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Iodine-123 iodoamphetamine and Thallium-201 SPECT in Two Patients with Primary Pulmonary Malignant Lymphoma

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Abstract Two patients with primary pulmonary malignant lymphoma were evaluated by iodine-123 iodoamphetamine (^{123}I-IMP) and thallium-201 (^{201}TlCl) SPECT. In both patients, radiographic differential diagnosis from benign conditions was difficult. Their ^{123}I-IMP SPECT revealed a defect of the lesion both on the early and delayed images, and ^{201}TlCl SPECT revealed prolonged retention of ^{201}TlCl activity in the lesion compared to benign disorders, and both scintigraphies highly suggestive of a malignancy. These findings indicate that ^{123}I-TMP and ^{201}TlCl SPECT can contribute to the differential diagnosis from other benign lesions in this rare entity.

Key Words : ^{123}I-IMP, ^{201}TlCl, Pulmonary malignant lymphoma, Lung neoplasms, Single photon emission computed tomography

Introduction

Primary pulmonary malignant lymphoma (PML) is rare and the disorder often begins as a small peripheral nodule or region of air space consolidation, but the lesions will progress to show mass-like consolidation and segmental or lobar distribution lobe, which named segmental or lobar PML[1,2]. On the other hand, other chronic air space diseases caused by a wide variety of malignant and benign disorders also can occasionally coalesce into the same radiographic manifestations. Therefore, the lesion is often misdiagnosed as a benign disease. Recently, lung scanning with iodine-123 iodoamphetomine (^{123}I-IMP) and thallium-201 chloride (^{201}TlCl) using single photon emission computed tomography (SPECT) has been applied to distinguish the malignant tumors from benign lesions[3-7].

In this paper, we present two patients with rare PML and document the diagnostic potentiality of ^{123}I-IMP and ^{201}TlCl SPECT as a non-invasive method for the differential diagnosis from benign conditions of this rare malignant entity.

^{123}I-IMP and ^{201}TlCl SPECT

A dose of lll MBq ^{123}T-IMP was injected intravenously, and planar static images were obtained 20 min and 24 hr later. Tomographic scans were also obtained at 24 hr. ^{201}TlCl SPECT was obtained at 20 min (early scan) and again at 3 hr (delayed scan) after intravenous injection of a dose of 222 MBq ^{201}TlCl. Both SPECT images were obtained using a rotating gamma camera system with a single head (Toshiba GCA-901). Sixty projection using a matrix size of 64×64, with an acquistition time of 20 sec each were stored. After reprocessing the data by nine-point weighted

smoothing, the reconstructed images were obtained with a Ramp filter following back projection using a Butterworth filter. The slice thickness was 4.6mm. Attenuation correction was not performed. On the ^{201}TlCl SPECT, regions of interest in the lesion and the contralateral normal lung field were examined. The lesion/normal lung uptake ratio of ^{201}TlCl activity was measured from average counts per voxel on both early (early uptake ratio) and delayed (delayed uptake ratio) scans. The retention index (degree of retention of ^{201}TlCl activity in the lesion) was calculated as follows; (delayed uptake ratio -early uptake ratio)/(early uptake ratio) × 100%.

Case peports

CASE 1

Three years ago, a 68-year-old man was referred to our hospital because of slight cough and sputum. Intitial chest radiography showed a massive consolidations adjacent to aortic arch in left upper lobe and small consolidation in tho right upper lobe. Although antituberculosis therapy initially administered on the suspition of tuberculosis, these shadows were not improved. Then, sputum cytology and bronchoscopic washing revealed abundant mature lymphocytes, and the patient was diagnosed as pseudolymphoma. The shadows were not improved despite steroid therapy, and the shadows gradually but slightly increcased in size during the 3 year follow-up period.

The patient again complained of increased cough and sputum, and was admitted for further examination. At the time of admission, physical examination revealed no swelling lymph node. The chest radiography showed a slightly extended consolidation in both lungs, compared to that at the initial examination (Fig-1A). On the chest CT (Fig -1B), a mass-like consolidation with shaggy borders and air-bronchogram was existed in the right upper lobe. The dilatated air bronchograms were seen within the consolodation of S^2. The constrictive change was appeared with the volume loss of left lung. Also, an ill -defined segmental consolidation with air bronchogram was seen in the right S^2. A

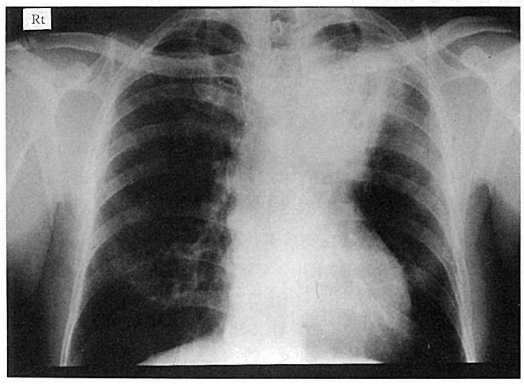

Fig. 1-A: Chest radiography showed a massive consolidation adjacent to aortic arch in the left upper lobe and segmental consolidation in the right upper lobe.

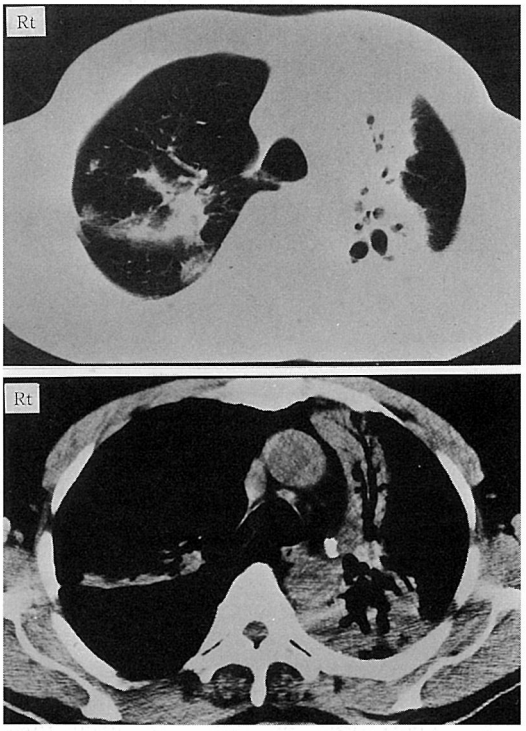

Fig. 1-B: Chest CT showing mass-like consolidation with shaggy borders and air bronchogram in the left lung. Also, ill defined scgmental consolidation was seen in the right upper lobe, with several small consolidations surrounding the lesion.

portion of the shadow extended over a major fissure into the right lower lobe (S^6), and several small consolidations were seen surrounding the lesion. No significant mediastinal Lymphadenopathy was not found. Gallium-67 scintigraphy showed intensive uptake in both lesions and no abnormal accumulation was found in the extrathorax. Early and delayed ^{123}I-IMP SPECT showed a defective or reduced ^{123}I-IMP utake within the lesions (Fig.1-C). The early and delayed ^{201}TlCl SPECT showed abnormal uptake in the lesion of left upper lobe with the ratios of 2.73 and 4.00, respectively. The retention index calculated by both uptake ratios was 46.5%, and the lesion of right upper lobe also showed abnormal uptake with an early uptake ratio of 1.15 and delayed uptake ratio of 1.38, and the retention index of 20.0% (Fig. 1-D).

Because the growing consolidations and both scintigraphic patterns were suggestive of malignancy, bronchoscopy was performed and biopsy findings revealed that the normal-lung parenchyma was effaced by a monotonous sheet of small round lymphocytes. Subsequent monoclonal antibody studies were consistent with non-Hogkin diffuse B-cell type lymphoma. After a 6-month follow-up period, no other extrathoracic lesions were found and the diagnosis of PML was made.

CASE 2

Six years ago, a 54-year-old female was referred to our hospital because of continuous dry cough. Initial chest radiography showed a segmental consolidation in the middle lobe. On the chest CT, a fan-shaped shadow mainly existed in the S^4 spreaded from the hilar region to the peripheral area, while it did not reach the visceral pleura. Bronchoscopy revealed a patent right middle lobe bronchus without tumor or inflammatory changes and bronchial washing showed no malignancy. The shadow was not improved despite the administration of antibiotics. The patient was asymptomatic and

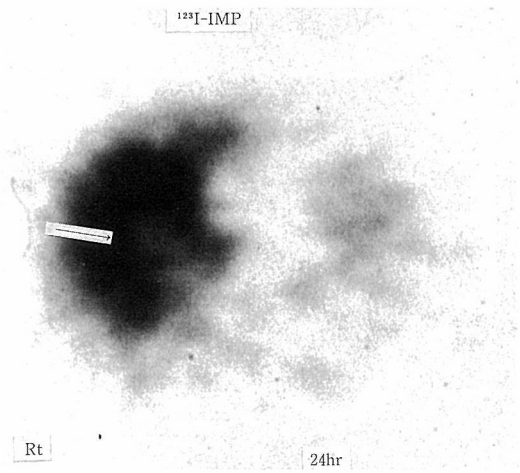

Fig. 1-C: ^{123}I-IMP SPECT obtained 24 hr after the injection showed reduced or defective uptake within the consolidations of the both lungs.

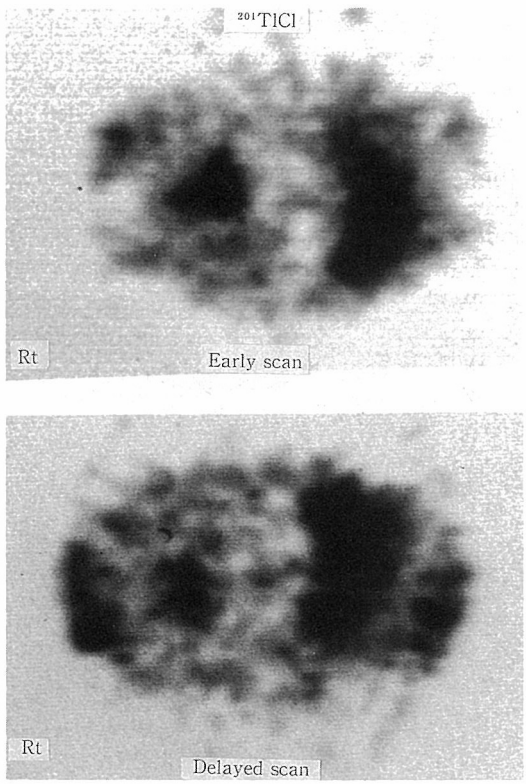

Fig. 1-D: Early and delayed images of ^{201}TlCl SPECT showed abnormal uptake in the lesions. In the lesion of the left upper lobe, the early ratio, the delayed ratio and the retention index was 2.73, 4.00 and 46.5%, respectively. Those of the lesion of the right upper lobe were 1.15, 1.38 and 20.0%, respectively.

followed up for 6 years as organizing pneumonia or middle lobe syndrome. The size of the consolidation had a tendency of gradual increase, while at one time the size shrinked slightly.

The patient was again admitted for the reccurent cough on July, 1992, and for further examination and therapy. At the time of admission, physical examination revealed no swelling of lymph nodes. The chest radiography (Fig.2-A) and CT showed a more extended, ill-defined, lobar consolidation occupying the entire middle lobe. On the chest CT, the fan-shaped shadow spread from hilar region to the peripheral area, and reached tho visceral pleura. The lesion partially extended from the right middle lobe into the right upper and lower lobe, and the margins had a irregular border. Within the shadow, an air bronchogram was observed from the proximal to the distal portion, and the consolidation was homogenous except for air bronchogram with no appreciable loss of volume (Fig.2-B). Gallium scintigraphy showed intensive uptake in the lesion and no abnormal accumulation was found in the extra-thorax. Both early ^{123}I-IMP planar images and SPECT obtained 24 hrs after the injection showed a defective or reduced ^{123}I-IMP uptake within the lesion (Fig.2-C). The early and delayed ^{201}TlCl SPECT showed intensive uptake with the ratios of 1.75 and 2.30, respectively. The retention index calculated by both uptake ratios was 31.4% (Fig.2-D). The chest CT findings of invasive consolidation into adjacent segments and both scintigraphic patterns suggested a malignancy. Bronchoscopy demonstrated a stenotic orifice of the rt-B^5. The transbronchial biopsy findings suggested malignant lymphoma.

A right thoracotomy was performed and a mass-like consolidation occupying the entire middle lobe was detected. Portions of the lesion extended from the RMI into the anterior segment of the right upper lobe and also into tho right lower lobe (S^8) across the minor fissure, and pulmonary lobectomy of middle lobe and partial resection of right

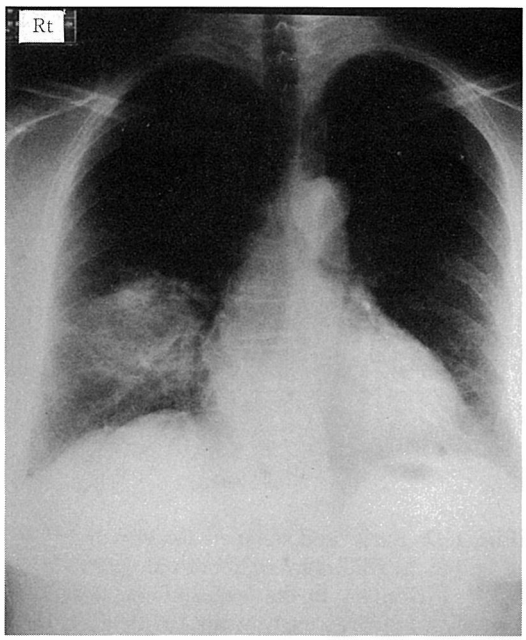

Fig. 2-A: Chest radiography showed ill defined lobar consolidation in the right middle lobe.

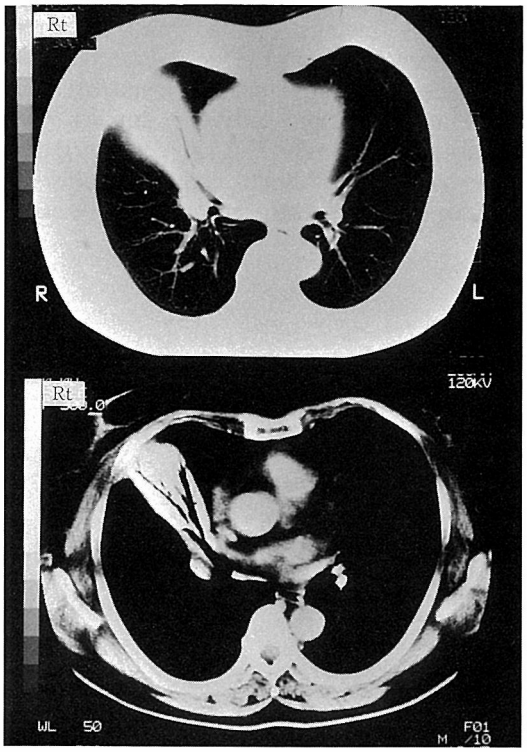

Fig. 2-B: Chest enhance CT revealed the consolidation was homgenously enhanced except for air bronchogram without appreciable loss of lung volume.

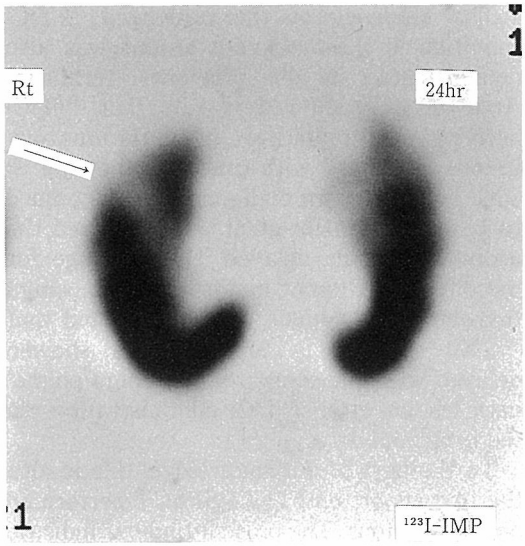

Fig. 2-C: ^{123}I-IMP SPECT obtained 24 hr after the injection showed defective uptake within the lesion.

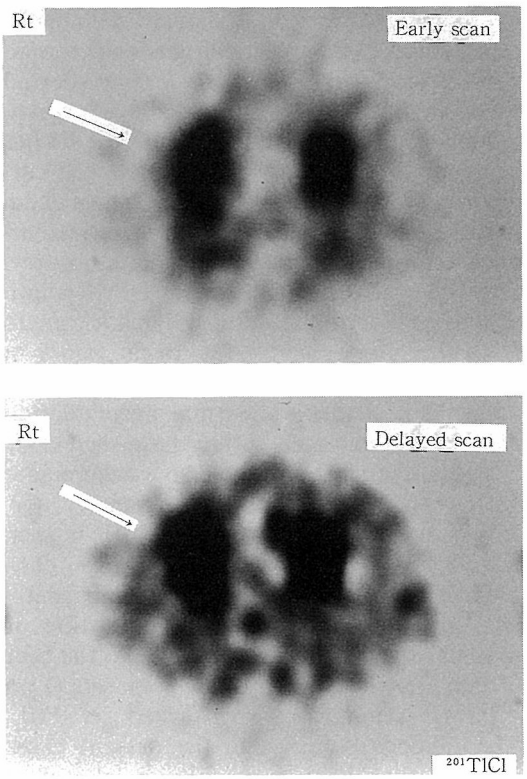

Fig. 2-D: Early and delayed images of ^{201}TlCl SPECT showed intensive uptake in the lesion, with the uptake ratios of 1.75 and 2.30, respectively. The retention index calculated by both uptake ratios was 31.4%.

upper and lower lobes were performed. No adenopathy or pleural effusion was found. Microscopically, the normal lung parenchyma was effaced by a monotonous sheet of small round lymphocytes and monoclonal antibody studies were consistent with non-Hogkin's diffuse B-cell type lymphoma.

Discussion

PMI is rare and the patients are often asymptomatic. On chest radiography, the disorder usually begins as a solitary or multiple small peripheral nodule or region of air space consolidation. Most of the lesions progress slowly, showing little change for months or even years, and will progress as mass like consolidations and rarely involve a segmental or entire lobe[1,2], as seen in the present cases. However, these consolidations, especially the segmental or lobar consolidations can be caused by a wide variety of disorders including both benign and malignant lesions[2,8-13]. Thus, PML is often a difficult clinicaland radiclogic diagnosis to make. Moreover, in PMI the diagnostic difficulty to differentiate from other inflammatory lesions with the transbronchial biopsy by bronchoscopy has been reported[8,12].

The brain perfusion agent, ^{123}I-IMP has recently been applied to various pulmonary diseases due to its high uptake by lung[14], and its use for differentiation malignant tumors from benign conditions has already been known[3-5]. The characteristic feature and kinetics of ^{123}I-IMP in the malignant lesions are that it is not accumulated intratumorally on either early or delayed images, while it is abnormally accumulated around the tumor on the delayed image. On the contrary, in benign lesions the prevalence of ^{123}I-IMP accumulation in the lesion is seen on the delayed image, although early images show a defect or reduced uptake[3-5].

In our institution, we have previously stud-

ied 64 patients with 39 malignant pulmonary tumors and 25 benign conditions due to wide variety of causes. All of the lesions showed the same results as mentioned above[4]. Nakajyo et al.[16] also reported that ^{123}I-IMP did not accumulate in the bronchioalveolar cell carcinoma, which manifested lobar consolidation resembling a pneumonia-like appearance on the chest radiography. Moreover, they reported the usefulness of ^{23}I-IMP scintigraphy to discriminate the malignant tumors from secondary changes due to the tumor in the obstructive pneumonia and/or atelectasis, because abnormal accumulation of ^{123}I-IMP was seen within these secondary changes, while ^{123}I-IMP could not accumulate within the causative malignant tumor.

Why no accumulation of ^{123}I-IMP is seen within malignant tumors has not been clarified. However, destruction of normal endothelial cells by tumor cells or alteration of physical supply are considered[3]. To the best of our knowledge, this is the first report on ^{123}I-IMP scintigraphy performed in PML. The findings obtained in the present cases indicate that PML consolidation also dose not accumulate ^{123}I-IMP as in the case for other malignant tumors. ^{123}I-IMP scintigraphy may contribute to differentiation of malignant lesions from other benign conditions, when the radiographic appearance is difficult as in our cases.

^{201}TlCl SPECT also has been recently used to differentiate malignant lesions from benign conditions[7,17,18], since Tonami et al.[6] initially used it for this purpose. One of the distinguishing features on ^{201}TlCl SPECT between malignant and benign lesions is the more prolonged retention of ^{201}TlCl activity in the malignant lesions, which appears as a higher retention index[6,7].

In our institution, we studied in 66 patiens with 33 malignant and 35 benign lesions. The retention indexs of malignant lesions ($26.07\pm0.43\%$) showed significantly higher than those of benign lesions ($-3.39\pm13.00\%$). When the cut-off value of the retention index was set at 10% and lesions showing higher values were defined as malignancy, the sensitivity was 81.8%, the specificity was 88.6% and the accuracy was 85.3%[7].

The tendency of the prolonged ^{201}TlCl retention in the malignant lesions was also demonstrated in the previous literatures. Ando et al.[19] showed in rats that ^{201}TlCl activity accumulating in inflammatory lesions decreased with time, but that the ^{201}TlCl washout from malignant tumors tended to be delayed. Ochi et al.[20] emphasized the usefulness of the delayed ^{201}TlCl image for the differentiation of malignant from benign thyroid tumor. Shindo et al.[21] reported that ^{201}TlCl activity in lung cancers showed delayed washout compared to benign pulmonary lesions after ^{201}TlCl administration via the bronchial artery.

To the best of our knowledge, this is also the first report on ^{201}TlCl SPECT performed on PML lcsions. The present findings indicate that this rare malignant entity also shows a higher value of the retention index as in the case for other malignant lesions. Therefore, ^{201}TlCl SPECT is considered to be potentially useful for differentiation of PML from other benign conditions.

Gallium-67 citrate, as an other agent for tumor scintigraphy, showed intensive uptake in the PML lesions. Although this agent may contribute to the detection of metastatic lesions and contribute to determine the clinical stage, it cannot differentiate malignancy frorm other benign lesions because of accumulation in both lesions.

When PML is confined to the lung parenchyma, without extention into the mediastinum, or chest wall, 5-year survival rates of 80-90% have been obtained when complete resection is achieved[1,2,8,10], suggesting the importance of early diagnosis in this entity. If one or both ^{123}I-IMP or ^{201}TlCl scintigraphy had been performed initially in the present patients, they would have contributed to earlier detection of malignant disorders. These scintigraphies are also helpful in the managerment of re-examination or further diagnostic procedure, when the bronchoscopic biopsy fails to diagnose the suspicion of malignant Icsion.

In conclusion, we performed ^{123}I-IMP or ^{201}TlCl scintigraphies in two cases of rare PML, and demonstrated that this malignant entity showed the same features and kinetics of these agents as other malignant lesions. In

the patient on whom radiographic features are difficult to differentiate from other benign conditions as in the present cases, these scans may be performed first to detect malignant disorder, as an noninvasive methods.

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