Lung cancer patients with previous or simultaneous the upper aerodigestive cancers

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ÖZET

Eş zamanlı veya tanılı üst hava yolu ve sindirim sistemi kanseri olan akciğer kanserli hastalar

Tanılı veya akciğer kanseriyle eş zamanda tanı almış olan üst hava yolu ve sindirim sistemi tümörü olan hastaların klinik özellikleriyle ilgili az sayıda çalışma bulunmaktadır. Bu özellikleri değerlendirmek üzere retrospektif bir çalışma yaptık. Bölümümüzde Ocak 1984 tarihinden Temmuz 2008 tarihine kadar olan sürede akciğer kanserli hastaların tıbbi kayıtları incelendi. Bin iki yüz kırk iki hastanın 21 (%1.7)'inde eş zamanlı veya tanı koyulmuş üst solunum yolu ve sindirim sistemi kanseri vardı. Yirmi hasta sigara içiyordu. Küçük hücreli dışı akciğer kanseri için 6 hastaya cerrahi rezeksiyon, 3 hastaya kemoterapi uygulandı. Küçük hücreli akciğer kanseri olan 3 hasta kemoterapi aldı. Komorbiditelere bağlı hiçbir ciddi komplikasyon gözlenmedi. Küçük hücreli dışı akciğer kanseri ve küçük hücreli akciğer kanseri için medyan sağkalım sırasıyla 15 ve 6 aydı. Üst solunum yolu ve sindirim sistemi kanseri olan hastalarda sigaranın bırakılması, akciğer grafi veya bigisayarlı tomografinin yılda bir kez tekrarlanması ve akciğer kanserini düşündüren belirti ve bulguların değerlendirilmesi önerilir.

Anahtar Kelimeler: *Üst solunum yolu ve sindirim sistemi kanseri, metakron, senkron, komorbidite.*

SUMMARY

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There have been few reports on clinical characteristics of lung cancer patients with previous or simultaneous upper aerodigestive cancers. To evaluate them, we conducted a retrospective study. The medical records of all lung cancer patients at our division from January 1984 through July 2008 were reviewed. Twenty-one (1.7%) of 1242 patients had previous or simultaneous upper aerodigestive cancers. Twenty patients were smokers. For non-small cell lung cancer (NSCLC), 6 patients underwent surgical resection and 3 were treated with chemotherapy. Three small cell lung cancer (SCLC) patients had chemotherapy. None of the severe complication related to the comorbidities were observed. The median survival for NSCLC and SCLC patients was 15 and 6 months, respectively. For patients with upper aerodigestive cancers, smoking cessation, a chest radiograph or computed tomography scan at least yearly and swift evaluation of signs or symptoms that are suggestive of lung cancer should be recommended.

Key Words: *Lung cancer, upper aerodigestive cancer, metachronous, synchronous, comorbid.*

Lung cancer patients sometimes have other malignancies (1-6). Among them, upper aerodigestive cancers such as vocal cord and laryngeal cancers seem to be incidentally detected during the workup of primary lung cancer. Etiologically, it is generally accepted that cigarette smoking may play an important role as carcinogenesis in lung cancer as well as upper aerodigestive cancers (7-9). Previous case-control studies had shown that smoking was an important cause of lung cancer (10,11). In addition, experimental studies had shown that painting of rabbit skin with tobacco tar induced cancers, and some of the carcinogens present in tobacco smoke had been identified (12). An International Working Group of experts established a positive association between tobacco smoking and cancers of the lung and upper aerodigestive cancers (13,14). However, there have been few reports on clinical characteristics of lung cancer patients with previous or simultaneous upper aerodigestive cancers (15). Additionally, it was scarcely reported the treatments for these patients and the outcomes of them (15). To evaluate such clinical information, we reviewed our experience with lung cancer patients who previously or simultaneously developed upper aerodigestive cancers.

MATERIALS and METHODS

The medical records and pathological reports of all patients at our division who had a diagnosis of primary lung cancer with previous or simultaneous upper aerodigestive cancers from January 1984 through July 2008 were reviewed. The data collected included gender, age at diagnosis of upper aerodigestive cancers, smoking history, comorbid diseases, histology of lung cancer and clinical stage, type of treatment, and survival from the date of diagnosis of lung cancer. Previous upper aerodigestive cancers were defined as those diagnosed and treated at least 1 year prior to the diagnosis of lung cancer. Simultaneous upper aerodigestive cancers were defined as those diagnosed during the workup of primary lung cancer and those diagnosed less than 1 year prior to the diagnosis of lung cancer. Diagnosis of both upper aerodigestive cancers and lung cancer were confirmed pathologically in all the patients studied. All the upper aerodigestive cancers were detected from symptom such as hemoptysis workup or detected incidentally during lung cancer workup. Upper aerodigestive tumors were staged according to the TNM classification (16). Histologic types of primary lung cancer were defined by the World Health Organization (WHO) classification (17). Staging procedure was performed for all lung cancer patients according to TNM classification using chest computed tomography (CT), brain, magnetic resonance imaging (MRI), bone scan as well as ultrasonograpy and/or CT of the abdomen (18). The pathology of the lung cancer and the upper aerodigestive cancer reviewed at the time of the 2nd diagnosis to be certain that this was a new primary tumor.

RESULTS

During the study period up to July 2008, 1242 patients with primary lung cancer were seen. Among them, 21 (1.7%) patients, including 20 men and 1 woman, had lung cancer and previous or simultaneous upper aerodigestive cancers. The number of current or former smokers

was 20 (95.2%). All but 1 of the male patients were smokers, and 18 of 19 male patients had 30 pack-year or more. The median age for diagnosis of upper aerodigestive cancers was 67 years (range, 47-82 years). Laryngeal and esophageal cancers were 2 of the most common aerodigestive cancers. All of the aerodigestive cancers were squamous cell carcinoma (Table 1). The median age at diagnosis of lung cancer was 73 years (range, 60-82 years). Symptomatic lung cancer was detected in 14 patients, but asymptomatic lung cancer was detected incidentally in 7 patients by follow-up chest radiography. The diagnosis of upper aerodigestive cancers preceded the diagnosis of lung cancer in all but 3 patients, for whom the diagnosis of upper aerodigestive cancers was made during the workup of primary lung cancer. In these patients, no distant metastasis was observed. The staging of lung cancer according to the TNM system at the time of diagnosis of lung cancer is shown in Table 1. Histologically, the lung cancers included 9 squamous cell carcinomas, 7 adenocarcinomas, 4 small cell lung cancers, and one large cell cancer. Therefore, 13 of 21 patients had smoking-related cell types of lung cancer. Six patients had smoking-related nonmalignant comorbid diseases (2: chronic obstructive pulmonary disease, 2: idiopathic pulmonary fibrosis, and 2: ischemic heart disease).

Types of therapy performed are summarized in Table 2. For non-small cell lung cancer (NSCLC), surgical resection was performed in 6 patients. Three patients had chemotherapy due to advanced stage of NSCLC, and 1 had post-operative chemotherapy. While, 4 patients had chest irradiation, and 4 NSCLC patients had best supportive care due to poor performance status (PS) or patient's refusal. Three of 4 small cell lung cancer (SCLC) patients had chemotherapy, but 1 of them received irradiation due to poor PS. Although there were 4 NSCLC patients treated with supportive care, 1 and 2 year survival of the 17 NSCLC patients was 58.8% and 29.4%, respectively. In 4 SCLC patients, 1 survived more than a year. The median survival following the diagnosis of lung carcinoma for NSCLC patients was 15 months (range, 1-55 months), and for small cell lung cancer (SCLC) it was 6 months (range, 3-12 months). The cause of death in the 15 patients who died in the study period was directly related to lung cancer, and recurrence of upper aerodigestive cancers was observed in none of the patients.

DISCUSSION

Extra-pulmonary cancers associated with lung cancer occur most commonly in the upper aerodigestive tract (3-5). In our present study, we identified 21 (1.7%) lung cancer patients with previous or simultaneous upper aerodigestive cancers. The incidence noted here reflected the sampling of patients who survived early upper aerodigestive cancers long enough to get lung cancer. Nineteen of them, lung cancer were detected several years after upper aerodigestive cancers were diagnosed. The reasons for this increased risk of developing a 2^{nd} primary lung cancer remain unexplained. However, it could in large part be due to a shared risk factor, such as cigarette smoking. It is generally accepted that cigarette smoking may play an important role as carcinogenesis in lung cancer as well as upper aerodigestive cancers. Although smoking induces all major histological types of lung cancer, the strongest associations are with squamous cell cancer and SCLC (19). In the present study, 20 of 21 (95.2%) patients were current or former smokers, and 13 of 21 (69.1%) patients had these 2 histological types of lung cancer. In addition to this, it also must be noted that there were less women than men with lung cancer with previous or simultaneous upper aerodigestive cancers. Most probably this is accounted by lower rate of smoking habit in women. In addition to cigarette smoking, some immunologic impairment caused by upper aerodigestive cancers might also contribute to this increased risk, but further studies are required to elucidate this.

In our experience, 5 NSCLC patients with good PS, who had stage IA and IIIA, could tolerate surgery and had favorable outcomes with no post-operative complications. Seven (4 NSCLC and 3 SCLC) patients were treated with platinum-based chemotherapy. None of these 7 patients developed life-threatening respiratory infection, although some of them had tracheostomy. The causes of death of the 15 patients,

Table 1. Characteristics of 20 patients with lung and aerodigestive cancers.

No.	Age/Sex	Smoking index	Performance status	Lung cancer		Aerodigestive ca.	Interval between two cancers
				Pathology	Stage		
1	77/Male	1800	0	Adenocarcinoma	3B	Laryngeal ca. (Sq)	8 years
2	75/Female	750	0	Adenocarcinoma	1B	Tongue ca. (Sq)	7 years
3	64/Male	0	1	Adenocarcinoma	1B	Esophageal ca. (Sq)	2 years
4	65/Male	1650	1	Small cell cancer	2B	Esophageal ca. (Sq)	4 years
5	69/Male	1500	1	Squamous cell cancer	2B	Laryngeal ca. (Sq)	10 years
6	78/Male	1850	1	Squamous cell cancer	3B	Esophageal ca. (Sq)	7 years
7	70/Male	600	4	Small cell cancer	3B	Maxillary sinuses ca. (Sq)	2 years
8	76/Male	1450	0	Squamous cell cancer	1B	Esophageal ca.(Sq)	7 years
9	75/Male	2000	1	Small cell cancer	4	Laryngeal ca. (Sq)	6 years
10	73/Male	1000	1	Squamous cell cancer	3B	Laryngeal ca. (Sq)	6 years
11	74/Male	500	1	Small cell cancer	3B	Oral ca.(Sq)	1 years
12	70/Male	2500	3	Squamous cell cancer	1A	Oral ca.(Sq)	13 years
13	75/Male	800	1	Squamous cell cancer	1B	Pharyngeal ca. (Sq)	13 years
14	65/Male	4000	1	Squamous cell cancer	3B	Laryngeal ca. (Sq)	Concurrent
15	70/Male	830	0	Large cell cancer	2A	Tongue ca. (Sq)	Concurrent
16	79/Male	600	1	Adenocarcinoma	4	Laryngeal ca. (Sq)	22 years
17	68/Male	1600	0	Adenocarcinoma	2B	Laryngeal ca. (Sq)	9 years
18	60/Male	920	2	Adenocarcinoma	4	Esophageal ca. (Sq)	13 years
19	82/Male	1200	0	Squamous cell cancer	3B	Esophageal ca. (Sq)	Concurrent
20	69/Male	1260	1	Adenocarcinoma	1A	Maxillary sinuses ca. (Sq)	3 years
21	81/Male	900	0	Squamous cell cancer	1B	Laryngeal ca. (Sq)	3 years

Ca: Cancer, Sq: Squamous cell cancer.

Table 2. Treatment and prognosis of 20 patients with lung and aerdigestive cancers.

No	Treatment		Survival from the diagnosis of lung cancer (months)	Alive or dead
	Lung cancer	Aerodigestive cancer		
1	Chemotherapy	Surgery	3	Dead
2	Supportive care	Surgery	24	Dead
3	Chemotherapy	Surgery	18	Dead
4	Chemotherapy	Surgery	12	Dead
5	Surgery	Surgery	47	Dead
6	Irradiation	Surgery	18	Dead
7	Irradiation	Surgery	3	Dead
8	Surgery	Surgery	15	Dead
9	Chemotherapy	Surgery	3	Dead
10	Supportive care	Surgery	9	Dead
11	Chemotherapy	Surgery, irradiation	8	Dead
12	Supportive care	Surgery	3	Dead
13	Surgery	Surgery, irradiation	55	Alive
14	Irradiation	Surgery	14	Dead
15	Irradiation	Surgery, irradiation	34	Alive
16	Irradiation	Surgery, irradiation	19	Dead
17	Surgery, chemotherapy	Surgery, irradiation	25	Alive
18	Supportive care	Surgery	1	Dead
19	Chemotherapy	Surgery	8	Alive
20	Surgery	Surgery, irradiation	3	Alive
21	Surgery	Surgery	1	Alive

who died in the study period, were directly related to lung cancer. Twelve of 17 NSCLC patients, who were unable to undergo surgical resection due to advanced stage, poor PS or patient's refusal, had poor outcomes. All the 6 patients, who are still alive, had surgical resection for NSCLC. These result suggested that lung cancer is more likely to be primary prognostic factor rather than upper aerodigestive cancers. In addition, appropriate evaluation of clinical stage of the disease and PS is essential to determine the best therapeutic strategy and to predict the patients' prognosis.

There were some limitations in this study. Patients with high stage tumors might have already died of upper aerodigestive cancer prior to developing lung cancer, when they preceded the lung cancers. Therefore, our patients may represent a selected group. The results should not be interpreted as 'population-based' and the study was under-powered to support a multivariate analysis. In addition, the retrospective design and small number of patients limit the generalization of results. However, patents with upper aerodigestive cancers should be counseled at diagnosis about their increased risk of developing 2nd cancers including lung cancer, and smoking cessation should be strongly recommended. In light of our experience, it is appropriate to consider heightened surveillance of upper aerodigestive cancer patients for lung cancer because early diagnosis and standard therapy appear to carry the only hope for long-term survival and cure. We recommended a chest radiograph or CT scan at least yearly and swift evaluation of signs or symptoms that are suggestive of lung cancer. Although the incidence may not be very high, future genetic and epidemiologic studies will clarify the potential connection between upper aerodigestive cancers and lung cancer.

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