

Intense and prolonged Tl-201 accumulation in a slow growing bronchioloalveolar carcinoma

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Thallium-201 SPECT was performed to evaluate a pulmonary lesion in a 73-year-old male which had been considered to be an inflammatory lesion for two years. The lesion has slowly increased in size on x-CT. Tl-201 was intensely taken up and retained in the lesion, suggesting a malignant lesion. Histological examination revealed that the lesion was bronchioloalveolar carcinoma. This case suggested that Tl-201 uptake of pulmonary carcinoma would not be necessarily related to cell growth rate.

Key words: Tl-201 SPECT, lung cancer, cell growth rate

INTRODUCTION

THALLIUM-201 CHLORIDE has been widely used for the assessment of malignant tumors of various organs.¹⁻¹⁰ Many factors might be involved in the mechanism of Tl-201 accumulation in tumors.¹¹⁻¹⁶ Cell activities such as glucose metabolism and (Na⁺-K⁺)ATPase pump activity are considered to be important factors while tumor blood flow, vascular permeability and vascular volume are also important for the initial distribution. There is a report showing that the level of (Na⁺-K⁺)ATPase activity is correlated with cell growth.¹⁷ Tl-201 uptake in gliomas is reported to be associated with the malignancy grade.⁸ Furthermore, other reports suggested that Tl-201 uptake by tumors could be related to the cell growth rate.^{9,10}

Recently we saw a case of a slow growing bronchioloalveolar carcinoma with intense and prolonged accumulation of Tl-201. The lesion has been considered to be an inflammation for two years.

CASE REPORT

An abnormal pulmonary shadow was pointed out on chest radiography in a screening examination in 1993 in a 73-

year-old male with an ex-smoking history (20 cigarettes/day for 30 years, cessation for 15 years) who had been followed up for prostate cancer at the first hospital since 1991. He had not complained of any respiratory symptom. Chest x-CT obtained in November, 1993 revealed consolidation with airbronchogram in the right S². No lymph node swelling was observed. The lesion had been considered to be an inflammation and was followed up with chest x-ray and x-CT. Follow-up x-CT was obtained in June, 1994 and interpreted by the clinician as showing no significant change in size in 7 months. He was referred to our hospital in July, 1995 by a urologist. The lesion was re-examined by x-CT, found to have become enlarged when compared to the previous x-CT and suspected of being alveolar cell carcinoma for the first time. The lesion was found to have somewhat increased in size through 1993 to 1994 when retrospectively checked. Tl-201 SPECT was performed in August, 1995 to characterize the lesion. A dose of 6.5 mCi (240 MBq) of Tl-201 chloride was intravenously injected, and tomographic scans were obtained at 15 min (early) and 3 hr (delayed) postinjection with a dual-headed rotating gamma camera (Prism-2000XP, Picker) with low-energy, high-resolution collimators. Both early and delayed images delineated intense tracer accumulation in the right pulmonary lesion, resulting in a diagnosis of lung cancer.^{1,3} The early ratio, delayed ratio and retention index were calculated to be 2.41, 2.72 and 13%, respectively. Specimens obtained by transbronchial lung biopsy and surgical resection

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confirmed bronchioloalveolar carcinoma. Laboratory examination revealed nothing unusual except mild anemia during the clinical course.

DISCUSSION

Tl-201 imaging has been suggested to have a potential for the *in vivo* characterization of various tumors.¹⁻¹⁰ It has been used for the differential diagnosis of pulmonary nodular lesions and for the detection of mediastinal lymph node metastases from lung cancer,¹⁻³ based on findings indicating that malignant lesions are likely to show intense and prolonged tracer uptake. This theory could also be adapted to tumors originating in bone and muscle structures.^{4,5} For brain tumor, Tl-201 SPECT has been reported to be effective for the diagnosis of tumor viability^{6,7} and be correlated with FDG uptake which has been supposed to depend on the malignancy of the tumor.¹⁸ Black et al. showed the correlation of Tl-201 uptake with the malignancy grade of glioma.⁸ Furthermore, Oriuchi et al.⁹ and Ishibashi et al.¹⁰ recently reported that Tl-201 uptake is associated with the cell proliferative activity of gliomas.

The mechanism of Tl-201 accumulation into tumors would include blood flow to the tumor, vascular permeability, vascular volume and cell activities such as glucose metabolism and $(\text{Na}^+-\text{K}^+)\text{ATPase}$ pump activity.¹¹⁻¹⁶ Since $(\text{Na}^+-\text{K}^+)\text{ATPase}$ pump activity is related to cell growth,¹⁷ Tl-201 uptake of tumor cells is supposed to be modified by cell growth rate.

The case presented in this report had a slow growing lung carcinoma with signs of intense initial uptake and prolonged retention of Tl-201 on the SPECT study. The lesion could be classified as a malignant tumor rather than an inflammatory process, although it had been followed for two years as the latter. Tumor doubling time estimated from the slices showing the biggest diameter of the lesion in each x-CT study by means of the equation of Schwartz¹⁹ was approximately 750 days. The estimation was made with x-CT because previous chest x-rays were not available. The mean doubling time of bronchioloalveolar carcinoma has been reported to be 300 days,²⁰ and that of the present case appears to be much longer than the reported length of time. There is as yet no report on the correlation between Tl-201 uptake and cell growth rate for lung cancers. Several papers indicated that the tumor doubling time of adenocarcinoma of lung is longer than that of other cell types.^{21,22} It was reported that the retention index of adenocarcinoma was not significantly different from that of other cell types and there was no difference in the uptake ratio among the various cell types except between adenocarcinoma and large cell carcinoma.³ These findings suggest that the cell growth rate would not be a major factor regulating Tl-201 uptake not only in the present case but also in lung carcinoma in general.

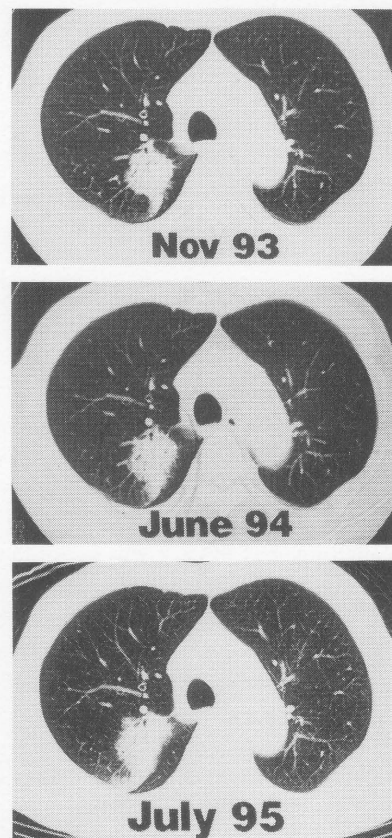


Fig. 1 Sequential x-CT images of the lung. The lesion in the right upper lobe slowly increased in size during two years.

Another example of the poor correlation between cell growth and Tl-201 uptake has been demonstrated for thyroid tumor. It is known that both differentiated adenocarcinoma of the thyroid gland and benign tumors such as adenoma accumulate Tl-201, and thyroid adenocarcinoma usually grows slowly. Kishida reported that both thyroid adenocarcinoma and adenoma had high $(\text{Na}^+-\text{K}^+)\text{ATPase}$ activity and Tl-201 uptake was well correlated with $(\text{Na}^+-\text{K}^+)\text{ATPase}$ activity irrespective of whether the tumor was malignant or benign.²³ Interestingly, microfollicular adenoma tended to have rather higher enzyme activity than adenocarcinoma. These results indicate that $(\text{Na}^+-\text{K}^+)\text{ATPase}$ activity is not necessarily associated with cell growth in thyroid tumor.

Although we did not examine $(\text{Na}^+-\text{K}^+)\text{ATPase}$ activity in the present case or could find any report on $(\text{Na}^+-\text{K}^+)\text{ATPase}$ activity in lung carcinoma, the findings in the present case suggest either that there would be a poor correlation between cell growth and $(\text{Na}^+-\text{K}^+)\text{ATPase}$ activity in this case as in thyroid tumor, or that the major mechanism of Tl-201 uptake in this case would not depend on $(\text{Na}^+-\text{K}^+)\text{ATPase}$ activity. Since alveolar cell carcinoma usually does not have intense vascularization, Tl-201 uptake in this case would not be fully explained by tumor blood circulation. Frankly we do not have a satis-

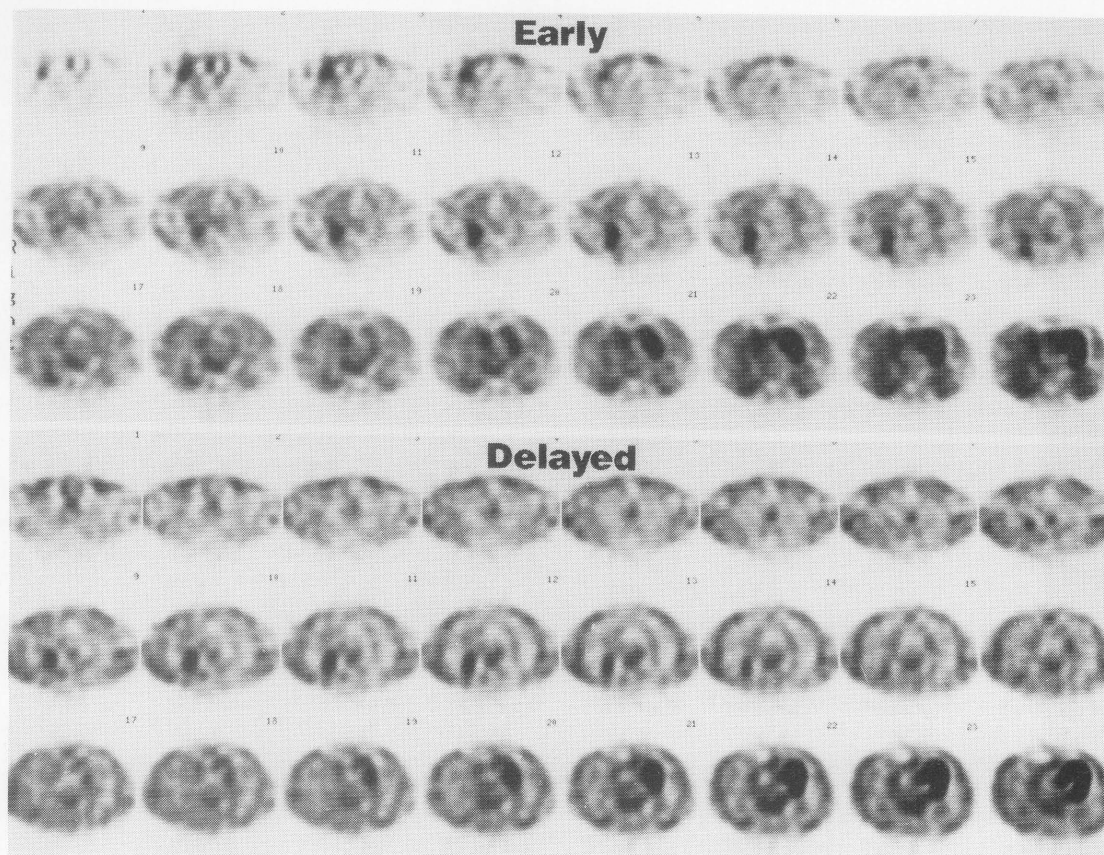


Fig. 2 Tl-201 SPECT performed in August 1995. The tracer was intensely taken up and retained in the pulmonary lesion, suggesting a malignant tumor. Histological examination revealed bronchioloalveolar carcinoma.

factory explanation for the intense Tl-201 uptake in this case. Since the lesion was resected by surgery, a slow growth rate after the Tl-201 study could not be confirmed. It is possible that the lesion would have progressed rapidly if not resected.

In conclusion, it can be imagined that there would be a variation in the correlation between Tl-201 uptake and cell growth rate according to the organ in which the tumor originated. Although a correlation between Tl-201 uptake and the proliferation of glioma is reported, it is likely that we could not adapt this theory to malignant lesions of the lungs as to thyroid tumors. We need to get more information about metabolic activities, including (Na⁺-K⁺)ATPase activity, in lung carcinoma to better understand the mechanism of Tl-201 accumulation in pulmonary lesions.

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