Evaluation of Pulmonary Metastases in Children by Non-Contrast Chest Computed Tomography

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Background: *Most of the metastatic lung lesions are relatively high contrast in comparison to the lung background and easily detected in non-contrast enhancement chest computed tomography alone (NECCT). Pediatric patients may get benefit from its minimal radiation dose and lack of adverse reaction from iodinated contrast agent.*
Objective: *To compare effectiveness of non-contrast enhancement chest computed tomography (NECCT) in detecting thoracic metastasis with full protocol chest computed tomography (FPCCT) (chest computed tomography with and without contrast) in non-hematologic extrathoracic malignancy in children.*
Material and Method: *Both NECCT and FPCCT were evaluated in 50 pediatric patients with non-hematologic extrathoracic malignancy retrospectively. Lung nodules, ground glass opacities, interlobular septal thickening, pleural effusion, pleural thickening, pericardial effusion, endobronchial lesion, and intravascular metastasis were evaluated separately on each CT protocol by two radiologists.*
Results: *Thirty boys and 20 girls were included in the present study (mean age = 10 years and 3 months). The lesions include nodule (333 detected by NECCT (median = 3), 336 detected by CECCT (median = 3)), ground glass opacity (12 detected by NECCT (median = 0), 15 detected by CECCT (median = 0)), interlobular septal thickening (12 detected by NECCT (median = 0), 11 detected by CECCT (median = 0)). There was 100 percent match of calcified nodules (n = 36), pleural effusion (n = 1), pleural thickening (n = 3), intravascular thrombus (n = 2), and mediastinal lymph node (n = 1) between NECCT and FPCCT studies. There was no statistically significant different in capability of demonstrating all lesions between NECCT and FPCCT. Most of the discrepancies between NECCT and FPCCT were from motion artifact, inadequate inspiration, and radiologist's opinion rather than effect of contrast agent administration itself.*
Conclusion: *NECCT is as effective as FPCCT in evaluation of pulmonary metastasis in non-hematologic extrathoracic malignancies. For evaluation of lung metastases in this population, NECCT alone is sufficient.*

Keywords: *Computed tomography, Non-contrast chest computed tomography, Lung metastasis, Radiation reduction, Radiation dose reduction*

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Thorax is one of the most common sites of metastasis in the patient affected by a variety of cancers. Chest computed tomography (CCT) is an excellent imaging modality in detecting lung metastatic nodules compared to surgical palpation and it has the ability to demonstrate a nodule as small as 1 millimeter in diameter[1,2]. However, because CCT has a relatively higher radiation dose than chest radiograph, it should be used with awareness of potential radiation injury especially in children[3,4]. Contrast agents are routinely administrated during CCT. However, a previous study reported 0.18% adverse reaction in pediatric population. There were 15% of the pediatric patients, affected by contrast adverse reaction, were classified as severe cases[5]. Because most of the metastatic lesions such as nodules, interlobular septal thickening, pleural effusion, pericardial effusion, endobronchial lesion present on CCT as focal hyperdense areas surrounded by low attenuation background of the lung parenchyma which are quite easily detected on non-contrast chest computed tomography (NECCT). The authors have made a hypothesis that a contrast study might not be necessary to identify these lesions and NECCT alone is probably sufficient to demonstrate thoracic metastatic

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lesions. The authors have excluded hematologic malignancies such as lymphoma and leukemia because they often manifest as mediastinal lymphadenopathy, which are best seen on contrast enhancement computed tomography (CECCT) and NECCT alone is not sufficient to evaluate lung involvement in this population.

The objective of the present study was to evaluate effectiveness of NECCT in demonstrating pulmonary and thoracic metastasis in comparison to those on full protocol computed tomography (FPCCT) (CCT with and without contrast) in children with non-hematologic extrathoracic malignancy.

Material and Method

The present study protocol was approved by the Ethics committee of the Faculty of Medicine Siriraj Hospital, Mahidol University (Si577/2009) in which the informed consent was waived due to its retrospective design.

Study population

The present study was retrospectively performed by searching a list of patients from the radiology report database who were younger than 15 years old and underwent CCT in Siriraj Hospital between September 2008 and September 2009. The exclusion criteria includes 1) no known history of malignancy 2) known case of primary intra-thoracic cancer 3) known case of hematologic malignancy 4) CCT done with protocols other than standard FPCCT 5) poor quality CCT. Of all 223 CCT studies retrieved from the database, only 96 studies were performed to evaluate thoracic involvement of known malignancy. After excluding cases of hematologic malignancy, there were only 50 cases eligible for analysis.

Imaging techniques

All of the imaging studies were performed with 64-slice CT scanners (Light speed VCT XTe, GE healthcare). The scan parameters including slice thickness (1.25-1.5 mm), kilovoltage (80 or 120 Kvp) and milli-ampere per second (60-120 mAs) were individually considered by pediatric radiologist to fit each patient with radiation dose awareness. The CECCT scans were performed by using standard non-ionic contrast agents through the peripheral venous access. The doses of the contrast agent vary between 1 and 2 milliliter/kilogram. In neonates, infants, or young children, the contrast agents were manually injected. However, in older children, the contrast agents were injected by using automated injector. The choice of manually or automated injection were judged individually by pediatric radiologists.

Data collection and image interpretation

The patient's clinical background including sex, age, weight, type of cancer, grading of cancer, vascular and lymphatic invasion, primary site of cancer, stage of cancer, site of metastasis, treatment complication, were recorded. The details of CCT technique such as milli-ampere, kilovoltage, and slice thickness were also recorded.

The images of each patient were divided into two sets, NECCT, and FPCCT images (combination of NECCT and CECCT images). These two sets of images of each patient were reviewed by an experienced chest radiologist (WS) and pediatric radiologist (IK) with the authors' standard PACS workstation (Fuji-synapse®) without knowing the patients' clinical background. Each set of images was randomly presented to the reviewers. When sets of NECCT were reviewed, the reviewers were not allowed to look at the CECCT series in the same case. The reviewers were allowed to perform image manipulation techniques such as window and level adjustment, multiplanar reformat, maximum intensity projection, average intensity projection, and minimum intensity projection. The final imaging findings were determined by consensus.

The lung nodule is defined as a round or irregular opacity, may be well or poorly defined, measuring up to 3 centimeters in diameter. Calcified nodule is defined as a nodule, which consisted of bone attenuation component. Ground glass (GG) nodule is defined as nodule with hazy increased attenuation in the lung that does not obliterate the bronchial and vascular margins. Consolidation appears as a homogenous increased in pulmonary parenchymal attenuation that obscures the margins of the vessels and airway walls. Interlobular septal thickening defined as thickening of interlobular septa, may be smooth or nodular. Intravascular and intracardiac thrombus is defined as filling defect in the pulmonary vessels and heart respectively that does not show enhancement on CECCT. The lymph node is considered to be significant if its short axis is greater than 1 centimeter. The reviewers were assigned to count the number of nodules, calcified nodules, ground glass nodules, and consolidation. For interlobular septal thickening, pleural effusion, pericardial effusion, endobronchial lesion, abnormal calcification, intracardiac thrombus,

intravascular thrombus, lymphadenopathy, and chest wall lesion, the reviewers were assigned to identify as presence or absence[6].

Statistical analysis

The Intraclass correlation and Wilcoxon sign-rank test was used to assess differences between two sets of images from the same patients. The p-values <0.05 indicate a statistically significance. The statistical analysis was calculated by using SPSS (SPSS: An IBM Company, version 16.0.2).

Results

Patient's data and scanning techniques

Of the 50 included cases, 30 were boys and 20 were girls. Average age was 10 years and 3 months (7 months old-16 years old). The average weight was 31.3 kilograms (7-63.8 kilograms). In terms of scanning technique, most of the cases were scanned with 1.25 mm slice thickness interval. However, four cases were scanned with 1.5 mm. Four cases scanned with kVp = 80 and the others were scanned with kVp = 120. The mAs ranged from 70 to 500 depending on size and weight of the patient. The list of primary malignancies is shown in Table 1.

CT chest findings

Of the 50 included cases, there were 333 and 336 non-calcified nodules detected by NECCT and FPCCT respectively. The median of non-calcified nodules detected by NECCT was 3 (0-36). The median of non-calcified nodules detected by FPCCT was 0 (0-36). There is no statistical significance between NECCT and FPCCT (p = 0.762).

There were 12 GG opacities detected on NECCT (median = 0) while 15 were detected by FPCCT (median = 0). Twelve interlobular septal thickenings were detected on NECCT (median = 0) while 11 were detected by FPCCT (median = 0). There is no statistical significance between NECCT and FPCCT in detection of GG opacity and interlobular septal thickening (p = 0.180 and 0.157 respectively).

There is 100% match of calcified nodules (n = 36), pleural effusion (n = 1), pleural thickening (n = 3), intravascular thrombus (n = 2), and mediastinal lymph node (n = 1) between NECCT and FPCCT studies. There is one case that the contrast study showed poor demonstration of paratracheal lymph node due to streak artifact from high concentration of contrast in left branchiocephalic vein. However, this group of lymph nodes was considered to be insignificant (less than 1 centimeter in short axis).

Table 1. Underlying primary malignancy diagnosed at time of CCT examination (n = 50)

Primary neoplasm	Number of patients (%)
Osteosarcoma	16 (32)
Ewing's sarcoma	6 (12)
Wilms tumor	6 (12)
Neuroblastoma	5 (10)
Rhabdomyosarcoma	5 (10)
Hepatoblastoma	4 (8)
Fibrosarcoma	2 (4)
Desmoplastic small round cell tumor	2 (4)
Adrenocortical carcinoma	2 (4)
Malignant peripheral nerve sheath tumor	1 (2)
Choriocarcinoma	1 (2)
Total	50 (100)

Discussion

Most of the pulmonary neoplasms are metastasis rather than primary in origin. The common pediatric pulmonary metastases include Wilms tumor, osteogenic sarcoma, Ewing's sarcoma and rhabdomyosarcoma[7]. With 16 channel multi-detector row CT scanner the tiny lung nodule as small as 1 mm in diameter can be easily detected with sensitivity and specificity as high as 97% and 54% respectively[1]. Because children have relatively more sensitive to radiation than adults, therefore CT protocol should be customized to lower the radiation dose as much as possible to prevent the risk of radiation injury and potential risk of cancer[8]. According to the fact that most of the metastatic nodules present with non-calcific nodule, calcific nodule, or ground glass nodules, which all of them have good contrast attenuation in comparison to the lung parenchymal background. For this reason, these nodules should be well demonstrated equally on both NECCT and CECCT.

Few researchers studied effectiveness of non-contrast enhancement CCT in evaluating lung metastasis. Margaritora et al (2002) has compared helical CT and HRCT (without contrast administration) in detecting lung metastasis in 356 surgical proven nodules. They have found that HRCT has slightly lower sensitivity in detecting lung metastasis (75%) than that of helical CT (82%). However, both modality have

limitation in assessment of pulmonary nodule less than 6 millimeters[9]. Hirakata et al (1993) has compared appearance of pulmonary metastasis on HRCT with autopsy findings. They have found good correlation between appearance of pulmonary nodule and histological findings on autopsy. They have also reported limitation of HRCT in detecting intravascular tumour emboli and lymphangitic spread[10]. In contrast, the present study shows no significant difference in detecting pulmonary nodules between NECCT and FPCCT.

FPCCT detected three nodules more than NECCT. The discrepant nodules occur due to poor inspiration seen on NECCT but the patient was able to perform adequate deep inspiration breath hold on CECCT, resulting in aerated lung parenchyma and better visualization of lung nodule. Other two missing nodules on NECCT occurred because of respiratory motion artefact. They were seen on NECCT but did not occur on post-contrast phase (Fig. 1).

GG opacity is one of the most common findings in CCT. This lesion is non-specific and could be found in both benign and malignant process[11]. In the present study, there were 12 GG opacities seen on NECCT while 15 GG were detected on FPCCT. The main reason for discrepancy is radiologist opinion rather than technical problem. After re-discussing between two radiologists, 15 GG opacities were unequivocally agreed on both NECCT and FPCCT. The authors concluded that there is no difference between NECCT and FPCCT in detecting ground glass opacity.

There were twelve interlobular septal thickening detected on NECCT while only 11 were seen on CECCT. The reason of discrepancy was motion artefact during CECCT obscuring visualization of the lesion in one of the cases (Fig. 2).

In terms of mediastinal lymph node evaluation, the result of the present study correlates with many previous studies comparing between NECCT and CECCT in detecting mediastinal lymph nodes in adult patients. Cascade et al (1998) demonstrated no statistically significant difference in detection of mediastinal lymph node between NECCT and CECCT of the chest in 50 adult patients with lung cancer. Similarly the results of Takahashi et al (2008) which showed contrast administration had low benefit in detection of mediastinal lymph nodes if thin slice axial and multiplanar reformatted were used. Haramati et al (1995) demonstrated effectiveness of 5 millimeters thickness NECCT in detection of mediastinal lymph node compared to that of 10 millimeters[12-14]. The authors concluded that with the appropriate scanning technique and image manipulation CECCT might not be necessary for evaluation mediastinal lymphadenopathy. One of the patients in the present study showed worse visualization of the mediastinal lymph node on CECCT due to beam hardening streak artifact from dense contrast material in left brachiocephalic vein obscuring enlarged lymph node in right paratracheal region. This artifact can be

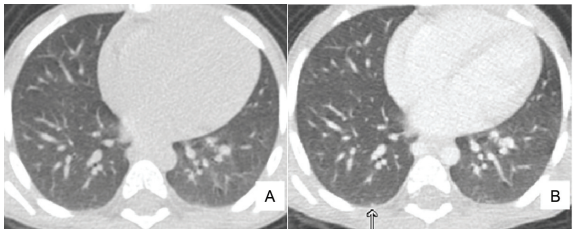

Fig. 1 A 1-year-old girl who had neuroblastoma with lung metastasis. (A) On NECCT there is subtle haziness at dependent part of the both basal lung due to relatively poor inspiration make the tiny nodule at the posterior right basal difficult to be detected. (B) On CECCT, with adequate inspiration, the tiny nodule (arrow) was better visualized in comparison to that on NECCT.

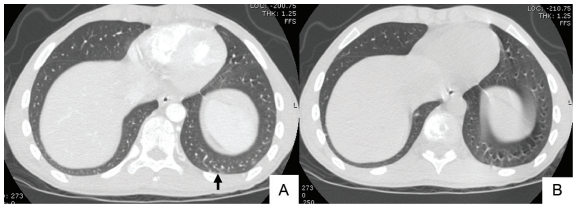

Fig. 2 A 12-year-old girl with choriocarcinoma of the pineal gland. (A) NECCT demonstrated interlobular septal thickening at the posterior left basal lung (black arrow). (B) On CECCT the interlobular septal thickening is obscured by motion artifact.

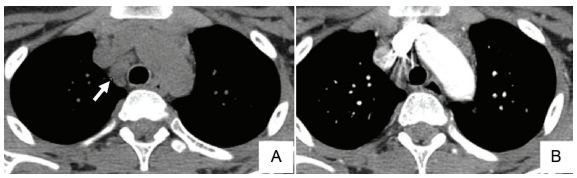

Fig. 3 A 13-year-old boy with adrenocortical carcinoma had significant lymphadenopathies at right paratracheal region which were better demonstrated on NECCT (arrow). (A) On post-contrast study (B) this lymph nodes were obscured by streak artifact due to high concentration of contrast in left brachiocephalic vein.

minimized by flushing brachiocephalic vein with dual chamber injector[15] (Fig. 3).

There is a perfect match between NECCT and FPCCT in detecting calcified nodule, pleural effusion, pleural thickening, pericardial effusion, endobronchial lesion. In the authors' opinion, contrast study is not necessary to identify these CT findings. Budoff et al (2000) reported excellent capability of electron beam CT in depicting pericardial sinus and pericardial fluid. The present study agrees with their result[16].

The present study demonstrated a perfect match between NECCT and FPCCT in detecting intravascular thrombus. However, this result was probably unreliable because all of the lesions found were pulmonary metastatses of osteosarcoma. The reason is that most metastatic osteosarcomas demonstrate calcifications due to new bone formation making intravascular metastases quite easy to be detected on NECCT. If the present study has non-calcific intravascular thrombus, FPCCT may show superior capability in demonstrating this kind of lesion. The authors have found that most of discrepancies in the present study are predominately due to radiologist opinion and technical error such as motion artifact or atelectasis rather than effect of contrast administration itself.

There are several limitations in the present study; first one is its retrospective design resulting in heterogeneity of the CT protocol. Due to the present study limiting to extrathoracic primary and non-hematologic malignancy so the result cannot be applied to other groups of malignancy. Some of the lesions were rare in the present study such as pleural thickening; pericardial effusion, pleural effusion endobronchial lesion, and intravascular thrombus make it difficult to do subgroup analysis. Finally, the present study mainly focuses on ability to demonstrate lesions in NECCT and FPCCT. However, the ability to make differentiation between benign and malignancy nodule is beyond scope of the present study.

Conclusion

NECCT is as effective as FPCCT in evaluation of pulmonary metastasis in non-hematologic extra-thoracic malignancies. For evaluation of lung metastases in this population, NECCT alone is sufficient.

Abbreviations

CT = computed tomography, CCT = chest computed tomography, NECCT = non-contrast enhancement chest computed tomography, CECCT = contrast enhancement chest computed tomography, FPCCT = full protocol chest computed tomography, GG = ground glass, HRCT = high resolution chest computed tomography

Potential conflicts of interest

None.

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ประสิทธิผลของการตรวจทรวงอกด้วยเอกซเรย์คอมพิวเตอร์โดยไม่ฉีดสารทึบรังสีในการตรวจหาก้อนมะเร็งแพร่กระจายมาที่ปอด

เกรียงไกร เอี่ยมสวัสดิกุล, สุวิมล วงศ์ลักษณะพิมล, วราลี มิ่งขวัญสุข, วิมลรัตน์ หล่อนิมิตดี

วัตถุประสงค์: *เพื่อศึกษาประสิทธิผลของการตรวจทรวงอกด้วยเอกซเรย์คอมพิวเตอร์ โดยไม่ฉีดสารทึบรังสีในผู้ป่วยเด็กที่เป็นมะเร็งปฐมภูมินอกทรวงอกนอกเหนือจากมะเร็งโลหิต โดยการเปรียบเทียบกับการตรวจเต็มรูปแบบ (ประกอบด้วยการตรวจชนิดทั้งฉีดและไม่ฉีดสารทึบรังสี)*

วัสดุและวิธีการ: *ผู้นิพนธ์ได้ศึกษาย้อนหลังโดยการวิเคราะห์ภาพเอกเรย์คอมพิวเตอร์ทรวงอกในผู้ป่วยเด็ก 50 ราย โดยใช้รังสีแพทย์ 2 คน ประเมินก้อนในปอดชนิดไม่มีหินปูน ก้อนในปอดชนิดมีหินปูน รอยฝ้าในเนื้อปอด ผนังกลีบปอดหนาตัว น้ำในช่องเยื่อหุ้มปอด เยื่อหุ้มปอดหนาตัว น้ำในช่องเยื่อหุ้มหัวใจ เยื่อหุ้มหัวใจหนา ลิ่มเลือดในหลอดเลือด และมะเร็งแพร่กระจายในต่อมน้ำเหลืองในภาพการตรวจเอกซเรย์คอมพิวเตอร์ทั้งแบบไม่ฉีดสารทึบรังสีและแบบปกติเต็มรูปแบบแยกกัน*

ผลการศึกษา: *กลุ่มตัวอย่างมีผู้ป่วยเด็กชาย 30 ราย และผู้ป่วยเด็กหญิง 20 ราย (อายุเฉลี่ย 10 ปี 3 เดือน) ความผิดปกติที่พบได้แก่ ก้อนในปอดชนิดไม่มีหินปูน (พบ 333 ก้อน (ค่ามัธยฐานเท่ากับ 3) และ 336 ก้อน (ค่ามัธยฐานเท่ากับ 3) จากการตรวจทรวงอกโดยเอกซเรย์คอมพิวเตอร์แบบไม่ฉีดสารทึบรังสีและการตรวจเต็มรูปแบบตามลำดับ) รอยฝ้าในเนื้อปอด (พบ 12 แห่ง (ค่ามัธยฐานเท่ากับ 0) และ 15 แห่ง (ค่ามัธยฐานเท่ากับ 0) จากการตรวจทรวงอกโดยเอกซเรย์คอมพิวเตอร์แบบไม่ฉีดสารทึบรังสีและการตรวจเต็มรูปแบบตามลำดับ) ผนังกั้นกลีบปอดหนา (พบ 12 แห่ง (ค่ามัธยฐานเท่ากับ 0) และ 11 แห่ง (ค่ามัธยฐานเท่ากับ 0) จากการตรวจทรวงอกโดยเอกซเรย์คอมพิวเตอร์แบบไม่ฉีดสารทึบรังสีและการตรวจเต็มรูปแบบตามลำดับ) ส่วนรอยโรคอื่น เช่น ก้อนในปอดชนิดมีหินปูน (พบ 36 ก้อน) น้ำในช่องเยื่อหุ้มปอด (พบ 1 แห่ง) เยื่อหุ้มปอดหนา (พบ 3 แห่ง) มะเร็งอุดหลอดเลือด (พบ 2 แห่ง) และต่อมน้ำเหลืองในทรวงอกโต (พบ 1 แห่ง) พบว่าการตรวจทั้งสองแบบเห็นตรงกัน ผลการศึกษานี้ไม่พบความแตกต่างอย่างมีนัยสำคัญของการเห็นรอยโรคระหว่างการตรวจทรวงอกด้วยเอกซเรย์คอมพิวเตอร์แบบไม่ฉีดสารทึบรังสีและแบบปกติเต็มรูปแบบ โดยสรุปแล้วความแตกต่างในการเห็นรอยโรคระหว่างการตรวจทั้งสองแบบส่วนมากมาจากปัญหาด้านเทคนิคการตรวจและความเห็นของรังสีแพทย์มากกว่าผลจากการฉีดสารทึบรังสี*

สรุป: *การตรวจทรวงอกด้วยเอกซเรย์คอมพิวเตอร์แบบไม่ฉีดสารทึบรังสีมีประสิทธิผลดีเท่ากับการตรวจเต็มรูปแบบ สำหรับการตรวจหามะเร็งแพร่กระจายมาที่ปอดในกลุ่มประชากรดังกล่าว การตรวจทรวงอกด้วยเอกซเรย์คอมพิวเตอร์แบบไม่ฉีดสารทึบรังสีมีประสิทธิผลเพียงพอสำหรับการวินิจฉัย*