Role of Chest Radiography in the Diagnosis and Follow-Up of Pulmonary Metastasis in Differentiated Thyroid Cancer

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Background: *Post-treatment I-131 whole body scan (WBS) is known to be a very sensitive test in detecting metastasis in differentiated thyroid cancer (DTC). Therefore, in the presence of this sensitive method, the role of chest radiography (CXR) in the diagnosis of pulmonary metastasis has been questioned.*
Objective: *The present study aimed to find the prevalence of pulmonary metastasis found on CXR in DTC patients who had negative post-treatment WBS.*
Material and Method: *Retrospective comparison was undertaken of CXR and post-treatment WBS routinely performed in 300 DTC patients during the time of I-131 treatment from January 2003 to December 2006 in the Department of Radiology. Radiographic patterns of pulmonary metastasis classified as single nodule, multiple nodules, lymphangitic metastasis and pleural metastasis were also recorded.*
Results: *Of the 300 DTC patients, 36 pulmonary metastases (12.0%) were diagnosed based on CXR and post-treatment I-131 WBS. Of these 36 cases, 11 (30.6%) were detected by both CXR and WBS, whereas 16 (44.4%) were detected by WBS alone and 9 (25.0%) by CXR alone. Seven of these 9 cases (77.8%) had lymphangitic pattern of pulmonary metastasis.*
Conclusion: *Although routine CXR has a limited role in the diagnosis of pulmonary metastasis in DTC patients being treated with I-131, it is helpful in detecting pulmonary metastasis in patients with negative post-treatment WBS.*

Keywords: *Differentiated thyroid cancer, Chest radiography, Whole-body scan, Pulmonary metastasis*

J Med Assoc Thai 2010; 93 (Suppl. 3): S52-60
Full text. e-Journal: *http://www.mat.or.th/journal*

Differentiated thyroid cancer (DTC) is the most common endocrine malignancy. Current standard treatment includes total or near-total thyroidectomy, followed by radioiodine (I-131) treatment and thyroid hormone suppressive therapy[1]. After initial treatment, life-long follow-up is mandatory to early detect tumor recurrence, and is usually performed by I-131 whole body scintigraphy (WBS), neck ultrasonography and serum thyroglobulin[2].

Distant metastasis is not uncommon during the course of DTC. One of the most common sites is in the lung[3-5]. This can be found either at the time of initial diagnosis or at a later stage, even after disease remission, with the reported rates varying approximately from 4-69%[6-8]. Pulmonary metastasis can be readily detected by post-treatment WBS performed 4-10 days after I-131 treatment despite a negative diagnostic I-131 WBS with 74-185 MBq of I-131[9]. Chest radiography (CXR) is another tool usually performed to detect and evaluate metastatic lesions in the lungs in patients with malignancy. However, there have been some studies reporting a significantly higher sensitivity of I-131 WBS compared to CXR in the detection of pulmonary metastasis in DTC patients[10,11]. Therefore, the role of CXR as a routine use in the detection and follow-up of pulmonary metastasis has been questioned, particularly with the presence of the more sensitive method of I-131 post-treatment WBS.

In order to evaluate whether the role of routine CXR should still exist in the management of DTC patients, the authors aimed to find the prevalence of lung metastasis i n DTC patients scheduled for I-131

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treatment, who had negative I-131 WBS but positive CXR.

Material and Method

Patients

A retrospective chart review was conducted of all consecutive DTC patients who received I-131 treatment at the Department of Radiology, Srinagarind Hospital, Khon Kaen University, from January 2003 to December 2006. The present hospital is a public tertiary care hospital and has approximately 150-170 new DTC patients a year referred for I-131 treatment. There were 630 patients admitted for high-dose I-131 treatment during the study period. The authors' inclusion criteria included patients who were administered high-dose I-131 treatment during this 4-year period and had both I-131 post-treatment WBS and CXR performed within 2 weeks. The authors excluded patients with a known history of primary cancer at other sites, patients with advanced DTC disease who received external radiation therapy or chemotherapy before the study period, and patients receiving contrast media for radiographic procedures within 8 weeks before I-131 treatment. There were 300 eligible patients meeting these criteria and they were all enrolled for analysis. Each patient was followed-up until June 2007 before analysis. The protocol was approved by the Ethics Committee for Human Research, Khon Kaen University, before commencing the study.

I-131 therapy and whole-body scan protocol

Of all 300 patients, 271 (90.3%) received I-131 treatment for the first time, mostly at 4-6 weeks post thyroidectomy, while 27 (9.0%) and 2 (0.7%) cases received I-131 treatment as the second and the third dose respectively.

I-131 was administered 4-6 weeks after thyroidectomy with the dose ranging from 3,700 to 7,400 MBq depending on the spread of the disease, documented mainly by clinical findings together with the pathology report and, in a very limited number of patients, on pre-treatment I-131 WBS. Post-operative pre-treatment I-131 WBS was not routinely performed. The exception was in the cases of suspected large thyroid remnant or brain metastasis. All patients took no thyroid hormone during this early postoperative period. Low-iodine diet for 2 weeks was recommended to all patients before I-131 therapy. On the day of hospital discharge or within 4 to 8 days after I-131 therapy, I-131 post-treatment WBS was performed to evaluate the presence of thyroid remnant and the extent of metastasis. Thyroid hormone suppressive therapy by thyroxin was initiated 2 to 3 days after I-131 treatment and serum TSH was monitored 3 months later to ensure that adequate suppression was achieved.

About 6 months after treatment, follow-up I-131 WBS using 74-185 MBq of I-131 was scheduled after a 4-week withdrawal of thyroxin. Re-treatment with I-131 was considered if there was residual thyroid remnant or persistent metastasis.

Chest radiography

CXR was routinely performed as a part of laboratory investigation on the day of hospital admission for a high-dose I-131 treatment irrespective of the presence of pulmonary symptoms. Diagnosis of pulmonary metastasis was documented if there was any one of the four radiographic findings suggestive of pulmonary metastatic pattern including single pulmonary nodule, multiple pulmonary nodules, lymphangitic metastasis, or pleural metastasis (Fig. 1).

Thyrotropin, thyroglobulin and anti-thyroglobulin antibody measurements

Serum thyrotropin (TSH), thyroglobulin (Tg) and thyroglobulin autoantibody (anti-Tg) were routinely measured on the day of hospital admission for high-dose I-131 treatment. Serum TSH was measured by radioimmunoassay using RIA-gnost®hTSH (Schering CIS Bio International). Serum Tg was measured using immunoradiometric assay of serum human Tg (CIS Bio International, France) which had a functional assay sensitivity of 0.2 ng/mL. Serum anti-Tg was measured using a semi-quantitative agglutination test (SERODIA®-ATG, Fujirebio Inc, Tokyo, Japan). Both serum Tg and anti-Tg tests were performed with assay kits from the same manufacturer during the entire study period.

Data analysis

The results of 300 paired studies, post-treatment I-131 WBS and CXR, performed at the time of I-131 treatment were analyzed. Although there were some patients receiving I-131 treatment more than once during the authors' study period, only the paired studies corresponding to the first I-131 treatment administered during this period were included. All relevant data were recorded including gender, age at the time of diagnosis, histologic types and tumor extension, type of surgery, pulmonary symptoms, date and number of the I-131 treatment, cumulative I-131 administered dose, and concomitant serum Tg, anti-Tg and TSH at the time of

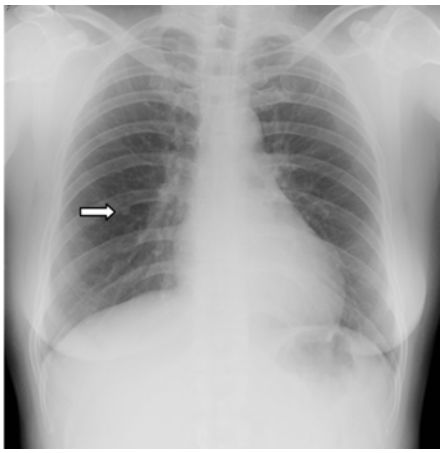

Fig. 1a Solitary pulmonary nodule.

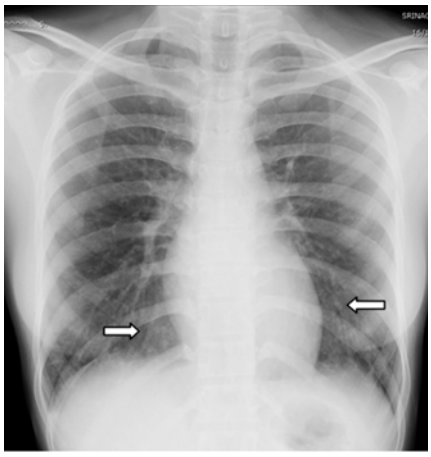

Fig. 1b Multiple pulmonary nodules.

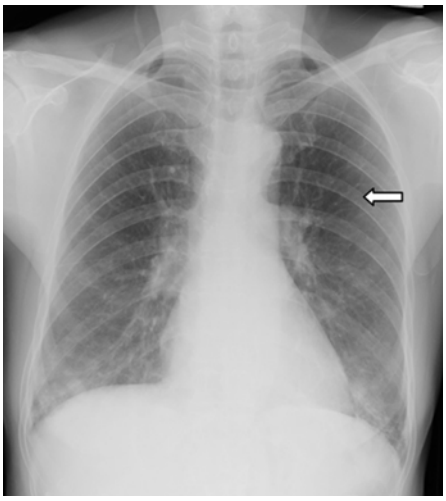

Fig. 1c Lymphangitic metastases.

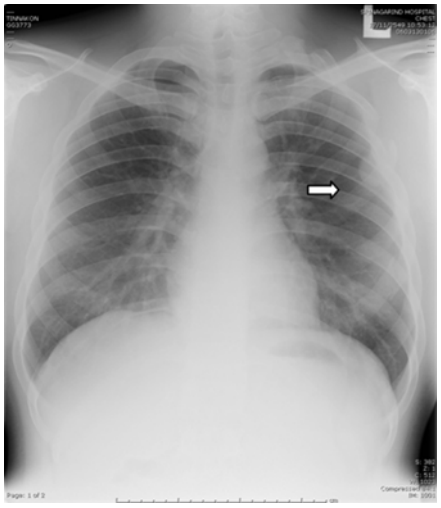

Fig. 1d Pleural metastases.

I-131 treatment.

Post-treatment WBS was independently reviewed by two nuclear medicine physicians (13 and 8 years experience). The discordant results were later discussed to reach a consensus. CXR was independently reviewed by two radiologists (9 and 2 years experience). A consensus was also reached by discussion.

Statistical analysis

Categorical data are shown as number and percentage, whereas continuous data are shown as mean and SD or median and interquartile range as appropriate. Un-weighted Kappa statistics were used to evaluate the degree of agreement between readers who reviewed CXR, between readers who reviewed post-treatment WBS, and for agreement between the two tests in the diagnosis of pulmonary metastasis.

Results

There were 300 eligible patients included for analysis. Of these, there were 243 cases (81.0%) with papillary carcinoma and 57 cases (19.0%) with follicular carcinoma. The mean age at the time of diagnosis was 43.4 years (SD 14.3, range 9-79). Ages younger or older than 45 years old were categorized according to known low and high risk of cancer mortality, respectively. The mean follow-up time was 22.1 months (SD 10.5, range 6-42). Total or near-total thyroidectomy was performed in 279 patients (93.0%), whereas subtotal thyroidectomy

was performed in 21 patients (7.0%). Pre-treatment I-131 WBS was performed in 9 patients (3.0%). Post-treatment WBS and CXR studies were mostly performed within one-week. Only nine studies (3.0%) were performed between 7 and 14 days apart. Two patients (0.7%) had hemoptysis during the time of I-131 treatment, while all the rest were asymptomatic. Characteristics of all patients are shown in Table 1.

Of 300 patients, 264 (88.0%) had negative pulmonary metastasis as shown by negative finding on both CXR and post-treatment WBS. However 10 of these 264 negative pulmonary metastatic cases (3.8%) revealed pulmonary non-metastatic disease detected on CXR. These included 6 with fibrosis, 2 with atelectasis, 1 with bronchiectasis and 1 with emphysema.

There were 36 of 300 cases (12.0%) diagnosed with pulmonary metastasis. The diagnosis was concordantly made by both CXR and post-treatment WBS in 11 cases, whereas in 16 cases the diagnosis was based only on WBS and 9 only on CXR (Table 2). There was a moderate agreement between two nuclear medicine physicians for I-131 WBS reading (Kappa 0.5), and a substantial agreement between the two radiologists on CXR interpretation (Kappa 0.68). The authors found a moderate agreement between WBS and CXR in the diagnosis of positive or negative pulmonary metastatic disease (91.7 percent agreement, Kappa 0.43).

Of 27 patients with positive pulmonary metastasis on the post-treatment WBS, the scan also revealed concomitant bone metastases in 2 patients and regional lymph node metastasis in another 3 patients.

Of 9 patients with negative WBS but positive CXR for pulmonary metastatic disease, 7 cases (77.8%) had radiographic appearance of lymphangitic metastasis, 1 (11.1%) with multiple nodular metastases and 1 (11.1%) with pleural metastasis. Considering radiographic appearance in 11 patients positive on both CXR and WBS, lymphangitic metastasis was found in only 3 cases (27.3%), whereas the most common radiographic finding in this group was multiple metastatic nodules (6 of 11 cases, 54.5%). Table 3 compares the frequency of radiographic patterns between the patients with negative and positive I-131 scans.

Of 9 patients undergoing pre-treatment I-131 WBS, 5 were negative for pulmonary metastasis on both CXR and post-treatment WBS, whereas the other 4 were CXR positive but I-131 WBS negative. Of these 4 cases of positive CXR, 2 were lymphangitic metastases; 1 was multiple nodular metastases and the other one was pleural metastasis. However, none of the pre-treatment WBS in these 9 patients showed positive radioiodine uptake in the lung.

The authors further explored the clinical course of 9 patients (7 women and 2 men) with positive CXR but negative I-131 WBS for pulmonary metastasis (Table 4). Of these 9 cases, follicular carcinoma was found in only 1 case, whereas the other 8 cases were papillary carcinoma. None of these patients had chest symptoms during the time of I-131 treatment.

Table 1. Patient characteristics (n = 300)

Characteristics	Value
Gender	
Male	53 (17.7%)
Female	247 (82.3%)
Age at the time of diagnosis *(year)	
≤ 45	171 (57.0%)
> 45	129 (43.0%)
Histopathology and tumor extension	
Papillary carcinoma	
- No extrathyroid extension	158 (52.7%)
- Regional lymph node metastasis	67 (22.3%)
- Extrathyroid local invasion	17 (5.7%)
- Both extrathyroid local invasion and regional lymph node metastasis	1 (0.3%)
Follicular carcinoma	
- No extrathyroid extension	54 (18.0%)
- Regional lymph node metastasis	3 (1.0%)
I-131 administered dose (MBq) *	
2,960	2 (0.7%)
3,700	169 (56.3%)
4,440	2 (0.7%)
5,550	122 (40.7%)
7,400	5 (1.7%)
Cumulative I-131 administered dose (MBq)	
Median (interquartile range)	3,700 (1,850)
Serum thyroglobulin (ng/mL)**	
Median (interquartile range)	7.3 (41.5)
Serum thyroglobulin autoantibody	
Negative	184 (61.3%)
Positive	42 (14.0%)
Data not available	74 (24.7%)

* The sum of the percentages is more than 100 percent due to rounding.
** Data from 252 patients (data not available in 48 patients).

Table 2. Concordance between I-131 whole body scan and chest radiograph in the diagnosis of pulmonary metastatic disease (Kappa = 0.43)

Test results n (%)		I-131 post-treatment scan		
		Negative	Positive	Total
Chestradiograph	Negative	264 (88.0%)	16 (5.3%)	280 (93.3%)
	Positive	9 (3.0%)	11 (3.7%)	20 (6.7%)
	Total	273 (91.0%)	27 (9.0%)	300 (100%)

Table 3. Chest radiographic pattern of pulmonary metastasis between patients with negative and patients with positive post-treatment whole body scan

Chest radiographic patterns	Post-treatment scan resultsn (%)	
	Negative (n = 9)	Positive (n = 11)
Solitary nodule	0 (0)	1 (9.1)
Multiple nodules	1 (11.1)	6 (54.5)
Lymphangitic metastasis	7 (77.8)	3 (27.3)
Pleural metastasis	1 (11.1)	1 (9.1)
Total	9 (100)	11 (100)

Discussion

Based on CXR and post-treatment I-131 WBS, 36 pulmonary metastases (12.0%) were diagnosed in 300 cases of the authors' cohort. Of these 36 cases, 11 (30.6%) were diagnosed by both CXR and WBS, whereas 16 (44.4%) were by WBS only and 9 (25.0%) by CXR only. Therefore, one-fourth of patients with pulmonary metastasis were able to be detected by CXR, but not by WBS. Of note, the majority of these cases (7 of 9 or 77.8%) had lymphangitic patterns of pulmonary metastasis.

CXR is generally the first examination performed in patients suspicious for pulmonary metastases. With a high sensitivity of post-treatment WBS in DTC however, the role of routine CXR in patients with DTC has been questioned. In 1994, Powell and co-workers[13] reported on the efficacy of CXR in the follow-up of 49 DTC patients treated at the Royal Marsden Hospital, London, and found that of 369 episodes of CXR during the mean follow-up time of 81 months, CXR was performed as a routine in 85%, whereas it was performed with a clear clinical indication in only 15%. Six of seven patients with abnormal chest radiograph were studied because they had elevated serum Tg, abnormal I-131 WBS or the presence of chest symptoms. They also found that none of the asymptomatic chest patients had abnormal findings on CXRon CXR. Powell and co-workers concluded that routine CXR was not cost-effective and was not sensitive enough to detect pulmonary metastasis in DTC patients and should be reserved for patients with chest symptoms or patients with positive anti-Tg.

The limited role of CXR was also extended to the pediatric group of thyroid cancer patients as reported by Bal and colleagues in 2004[14]. They found that 28 of 122 patients (23.0%) under the age of twenty had pulmonary metastases, and 21 of those 28 patients (75.0%) had negative CXR. In contrast, all of those 28 patients showed abnormal I-131 WBS. Therefore, they concluded that I-131 WBS, instead of CXR, should be used as a tool in the follow-up of pulmonary metastases in pediatric DTC patients.

Recently, a report on a 20-year follow-up retrospective study of the benefit of routine CXR in DTC patients from MD Anderson by Habra and co-workers[15] revealed that abnormal CXR was found in only 22 of 333 patients (6.6%). The authors recommended that without coexisting evidence, routine

Table 4. Clinical course of 9 patients with positive chest radiograph but negative I-131 whole body scan for pulmonary metastasis

Case No., Gender, Histology	I-131 treatment; dose (MBq)	Serum Tg	Serum anti-Tg	CXR finding	Site of I-131 uptake apart from the lung on post-treatment WBS
	Clinical course				
1, Female, Papillary carcinoma	1st; 5, 550	3.9	Pos	Lymphangitic	Remnant
	She received subsequent 3 episodes of 5,550 MBq of I-131 ablation and had persistent positive serum anti-Tg and persistent lymphangitic pattern on CXR but without lung uptake on post-treatment WBS.				
2, Female, Papillary carcinoma	2nd; 5, 550	6.5	Neg	Lymphangitic	Regional lymph nodes
	She developed bone metastasis at the sternum and progressive regional lymph node metastases early post I-131 treatment, and was lost to follow-up.				
3, Male, Papillary carcinoma	1st; 5, 550	30.3	Neg	Lymphangitic	Nil
	He received a subsequent empiric 3,700 MBq I-131 treatment and still had elevated serum Tg, negative serum anti-Tg, negative post-treatment WBS but persistent lymphangitic pattern on CXR.				
4, Male, Papillary carcinoma	1st; 5, 550	55.4	Neg	Lymphangitic	Remnant
	He developed right cervical lymph node metastases early after I-131 treatment and was lost to follow-up since then.				
5, Female, Papillary carcinoma	1st; 3, 700	0.9	Pos	Lymphangitic	Remnant
	She received subsequent 2 episodes of 3,700 MBq I-131 for remnant ablation and showed undetectable serum Tg and negative serum anti-Tg but persistent lymphangitic pattern on CXR, without lung uptake on post-treatment WBS. No recurrence was detected.				
6, Female, Papillary carcinoma	2nd; 5, 550	6.9	Neg	Lymphangitic	Remnant
	She had negative follow-up I-131 WBS 6 months after I-131 treatment with undetectable serum Tg and anti-Tg. No recurrence was detected.				
7, Female, Follicular carcinoma	1st; 5, 550	1,068.5	Neg	Pleural metastasis	Remnant and multiple bones
	She received 7,400 MBq of I-131 treatment 7 months after the first dose with evidence of multiple bony metastases but no lung uptake on post-treatment WBS. The concurrent CXR showed decrease in size of pleural metastatic lesion.				
8, Female, Papillary carcinoma	1st, 150	947.2	Neg	Multiple nodules	Remnant
	She was lost to follow-up since I-131 treatment.				
9, Female, Papillary carcinoma	1st, 100	0.1	Pos	Lymphangitic	Remnant
	She had negative follow-up I-131 WBS for 2 times with concomitant undetectable serum Tg, even persistently positive anti-Tg. No recurrence was detected.				

CXR, chest radiograph, Tg, thyroglobulin (ng/mL), Anti-Tg, thyroglobulin autoantibody, WBS, whole body scan, Pos, positive, Neg, negative

CXR has a very limited role in the follow-up of these patients.

The results of the authors' study were in accordance with those from the previous studies. Since pulmonary metastasis was found in only 12% of patients in the authors' cohort and one-fourth of them could be diagnosed exclusively by CXR, performing routine CXR in every patient to detect pulmonary metastasis would not be cost-effective. The authors recommend that CXR be performed only in patients with negative pulmonary metastasis on post-treatment WBS, in particular if there is other evidence suggestive of pulmonary metastasis such as unexplained elevated serum thyroglobulin.

High serum Tg level has been associated with the presence of metastatic disease in DTC patients particularly after successful remnant ablation[16]. In fact, Bachelot and colleagues proposed that one gram of DTC tissue could elevate serum Tg by 0.5-1 ng/mL[17]. However, serum Tg measurement can not locate the site of metastasis which is crucial information for further management.

Post-treatment WBS performed shortly after I-131 treatment has been established to provide a high sensitivity in determining the presence and

demonstrating the extent of metastatic lesions including in the lungs. In addition, the presence of radioiodine uptake in the lungs suggests that the metastatic cells are functioning and this had been reported to be associated with better prognosis compared with non-functioning pulmonary metastatic lesions[7]. However, false-negative pulmonary metastasis on I-131 WBS could occur in the presence of a large thyroid remnant because it may make radioiodine concentration in the pulmonary metastatic lesions indiscernible[18,19].

It is interesting that of all 20 cases with pulmonary metastases seen on the CXR, lymphangitic metastasis was the most frequently found in the negative WBS group (7/9 cases, 77.8%), whereas multiple pulmonary nodular pattern was most frequently found in the positive WBS group (6/11 cases, 54.5%). This may be explained, in part, by the size of pulmonary metastatic lesions, which was considered smaller in the lymphangitic pattern and hence was more difficult to visualize on WBS.

The present study has a limitation. The authors did not have cytology or histology of lung lesions seen on the CXR to prove the evidence of pulmonary metastasis. In endemic areas of tuberculosis such as in the authors' country, pulmonary tuberculosis can cause abnormal CXR findings similar to those of pulmonary metastases, particularly in patients with lymphangitic pattern. Therefore, these cases might actually be free of pulmonary metastasis from DTC. Although serum Tg might help indicate the presence of pulmonary metastasis, it was of no use in cases of co-existing metastasis at other sites (case number 7 in Table 4) and in the presence of anti-Tg (case number 1, 5 and 9). Furthermore, undetectable serum Tg could even be found in the presence of pulmonary metastasis shown on the post-treatment WBS[20]. Two of seven WBS-negative, lymphangitic pulmonary metastatic patients in the authors' study were lost to follow-up (case number 2 and 4). Three of these seven cases received subsequent doses of I-131 during the time of the authors' study period and all showed persistent lymphangitic pattern with persistent negative pulmonary metastasis on WBS (case number 1, 3 and 5), while the other two (case number 6 and 9) had disease remission on the follow-up without further treatment. None of these cases received anti-tuberculous drug regimen.

Conclusion

Although CXR has a limited role as a routine investigation for detection of pulmonary metastasis in DTC patients, it may play an additional role in detecting pulmonary metastasis for patients with negative pulmonary metastasis on the post-treatment WBS.

Acknowledgements

This work was supported by the Thyroid Cancer Research Group and the Invitation Research Grant (Grant Number I 50206) from Faculty of Medicine, Khon Kaen University, Thailand. The authors thank Emeritus Professor James A. Will for assistance with the English-language presentation of the manuscript.

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บทบาทของภาพรังสีปอดในการวินิจฉัย และติดตามการกระจายของมะเร็งไปที่ปอด ในผู้ป่วยมะเร็งไทรอยด์ชนิดดิฟเฟอเรนชิเอดเตด

จรูญศักดิ์ สมบูรณ์พร, พรรณิภา สิมธรรมนิมิต, วรินทร พุทธรักษ์, ปาณยา ทุมสท้าน, เชษฐา งามจรัส, กฤษณา ร้อยศรี

ภูมิหลัง: *การตรวจสแกนทั้งตัว (WBS) หลังการรักษาด้วยสารไอโอดีนกัมมันตรังสี (I-131) มีความไวสูงในการตรวจการกระจายของมะเร็งไทรอยด์ชนิดดิฟเฟอเรนชิเอดเตด (DTC) ทำให้เกิดคำถามว่า การถ่ายภาพรังสีปอด (CXR) ยังมีบทบาทในการใช้วินิจฉัยการกระจายของมะเร็งไปที่ปอดในผู้ป่วยกลุ่มนี้หรือไม่*

วัตถุประสงค์: *เพื่อหาความชุกของการกระจายของมะเร็งไปที่ปอดที่วินิจฉัยได้จาก CXR แต่ WBS ให้ผลลบ*

วัสดุและวิธีการ: *ผู้นิพนธ์ศึกษาย้อนหลังเพื่อเปรียบเทียบ CXR และ WBS ที่ทำเป็นประจำขณะรักษาด้วย I-131 ในผู้ป่วย DTC 300 ราย ในช่วงปี พ.ศ. 2546 ถึง พ.ศ. 2549 ลักษณะการกระจายของมะเร็งไปที่ปอดที่พบใน CXR แยกเป็น 4 แบบ ได้แก่ แบบก้อนเดี่ยว แบบหลายก้อน แบบกระจายตามท่อน้ำเหลือง และแบบกระจายไปที่เยื่อหุ้มปอด*

ผลการศึกษา: *พบลักษณะการกระจายของมะเร็งไปที่ปอดในผู้ป่วย 36 จาก 300 ราย (ร้อยละ 12.0) ในจำนวนผู้ป่วยที่มีการกระจายของมะเร็งไปที่ปอดทั้งหมด 36 รายนี้ มี 11 ราย (ร้อยละ 30.6) ที่วินิจฉัยได้จากทั้ง CXR และ WBS อีก 16 ราย (ร้อยละ 44.4) วินิจฉัยได้จาก WBS อย่างเดียว และอีก 9 ราย (ร้อยละ 25.0) วินิจฉัยได้จาก CXR อย่างเดียว และพบว่าผู้ป่วย 7 ใน 9 รายในกลุ่มนี้ มีภาพ CXR เป็นแบบกระจายตามท่อน้ำเหลือง*

สรุป: *แม้ว่าการตรวจ CXR แบบเป็นประจำทุกรายขณะรับการรักษาด้วย I-131 ในผู้ป่วยมะเร็งไทรอยด์ชนิดดิฟเฟอเรนชิเอดเตด จะได้ประโยชน์ค่อนข้างน้อยในการวินิจฉัยภาวะการกระจายของมะเร็งไปที่ปอด แต่ก็มีประโยชน์ในผู้ป่วยที่ WBS ให้ผลลบ*