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Piyavisetpat N, Wettawong K, Assanasen T, Wannakrairot P. Intrathoracic manifestations of lymphoma detected by CT. Chula Med J 2010 Jul - Aug; 54(4): 335 - 45

Introduction : *Computed tomography (CT) has been frequently supplemented to stage intrathoracic disease, monitor response to treatment, evaluate recurrence, and diagnose complications. Geographic variations in the incidence of malignant lymphoma are well documented. However, there is no radiologic study of intrathoracic disease of lymphoma in Thailand.*

Objective : *To describe intrathoracic diseases of both Hodgkin disease (HD) and non-Hodgkin's lymphoma (NHL) demonstrated on CT.*

Setting : *King Chulalongkorn Memorial Hospital*

Research design : *A retrospective study*

Patients : *Lymphoma patients who obtained chest CT as an initial staging in between January and December 2003.*

Methods : *We reviewed chest CT obtained as an initial staging within 1 month either before or after diagnosis of lymphoma patients. Each chest CT was reviewed by a chest radiologist.*

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Results : *A total of 62 patients of lymphoma met inclusion criteria (39 men, 23 women; mean age, 46.6 years); 9 were HD and 53 were NHL. Intrathoracic diseases were present in 6 of 9 patients with HD and in 38 of 53 patients of NHL. In HD, 5 had enlarged nodes; 1 had lung involvement; 3 had pleural effusions; 2 had pericardial effusion, and one had distant bone lesion. In NHL, 30 had enlarged nodes; 4 had lung involvement; 28 had pleural abnormalities; 6 had pericardial effusion; 1 had cardiac involvement and distant bone lesion each.*

Conclusions : *The incidence of intrathoracic involvement of HD and NHL is approximately 70% and the most common intrathoracic manifestation is nodal enlargement. The most common nodal group involved in HD is anterior mediastinal group whereas in NHL is paratracheal group.*

Keywords : *Intrathoracic manifestation, Malignant lymphoma, Hodgkin disease, non-Hodgkin's lymphoma, Computed Tomography (CT).*

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นิทรา ปิยะวิเศษพัฒน์, กชกฤษณ์ เวทวงศ์, ธรรมธร อาศนะเสน, พงษ์ศักดิ์ วรรณไกรโรจน์. ความผิดปกติในช่องทรวงอกของผู้ป่วยมะเร็งต่อมน้ำเหลืองที่ตรวจพบโดยเอกซเรย์คอมพิวเตอร์. จุฬาลงกรณ์เวชสาร 2553 ก.ค. – ส.ค.; 54(4): 335 – 45

บทนำ : *เครื่องเอกซเรย์คอมพิวเตอร์ได้ถูกใช้อย่างแพร่หลายในการแบ่งระยะ และการประเมินผลการรักษาของโรคมะเร็งต่อมน้ำเหลือง ทั้งชนิด Hodgkin disease และ non-Hodgkin's lymphoma (NHL) มีการศึกษาอย่างกว้างขวางว่าชนิดของโรคมะเร็งต่อมน้ำเหลืองมีความแตกต่างกันในแต่ละภูมิภาค แต่ไม่เคยมีการศึกษาของความผิดปกติที่พบในช่องทรวงอกจากการตรวจด้วยเครื่องเอกซเรย์คอมพิวเตอร์ในประเทศไทย*

วัตถุประสงค์ : *เพื่อบรรยายความผิดปกติในช่องทรวงอกของผู้ป่วยมะเร็งต่อมน้ำเหลืองจากการตรวจด้วยเครื่องเอกซเรย์คอมพิวเตอร์*

สถานที่ที่ทำการศึกษา : *โรงพยาบาลจุฬาลงกรณ์*

รูปแบบการวิจัย : *การศึกษาย้อนหลัง*

ผู้ป่วยที่ทำการศึกษา : *ผู้ป่วยมะเร็งต่อมน้ำเหลืองที่ได้รับการตรวจด้วยเครื่องเอกซเรย์คอมพิวเตอร์เพื่อแบ่งระยะของโรคระหว่างเดือนมกราคม ถึง ธันวาคม 2548*

วิธีการศึกษา : *ผู้วิจัยได้ทำการหาความผิดปกติที่พบในช่องทรวงอกจากการตรวจด้วยเครื่องเอกซเรย์คอมพิวเตอร์ โดยที่การตรวจนั้นจะต้องอยู่ภายในระยะเวลา 1 เดือนก่อนหรือหลังได้รับการวินิจฉัยโดยรังสีแพทย์*

ผลการศึกษา : *ผู้ป่วยโรคมะเร็งต่อมน้ำเหลืองจำนวน 62 ราย (ชาย 39 ราย หญิง 23 ราย อายุเฉลี่ย 46.6 ปี) โดยเป็น HD 9 ราย และ NHL 53 ราย ในจำนวนผู้ป่วย HD 9 รายพบความผิดปกติในช่องทรวงอก 6 ราย โดยพบว่ามีต่อมน้ำเหลืองโต 5 ราย มีความผิดปกติในปอด 1 ราย มีน้ำในช่องปอด 3 ราย มีน้ำในช่องเยื่อหุ้มหัวใจ 2 ราย และมีความผิดปกติในกระดูก 1 ราย ในจำนวนผู้ป่วย NHL 53 ราย พบความผิดปกติในช่องทรวงอก 38 ราย โดยพบว่ามีต่อมน้ำเหลืองโต 30 ราย มีความผิดปกติในปอด 4 ราย มีความผิดปกติของเยื่อหุ้มปอด 28 ราย และมีน้ำในช่องเยื่อหุ้มหัวใจ 6 ราย และมีความผิดปกติในหัวใจและกระดูกอย่างละ 1 ราย*

วิจารณ์และสรุป : *อุบัติการณ์การเกิดความผิดปกติในช่องทรวงอกใน HD และ NKL พบได้มากถึงร้อยละ 70 โดยความผิดปกติที่พบบ่อยที่สุดคือต่อมน้ำเหลืองโต โดยกลุ่มต่อมน้ำเหลืองที่พบบ่อยที่สุดใน HD คือกลุ่มที่อยู่ทางด้านหน้าของ mediastinum และใน NHL คือกลุ่มที่อยู่ด้านข้างของหลอดลม*

คำสำคัญ : *ความผิดปกติในช่องทรวงอก, มะเร็งต่อมน้ำเหลือง, Hodgkin disease, non-Hodgkin's lymphoma, เอกซเรย์คอมพิวเตอร์.*

Geographic variations in the incidence of malignant lymphoma are well recognized. For instance, the incidence of Hodgkin disease (HD) and follicular lymphomas in the Asia is lower than that of Western countries [1] and among non-Hodgkin's lymphoma (NHL), the low grade lymphoma is less common in Thailand than in the U.S. [1, 2]

Computed tomography (CT) has been frequently supplemented to stage intrathoracic disease, monitor response to treatment, evaluate recurrence, and diagnose complications such as pneumonia and radiation injury. To our knowledge; however, there is no radiologic study of intrathoracic disease of lymphoma in Thailand. The purpose of our study is to describe diseases of both HD and NHL at various intrathoracic sites demonstrated on CT.

Materials and Methods

We retrospectively reviewed the patients with histologically proven lymphoma from our institution's medical record from January to December 2003. All these patients who obtained chest CT as initial staging were provisionally included. Patients were excluded if the initial chest CT was obtained more than 1 month either before or after diagnosis and no available CT to review. The chest CT scans were reviewed by a chest radiologist and all pathological reports were reviewed and reclassified by pathologists.

There were 421 patients who had histological proven of HD and NHL. One hundred and fifty two patients obtained CT scans of the chest, 62 patients met inclusion criteria. Ninety patients were excluded either due to no initial chest CT in determined 1-month period (n = 56) and no available chest CT to review (n = 34).

All CT examinations were performed with Siemens Somatoms Sensation 4 or 16. CT scans were acquired during a single breath hold with the patient lying in the supine position. These CT scans extended from the lung apices to adrenal glands. Of 62 scans, one patient underwent CT with 2-mm collimation, 18 patients underwent CT with 5-mm collimation, and 43 patients underwent CT with 8-mm collimation throughout the lungs. Only one CT scan performed without contrast administration, the remaining scans performed with 80 - 100 ml intravenous contrast administration using a power injector.

All initial chest CT scans were reviewed regarding the following parameters; enlarged intrathoracic nodes ($\geq$ 1 cm in short axis diameter), pulmonary parenchymal abnormalities interpreted as consistent with lymphomatous involvement, pleural or pericardial effusion or thickening, abnormalities of airway, and chest wall abnormality. The location of involved lymph nodes were categorized as highest mediastinal, anterior mediastinal (prevascular and aortopulmonary), paratracheal, subcarinal, posterior mediastinal (paraesophageal, retrocrural and paravertebral), superior diaphragmatic and internal mammary nodes.

Enlargement of other nodes such as supraclavicular, cervical, axillary and intraabdominal lymph nodes as well as hepatic and splenic lesion from included upper abdomen was also recorded but was not evaluated for this study.

Results

Of the 62 patients included in our study group, 39 patients were men and 23 were women. The average age was 46.6 years (age range, 8 - 80 years).

Nine patients were HD and 53 patients were NHL. The diagnosis of lymphoma was diagnosed by bone marrow biopsy in 24 patients and nodal biopsy in 31 patients, gastrointestinal tract in 5 patients, skin and subcutaneous tissue in 2 patients and from other sites such as brain, breast and testis. Regression or progression of abnormality on follow-up examinations was attributed to support lymphomatous involvement.

Of the 9 patients with HD, 6 were mixed cellularity and 3 were nodular sclerosis subtypes. Of the 53 patients of NHL, 24 were diffuse large B-cell lymphoma; 3 were follicular lymphoma, mantle cell lymphoma, MALT lymphoma, and T-lymphoblastic lymphoma each; 2 were small lymphocytic lymphoma, lymphoplasmacytic lymphoma, peripheral T-cell lymphoma and anaplastic large cell lymphoma each; and 1 was Burkitt's lymphoma, angioimmunoblastic T-cell lymphoma, extranodal NK/T-cell lymphoma, aggressive NK cell lymphoma, mycosis fungoides and subcutaneous like T-cell lymphoma each. The rest were unclassified NHL due to lack of phenotypic classification.

Hodgkin disease

Of 9 patients with HD, intrathoracic diseases were present in 6 patients (66.7%) (Table 1). Five of 6 patients (83.3%) had enlarged intrathoracic nodes. Of enlarged nodes, there were anterior mediastinal (n = 5), highest mediastinal (n = 3), paratracheal (n = 2), subcarinal (n = 2), and retrocrural (n=1) as shown in Table 2. One patient had bulky mass which encasing and narrowing the left brachiocephalic vein (Fig. 1). Three of 5 patients also had accompanying enlarged intraabdominal nodes from included upper abdomen.

One of 6 patients had parenchymal consolidation in accompanying with multiple pulmonary nodules containing air bronchograms and cavitation (Fig 2). This patient also had massive left pleural effusion and enlarged intrathoracic node.

Table 1. Prevalence of intrathoracic disease in HD and NHL detected with chest CT at specific anatomic sites.

Anatomic site	No. of patients (%)	
	Hodgkin disease (n = 6)	NHL (n = 38)
Lymph nodes	5 (83.3)	30 (79)
Lung parenchyma	1 (16.7)	4 (10.5)
Pleural effusion	3 (50)	28 (73.7)
Pleural thickening	0	2 (5.3)
Pericardium	2 (33.3)	6 (15.8)
Heart	0	1 (2.6)
Chest wall	1 (16.7)	1 (2.6)
Intrathoracic disease	6 (66.7)	38 (71.7%)

Table 2. Distribution of enlarged intrathoracic nodes in HD and NHL.

Location	No. of patients (%)	
	Hodgkin disease (n = 5)	NHL (n = 30)
Highest mediastinal	3 (60)	2 (6.67)
Paratracheal	2 (40)	21 (70)
Anterior mediastinum	5 (100)	17(56.7)
Internal mammary	-	3 (10)
Subcarina	2 (40)	16 (53)
Posterior mediastinum	1 (20)	4 (13.3)
Hilar & intrapulmonary	-	9 (30)
Superior diaphragmatic	-	11 (36.7)

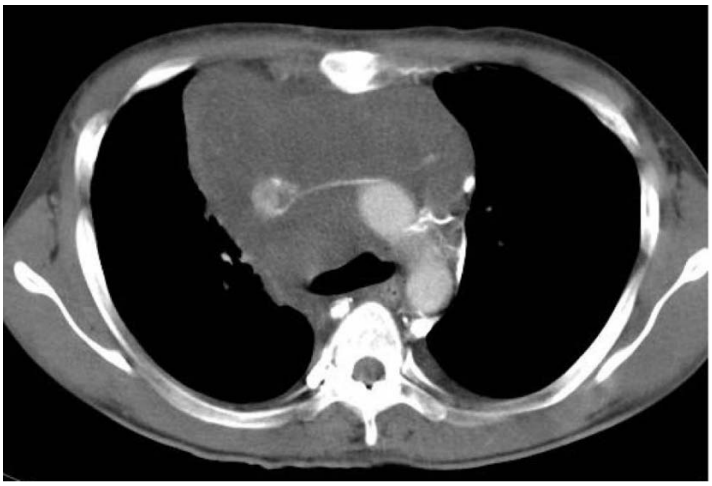

Figure 1. A 22-year-old-man of HD, chest CT at the level of aortic arch showing bulky mediastinal mass, encasing and stretching the left brachiocephalic vein.

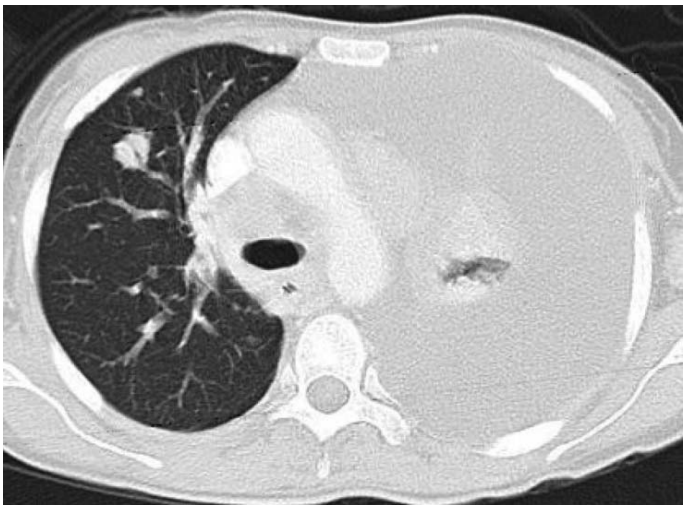

Figure 2. A 23-year-old-woman of HD, chest CT at the level of aortic arch showing a small nodule with air bronchogram in anterior segment of RUL. Note large left pleural effusion and enlarged mediastinal nodes.

Three of 6 patients (50%) had pleural effusion. All patients had enlarged intrathoracic nodes. One of 3 patients had bilateral pleural effusions. Two patients had pericardial effusion in accompanying with pleural effusion and enlarged intrathoracic nodes.

One patient had distant focal osteolytic lesion at thoracic vertebra without enlarged intrathoracic node. However, enlarged axillary, supraclavicular and cervical nodes were present. This lesion has become sclerotic after treatment.

Non-Hodgkin's Lymphoma

Of 53 patients of NHL, there were intrathoracic diseases in 38 patients (71.7%). Intrathoracic node enlargement was present in 30 patients (79%) as shown in Table 1. The involved nodes were paratracheal (n = 21), anterior mediastinal (n = 17), subcarinal (n = 16) and superior diaphragmatic nodes (n = 11) (Table 2). Two patients had bulky mass at prevascular region which compromising SVC. Six of 30 patients (20%) had no other intrathoracic diseases, eight patients had other intrathoracic disease without intrathoracic node enlargement. Of 11 patients with enlarged superior diaphragmatic nodes, 4 had accompanying intraabdominal node enlargement.

Four patients (10.5%) had pulmonary parenchymal abnormalities. Three of 4 patients had accompanied enlarged mediastinal node. Three of them had multiple irregular-marginated pulmonary nodules; one of these also had parenchymal consolidation. Nodules in 1 patient also had air bronchogram. Another one patient had a 4-cm lobulated mass at left lower lobe without enlarged intrathoracic node.

Of 38 patients, 28 (73.7%) had pleural effusion, 15 were bilateral and 13 were unilateral pleural effusion. Two of 28 patients (7.1% of pleural disease, 5.3% of intrathoracic abnormality) also had pleural thickening, one was bilaterally involved (Fig. 3). Of 28 patients, 7 had pleural effusion without intrathoracic node enlargement.

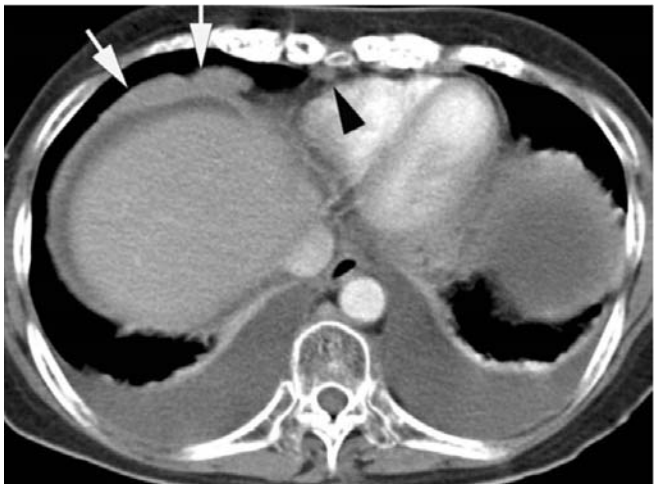

Figure 3. A 54-year-old-woman with NHL, chest CT at the level of dome of right hemidiaphragm reveals lobulated pleural nodules (arrows). There are also bilateral pleural effusions and a small right anterior superior diaphragmatic node (arrowhead).

Six of 38 patients (15.8%) had small pericardial effusion, all of these had intrathoracic node enlargement. Five of 6 patients had both pericardial and pleural effusion. One patient had cardiac involvement manifested as thickened interventricular septum and infiltrative soft tissue encasing left coronary artery (Fig 4).

Only one patient had a single distant osteolytic lesion at thoracic vertebra. Bilateral pleural effusion, pulmonary nodules and consolidation and liver mass were also present in this patient.

The details of involvement is shown in table 3.

Discussion

The incidence of lymphoma has been increasing in Thailand. [2] In Asia, low grade lymphoma is less common whereas intermediate to high grade lymphomas are more common than in the U.S.[1, 2], and the incidence of follicular lymphoma, T-cell lymphoma as well as HD is lower than in the U.S. [1], but is comparable to the Western population. [1,2] Various environmental agents and inherited genetic abnormalities are possibly responsible for these differences. [1]

In our study, there was no difference in the incidence of intrathoracic involvement between HD (66.7%) and NHL (71.7%), in contrast to the studies reported by Filly *et al* [3] and Castellino *et al* [4] that demonstrated a higher incidence of intrathoracic disease at presentation in HD than in NHL. This difference is probably due to our study based on CT imaging which is more sensitive in detecting intrathoracic disease than chest radiograph. In our study, intrathoracic node involvement was seen on the imaging in 83% of patients at presentation in HD, which is comparable to the study reported by Castellino *et al* . [5] Prevascular and aortopulmonary window nodes were involved in all HD with intrathoracic disease, similar to the previous studies reported that prevascular and paratracheal nodes (superior mediastinal nodes) were the most frequent site of disease in HD. [3, 6] Intrathoracic disease without concomitant mediastinal node disease did not occur

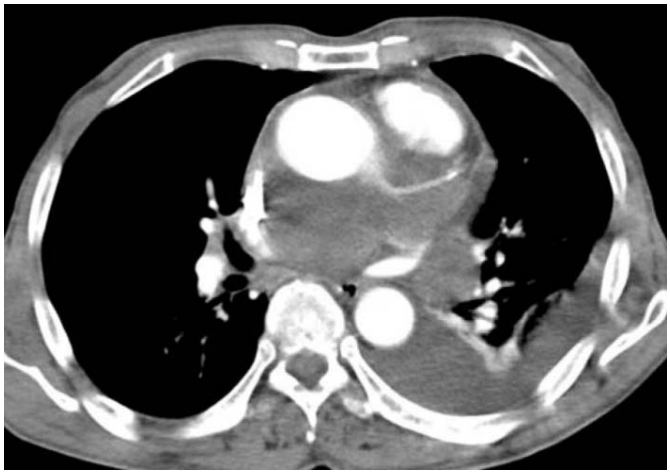

Figure 4. A 77-year-old-man with NHL, chest CT at the level of aortic root showing an infiltrative soft tissue mass in the pericardial space encasing the left coronary artery.

Table 3. Intrathoracic abnormalities of each type of NHL.

Type	Nodes	Pleural effusion	Pleural thickening	Pericardial effusion	Lung	Cardiac	Bone	Negative
Diffuse large B cell (24)	14	14	0	3	3	1	1	5
Small lymphocytic (2)	0	0	0	0	0	0	0	2
Lymphoplasmacytic (2)	2	0	0	0	1	0	0	0
MALT (3)	0	0	0	0	0	0	0	3
Follicular (3)	3	2	1	1	0	0	0	0
Mantle (3)	2	1	0	0	0	0	0	0
Burkitt's (1)	1	1	0	0	0	0	0	0
Aggressive NK cell (1)	0	1	0	0	0	0	0	0
Extranodal NK/T- cell (1)	0	0	0	0	0	0	0	1
Subcutaneous panniculitis like T- cell (1)	0	0	0	0	0	0	0	1
Mycosis fungoides (1)	0	0	0	0	0	0	0	1
T-lymphoblastic (3)	3	3	1	1	0	0	0	0
Peripheral T cell (2)	1	1	0	0	0	0	0	1
Angioimmunoblastic T- cell (1)	1	1	0	0	0	0	0	0
Anaplastic large cell (2)	2	2	0	1	0	0	0	0
Nonspecified (3)	1	2	0	0	0	0	0	1

in their study. [6] The presence of intrathoracic disease without nodal involvement, particularly prevascular nodal group, should be prompt the radiologist either to raise the possibility of disease other than HD or an alternative second concomitant disease process. [5] The bulky, confluent masses in HD tend to displace, rather than constrict or invade, adjacent tissues.[5]

In NHL, intrathoracic nodes were involved in 79% of patients in this series. The paratracheal nodes were most commonly involved, followed by prevascular and aortopulmonary nodes, which is similar to study of Castellino *et al* . [4] In comparison with HD, NHL shows a lower frequency of superior mediastinal lymphadenopathy.[7] Presence of other thoracic diseases without enlarged intrathoracic nodes in NHL is also much more common than in HD. [4] Single lymph node involvement as the only manifestation of intrathoracic disease, particularly posterior mediastinum, is also not infrequently present in patients with NHL. Cardiophrenic angle adenopathy was usually associated with extensive disease at other intrathoracic sites. [8]

Pleural effusions are not uncommon at presentation and account for 13% of patients with HD [5] and 20% of patients with NHL.[4] In our study, pleural effusions in all of patients with HD and in 92.9% of patients of NHL had associated mediastinal lymphadenopathy, similar to the studies of Aquino *et al* and Castellino *et al*. [5, 9] In the absence of pleural masses identified, it is generally assumed to result

from lymphatic or venous obstruction rather than direct tumor involvement of pleura. [6] Solid pleural masses occur less frequently than pleural effusion and represent an underappreciated site of lymphoma.[10]

Cardiac or pericardial involvement of lymphoma may result from retrograde lymphatic spread, hematogenous spread and direct extension from intrathoracic masses. [11] In our study, pericardial disease including effusion and mass accounted for approximately 22% in patients with HD and 11% in patients with NHL, which were fairly high as compared with study of Castellino *et al*, which were only 6% and 8%, respectively.

Lymphomatous involvement of the lung is more frequently in secondary or recurrent disease than as a primary manifestation, particularly in HD. [6] Pulmonary parenchymal involvement in newly diagnosed HD occurs approximately 8% of patients; [6] in relapsed HD is 12% [12]; and in patients with NHL occurs 4 - 13%. [3, 4] There are a wide variety of radiologic appearance including direct extension into the parenchyma from involved mediastinal nodes, small irregular nodules along the bronchovascular bundle extending out from the hila, cavitation in nodules or masses, segmental or lobar opacities with air bronchogram, thickening of peribronchovascular bundle and septal lines. The most common findings in both HD and NHL are mass or masslike consolidation and nodules less than 1 cm. [3, 12] Peribronchovascular thickening is also fairly common. [12] The presence of multiplicity of CT findings, which can be explained on the basis of the anatomy of the lymphatic system in the lungs, may help differentiate lymphoma involving the lung parenchyma from other processes that tend to have a predominantly single pattern. [12] However, other diseases such as Kaposi sarcoma, sarcoidosis, or bronchioloalveolar cell carcinoma can also have a combination of various CT findings similar to lymphoma, thus knowing the clinical history is still crucial. [12] In untreated HD, presence of lung involvement without lymphadenopathy is very rare and most likely represents another process. [3, 6]

Chest wall involvement in both HD and NHL is unusual at presentation. [4, 5] In HD, chest wall involvement is frequently related to direct extension from enlarged bulky lymphadenopathy [5], whereas in patients with NHL, the prevalence of direct extension from adjacent enlarged nodes and distant bone involvement from lymphadenopathy are in approximately equal proportion. [4] Bone lesion in lymphoma is characteristically mixed with a strong blastic component. [6] In HD, involvement of cortical and medullary bone is unusual at presentation and is frequently caused by enlarged node which directly infiltrates the adjacent skeletal structure. [6]

There were several limitations in this study. First, there were small numbers of patients, particularly in HD, Second, it is difficult to distinguish these CT findings from those associated with infection or hemorrhage in lymphoma and only few cases had histopathologic confirmation of lymhomatous involvement.

In conclusion, the incidence of intrathoracic disease of both HD and NHL is approximately 70%, and enlarged mediastinal node is the most common intrathoracic manifestation. The most common nodal group involved in HD is anterior mediastinal group and in NHL is paratracheal group. Despite different

distribution in the incidence of various subtypes of malignant lymphoma in that of Western countries, there is no difference in radiologic findings.

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