharyngeal carcinoma (r = 0.328, p < 0.001). Older age, smoking, body weight loss, and lower cranial nerve (vagus or hypoglossal nerve palsy) were significant predictors of multiple episodes of pneumonia ($r^2 = 0.687$, p = 0.033, 0.034, 0.036, and 0.027, respectively).

Conclusion: We concluded that old age, smoking, body weight loss, and lower cranial nerve palsies are predisposing factors for multiple episodes of pneumonia in post-irradiated NPC patients. Metastatic cancer status usually leads to a lethal outcome. Early interventions to manage dysphagia in high-risk patients are necessary.

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Keywords: Aspiration pneumonias; Deglutition disorder; Enteral nutrition; Nasopharyngeal carcinoma; Risk factors

1. Introduction

Pneumonia is a leading cause of death due to infection globally. Pneumonia usually affects the elderly. ^{1, 2} Furthermore,

the presence of comorbidities including chronic respiratory and cardiovascular diseases, dementia, dysphagia, and chronic renal or liver diseases increase the risk of pneumonia.² Patients with head and neck cancers (HNCs) are prone to developing pneumonia. An important etiology for pneumonia in HNC patients is deglutition disorder. The anatomical changes of the upper aerodigestive tract resulting from tumor destruction or surgeries result in deglutition disorder. In addition, chemoradiotherapy is an important treatment modality for HNCs. Deglutition disorder is a major late treatment side effect after chemoradiotherapy for HNCs, and may lead to malnutrition and aspiration pneumonia.³⁻⁶ Nasopharyngeal carcinoma (NPC) is a common

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neoplasm in southern China, Hong Kong, and Taiwan.⁷ The primary treatment modality for NPC is chemoradiotherapy. Our recent analysis using Taiwan's National Health Insurance Research Database found that the incidence of pneumonia in the post-irradiated NPC population in Taiwan was around 5.5%.⁸ However, this database did not provide sufficiently detailed information to allow an exploration of risk factors for developing pneumonia. It had been reported that approximately 90% of deaths due to pneumonia occur in people aged over 65 years.² The outcome of pneumonia in middle-aged NPC patients had not been reported. In our experience, the prognosis of pneumonia in NPC patients is generally poor. The purpose of this retrospective study was to investigate the risk factors and outcomes of NPC patients who were hospitalized with pneumonia at a teaching hospital.

2. Methods

The Ethics Committee of Taichung Veterans General Hospital approved this study. A retrospective chart review was conducted from January 2004 to December 2014. NPC patients who had been hospitalized for pneumonia in the study hospital were enrolled. The diagnosis of pneumonia was based on radiological evidence of chest inflammation and clinical symptoms including fever, cough, or dyspnea. Patients under 20 years of age were excluded. Patients' characteristics including demographic data, hospital course, and outcome of pneumonia were collected by chart review and analyzed. NPC cancer staging was performed according to the 7th edition of the American Joint Committee on Cancer system. If a patient died within 30 days of a pneumonia episode and a causal relationship was established, then pneumonia was recorded as the cause of death.

Continuous variables are presented with means (standard deviation). Spearman correlation coefficient was used to analyze the relationship between pairs of variables. Furthermore, multivariable logistic regression analysis was performed to assess the risk factors associated with multiple episodes of pneumonia. A two-sided p < 0.05 was considered statistically significant. Statistical analyses were performed using SPSS 17.0 (SPSS, Inc., Chicago, IL, USA).

3. Results

The numbers of patients received treatment or follow-up for NPC, hospitalized for pneumonia, or for both diseases in the study hospital are listed in Table 1. There were 6,651 NPC patients and 16,130 hospitalized pneumonia patients during the study period. Two hundred and sixteen NPC patients had been hospitalized for pneumonia. The estimated incidence of hospitalized for pneumonia in NPC patients was 3.2%. We performed a retrospective chart review enrolling 113 NPC patients who had been admitted to our department for pneumonia. We found that 96 NPC patients had pneumonia after radiotherapy. The other 17 patients did not receive radiotherapy or had pneumonia during or before the radiotherapy. The demographic data of the study subjects are shown in Table 2.

Table 1 Numbers of patients who received treatment for nasopharyngeal carcinoma, pneumonia, or both diseases during the study period.

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Year	NPC ^a	Pneumonia ^b	Both
2004	1,199	1,581	12
2005	1,175	1,511	20
2006	1,303	1,362	18
2007	1,271	1,371	21
2008	1,249	1,470	27
2009	1,353	1,571	17
2010	1,325	1,886	22
2011	1,433	1,845	22
2012	1,365	1,812	26
2013	1,278	1,743	30
2014	1,266	1,976	24
2004-2014	6,651	16,130	216

^a Number of patients with diagnosis of nasopharyngeal carcinoma who received in-hospital or outpatient treatment.

Table 2 Characteristics of post-irradiated patients with nasopharyngeal carcinoma admitted for pneumonia in the study hospital.

Characteristics	N = 96	Percentage	
Sex F/M (N)	19/77	19.8% vs. 80.2%	
T stage ^a			
T1	12	12.5%	
T2	23	24%	
T3	18	18.8%	
T4	27	28,1%	
Unknown	16	16.7%	
N stage ^a			
N0	10	10.4%	
N1	12	12.5%	
N2	39	40.6%	
N3	18	16.7%	
Unknown	18	16.7%	
M stage ^a			
M0	64	66.7%	
M1	19	19.8%	
Unknown	13	13.5%	
Comorbidity ^b	30	31.3%	
Smoking ^c	49	51%	
Lower cranial nerve palsy ^d	38	40.6%	
Disease status at pneumonia diagram	nosis		
No evidence of cancer	32	33.3%	
Metastatic disease	36	37.5%	
Loco-regional disease	26	27.1%	
Second cancer	2	2.1%	
Radiotherapy (RT)			
CRT ^e	11	11.5%	
$\mathbf{IMRT}^{\mathrm{f}}$	66	68.8%	
Unknown	19	19.8%	
Received 2nd course RT	32	33.3%	

^a AJCC 7th edition, initial cancer stage.

b Number of hospitalized patients with diagnosis of pneumonia.

^c Number of hospitalized patients with diagnosis of nasopharyngeal carcinoma and pneumonia.

^b Comorbidity = pre-existing diabetes, respiratory or cardiovascular diseases, chronic renal or liver diseases, autoimmune disease.

^c Current or ex-smokers.

^d Vagus nerve or hypoglossal nerve palsies at the time of pneumonia.

^e Conventional two-dimensional radiotherapy.

^f Intensity modulated radiotherapy.

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