J Korean Radiol Soc 1999;41:1139-1145

CT Findings of Pleural Dissemination from Lung Cancer[1]

Du Hwan Choe, M.D., Jeong Eun Sohn, M.D., Tae Hyun Lee, M.D., Kie Hwan Kim, M.D., Soo Yil Chin, M.D., Jae Ill Zo, M.D.[2]

Purpose: The purpose of our study was to identify the CT findings that help detect pleural dissemination from lung cancer and to evaluate the usefulness of selected diagnostic criteria.

Materials and Methods: After a computerized database search of 606 patients who had undergone thoracotomy for primary lung cancer, 23 patients were identified as having surgically documented pleural dissemination. From the same database, 50 patients without pleural dissemination during thoracotomy were randomly selected as controls. Preoperative CT scans and medical records were reviewed retrospectively, and findings were compared between the two groups.

Results: One or more of three types of pleural thickening (plaque-like, nodular, and fissural) were identified on CT as the most discriminating finding (sensitivity, 74 %; specificity, 60 %; $p = 0.007$). The following findings were also significantly discriminating ($p < 0.05$): contiguity of primary tumor with the pleural surface as seen on CT; adenocarcinoma in cell type; and a peripheral tumor defined as one in which bronchoscopy revealed no endobronchial lesion. The use of combinations of these findings in addition to pleural thickening rendered diagnostic criteria more specific at the cost of the sensitivity.

Conclusion: During preoperative CT evaluation of lung cancer, the recognition of subtle pleural thickening helps detect pleural dissemination. The likelihood that subtle pleural thickening represents pleural dissemination is increased when a primary tumor is contiguous with the pleural surface, is an adenocarcinoma, or is peripherally located.

Index words : Lung neoplasms, CT
Lung neoplasms, metastases
Lung neoplasms, staging
Pleura, CT
Pleura, neoplasms.

Pleural metastasis from lung cancer forewarns a poor prognosis and it is generally considered incurable by surgical resection (1, 2) although extensive resection has been tried in some cases (3, 5). Preoperative diagnosis of pleural metastasis from lung cancer is advantageous since it has been a common cause of unnecessary thoracotomy, so-called open and close operation, in spite of preoperative efforts to assess unresectability (3, 4, 6, 7).

Pleural dissemination as an early form of pleural metastasis has been difficult to diagnose preoperatively. When the amount of pleural effusion associated with

[1]Department of Radiology, Korea Cancer Center Hospital
[2]Department of Thoracic Surgery, Korea Cancer Center Hospital
Received February 27, 1999 ; Accepted September 16, 1999
Address reprint requests to : Du Hwan Choe, M.D., Department of Radiology, Korea Cancer Center Hospital
#215-4 Gongneung-dong, Nowon-gu, Seoul 139-706, Korea.
Tel. 82-2-970-1255 Fax. 82-2-972-3093
E-mail: choe@kcchsun.kcch.re.kr

lung cancer is sufficient for thoracentesis, the fluid can be obtained for cytological examination to determine operability. In some cases, however, pleural metastasis is found at the stage of pleural dissemination alone, without pleural effusion or with only minimal effusion. CT has been used routinely for the preoperative staging of lung cancer in recent years, and the characteristic CT features of metastatic pleural disease showing diffuse pleural thickening have been described well (8). However, pleural dissemination has not yet been diagnosed on the basis of CT findings; it is thus often detected at thoracotomy or after pleural effusion has developed with the progression of pleural involvement (3, 4).

A few reports have suggested that some pleural abnormalities were retrospectively found on the CT scans of patients with pleural dissemination that had been discovered at thoracotomy (5, 9, 10). However, the lack of control groups in these studies potentially renders their CT findings less reliable. The pleural abnormalities described in these studies may also appear in various pleuritic processes. To ascertain the diagnostic value of CT findings for detecting pleural dissemination from lung cancer, a study that compares findings between patients with and those without pleural dissemination is necessary.

The purpose of our study was to identify the CT findings that help detect pleural dissemination from lung cancer and to evaluate the usefulness of selected diagnostic criteria, in the hope that unnecessary surgery for lung cancer can be avoided.

Materials and Methods

We performed a computerized database search of 606 patients who underwent thoracotomy for primary lung cancer at our institution between January 1991 and April 1998. We identified 23 patients in whom lung cancer was unresectable or not curatively resectable because of unexpected pleural dissemination that had been unrecognized preoperatively but subsequently discovered at thoracotomy. The study group consisted of 15 men and eight women, ranging in age from 38 to 70 years (mean, 59 years). Surgical records revealed that diagnoses of pleural dissemination had been confirmed pathologically during surgery in all patients of the study group. Because fluid was absent or insufficient for thoracentesis, no patient underwent preoperative cytological examination for pleural effusion.

Fifty control patients were randomly selected from the same database. The control patients were 41 men and nine women ranging in age from 41 to 84 years (mean, 60 years). The surgical records of these patients included no mention of pleural dissemination. Preoperative CT scans and medical records were retrospectively reviewed in both the study group (n = 23) and the control group (n = 50).

Chest CT was performed as part of the preoperative staging for lung cancer. Because CT scans obtained outside our institution were included, a variety of CT scanners and protocols was used. The scanners included 9800, HiLite, HiSpeed Advantage (GE Medical Systems, Milwaukee, Wis, U.S.A.), Somatom DR, and Somatom Plus (Siemens, Erlangen, Germany) models. Contiguous 10-mm-thick (n = 30), 10 and 5-mm-thick (n = 33), 8-mm-thick (n = 7), 7-mm-thick (n = 2), and 5-mm-thick (n = 1) scans were acquired from lung apices to the adrenals. Spiral technique was used in 39 examinations. All CT examinations except two were contrast-enhanced. The images were photographed at window settings appropriate for lung parenchyma and mediastinum. In no patient did the time interval between CT scanning and surgery exceed one month.

To obtain a set of findings for assessment, a board-certified chest radiologist first reviewed the CT scans of patients with proven pleural dissemination. All CT scans of patients with and without pleural dissemination were randomly mixed together and then reviewed by two general radiologists who were instructed to assess following findings on each scan. In each case, the two observers were unaware of whether or not pleural dissemination was found at surgery and reached their conclusions by consensus.

Each CT scan was assessed for the presence of pleural thickening, the type of which was classified as plaque-like, nodular, or fissural. Plaque-like thickening was characterized as a circumscribed area of pleural thickening about 1-4 mm in thickness and less than 4 cm in length. Special attention was paid to distinguish between this and the so-called intercostal stripe as suggested in a previous study (11). Nodular thickening was characterized as a round or oval area of pleural thickening about 1-4 mm in diameter. The location of plaque-like and nodular thickening was classified as costal, mediastinal, diaphragmatic, or interlobar. No attempt was made to differentiate between parietal and visceral pleural involvement. Fissural thickening was defined as an interlobar fissure appearing as either a poorly marginated, broad, hyperattenuating band or a sharply de-

fined thick line, apart from plaque-like or nodular thickening of the interlobar fissure. Special attention was paid to distinguish this type of thickening from the normal interlobar fissure that sometimes appears as a line or hyperattenuating band (12).

The presence or absence of the following CT findings was also assessed: contiguity of primary tumor with the pleural surface, small amount of pleural effusion, pleural retraction by tumor, chest wall invasion by tumor, and mediastinal adenopathy (greater than 10 mm in short-axis diameter). The size of a primary tumor was estimated by calculating the mean of two representative perpendicular diameters. If a substantial part of the tumor edge was obscured, a representative single diameter was used instead.

Cell type of primary tumors and preoperative bronchoscopic findings were assessed during the review of medical records. Cell type was determined by pathologic examination of surgical specimens in 52 patients who underwent tumor resection. In the remaining 21 patients who underwent exploratory thoracotomy only, cell type was determined by the tissue obtained during sugery (n = 12), by bronchoscopic biopsy (n = 7), or by percutaneous needle biopsy (n = 2). On the basis of preoperative bronchoscopic findings, the location of primary tumor was classified as either peripheral or central. If no endobronchial lesion was noted during bronchoscopy, the tumor was defined as peripheral. The number of patients with adenocarcinoma and peripheral tumor was noted.

The frequencies of individual CT findings, adenocarcinoma in cell type, and peripheral tumor determined on the basis of bronchoscopic findings were compared between the study and the control group using the chi-square test. Student's t test was used to compare tumor sizes. A p value less than 0.05 was considered significant. After determining which findings were significantly discriminating, the usefulness of various combinations of these findings was evaluated by calculating sensitivity and specificity for the purpose of improving diagnostic ability to detect pleural dissemination.

Results

The CT, pathologic, and bronchoscopic findings in both the study and the control group are summarized in Table 1. Retrospective review of the CT scans of the 23 patients with pleural dissemination identified subtle pleural thickenings that had been overlooked or interpreted as benign at initial CT examination. Of three types of pleural thickening, plaque-like type was present in 12 patients (52%) (Figs. 1 and 2A). The costal pleura was involved in 11 patients, the mediastinal pleura in two, and the interlobar fissure in one. Nodular type of pleural thickening was present in nine patients (39%) (Figs. 2B and 3). The interlobar fissure was involved in six patients, the costal pleura in two, the diaphragmatic pleura in two, and the mediastinal pleura in one. Fissural thickening as a type of pleural thickening was identified in eight patients (35%) (Fig. 3). In 17 (74%) of the 23 patients with pleural dissemination, one or more of these three types of pleural thickening were present. The same findings were identified in 20 (40%) of the 50 patients without pleural dissemination. This difference between the study and the control group was statistically significant ($p < 0.05$).

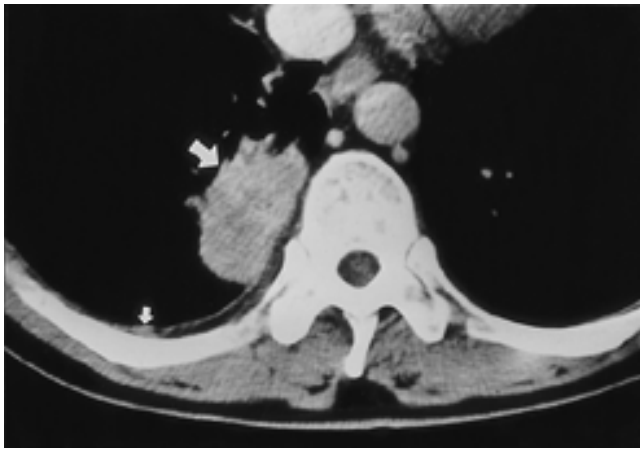


Fig. 1. A 38-year-old man with pleural dissemination from adenocarcinoma of the lung. Contrast-enhanced CT scan (10-mm collimation) shows a primary tumor (large arrow), located in the peripheral portion of the right lower lobe, with contiguity to the pleural surface. A plaque-like thickening of the pleura (small arrow), about 3 mm in thickness, is identified on the costal surface. Surgery revealed pleural dissemination that had been overlooked at preoperative CT examination.

Contiguity of primary tumor with the pleural surface was noted in 19 patients (83%) of the study group (Fig. 1) and in 27 patients (54%) of the control group. This difference was significant ($p < 0.05$). The frequencies of other CT findings were not significantly different between the two groups. In terms of mean size, primary tumors with pleural dissemination were not significantly larger than those without pleural dissemination (3.9 cm versus 3.6 cm, $p = 0.36$).

Among the study group, the cell type of primary tumor was adenocarcinoma in 13 patients (57%), squamous cell carcinoma in seven (30%), large cell carcino-

ma in one (4%), sarcomatoid carcinoma in one (4%), and unclassified carcinoma in one (4%). On the basis of preoperative bronchoscopic findings, the tumors of 16 patients (70%) in the study group were classified as peripheral. The frequencies of both adenocarcinoma and peripheral tumor were significantly higher in patients with pleural dissemination than in those without pleural dissemination ($p < 0.05$).

Pleural thickening on CT regardless of type, contiguity of tumor with the pleura as seen on CT, adenocarcinoma in cell type, and peripheral tumor based on bronchoscopy were selected as the set of findings which were significantly discriminating. On the basis of pleural thickening regarded as the most discriminating finding, 74% of pleural dissemination could be detected, but specificity, at 60%, was relatively low. To improve

Table 1. CT, Pathologic, and Bronchoscopic Findings in Patients with or without Pleural Dissemination at Thoracotomy for Lung Cancer

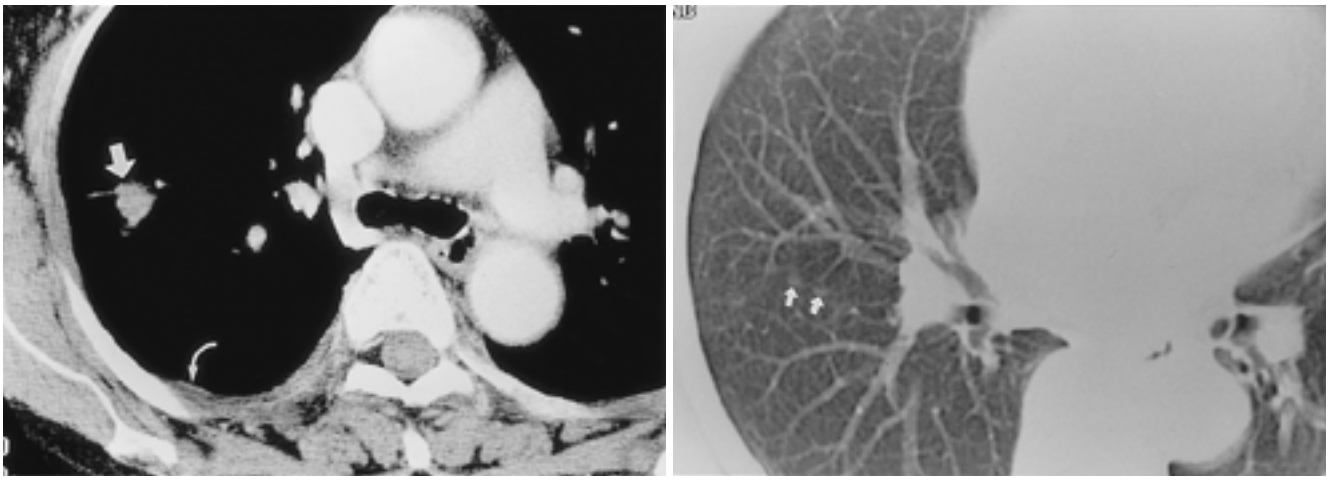
Finding	With Pleural Dissemination (n = 23)	Without Pleural Dissemination (n = 50)	p value
Pleural thickening*	17 (74)	20 (40)	0.007†
Plaque-like	12 (52)	15 (30)	0.068
Nodular	9 (39)	9 (18)	0.052
Fissural	8 (35)	9 (18)	0.115
Contiguity of tumor with pleura	19 (83)	27 (54)	0.019†
Pleural effusion	5 (22)	7 (14)	0.407
Pleural retraction by tumor	7 (30)	12 (24)	0.561
Chest wall invasion by tumor	1 (4)	1 (2)	0.568
Mediastinal adenopathy	8 (35)	18 (36)	0.920
Size of tumor (mean±SD, cm)	3.9 ±1.2	3.6 ±1.7	0.364
Adenocarcinoma in cell type	13 (57)	16 (32)	0.047†
Peripheral tumor‡	16 (70)	20 (40)	0.019†

Note: Data are numbers of patients with finding, except for size of tumor. Numbers in parentheses are percentages. SD = standard deviation.

* Includes patients whose CT scans showed at least one of the three types of pleural thickening below.

‡ Defined as a tumor showing no endobronchial lesion on preoperative bronchoscopy.

† Indicates significant p values



A B

Fig. 2. A 63-year-old woman with pleural dissemination from adenocarcinoma of the lung.

A. Contrast-enhanced CT scan (5-mm collimation) obtained with a mediastinal window shows upper part of a primary tumor (large arrow) located in the peripheral portion of the right upper lobe. A plaque-like thickening (curved arrow) is identified on the costal surface of the pleura.

B. A more caudal section (10-mm collimation) obtained with a lung window demonstrates nodular thickenings of the pleura (small arrows) along the interlobar fissure. Pleural dissemination was not diagnosed at initial interpretation of CT but it was found at thoracotomy.

Table 2. Usefulness of Various Diagnostic Criteria for Detecting Pleural Dissemination from Lung Cancer

Diagnostic Criteria	Sensitivity (%)	Specificity (%)
Pleural thickening*	74	60
Pleural thickening* with one or more of CP, ADC, or PT	74	68
Pleural thickening* with two or more of CP, ADC, or PT	65	88
Pleural thickening* with all of CP, ADC, and PT	26	96

Note: CP = contiguity of primary tumor with the pleural surface as seen on CT, ADC = adenocarcinoma in cell type, PT = peripheral tumor defined as one in which bronchoscopy revealed no endobronchial lesion.
*Indicates one or more of three types (plaque-like, nodular, or fissural) of pleural thickening on CT.

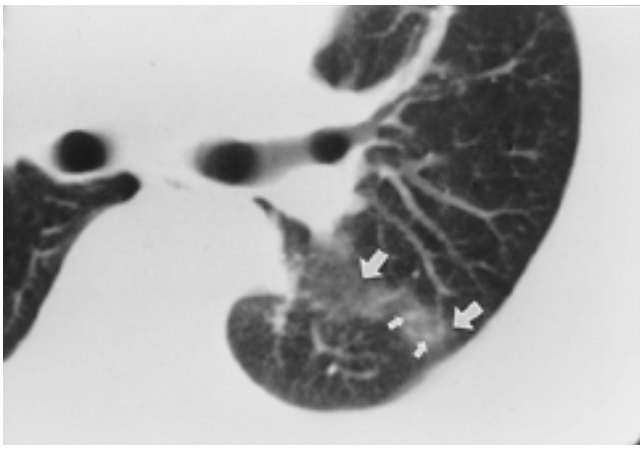


Fig. 3. A 57-year-old man with pleural dissemination from adenocarcinoma (not shown) in the peripheral portion of the left lower lobe. CT scan (10-mm collimation) obtained through the carina using a lung window setting shows a poorly marginated band indicating fissural thickening (large arrows). Small nodular thickenings of the pleura (small arrows) are noted along the interlobar fissure. These lesions were not attributed to pleural dissemination at preoperative CT examination. However, surgery revealed pleural dissemination.

specificity, combinations of the remaining three findings in addition to pleural thickening were used as diagnostic criteria (Table 2). When pleural thickening was combined with at least one of the remaining three findings, specificity (68%) was improved a little at no cost of sensitivity (74%). When pleural thickening was combined with either at least two or all of the three findings, high specificity was obtained (88% and 96%, respectively) at the cost of sensitivity (65% and 26%, respectively).

Discussion

In our study, unexpected pleural dissemination was present in 23 (3.8%) of 606 patients who had undergone thoracotomy for lung cancer. This prevalence compares well with the results of 3.3% and 5.7%, observed by Shimizu et al. (3) and Ishida et al. (4), respectively. Overall, pleural dissemination was the most common cause of unexpected unresectability and T4 disease at our institution and according to the results of Ishida et al. (4). Prospective detection of pleural dissemination on a noninvasive preoperative examination such as CT would therefore be very useful.

In retrospect, we found that 74% of patients with pleural dissemination had at least one of the three types of subtle pleural thickening that had been overlooked or interpreted as benign at initial CT examination. No patient in the study group had sufficient pleural effusion for thoracentesis or remarkable thickening of the pleura on CT. Because no method for the staging of lung cancer, except surgical exploration, was able to detect pleural dissemination preoperatively, we presumed that they had pleural metastases of early stage. Thus, the sensitivity of CT for detecting pleural metastasis of early stage (i.e. pleural dissemination) is estimated at 74% when using pleural thickening as diagnostic criteria. The specificity of 60%, however, remains poor.

We do not believe that the above-mentioned pleural thickening is specific for pleural dissemination from lung cancer. Tuberculosis, asbestosis, and various other pleuritic processes can manifest as the above-mentioned pleural thickening, but there are no radiological criteria that reliably distinguish benign pleural disease from malignant. Even if subtle pleural thickening is prospectively detected, there is a problem of false-positive diagnosis. The results of this study suggest that a diagnosis of pleural dissemination can be made more specific and more reliable if other discriminating findings (contiguity with the pleural surface, adenocarcinoma in cell type, and peripheral location of primary tumor) are noted in addition to pleural thickening.

When the above diagnostic criteria suggest pleural dissemination, we believe that video-assisted thoracoscopy (VAT), performed prior to thoracotomy, may serve as a less invasive procedure to make a definite diagnosis. VAT allows visualization of the pleural surface, pro-

vides access for surgical manipulation including pleural biopsy, and obviates the attendant morbidity and potential mortality of an exploratory thoracotomy (13).

Our results are generally in agreement with those of Lee et al (9) who reported that 79 % of patients with pleural dissemination had at least one pleural abnormality on CT. In that series of 19 patients, pleural thickening was noted in 11 patients, pleural irregularity in 10, and pleural nodules in 12. The results differ in some respects, especially in that they did not consider diffuse thickening of the interlobar fissure as a pleural abnormality. With regard to the pleural thickening and irregularity described in that study, we think that both findings correspond to plaque-like thickening of the pleura described in our study. Murayama et al. (10) reported a somewhat lower prevalence (52 %) of pleural abnormalities including thick major fissures or pleural nodules. A study by Akaogi et al. (5) found small pleural nodules in 38 % of 21 patients, a result that matched the 39 % prevalence of nodular thickening of the pleura seen in our study. Our relatively high frequency of findings such as contiguity of primary tumor with the pleural surface, adenocarcinoma in cell type, and peripheral location of primary tumor is also in accordance with the results of previously reported series (5, 9, 10).

Our study has several limitations. First, the imaging protocol was not standardized. Because our study included numerous CT scans obtained prior to referral to our institution, a variety of CT scanners and protocols were used. Although technical consideration is not possible in our study, narrow collimation would be expected to improve the visibility of subtle pleural thickening by reducing partial volume averaging. A second limitation is that we could not perform precise one-to-one correlation between the pathologic and CT findings of pleural thickenings because our study was retrospective. A prospective study is needed to determine whether the pleural thickening described in our study really represents pleural metastases and whether the unnecessary thoracotomy rate can be reduced actually by using the above-mentioned diagnostic criteria in combination with VAT.

In conclusion, we believe that the recognition of subtle pleural lesions such as plaque-like, nodular, or fissural thickening is helpful for detecting pleural dissemination during the preoperative CT evaluation of lung cancer. Pleural dissemination can be suggested more reliably when other discriminating findings (contiguity with the pleural surface, adenocarcinoma in cell type, or peripheral location of primary tumor) are present in addition to pleural thickening.

References

1. Mountain CF. Prognostic implications of the international staging system for lung cancer. *Semin Oncol* 1988;15:236-245
2. Naruke T, Goya T, Tsuchiya R, Suemasu K. Prognosis and survival in resected lung carcinoma based on the new international staging system. *J Thorac Cardiovasc Surg* 1988;96:440-447
3. Shimizu J, Oda M, Morita K, et al. Comparison of pleuropneumonectomy and limited surgery for lung cancer with pleural dissemination. *J Surg Oncol* 1996;61:1-6
4. Ishida T, Kohdono S, Hamatake M, et al. Malignant pleurisy and intrathoracic dissemination in carcinoma of the lung: diagnostic, therapeutic and prognostic implications. *Int Surg* 1995;80:70-74
5. Akaogi E, Mitsui K, Onizuka M, Ishikawa S, Tsukada H, Mitsui T. Pleural dissemination in non-small cell lung cancer: results of radiological evaluation and surgical treatment. *J Surg Oncol* 1994;57: 33-39
6. Whittlesey D. Prospective computed tomographic scanning in the staging of bronchogenic cancer. *J Thorac Cardiovasc Surg* 1988;95: 876-882
7. Weiman DS, Bolton JWR, Howard ML, Olsen GN, Almond CH, Greene FL. Failure of preoperative staging to assess unresectability in M0 bronchogenic carcinoma. *Cancer* 1989;63:767-768
8. Müller NL. Imaging of the pleura. *Radiology* 1993;186:297-309
9. Lee YC, Chen W, Shih TF. Computed tomography in the evaluation of pleural dissemination in lung cancer. *J Formos Med Assoc* 1990;89:1063-1066
10. Murayama S, Murakami J, Yoshimitsu K, Torii Y, Ishida T, Masuda K. CT diagnosis of pleural dissemination without pleural effusion in primary lung cancer. *Radiat Med* 1996;14:117-119
11. Im JG, Webb WR, Rosen A, Gamsu G. Costal pleura: appearance at high-resolution CT. *Radiology* 1989;171:125-131
12. Glazer HS, Anderson DJ, DiCroce JJ, et al. Anatomy of the major fissure: evaluation with standard and thin-section CT. *Radiology* 1991;180:839-844
13. Wain JC. Video-assisted thoracoscopy and the staging of lung cancer. *Ann Thorac Surg* 1993;56:776-778

J Korean Radiol Soc 1999;41:1139-1145

대한방사선의학회지 1999;41:1139-1145

폐암에 의한 흉막 파종의 전산화단층촬영 소견[1]

[1]원자력병원, 진단방사선과, [2]원자력병원, 흉부외과

최두환 · 손정은 · 이태현 · 김기환 · 진수일 · 조재일[2]

목적: 폐암의 흉막 파종(Pleural dissemination)의 CT소견과 그 진단적 가치에 대하여 알아보고자 하였다.
대상 및 방법: 원발성 폐암으로 개흉술을 시행한 환자들의 전산화된 자료로부터, 개흉술 시에 흉막 파종이 확인된 23명을 대상으로 하였고, 같은 자료로 부터 흉막 파종이 없었던 50명의 대조군을 무작위로 추출하였다. 이들 환자의 의무 기록과 수술전 CT 소견을 후향적으로 분석하였으며, 각 소견의 빈도를 대상군과 대조군 사이에서 비교하였다.
결과: 흉막 파종이 있었던 23명의 CT상에서 세가지 형태의 흉막 비후 (플라크형, 결절형, 엽간열의 비후) 중에서 한가지 이상을 보였던 경우가 17예로, 가장 의미있는 판별력을 보였다 (민감도, 74%; 특이도, 60%; $p = 0.007$). 그밖에 CT상 종양이 흉막과 인접하고 있는 소견, 종양의 조직학적 유형이 선암인 경우, 및 수술전 기관지경 검사상에서 기관지내의 병변이 없었던 경우 등이 판별력이 있는 소견으로 나타났다 ($p < 0.05$). 흉막 비후의 소견과 함께 이들 소견의 조합을 이용하여 흉막 파종을 진단하면 특이도를 향상시킬 수 있었다.
결론: 폐암의 수술전 CT상에서 미세한 흉막 비후일지라도 이를 인식하면 흉막 파종의 진단에 도움을 줄 것으로 기대된다. 특히, 종양이 CT상에서 흉막과 인접하여 있거나, 조직학적으로 선암이거나, 기관지내의 병변을 보이지 않는 경우에 흉막 파종의 가능성은 더욱 높아진다고 생각된다.