Distinguishing Small Primary Lung Cancer from Pulmonary Tuberculoma Using 64-Slices Multidetector CT

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Objective: *To evaluate which CT findings help in distinguishing small primary lung cancer from tuberculoma.*
Material and Method: *Forty-two chest CT studies with pathological diagnosis of primary lung cancer (n = 27) and tuberculoma (n = 15) were retrospectively reviewed by two radiologists who were blind to the pathological results. The CT findings of number, size, shape, border, and location of the nodules, the presence or absence of satellite nodule, contrast enhancement, internal air bronchogram, internal calcification, internal cavitation, bronchovascular invasion, and bony destruction were evaluated.*
Results: *About 96% of primary lung cancer had a solitary lesion compared to only 60% among tuberculoma ($p < 0.05$). The nodule size > 2-3 cm is more likely to be primary lung cancer compared with tuberculoma ($p = 0.058$). Both primary lung cancer and tuberculoma can occur in all lobes of both lungs but more frequently in the upper lobe, which has no statistically significant difference between these two groups. Tuberculoma seems to be round or polygonal shape and primary lung cancer is more likely to be lobulated shape. The smooth border nodule is found only in tuberculoma (27%) whereas 93% of primary lung cancer had spiculated border compared to 73% among tuberculoma ($p < 0.05$). Tuberculoma seems to have more satellite nodule than primary lung cancer (47% vs. 22%, $p = 0.163$). The enhancement of nodule and air bronchogram are significantly found in primary lung cancer compared with tuberculoma ($p < 0.05$). Tuberculoma seems to have dense central calcification and primary lung cancer seems to have punctate calcification ($p < 0.05$). Most of the primary lung cancer and tuberculoma do not have internal cavity. The presence of bronchovascular invasion was significantly found in primary lung cancer compared with tuberculoma ($p < 0.05$). No evidence of bony destruction was observed in both pulmonary tuberculoma and primary lung cancer groups.*
Conclusion: *The solitary lesion size ≤ 3 cm in diameter with spiculated border, contrast enhancement, presence of air bronchogram, punctate calcification and bronchovascular invasion are useful CT findings for diagnosis of primary lung cancer. However, the lesions with inconclusive findings, tissue diagnosis may be necessary.*

Keywords: *Air bronchogram, Multidetector CT, Primary lung cancer, Pulmonary tuberculoma, Satellite nodule*

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Primary lung cancer is the common leading causes of cancer deaths. In The Thai population, it is the most common cancer in males and the fourth most common cancer in females following breast, cervix, and colonic cancers. Most patients present with advanced stage of disease and beyond surgical treatment[1]. Early diagnosis of primary lung cancer is important for improvement of the prognosis.

Pulmonary TB is the common disease in the Thai population. There are many radiological features of pulmonary TB. Tuberculoma is one of the more common lesions presenting a small pulmonary nodule. Most tuberculomas are less than 3 cm in diameter, smooth marginated, however fibrosis related to vessels, interlobular septa, or lung parenchyma adjacent to the nodule may result in a spiculated margin[2]. Therefore, differentiation of primary lung cancer from tuberculoma is still a common diagnostic problem. If a small lung cancer was diagnosed and resected early, the prognosis is excellent. On the other hand, if a pulmonary nodule is more favor to be tuberculoma, unnecessary operation could be avoided.

Nowadays, computed tomography (CT) scan has a very important role in detection and characterization of the pulmonary nodule. The goal of CT scan is distinguishing between benign and

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malignant nodule for further proper management. However, there is an overlap in CT findings of benign and malignant lesion. Therefore, CT scan cannot differentiate primary lung cancer from tuberculoma in some cases. The previous study conducted by Chawalparit et al[3] studied HRCT findings of pulmonary TB in Siriraj Hospital's patients but with no malignancy cases for comparison. The aim of the present study was to evaluate which CT findings help in distinguishing small primary lung cancer from tuberculoma.

Material and Method

Subjects

This retrospective study was approved by the Ethics Committee of Siriraj Hospital (No.Si 072/2009). The present study included cases with diagnosed primary lung cancer and pulmonary tuberculoma who had completely pretreatment CT imaging. The inclusion criterion of nodule was size of $\leq$ 3 cm in diameter.

Five hundred nine pathological reports from the pathology department, Siriraj Hospital with diagnoses of primary lung cancer and pulmonary tuberculoma between January 2006 and December 2009 were collected. Four hundred and sixty seven patients were excluded from the present study due to an absence of pretreatment or post contrast CT study, had only thicken section CT imaging, and no CT data in PACS. The pulmonary lesions greater than 3 cm were also excluded because the larger nodule (greater than 3 cm in diameter), the more likely it is to be malignant[4] (Fig. 1).

The remaining 42 patients were included in the present study, including 27 cases of primary lung cancer (13 men, 14 women; age range 46 to 81 years; mean age 64 years) and 15 cases of tuberculoma (9 men, 6 women; age range 21 to 71 years; mean age 53 years).

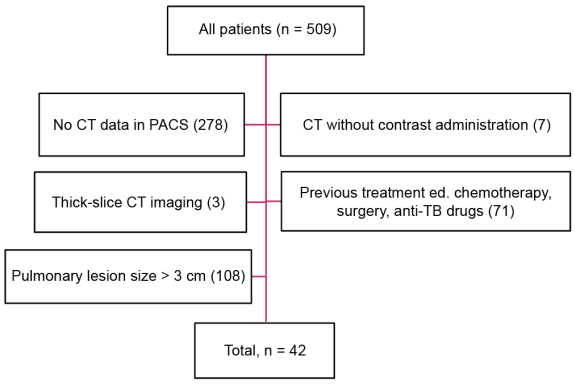

Fig. 1 Patient selection

CT scanning

Forty-one CT of the chests were performed with GE LightSpeed scanner at 1.25 mm slice thickness (15 patients with tuberculoma, and 26 patients with primary lung cancer) and one CT of the chest was performed with Siemens Somatom scanner at 1.5 mm slice thickness (1 patient with primary lung cancer). The MDCT of the chest was performed from the level of the thyroid gland to the level of the adrenal glands. The exposure parameters for the CT scans were 120 kVp and 250 to 300 mAs for both scanners. The CT scans were obtained before and after injection of non-ionic contrast medium (70-80 cc, rate 2 cc/sec) with delay scan time 45 seconds. Evaluation was done in both mediastinal and lung window settings.

Image interpretation

Two radiologists who had more than ten years of experience in a chest CT interpretation retrospectively reviewed the chest CT scans from PACS, independently. Both radiologists were blind to the pathological results. The radiologists evaluated number, size, shape (round, oval, lobulated, or polygonal), border (smooth, irregular, or spiculation), location of the nodules, the presence or absence of satellite nodule, contrast enhancement, internal air bronchogram or bubble-like lucency, internal calcification (uniform or homogenous, concentric or laminated, dense central, and punctate or stipple), internal cavitation, bronchovascular invasion, and bony destruction.

The terms used in the present study were described as: satellite nodule; small nodule adjacent to a dominant nodule[5], round shape; a shape that is curved and without sharp angles[6], oval shape; an egg-shaped or elliptical form or figure[6], lobulated shape; a simple closed curve that cannot be described as borders of the same circle[7], polygonal shape; a closed plane figure bounded by straight sides[6], smooth border; a simple closed curve with borders of the same circle[4], spiculated border; the spikes or points on the surface[8], irregular border; the border that was not smooth or spiculated, air bronchogram; an air-filled bronchus against surrounding opacified alveoli[9], cavitation; an unfilled space within a nodule[10], and bronchovascular invasion; the act of invading bronchial or vascular structure[10]. For the term 'enhancement', the present study was defined as

an increased CT number of nodule on post contrast image more than 15 Hounsfield unit (HU), due to the results of the multicenter study corroborated the hypothesis that absence of significant lung nodule enhancement (≤ 15 HU) at CT was strongly predictive of benignity[11]. The pattern of shape and border was shown in Fig. 2. If there were any disagreement, the final interpretation would be solved by consensus.

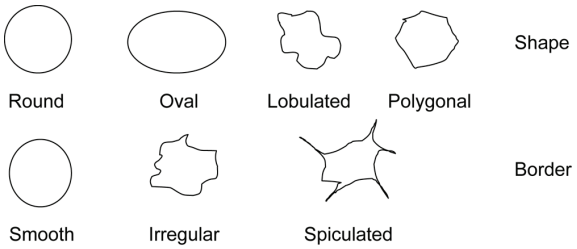

Fig. 2 The patterns of shape and border

Statistical analysis

Kappa statistic and its 95% confidence interval (CI) were employed to determine agreement in characterized CT findings between two radiologists. Degree of interobserver agreement was graded as follows: Kappa values of 0 to 0.20 poor or slight agreement, 0.21 to 0.40 fair agreement, 0.41 to 0.60 moderate agreement, 0.61 to 0.80 good or substantial agreement, and 0.81 to 1.00 very good or almost perfect agreement.

Fisher's exact test was used to test the difference in CT patterns between primary lung cancer and tuberculoma. A p-value of less than or equal 0.05 was considered statistically significant. The SPSS statistical software (version 18) was used for the statistical evaluation.

Results

Interobserver agreement

Interobserver agreement in characterized CT findings of primary lung cancer and tuberculoma are shown in Table 1. There was perfect agreement in size, internal cavitation, and bony destruction (Kappa, [95% CI] = 1, [1.00, 1.00]). Agreement in CT findings of number of lesions and enhancement were very good (Kappa, [95% CI] = 0.83, [0.60, 1.00] and 0.81, [0.66, 0.97], respectively). Satellite nodule and internal air bronchogram were good agreement (Kappa, [95% CI] = 0.70, [0.46, 0.94] and 0.61, [0.38, 0.85], respectively). Moderate agreement were observed on the CT findings of shape, border, internal calcification, and bronchovascular invasion (Kappa, [95% CI] = 0.55, [0.35, 0.76]; 0.53, [0.23, 0.83]; 0.60, [0.24, 0.95]; and 0.50, [0.22, 0.77], respectively).

CT characteristics

About the location, both primary lung cancer and tuberculoma can occur in all lobes of both lungs but more frequently in the upper lobe. Right upper lobe is the most common location for primary lung cancer whereas both right and left upper lobes are the common locations for tuberculoma (Table 2). No statistically significant difference of location between these two groups (p > 0.05). The details of CT findings are summarized in Table 3. As high as 96% of primary lung cancer had solitary lesion compared to only 60% among tuberculoma. On the other hand, multiple lesions were found in 4% of primary lung cancer and 40% with tuberculoma (p = 0.005). About size of the lesion, the nodule > 2 to 3 cm in diameter is more likely to be primary lung cancer compared with tuberculoma (59% vs. 27%, p = 0.058). Regarding shape of the

Table 1. Interobserver agreement in characterized CT findings of primary lung cancer and tuberculoma (n = 42)

Findings	Kappa	95% CI
Number of lesion(s)	0.83	(0.60, 1.00)
Satellite nodule	0.70	(0.46, 0.94)
Maximum diameter	1.00	(1.00, 1.00)
Shape	0.55	(0.35, 0.76)
Border	0.53	(0.23, 0.83)
Enhancement	0.81	(0.66, 0.97)
Air bronchogram	0.61	(0.38, 0.85)
Calcification	0.60	(0.24, 0.95)
Cavity	1.00	(1.00, 1.00)
Bronchovascular invasion	0.50	(0.22, 0.77)
Bony destruction	1.00	(1.00, 1.00)

Table 2. Location of primary lung cancer and pulmonary tuberculoma

Location	Primary lung cancer (lesion = 28)	Pulmonary tuberculoma (lesion = 21)	p-value
RUL	14 (50.00%)	8 (38.10%)	1.000
RML	2 (7.14%)	2 (9.52%)	0.608
RLL	2 (7.14%)	2 (9.52%)	0.164
LUL	7 (25.00%)	8 (38.10%)	0.100
LLL	3 (10.71%)	1 (4.76%)	1.000

Table 3. Differences CT findings between primary lung cancer and pulmonary tuberculoma

Findings	Primary lung cancer (n = 27)	Pulmonary tuberculoma (n = 15)	p-value
Number of lesion(s)			0.005
Solitary	26 (96.3%)	9 (60.0%)	
Multiple	1 (3.7%)	6 (40.0%)	
Maximum diameter (cm)			0.058
≤ 2	11 (40.7%)	11 (73.3%)	
> 2-3	16 (59.3%)	4 (26.7%)	
Shape			0.179
Round	4 (14.8%)	5 (33.3%)	
Oval	2 (7.4%)	1 (6.7%)	
Lobulated	18 (66.7%)	5 (33.3%)	
Polygonal	3 (11.1%)	4 (26.7%)	
Border			0.012
Smooth	0 (0%)	4 (26.7%)	
Irregular	2 (7.4%)	0 (0%)	
Spiculated	25 (92.6%)	11 (73.3%)	
Satellite nodule			0.163
Present	6 (22.2%)	7 (46.7%)	
Absent	21 (77.8%)	8 (53.3%)	
Enhancement			0.001
Non-enhancement	3 (11.1%)	10 (66.7%)	
Enhancement	24 (88.9%)	5 (33.3%)	
Air bronchogram			0.003
Present	22 (81.5%)	5 (33.3%)	
Absent	5 (18.5%)	10 (66.7%)	
Calcification			0.040
Punctate	2 (7.4%)	0 (0%)	
Dense central	0 (0%)	3 (20.0%)	
Absent	25 (92.6%)	12 (80.0%)	
Cavity			0.357
Present	0 (0%)	1 (6.7%)	
Absent	27 (100%)	14 (93.3%)	
Bronchovascular invasion			0.016
Present	25 (92.6%)	9 (60.0%)	
Absent	2 (7.4%)	6 (40.0%)	
Bony destruction			-
Present	0 (0%)	0 (0%)	
Absent	27 (100%)	15 (100%)	

nodule, there was no statistically significant difference between these two groups (p = 0.179) but tuberculoma seem to be round or polygonal shape than primary lung cancer (33% vs. 15% and 27% vs. 11%). Primary lung cancer is more likely to be a lobulated shape than a tuberculoma (67% vs. 33%). Concerning the border of the nodule, the smooth border nodule was found only in tuberculoma (27%) where as 93% of primary lung cancer had a spiculated border compared to 73% among tuberculoma (p = 0.012). Regarding satellite nodule, tuberculoma seem to have more satellite nodule than primary lung cancer (47% vs. 22%, p = 0.163) (Fig. 3). About nodule enhancement, the enhancement of nodule is significantly found in primary lung cancer compared with tuberculoma (89% vs. 33%, p = 0.001) (Fig. 4). The nodule containing air bronchogram was found in 82% with primary lung cancer and 33% with tuberculoma which is statistically significant difference (p = 0.003) (Fig. 5). About the presence of calcification in the nodule, tuberculoma seem to have dense central calcification compared with primary lung cancer (20% vs. 0%) and primary lung cancer seem to have punctate calcification compared with tuberculoma (7% vs. 0%) (p = 0.040) (Fig. 6). Most of the primary lung cancer and tuberculoma do not have internal cavity (100% vs. 93%, p = 0.357). The presence of bronchovascular invasion was significantly found

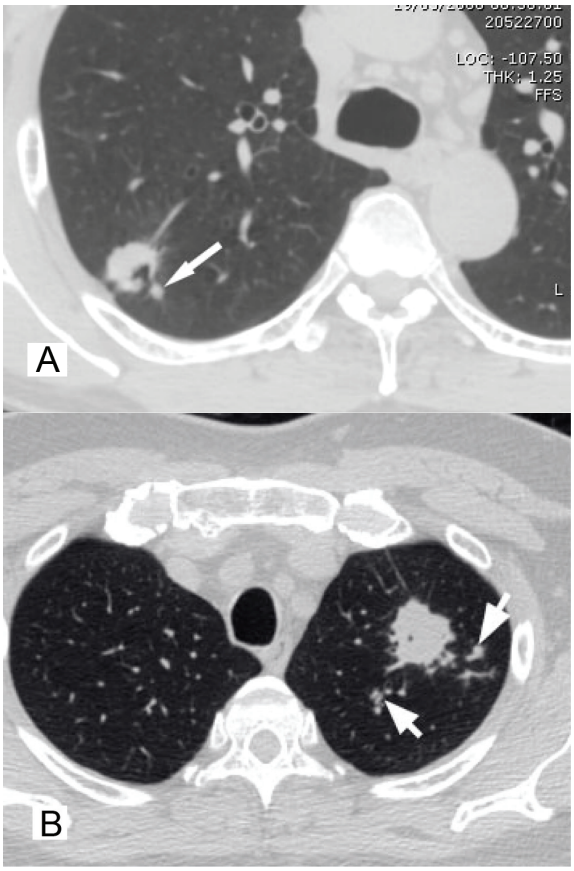

Fig. 3 MDCT scan of chest shows satellite nodules (arrow) surrounding the pulmonary nodules in patients with non-small cell lung cancer (A) and pulmonary tuberculoma (B)

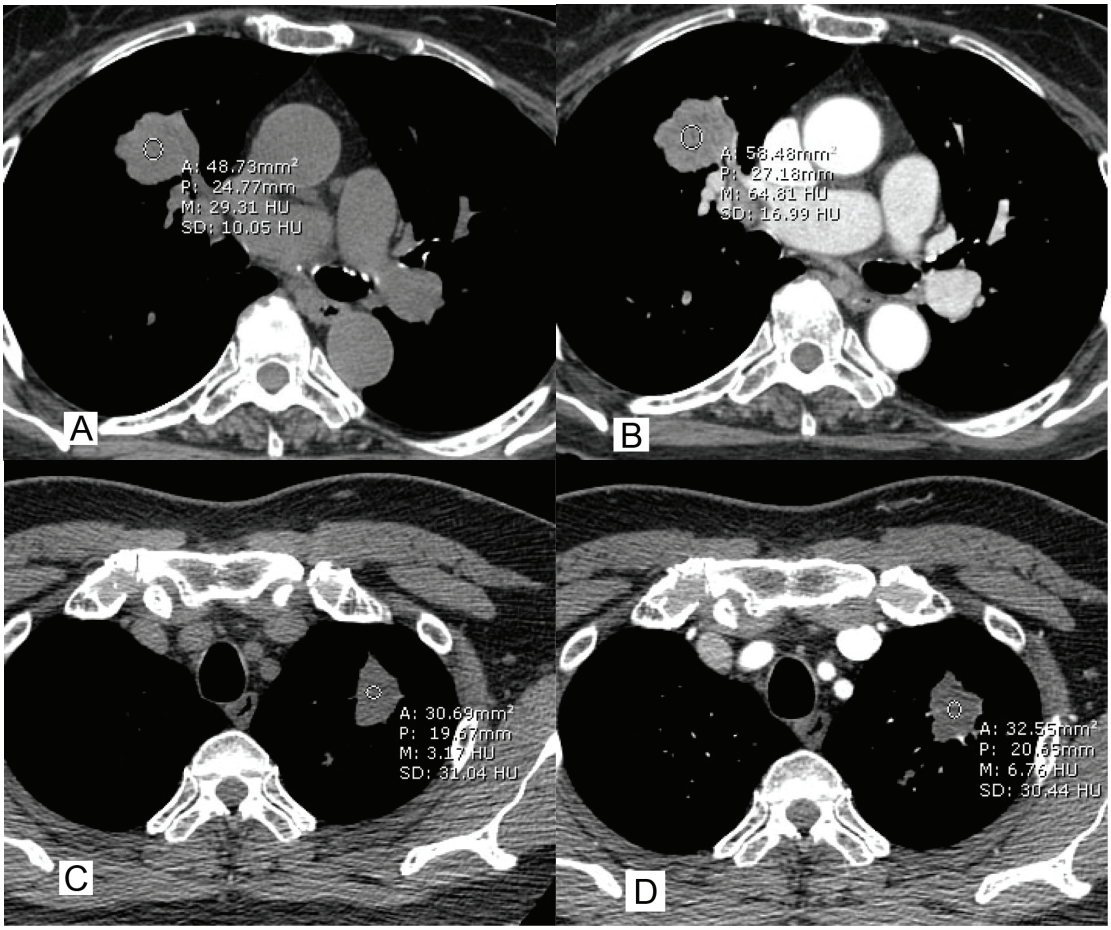

Fig. 4 MDCT scan of chest shows a homogeneous enhancing lobulated nodule at right upper lobe in a patient with adenocarcinoma of the lung (A: precontrast scan, B: postcontrast scan) and a non-enhancing polygonal shape nodule at left upper lobe in a patient with pulmonary tuberculoma (C: precontrast scan, D: postcontrast scan)

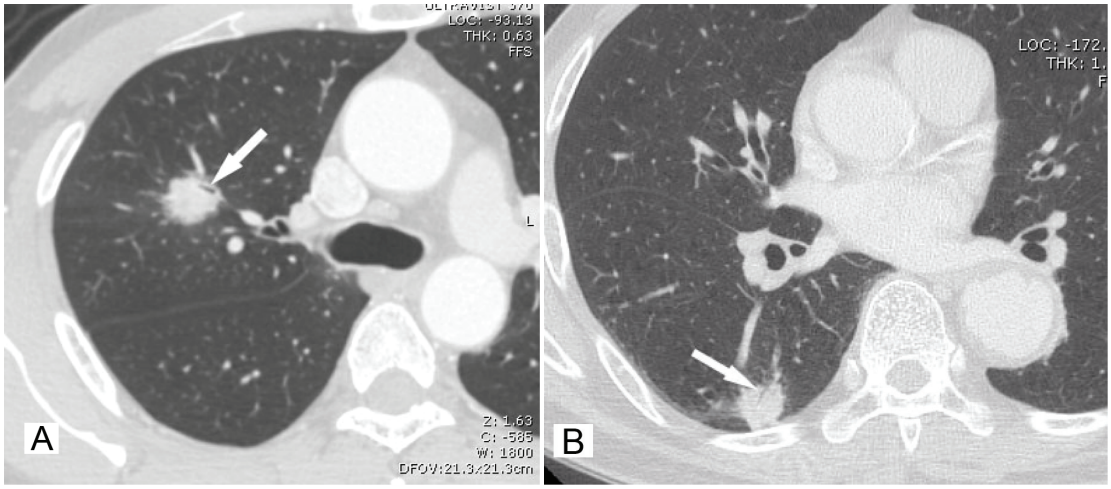

Fig. 5 MDCT scan of chest shows air bronchogram (arrow) within the pulmonary nodules in patients with adenocarcinoma of the lung (A) and pulmonary tuberculoma (B)

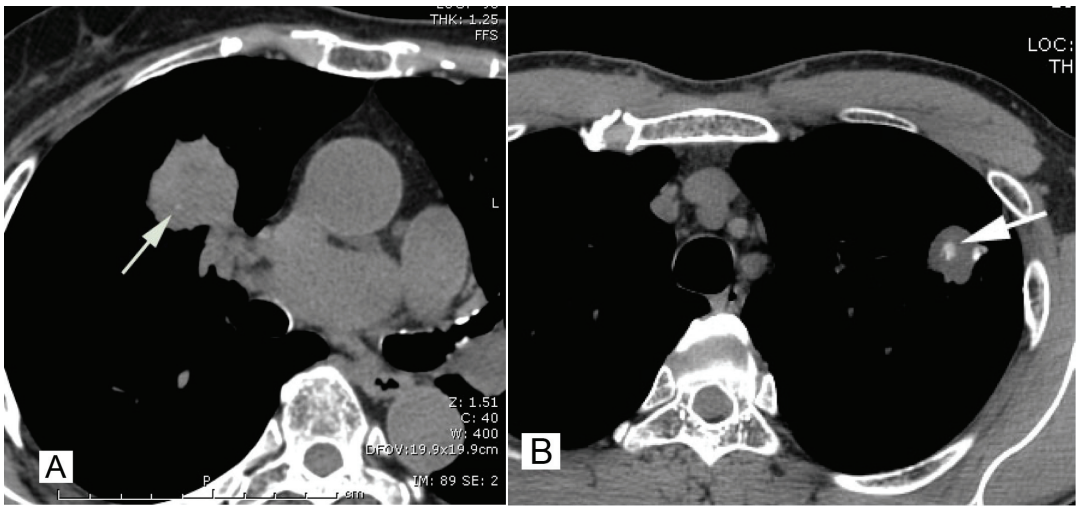

Fig. 6 Precontrast MDCT scan of chest shows punctatecalcification (arrow) within the pulmonary nodule in a patient with adenocarcinoma of the lung (A) and dense central calcification (arrow) within the pulmonary nodule in a patient with pulmonary tuberculoma (B)

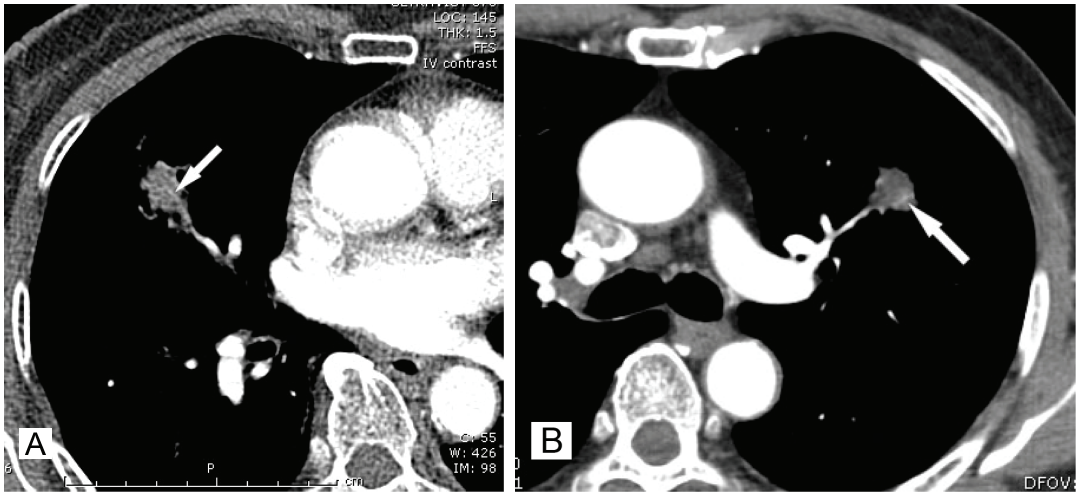

Fig. 7 Postcontrast MDCT scan of chest shows pulmonary nodules with vascular invasion (arrow) in patients with adenocarcinoma of the lung (A) and pulmonary tuberculoma (B)

in primary lung cancer compared with tuberculoma (93% vs. 60%, p = 0.01) (Fig 7). No evidence of bony destruction was observed in all CT images of both pulmonary tuberculoma and primary lung cancer groups.

Discussion

The pulmonary nodules refer to a round or oval opacity smaller than 3 cm in diameter. To give a definite diagnosis of pulmonary nodules are a diagnostic challenge because there are many differential diagnosis of pulmonary nodule. The most important diagnostic goal is to differentiate lung cancer from other benign lesions.

Several previous studies concluded that nodules less than 2 cm, smooth border, exhibits benign calcification (central, laminated, popcorn or diffuse), enhancement less than or equal 15 HU and cavity wall thickness less than or equal 16 mm are favored to be benign nodules. On the other hand, nodules larger than 3 cm, lobulation, irregular spiculated edge, indeterminate calcification (stipple or eccentric), presence of air

bronchogram, enhancement more than 15 HU, cavity wall thickness more than 16 mm, nonsolid, and partially solid nodules are more likely to be malignant[12-16].

In present study, the number of nodules was a significant factor to differentiate primary lung cancer from tuberculoma. If there are multiple lesions, it is more likely to be tuberculoma. The size of nodule $\leq$ 2 cm is seem to be tuberculoma more than primary lung cancer (73% vs. 41%, p = 0.058). This result supports a previous report [12] that more than 90% of nodules smaller than 2 cm in diameter are benign. The most common location for primary lung cancer in this study is right upper lobe, which also confirm the previous report[12]. Takashima et al[17] found that polygonal shape and concave margin were specific to benign lesion and the prevalence of groudglass opacity and air bronchogram were significantly greater in malignant lesions. Chawalparit et al[3] reported 77% of pulmonary TB had spiculated margin and 54% of pulmonary TB had polygonal shape. The present study may be concluded by using significant difference in percentage of CT findings that tuberculoma is more likely to be round or polygonal shape and smooth border whereas primary lung cancer seem to be lobulated shape and irregular spiculated border, although there is no statistically significance (p = 0.179) that could be from a small number of patients.

Kim et al[14] reported that a satellite lesion and cavitation on CT chest could be useful predictors for benign nodule in TB-endemic area. In present study tuberculoma seem to have more satellite nodules than primary lung cancer (47% vs. 22%), although there is no statistical significance (p = 0.163) that could be from a small number of patients. The enhancement of nodule was a significant factor to differentiate primary lung cancer from tuberculoma in the present study.

In the study of Kuriyama et al[15], 72% of adenocarcinomas demonstrated air bronchogram and they suggested that the presence of air bronchogram in a lung nodule is a useful finding to help differentiate adenocarcinoma from benign lesion. In present study, the presence of air bronchogram in a nodule was a significant indicator for malignancy in particular adenocarcinoma, concordant with prior study.

There is no statistically significant difference of the presence of calcification in the nodule between primary lung cancer and tuberculoma. However, when the nodule exhibit dense central calcification, the diagnosis of tuberculoma should be of concern. The presence of cavity in the nodule also showed no statistically significant difference between these two groups. Bronchovascular invasion was a significant indicator of malignancy in the present study.

There are limitations in the present study. First, this is a retrospectively study with a limited possibility of diagnosis (primary lung cancer and tuberculoma) that may affect imaging interpretation and cause many bias. Second, no dynamic enhancement technique was used for evaluate nodule enhancement in this retrospective study. Therefore, this may effect nodule enhancement analysis. Third, the number of subjects is small, especially the pulmonary tuberculoma group. This could be due to most favor benign nodules were not confirmed by tissue diagnosis. The small number of subjects affects the statistical analysis. Because of this limitation, the authors suggested that further study with a larger group would help radiologists to differentiate primary lung cancer from pulmonary tuberculoma with more confidence.

In conclusion, the solitary lesion with spiculated border, contrast enhancement, presence of air bronchogram, punctate calcification, and bronchovascular invasion are useful CT findings for diagnosis of primary lung cancer. However, the lesions with inconclusive findings, tissue diagnosis may be necessary.

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Potential conflicts of interest

None.

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การวินิจฉัยแยกก้อนมะเร็งปอดขนาดเล็กจากวัณโรคปอดชนิดเป็นก้อนโดยใช้เอกซเรย์คอมพิวเตอร์ชนิด 64 สไลด์

กันยารัตน์ โตธนะรุ่งโรจน์, สุธาสินี เชานโพธิ์ทอง, ตรงธรรม ทองดี

วัตถุประสงค์: *เพื่อศึกษาว่าลักษณะทางเอกซเรย์คอมพิวเตอร์ใดที่ช่วยในการวินิจฉัยแยกก้อนมะเร็งปอดขนาดเล็กจากวัณโรคปอดชนิดเป็นก้อน*

วัสดุและวิธีการ: *รังสีแพทย์ 2 คน ทำการศึกษาลักษณะทางเอกซเรย์คอมพิวเตอร์ทรวงอกของก้อนในปอดขนาดเส้นผ่าศูนย์กลาง ≤ 3 ซม. ในผู้ป่วยที่ได้รับการวินิจฉัยว่าเป็นมะเร็งปอด (27 ราย) และวัณโรคปอด (15 ราย) ลักษณะทางเอกซเรย์คอมพิวเตอร์ของก้อนเนื้องอกที่ศึกษา ได้แก่ จำนวน, ขนาด, รูปร่างและขอบของก้อน, ตำแหน่ง, ก้อนขนาดเล็กที่อยู่โดยรอบ, การเพิ่มขึ้นของค่าความทึบรังสีหลังฉีดสารทึบรังสี, ส่วนประกอบภายในก้อน ได้แก่ ลมในหลอดลม, หินปูนและโพรงอากาศ, การลุกลามของหลอดเลือดและหลอดลม และการทำลายกระดูกที่พบร่วมด้วย*

ผลการศึกษา: *ประมาณร้อยละ 96 ของมะเร็งปอดพบเป็นก้อนเดี่ยว ในขณะที่วัณโรคปอดชนิดเป็นก้อนพบประมาณร้อยละ 60 ก้อนขนาดใหญ่กว่า 2 ซม. ถึง 3 ซม. มีโอกาสเป็นมะเร็งปอดมากกว่าวัณโรคปอดชนิดเป็นก้อน ทั้งมะเร็งปอดและวัณโรคปอดชนิดเป็นก้อนสามารถพบได้ทุกส่วนของปอดแต่จะพบบ่อยที่ปอดกลีบบน วัณโรคปอดชนิดเป็นก้อนมักจะมีรูปร่างกลม หรือ เป็นรูปหลายเหลี่ยมและขอบเรียบ ในขณะที่ก้อนมะเร็งปอดมักจะรูปร่าง lobulate และขอบไม่เรียบ วัณโรคปอดชนิดเป็นก้อนมักจะมีก้อนขนาดเล็กที่อยู่โดยรอบมากกว่าก้อนมะเร็งปอด ถึงแม้จะไม่มีนัยสำคัญทางสถิติ วัณโรคปอดชนิดเป็นก้อนมักจะพบหินปูนแบบก้อนตรงกลาง ส่วนก้อนมะเร็งปอดมักจะพบหินปูนแบบ punctate ส่วนใหญ่ก้อนมะเร็งปอดและวัณโรคปอดชนิดเป็นก้อนไม่พบโพรงอากาศภายในก้อน การเพิ่มขึ้นของค่าความทึบรังสีหลังฉีดสารทึบรังสี, พบลมในหลอดลมภายในก้อน, และการลุกลามของหลอดเลือดและหลอดลมข้างเคียง จะพบในก้อนมะเร็งปอดมากกว่าวัณโรคปอดชนิดเป็นก้อนอย่างมีนัยสำคัญทางสถิติ ($p < 0.05$) ไม่พบการทำลายกระดูกในภาพเอกซเรย์คอมพิวเตอร์ของก้อนมะเร็งปอดและวัณโรคปอดชนิดเป็นก้อน*

สรุป: *ลักษณะทางเอกซเรย์คอมพิวเตอร์ของก้อนเดี่ยวในปอดที่มีขอบเขตไม่เรียบ, พบหินปูน ชนิด punctate และลมในหลอดลมภายในก้อน, มีการเพิ่มขึ้นของค่าความทึบรังสีหลังฉีดสารทึบรังสี และมีการลุกลามของหลอดเลือดและหลอดลมข้างเคียง จะช่วยในการวินิจฉัยมะเร็งปอดขนาดเล็กได้ แต่ในบางกรณีการอาศัยลักษณะทางเอกซเรย์คอมพิวเตอร์ของก้อนในปอดเพียงอย่างเดียวก็ไม่สามารถให้การวินิจฉัยได้อย่างมั่นใจ ต้องอาศัยการพิสูจน์ชิ้นเนื้อร่วมด้วย*