Lung Cancer 102 (2016) 60–64

Contents lists available at ScienceDirect

Lung Cancer

journal homepage: www.elsevier.com/locate/lungcan

Prognostic impact of pleural lavage cytology in patients with primary lung cancer

Kenji Tomizawa[a], Masaya Nishino[a], Yuichi Sesumi[a], Yoshihisa Kobayashi[a], Katsuaki Sato[a], Masato Chiba[a], Masaki Shimoji[a], Kenichi Suda[a], Shigeki Shimizu[b], Takao Sato[b], Toshiki Takemoto[a], Tetsuya Mitsudomi[a,*]

[a] Division of Thoracic Surgery, Department of Surgery, Kindai University Faculty of Medicine, Ohno-Higashi, Osaka-Sayama, Japan
[b] Department of Pathology, Kindai University Faculty of Medicine, Ohno-Higashi, Osaka-Sayama, Japan

ARTICLE INFO

Article history:
Received 26 July 2016
Received in revised form 7 October 2016
Accepted 22 October 2016

Keywords:
Non-small cell lung cancer
Pleural lavage cytology
TNM classification
Prognostic

ABSTRACT

Objectives: Positive pleural lavage cytology (PLC) has been reported to have a negative prognostic impact in patients with surgically resected non-small cell lung cancer (NSCLC). However, positive PLC does not upgrade the stage according to the 7th edition of TNM classification for lung cancer. The objectives of this study were to evaluate the prognostic impact of positive PLC in patients with NSCLC and to clarify its contribution to TNM classification.
Materials and methods: Seven hundred fifty-four patients who underwent surgical resection of NSCLC from January 2007 through December 2013 were retrospectively studied. PLC was performed using 50 ml of saline immediately after thoracotomy.
Results: Thirty-eight of the 754 patients were positive for PLC (5.1%). The overall survival (OS) of patients with positive PLC was significantly shorter than that of those with negative PLC ($P = 0.007$, log-rank test). In multivariate analyses of OS, positive PLC was a significant independent prognostic factor (hazard ratio = 2.21, 95% confidence interval: 1.21–4.04, $P = 0.009$). The OS of patients with positive PLC was significantly shorter than that of those with negative PLC and pT1 ($P < 0.0001$) or negative PLC and pT2 ($P < 0.0001$) and almost overlapped with that of those with negative PLC and pT3 disease ($P = 0.601$).
Conclusion: Positive PLC is an independent prognostic factor in patients with resected NSCLC. Based on our analyses, we propose that patients with positive PLC be staged as pT3.
© 2016 Elsevier Ireland Ltd. All rights reserved.

1. Introduction

Pleural lavage cytology (PLC) is a cytological examination that is performed to detect subclinical disseminated malignant cells in the thoracic cavity of patients without detectable pleural effusion. In 1958, Spjut et al. were the first to report performing PLC immediately after a thoracotomy in patients with non-small cell lung cancer (NSCLC) [1]. Thereafter, many researchers have reported that PLC is a negative prognostic factor in patients with surgically resected NSCLC, although different PLC methods are used by different institutions [2–17]. According to the seventh edition of the tumour node metastasis (TNM) classification for lung cancer [18], pleural invasion (PL) is regarded as T2 disease [18–20]. Pleural dissemination and malignant pleural effusion are regarded as M1a diseases. A positive PLC suggests that during primary lung cancer progression, malignant cells migrated into the thoracic cavity through a hole created by a pleural invasion. The presence of malignant cells in the pleural lavage is thought to indicate the prodromal stage of pleural dissemination and malignant pleural effusion. However, according to the seventh edition of TNM classification [18], positive PLC does not change the stage of NSCLC. In this study, we evaluated the prognostic impact of PLC status in patients with resected NSCLC and the incorporation of positive PLC into the TNM classification on patient prognosis.

2. Materials and methods

2.1. Patients

We examined 860 consecutive patients with NSCLC who underwent surgery at the Division of Thoracic Surgery in the Department of Surgery at Kindai University Faculty of Medicine from January 2007 through December 2013. We excluded 85 patients who did

* Corresponding author at: Division of Thoracic Surgery, Department of Surgery, Kindai University Faculty of Medicine, 377-2 Ohno-Higashi, Osaka-Sayama 589-8511, Japan.
E-mail addresses: mitsudom@surg.med.kindai.ac.jp, mitsudom@gmail.com (T. Mitsudomi).

http://dx.doi.org/10.1016/j.lungcan.2016.10.009
0169-5002/© 2016 Elsevier Ireland Ltd. All rights reserved.

not undergo PLC as well as 21 patients with M1 disease, including 20 with pleural dissemination or malignant pleural effusion (M1a) and one with brain metastasis (M1b). The remaining 754 patients were analysed in this study. There were 290 males and 464 females, and the patients ranged in age from 37 to 88 years, with a median age of 70 years. Twenty-three of the patients underwent pneumonectomy, 652 underwent lobectomy, and 79 underwent segmentectomy or partial resection. Using the definitions provided in the seventh edition of the TNM classification for lung cancer, there were 521 patients with pathological-stage (p-stage) I disease, 128 with p-stage II, and 105 with p-stage III. PL was pathologically evaluated and scored from PL0 to PL3 as follows: PL0, tumour under elastic layer; PL1, invasion beyond elastic layer; PL2, invasion to visceral pleural; and PL3, invasion to parietal pleura [19]. After pulmonary resection, adjuvant chemotherapy was administered according to pathological findings and the general condition of the patients. Patients with p-stage I disease and tumours larger than 2 cm received oral UFT, while patients with p-stage II or III disease received platinum-based doublet chemotherapy. Patients were routinely followed up at a 3- to 6-month interval for 5 years. The evaluations included a physical examination, chest radiography or CT, and tumour marker analysis. When recurrence was suspected, brain magnetic resonance imaging, bone scintigraphy, or positron emission tomography scans were performed as needed. The medical records of all the included patients were reviewed to extract data regarding clinicopathological characteristics and prognosis. This study was reviewed and approved by the Ethics Committee of the Faculty of Medicine at Kindai University (28-046). Because many of the patients were already dead or lost to follow-up, we posted information on this research plan on our website (http://www.kindai-geka.jp/biomarker/2016/06/post-15.html) for those from whom informed consent could not be obtained. We also provided an opportunity to exclude their data from the analyses upon request through the website, according to the instructions of the IRB.

2.2. Pleural lavage cytology

When pleural effusion or dissemination was not present after thoracotomy, the pleural cavity was carefully lavaged with 50 ml of saline, and the fluid was cautiously retrieved so as to not touch a pleural surface of the tumour. The fluid was centrifuged at 1500 rpm for 5 min using an Auto Smear CF-120 (Sakura, Tokyo, Japan). Four slides were stained using Papanicolaou, and one was stained with Giemsa. A screener and a pathologist examined these slides, and the cytology results were reported as negative or positive.

2.3. Statistical analysis

A chi-square test or Fisher's exact test was used to compare proportions. A logistic regression analysis was performed to detect independent factors that were associated with positive PLC. The Kaplan–Meier method was used to plot survival curves, and the log-rank test was used to evaluate differences between groups. Cox proportional hazards modelling was used to perform univariate and multivariate analyses of overall survival (OS). The two-sided significance level was set at $p < 0.05$. Statistical calculations were performed using a statistical software package (StatView version 5.0; SAS Institute Inc., NC).

3. Results

3.1. Clinicopathological characteristics of patients with positive PLC

The clinicopathological patient characteristics are shown in Table 1 according to PLC status. Patients with positive PLC were older than those with negative PLC (median: 73 vs 69 years; $P = 0.045$). The frequencies of lymph node metastasis (24% vs 20% for positive vs negative PLC; $P = 0.017$) and PL1-3 (71% vs 25%, respectively; $P < 0.0001$) were significantly higher in patients with positive PLC than in those with negative PLC. No significant differences were detected between the two groups in other clinicopathological characteristics. A logistic regression analysis was performed to analyse correlations between positive PLC and clinicopathological factors. Positive PLC was independently associated with PL1-3 (odds ratio: 6.64, 95% confidence interval: 3.17–13.9, $P < 0.0001$) and older age ($P = 0.002$) (Table 2).

3.2. Independent prognostic factors in patients with resected NSCLC

The median follow-up period after surgery was 3.5 years. The OS of patients with positive PLC was significantly shorter than that of those with negative PLC (log-rank test, $P = 0.007$; Fig. 1A). We performed multivariate Cox proportional analysis of OS in this cohort. Positive PLC was found to be a significant independent prognostic factor of poor OS (hazard ratio: 2.25, 95% confidence interval: 1.23–4.11, $P = 0.009$), as were old age ($P = 0.004$), male sex ($P = 0.021$), high CEA value ($P = 0.023$), pT3-4 ($P = 0.014$), pN1-2 ($P = 0.001$), and non-adenocarcinoma histology ($P = 0.017$) (Table 3).

3.3. Incorporation of positive PLC into the seventh edition of TNM classification

Because positive PLC significantly affected the OS of patients, we incorporated positive PLC into the TNM classification. We regarded it appropriate to reflect the PLC results on T descriptor, because positive PLC was thought to be minimal pleural dissemination. Indeed, positive PLC was associated with PL status (Table 2). When we evaluated the impact of T status on the OS of 38 patients who were positive for PLC, there was no significant difference, although the number of patients was limited (Fig. 1B). Next, the OS of 716 patients with negative PLC was stratified by pT status, and they were compared to the 38 patients with positive PLC. The OS curve of patients with positive PLC almost overlapped with that of those with negative PLC and pT3 disease (Fig. 1C).

4. Discussion

In this study, we retrospectively examined PLC status in 754 patients with resected NSCLC. Of them, 38 were positive for PLC (5.1%). The previously reported incidence of positive PLC has ranged from 3.5 to 13.1% [2–17], with a median of 4.7% (Table 4). The differences in reported incidence are thought to be due to sampling methods across institutions (Table 4). The diagnostic criteria at most institutions state that samples are divided into two categories, similar to the procedure in this study. It is important to standardize sampling methods for PLC in patients with resected NSCLC.

Positive PLC was an independent prognostic factor in patients with resected NSCLC. The 5-year OS of patients with positive PLC was 33.1% in our institution, which is similar to that in previous reports (5-year OS: 28–51%, Table 4) [2–8,10,12–15]. In this study, the OS curve of patients with positive PLC overlapped with that of those with negative PLC and pT3 disease. The clinicopathological

Download English Version:

https://daneshyari.com/en/article/5528463

Download Persian Version:

https://daneshyari.com/article/5528463

Daneshyari.com