Lymphangitic Carcinomatosis of the Lung:
Serial Changes on High-Resolution CT

Jae Woong Hwang, M.D., Yookyung Kim, M.D., Jung Hwa Hwang, M.D.
Tae Sung Kim, M.D., Duk Woo Ro, Ph.D., Kyung Soo Lee, M.D.

Purpose: To present initial and follow-up HRCT findings of lymphangitic carcinomatosis of the lung.

Materials and Methods: Both initial and follow-up HRCT scans were obtained in 18 patients with lymphangitic carcinomatosis of the lung. After dividing the patients into two groups (with anticancer chemotherapy \( n=12 \) and without chemotherapy \( n=6 \)), changes of pulmonary parenchymal abnormalities (percentile increase or decrease in the extent of each pattern) were assessed and compared on initial and follow-up HRCTs.

Results: Findings on initial CT were interlobular septal thickening \((n=18)\) (smooth in 15 and mixed smooth and nodular in three), thickening of bronchovascular bundles \((n=17)\), areas of ground-glass opacity \((n=15)\), polygonal lines \((n=15)\), and nodules \((n=10)\). With chemotherapy, the finding of polygonal lines decreased by 20.3%, while findings of ground-glass opacity, bronchovascular bundle thickening, septal thickening, and nodules remained stable. Without chemotherapy, all CT patterns of abnormalities except nodules increased by 45–88%. In three patients who did not undergo chemotherapy, smooth interlobular septal thickening changed to nodular thickening.

Conclusion: Lymphangitic carcinomatosis of the lung manifests initially as smooth thickening of the interlobular septae, bronchovascular bundle thickening, areas of ground-glass opacity, and polygonal lines, as seen on HRCT. Without chemotherapy, the extent of CT findings increases and there is a tendency for smooth septal thickening to change to nodular thickening. Chemotherapy induces improvement or cessation of the progression of CT findings.

Index Words: Lung neoplasms, metastases
Lymphatic system, neoplasms
Lung neoplasms, CT

Pulmonary lymphangitic carcinomatosis (PLC) refers to the condition involving tumor growth in the lymphatics of the lung and associated changes mainly involving the pulmonary interstitium. The pathologic findings of PLC are gross thickening of the bronchovascular bundles and interlobular septae as well as a fine accentuation of the pleural lymphatic network(1), and are caused by tumor cell growth, lymphatic dilatation, associated fibrosis and edema within the lymphatics (1).

Reported high-resolution (HR) CT findings of PLC include smooth or nodular thickening of the bronchovascular bundles and interlobular septae, polygonal lines, fissural thickening, and hilar or mediastinal adenopathy; polygonal lines in fact represent secondary pulmonary lobules outlined by thickened interlobular septae(2-6). The lesions are focal or diffuse in distribution, with preservation of normal lung architecture. The early HRCT findings of PLC are not
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exact ly known, however, and serial CT scans have not revealed how the disease evolves with and without treatment. In addition, modern chemotherapy results in stability or only gradual progression of PLC, as shown by radiology. The chronic nature of these findings may, however, preclude the radiologic diagnosis of PLC(5, 7-9).

The aims of this study were to present the initial HRCT findings of PLC and to clarify the changes in CT findings over time, with or without chemotherapy.

Materials and Methods

Our study involved 18 consecutive patients diagnosed with PLC at our institution. For all patients, initial and follow-up HRCT studies were available.

The mean duration between the diagnosis of primary tumors and PLC was 2.4 years (0 - 144 months) and the duration between initial and follow-up HRCT scans ranged from two to eight (average, 3.9) months. The patients were 12 women and six men ranging in age from 36 to 73 (mean, 54) years. Symptoms reported at the time of diagnosis included cough and sputum production in five patients and dyspnea in four; the remainder had no pulmonary complaints. All patients had suspicious or obviously abnormal pulmonary parenchymal opacities or mediastinal abnormalities. The primary tumor sites were breast (n=7), lung (n=6), stomach (n=2), rectum (n=1), and unknown primary site (n=2). Except in one patient, who had squamous cell carcinoma of the lung, the primary tumor cell type was adenocarcinoma. In all patients, PLC was diagnosed histopathologically using transbronchial lung biopsy obtained within 4 days of initial CT scans.

Twelve patients underwent systemic chemotherapy (2 - 6 cycles) for PLC during the period between initial and follow-up CT scans: combination chemotherapy of 5-fluorouracil (Choongwae, Korea), leucovorin (Pharma Chemi B.V., The Netherlands), ifosfamide (Asta Medica, Germany), and cisplatin (Dong-A, Korea) for patients with PLC arising from adenocarcinoma of the lung; 5-fluorouracil and cisplatin for patients in whom it arose from stomach or rectal cancer; cyclophosphamide (Choongwae, Korea), methotrexate (Yuhan, Korea), and 5-fluorouracil for patients with initial breast cancer; cyclophosphamide, adriamycin (Dong-A, Korea), and cisplatin for patients whose primary site was unknown. In the remaining six patients, no systemic anticancer chemotherapy was given during this period, mainly because this was the wish of the patients themselves.

All HRCT scans were obtained using a GE HiSpeed Advantage scanner (GE Medical Corp., Milwaukee, Wis.). Scan parameters were 250 mA, 140 kVp, 2-second exposure time with 1.0-mm collimation and at 10-mm intervals through the thorax. A bone algorithm was used to reconstruct the images, which were photographed with both lung and mediastinal windows (window width: 1,500 HU and 400 HU; window level: -700 HU and 30 HU, respectively).

![Fig. 1. Pulmonary lymphangitic carcinomatosis from lung cancer in a 58-year-old man.](image)

A. Initial HRCT scan demonstrates smooth thickening of interlobular septae and bronchovascular bundles, involving mainly right lower lobe. Also note primary lung cancer (arrows) in left lower lobe.

B. Follow-up CT scan obtained two months after (A) without chemotherapy shows aggravation with increased extent of lesions. Note nodular thickening of interlobular septae and bronchovascular bundles (arrows).
Initial and follow-up HRCT scans were randomized and evaluated by the consensus of three chest radiologists who did not know whether the scan represented an initial or follow-up examination, and were blinded to the identity of each patient and to pertinent clinical information. Patterns of abnormalities were classified as bronchovascular bundle thickening, ground-glass opacity (GGO), interlobular septal thickening (smooth, nodular, or mixed), polygonal lines, and nodules (less than 20 mm in diameter). The distribution of abnormalities was recorded by dividing the lungs into six lobes, each representing a lingular segment. The extent of each abnormality in each lobe was classified as follows: 0, no involvement; 1, mild (less than one segment); 2, moderate (less than two segments); and 3, diffuse (more than three segments). The apicoposterior segment of the left upper lobe and anteromedial basal segment of the left lower lobe were both divided into two segments and by adding the degree of involvement in each lobe, the total extent of each pattern of abnormality in each patient was classified into 16 degrees (0-3 degrees in the bilateral upper and lower lobes and 0-2 degrees in the right middle lobe and lingular segment of the left upper lobe).

The chest radiographs of all patients were available; images had been obtained not more than three days before or after initial and follow-up HRCT scans. Their hospital records were also reviewed.

The patients were subdivided into two groups: group 1 (n=6) without anticancer chemotherapy, and group 2 (n=12) with chemotherapy. In group 1, the mean duration between initial and follow-up CT scans was 2.3 (range, two to three) months; follow-up CT could not be performed because of loss to follow-up or

### Table 1. Serial HRCT Findings of 18 Patients with Lymphangitic Carcinomatosis

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<td>Group 1 (n=6)</td>
<td>Group 2 (n=12)</td>
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<td>69 / 11</td>
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<td>45 / 6</td>
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<td>34 / 10</td>
<td>54 / 15</td>
<td>36 / 6</td>
<td>35 / 10</td>
<td>71 / 16</td>
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<tr>
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<td>18 / 4</td>
<td>47 / 6</td>
<td>65 / 10</td>
<td>18 / 4</td>
<td>46 / 6</td>
<td>64 / 10</td>
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Group 1; untreated, group 2; treated with anticancer chemotherapy

* added degrees in extent, + patient number, BV: bronchovascular, GGO: ground-glass opacity.

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**Fig. 2.** Metastatic pulmonary disease from unknown primary cancer in a 40-year-old woman.

A. Initial HRCT scan obtained at the level of lower lobar bronchus demonstrates smooth thickening of interlobular septae and bronchovascular bundles, involving mainly right middle lobe and lingular segment of left upper lobe.

B. Follow-up CT scan obtained two months after (A) without chemotherapy shows aggravation with increased extent of lesions. Patchy areas of ground-glass opacity (open arrows) are also seen. Note nodular thickening of interlobular septae (arrows).
death. Six group 2 patients underwent two or more follow-up CT scans, and the last of these was included for analysis. The mean duration between initial and follow-up CT scans in group 2 was 4.3 (range, two to eight) months, and after each of these procedures, the presence of each pattern of parenchymal abnormalities as well as the extent of each pattern in each group was evaluated. By comparing the extent (added degree of involvement on CT) of each parenchymal abnormality on initial and follow-up CT scans, the percentile increase or decrease of parenchymal abnormality was calculated. Because we had frequently encountered cases of PLC with smooth rather than nodular or beaded thickening of interlobular septae, particular attention was paid to any changes in the type of interlobular septal thickening (smooth, nodular or mixed) between initial and follow-up CT scans.

Results

The predominant findings of PLC on initial CT were interlobular septal and bronchovascular bundle thickening(Figs. 1 and 2). On initial CT scans, interlobular septal thickening was seen in all 18 patients and involved 60 lobes, while bronchovascular bundle thickening was seen in 17 patients and involved 56 lobes(Table 1). Interlobular septal thickening was smooth in 15 patients and mixed smooth and nodular in three (1/6 group 1 patients; 2/12 group 2 patients). Bronchovascular bundle thickening (20, 16, and 20 lobes in the upper, middle, and lower lobes, respectively) and interlobular septal thickening (22, 18, and 20 lobes in the upper, middle, and lower lobes, respectively) were randomly distributed. Polygonal lines, nodules, and areas of GGO (Fig. 3) were seen in 15, 10 and 15 patients, respectively(Table 1). Areas of GGO were more commonly seen in the upper (n=14) than in the middle (n=7) or lower lobes (n=9). Polygonal lines (18, 15, and 13 lobes in the upper, middle, and lower lobes, respectively) and nodules (9, 6, and 10 lobes in the upper, middle, and lower lobes, respectively) showed no zonal predominance. Parenchymal lung lesions of PLC were confined in one patient to only one lobe, and in three patients to only one lung.

In six group 1 patients, the extent of all CT patterns of abnormalities, except nodules, was greater than on initial scans(Figs. 1 and 2): 44.7% of thickening of bronchovascular bundles, 57.1% of interlobular septal thickening, 87.5% of polygonal lines, and 80% of GGO(Table 1). Among the twelve group 2 patients, polygonal lines were 20.3% less than on initial scans. The extent of bronchovascular bundle thickening, interlobular septal thickening, GGO and nodules showed no significant change. In one patient, however, all PLC findings showed marked improvement after chemotherapy(Fig. 4). Overall, as seen on follow-up CT scans, the extent of bronchovascular bundle thickening, interlobular septal thickening, GGO, and polygonal lines increased(Table 1). In three patients who had not undergone anticancer chemotherapy, initial smooth thickening of interlobular septae changed to nodular or beaded thickening(Figs. 1 & 2). The extent of nodules remained unchanged(Table 1), and regardless of progression or stability, no zonal predominance was noted.

Discussion

In PLC, the tumor disseminates hematogenously to the lungs, penetrates the vessels secondarily, and invades into the surrounding interstitium. Although tumor is present in the lymphatic vessels, most radiographically visible tumor is in the interstitium around the lymphatics(1, 10).

Reported characteristic HRCT findings of PLC are uneven thickening of the bronchovascular bundles, nodular or beaded thickening of the interlobular septae, and the presence of polygonal lines(2–4, 11). These findings are believed to result from the dilatation of lymphatics behind central tumor deposits, tumor-filled lymphatics, tumor cells within the interstitium, interstitial pulmonary edema, and interstitial fibrosis due to desmoplastic reaction to the
tumor(1, 3, 11). In our study, initial CT scans showed bronchovascular bundle thickening, interlobular septal thickening, areas of GGO, polygonal lines, and nodules. In three patients, interlobular septal and bronchovascular bundle thickening was smooth rather than beaded or nodular. These results are different from those described in previous reports by Munk (3) and Ren(11), who stated that beaded or uneven thickening was seen in more than 90% of PLC patients. With regard to nature of interlobular septal and bronchovascular bundle thickening, the difference between previous studies (3, 11) and ours is probably due to the fact that previous studies were performed in patients in whom PLC was advanced, or in autopsy cases. In our study, however, a change from smooth thickening of the interlobular septae to nodular or beaded thickening could be observed on follow-up CT scans.

In our study, areas of GGO, which had not been suggested as a finding of PLC, were seen in 15 patients (83%). Because in most previous studies, conventional 10-mm collimation scanning was performed, or because the number of HRCT (1.5-mm collimation) scans was limited to three, areas of GGO may have been difficult to notice. On HRCT scans, GGO can reflect minimal thickening of the septal or alveolar interstitium or the presence of cells or fluid, which partially fill/fills the alveoli(1, 10, 12—14). Because CT-pathologic correlation was not performed in the area of GGO on HRCT, we do not know what GGO represents pathologically. Furthermore, we do not know why some areas of PLC show interlobular septal thickening, bronchovascular bundle thickening, and polygonal lines and other areas show GGO. We speculate that these areas of GGO in our study represent the findings of PLC with tumor cells or edema partially filling the alveolar space or edema and fibrosis in the alveolar walls due to lymphatic obstruction.

PLC most often complicates carcinomas of the breast, lung, stomach, colon, prostate, and pancreas, as well as cases of diffuse metastatic adenocarcinoma arising from an unknown primary tumor(15). The prognosis of PLC is grave, with survival measured in weeks or months. Once it has developed, clinical deterioration follows quickly, reflecting widespread rapidly advancing disease. Before the introduction of modern chemotherapy for metastatic breast cancer, for example, about half of all affected patients died within 3 months and only 15% of patients survived beyond 6 months(16). The introduction of combined chemotherapy for PLC has in some patients, however, induced objective regression of the extent of disease and prolonged survival(5, 7—9). In our study, the follow-up period was longer in patients who underwent anticancer chemotherapy (mean, 4.3 months; range, two to eight months) than in patients who did not (mean, 2.3 months; range, two to three months). In a study by Ikezoe et al(5), ten patients with proven lymphangitic carcinomatosis survived for at least 11 months with chemotherapy. Either their condition was relative stable or a slow progression of pulmonary
radiographic abnormalities was seen. In their study, radiographic abnormalities and pulmonary symptoms initially regressed in six patients, but despite therapy, serial transbronchial lung biopsy and autopsy confirmed persistent lymphangitic carcinomatosis. On serial chest radiography or detailed CT scanning, however, they did not show interval changes of each pattern of pulmonary lesion.

In our six untreated patients, follow-up CT scans showed that all findings (bronchovascular bundle and interlobular septal thickening, polygonal lines, and GGO) increased to a varying extent (by between 45 and 88%). In 12 patients who underwent chemotherapy, the above findings were either stable or showed improvement. In one patient, the extent of PLC was seen to have markedly decreased after chemotherapy.

Initial HRCT findings of PLC should be differentiated from the findings of interstitial pulmonary edema and sarcoidosis. HRCT findings of pulmonary edema consist of smooth interlobular septal thickening, bronchovascular bundle thickening, and areas of GGO with or without pleural effusion, and are very similar to the initial CT findings of PLC. The disappearance of abnormal findings on short-term follow-up radiograph, particularly when diuretics were administered, suggests pulmonary edema. HRCT in patients with pulmonary sarcoidosis shows nodules along the bronchovascular bundles, centrilobular and perilobular regions, including the subfissural areas, so called perilymphatic distribution. Interlobular septal thickening and polygonal lines are, however, unusual in pulmonary sarcoidosis.

Our study is limited by the relatively small number of patients and short duration of follow-up. In PLC cases, it is difficult to obtain pathologic specimens and follow-up CT scans in all patients who showed suspicious pulmonary abnormalities on chest radiograph and in whom primary malignancy was known to be present. This clinical condition precluded the inclusion of a large number of patients. In our study, pulmonary lesions seen on follow-up CT scans might not have been those of PLC, since pathologic proof of the nature of all these lesions was not obtained. However, we clinically eliminated the possibility of infection, drug reaction, hemorrhage, edema or bronchiolitis obliterans organizing pneumonia, and furthermore, the lesions did not change rapidly for at least one month.

In conclusion, HRCT in patients with PLC initially shows smooth rather than nodular thickening of the interlobular septae, bronchovascular bundle thickening, areas of GGO, polygonal lines, and nodules. Overall, the extent of these findings progresses on follow-up to varying degrees. The progressive thickening of bronchovascular bundles and septae, and the presence of polygonal lines and areas of GGO on follow-up CT scan is apparent, especially in patients who do not undergo anticancer chemotherapy. Smooth interlobular septal thickening tended to change to nodular thickening. In patients who underwent chemotherapy, however, improvement or stability was seen with regard to the thickening of bronchovascular bundles, GGO, and polygonal lines; these findings thus indicated that the condition had become chronic.

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임파성 폐전이암: 고해상 전산화단층촬영에서의 시간적 변화

1성균관대학교 의과대학 삼성서울병원 진단방사선과
황재웅·김유경·황정화·김태성·노덕우·이경수

목적: 임파성 폐전이암의 초기 그리고 추적 고해상 전산화단층촬영 소견을 알아보고자 하였다.

대상 및 방법: 임파성 폐전이암을 가진 환자 중 초기 그리고 추적 고해상 전산화단층촬영을 시행한 18명의 환자 를 대상으로 하였다. 이 환자들은 두군으로 나누고(12명의 항암치료를 받은 환자군과 6명의 받지 않은 환자군), 초기 그리고 추적 고해상 전산화단층촬영에서 패실질 이상 소견의 변화를 알아보고, 이를 두 군간에 비교하였다.

결과: 초기 고해상 전산화단층촬영 소견은 소엽간 중격 비후(n=18) (부드러운 비후 15명, 결절성 비후를 포함한 혼합형 3명), 중심부 폐간질(bronchovascular bundle)의 비후(n=17), 마쇄상 음영(ground-glass opacity)(n=15), 다각형 선(n=15), 그리고 결절(n=10)이었다. 항암치료를 시행하였을 때 다각형 선은 그 정도가 감소하였으며 마쇄상 음영, 중심부 폐간질 비후, 소엽간 중격 비후와 결절의 범위는 큰 변화가 없었다. 항암치료를 시행하지 않았을 때는 결절을 제외한 모든 소견의 범위가 증가하였으며(45~88%), 3명의 환자에서 부드러운 소엽간 중격 비후가 결절성의 비후로 바뀌었다.

결론: 임파성 폐전이암의 초기 고해상 전산화단층촬영 소견은 부드러운 소엽간 중격 비후, 중심부 폐간질 비후, 마쇄상 음영과 다각형 선이다. 이들 소견들은 항암치료를 받지 않았을 때 증가하며 부드러운 소엽간 중격 비후가 결절성의 비후로 변하는 경향이 있다. 그러나 항암치료는 이런 소견들의 진행을 멈추게 하거나 호전을 가져온다.
진단방사선과 전문의시험 출제 경향 안내

1. 전문의 시험 분야별 출제비율

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2. 핵의학 분야의 수련은 현행대로 2개월 이상 의무적으로 수련해야 하며 전문의 시험에도 핵의학을 현행 비율대로 계속 출제 할 것임.

3. 동위원소 취급 특수면허 취득을 위한 교육이나 동 면허취득으로 상기 2항의 수련 의무를 대신하지 못함.

4. 상기 출제 비율은 당해연도 문제 선택위원의 성향 또는 문제은행의 문제 성향 등에 따라 증감될 수 있음.

5. 전공의의 전문의시험 응시자격을 위한 논문은 응시서류 제출시 별책을 제1저자 원저 1편과 공저자 2편을 제출하여야 함(단. 증례보고와 논문게재 확인 증명서는 안됨.)