

Incidental Detection of an Invasive Thymoma during Thallium-201 Imaging for Coronary Artery Disease

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Thallium-201 (Tl-201) is widely used for myocardial perfusion imaging, but is also reported to have potential tumor-seeking properties. Tl-201 uptake has been described in various malignant diseases, including thymic tumors. Thymomas are the most frequent tumors of the anterior mediastinum, and chest pain is one of the major presentation symptoms. Sometimes, a thymoma may be overlooked on chest plain film. We report on a case of a 63-year-old man who had a history of hypertension and suffered from intermittent chest pain for several weeks. He underwent a Tl-201 stress test to evaluate the presence of coronary artery disease, and during the test, abnormal uptake over focal extracardiac activity in the left upper mediastinum was incidentally revealed. Furthermore, chest computed tomography identified a 6-cm left anterior mediastinal mass. Mediastinal tumor resection was carried out, and the pathological examination demonstrated an invasive epithelial-type thymoma, which had invaded the left innominate vein. Subsequently, the patient received postoperative radiotherapy and thenceforth responded well to treatment. A Tl-201 scan has the potential to play a part in tumor detection and clinical assessment of therapeutic effects. (*Chang Gung Med J* 2004;27:138-42)

Key words: thallium-201, anterior mediastinal tumor, invasive thymoma.

Thallium is a metallic element in group III-A of the periodic table. The use of thallium-201 (Tl-201) as a myocardial perfusion imaging agent is based on its cellular physiological similarities to ionic potassium.^(1,2) A number of studies have described the uptake of Tl-201 by tumors, including thymomas and invasive thymomas; thymic,⁽³⁾ bronchogenic, brain, and bone carcinomas; Hodgkin's and non-Hodgkin's lymphomas; breast cancer; esophageal cancer; osteosarcomas; and most cases of thyroid carcinomas.⁽⁴⁾ In the literature, 70% of thymomas⁽⁵⁾ are positive on post-diagnostic Tl-201 scanning. We report an interesting patient who underwent noninvasive cardiac testing, in which Tl-201

myocardial perfusion scintigraphy with the aid of single photon emission computed tomography (SPECT) testing led to a diagnosis of a previously unsuspected malignant thymoma.

CASE REPORT

A 63-year-old man, with a history of hypertension and gouty arthritis for several years without regular medication control, came to our cardiovascular outpatient department complaining of new onset of sharp chest pain lasting one month. The pain was intermittent in the retrosternal area, and was associated with back radiation, right limb weakness, and

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cold sweating. He visited our cardiovascular outpatient department. Under the impression of acute coronary syndrome, Tl-201 myocardial perfusion scintigraphy with the aid of single photon emission computed tomography (SPECT) was arranged, but he did not have a chest X-ray as routine at that time. Stress images of Tl-201 myocardial perfusion scintigraphy were performed 5 min after intravenous injection of 0.143 mg/kg/min dipyridamole for 4 min, while delayed images were taken after 4 hours of rest. For imaging, 2 energy windows were set over the 80- (20%) and 167-keV (20%) photopeaks of Tl-201 by a SMV DST-XLi dual-head camera equipped with low-energy, high-resolution, para-hole collimators. The SPECT acquisition was performed using 180° rotational tomography, extending from the 45° right anterior oblique position to the 45° left posterior oblique position. Thirty-two projections were obtained during the 180° rotation, with each being imaged for 60 s. All projections were stored as a 64×64, 32-bit matrix. Ordered subset expectation maximization (OSEM) was used for image reconstruction. The result showed uniform myocardial perfusion of the left ventricle. Furthermore, abnormal focal left upper mediastinal activity was visualized on both the stress and delayed images (Fig. 1). Chest computed tomography demonstrated a 6-cm, heterogeneously enhanced mass in the left upper anterior mediastinum (Fig. 2).

The patient was referred to a chest surgeon, and total resection of the anterior mediastinal tumor was performed. The tumor was severely adherent to the pulmonary artery and aorta and had invaded the left innominate vein. Pathological examination revealed a well-circumscribed tumor, focally invading the attached fat tissue. Microscopically, the tumor consisted of clusters, sheets, or solid groups of polygonal cells and had vesicular round to oval nuclei with light eosinophilic cytoplasm and indistinct nucleoli (Fig. 3). The mitotic count measured up to 6 per 10 high-power fields. The tumor was noted to involve the vessel wall of the innominate vein. According to the classification of thymic epithelial tumors, the present tumor was an invasive thymoma of the polygonal cell type (Shimosato and Mukai, 1997). The patient received 51 Gy of postoperative mediastinal radiation and recovered well.

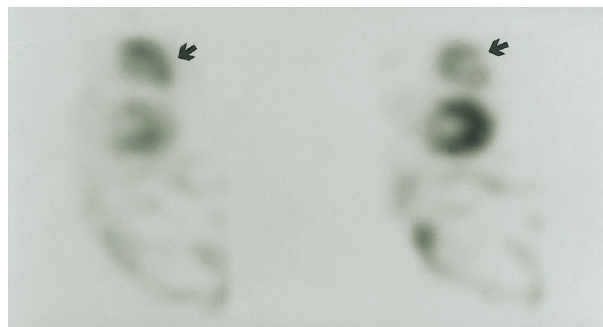


Fig. 1 ^{201}Tl SPECT coronal images showing intense focal uptake above the heart in the anterior mediastinum (black arrow).

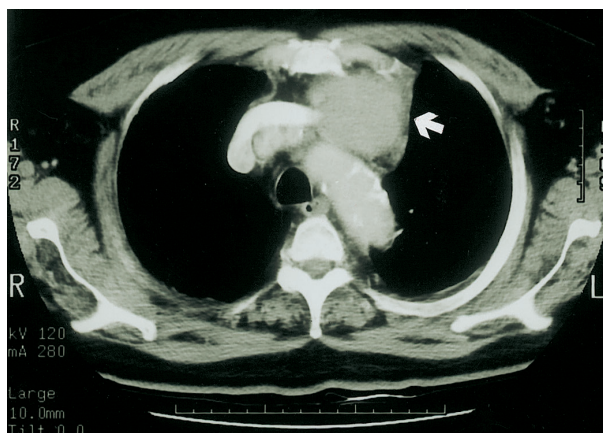


Fig. 2 CT scan demonstrating an anterior mediastinal mass (white arrow).

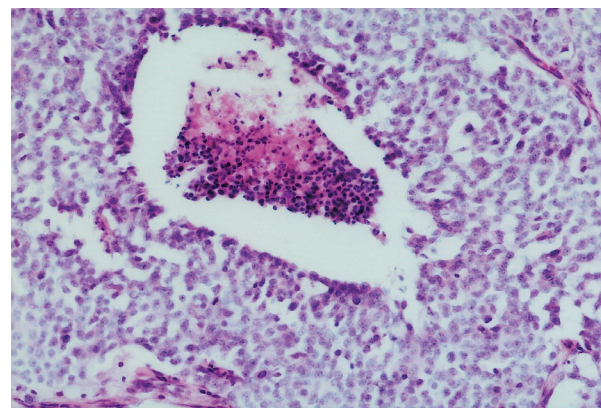


Fig. 3 Tumor cells involving the vessel wall of the innominate vein (marked by Indian ink). (H&E, 40×)

DISCUSSION

Tl-201 uptake has been reported to occur with various mediastinal tumors, including thymomas, seminomas, lymphomas, and lung cancer.^(1,6) Tl-201 is in the form of thallous chloride, and behaves as a potassium analogue in the body on the basis of cellular physiology. It has been shown to be preferentially localized^(1,2) in the myocardium, and to participate in ionic active pumping mechanisms. Ischemic and necrotic areas show up as cold spots on Tl-201 myocardial perfusion imaging, which may be due to non-functioning cell membrane pump activity of cell membranes.⁽⁷⁾ Myocardial Tl-201 uptake is generally accepted to reflect both blood flow and Na-K ATPase-dependent pump activity. Thallium uptake by a tumor occurs rapidly in parallel with myocardial uptake. The similarity in tumor and myocardial Tl-201 uptake has led researchers to hypothesize that the mechanism of Tl-201 uptake by tumor cells is related to a function of blood flow and the Na-K ATPase cell membrane pump, just as for Tl-201 myocardial uptake. Tumors often have abnormal vascularity, and Tl-201 may rapidly accumulate⁽¹⁾ in the extracellular space due to either increased permeability of new vessels with large intracapillary pores or simply because of increased vascularity. The mechanism of intracellular uptake of Tl-201 by tumors may be related to the viability and metabolic activity of pathological cells rather than being a purely flow-dependent process. Venuta et al.⁽⁸⁾ compared the uptake of thallium in rat thyroid tumor cells to normal rat thyroid tissue, and found that transformed cells took up thallium faster and concentrated it more effectively than did normal cells. Moreover, Venuta et al. also found that faster-growing cells took up thallium more quickly than did slowly growing ones.

Thymomas are the most common primary mediastinal neoplasms in adults and the most frequent tumor of the anterior mediastinum. Chest pain is one of the major clinical manifestations. Sometimes, a small thymoma is hidden within the mediastinal structure and can be missed by chest radiography. Chest tomography is useful for advanced imaging study. The treatment of an invasive thymoma confined to the mediastinum is surgical resection and postoperative radiation. Delayed recurrence of a thymoma may occur, even in patients who have completely resected lesions, and thus long-term follow

up should be emphasized. Fukuda et al.⁽⁹⁾ first described the high uptake of Tl-201 in a thymoma. Subsequently, several reports have described a similar high uptake of Tl-201. Yuzuriha et al.⁽⁵⁾ reported that 70% of all thymomas, regardless of cell type, are positive on Tl-201 scans. The uptake of Tl-201 seems to be related to the vascularity of tumor and can possibly serve as an index for the suitability of supplementary chemo- and radiotherapy. Moreover, Tl-201 and technetium (Tc-99m) tetrofosmin uptake can be used to detect a recurrent thymoma after surgery and radiation.⁽¹⁰⁾ Kageyama et al.⁽¹¹⁾ reported the use of Tl-201 SPECT for detecting 2 cases of thymic carcinoma and documented the absence of uptake of Tl-201 by residual tissue indicating a lack of tumor viability. In the current case, the uptake of Tl-201 by the thymoma was remarkable, and pathological examination documented that it was the invasive type. Postoperative radiation was arranged in order to reduce the possibility of local recurrence. Tl-201 can be considered a tool for long-term follow-up to detect local recurrence.

A few cases of unsuspected thymoma discovered during Tl-201 and Tc-99m tetrofosmin SPECT exercise stress testing have been reported.^(2,6,12,13) Initial suspicions in those cases were of coronary artery disease, due to complaints of chest pain, and thus heart scintigraphy was arranged for ischemic heart study. This illustrates that the characteristics of chest pain of a thymoma may mimic a heart origin and can mislead physicians into having a wrong initial impression.

In summary, the tumor-seeking property of Tl-201 is not widely used for clinical purposes, although it is taken up by various tumors. A lack of high sensitivity and specificity is the major reason. Most reports are described as being particularly interesting tumor cases. We present this case of the incidental discovery of an invasive thymoma during Tl-201 SPECT stress testing. The finding of extracardiac uptake led to further studies which diagnosed a mediastinal tumor. Tl-201 SPECT can serve as a potential method for postoperative follow-up in this patient.

REFERENCES

1. Schweil AM, McKillop JH, Milroy R, Wilson R, Abdel-Dayem HM, Omar YT. Mechanism of Tl-201 uptake in

- tumor. *Eur J Nucl Med* 1989;15:376-9.
2. Cox PH, Belfer AJ, Van der Pompe WB, Delpart CC, Marcuse HR, de Vijlder JJ. Thallium-201 chloride uptake in tumors, a possible complication in heart scintigraphy. *Br J Radiol* 1976;49:767-8.
3. Seto H, Kageyama M, Shimizu M, Wu YW, Kamei T, Kakishita M. Assessment of residual tumor viability in thymic carcinoma by sequential Thallium-201 SPECT: Comparison with CT and biopsy findings. *J Nucl Med* 1994;35:1659-61.
4. Hoefnagel CA, Delprat CC, Marcuse HR. Role of Thallium-201 total body scintigraphy in follow-up of thyroid carcinoma. *J Nucl Med* 1986;27:1854-7.
5. Yuzuriha H, Morimoto M, Inokawa K, Hikita H, Iida F. Scintiscanning demonstration of thymoma: comparative study on scintiscans using Tl-201, Ga 67, Se 75. *Jpn J Surg* 1986;16:250-6.
6. Paull DE, Graham J, Forgetta J, Turissini T, Saidman B. Detection of occult thymoma during exercise Thallium-201, Technetium 99m Tetrofosmin imaging for coronary artery disease. *Chest* 2000;118:550-1.
7. Elgazzar AH, Fernandez-Ulloa M, Silberstein EB. ²⁰¹Tl as a tumor-localizing agent: current status and future considerations. *Nucl Med Commu* 1993;14:96-103.
8. Venuta S, Ferraiuolo R, Morrone G, Ambei-Impimbato FS, Mansi L, Salvatore M. The uptake of Tl-201 in normal and transformed thyroid cell lines. *J of Nucl Med & Allied Sci* 1979;23:163-6.
9. Fukuda T, Itami M, Sawa H, Fumkawa T, Fukawa T, Fukakusa S, Tsuchihashi N, Kakehi H, Takahashi Y, Fujimoto Y, Futonaka H, Takemura T. A case of thymoma arising from undescended thymus. High uptake of Thallium-201 Chloride. *Eur J Nucl Med* 1980;5:465-8.
10. Ohta H, Taniguchi T, Watanabe H, Watanabe H, Komibuchi T, Nakade M, Kohno K. Tl-201 and Tc99m HMPAO SPECT in a patient with recurrent thymoma. *Clin Nucl Med* 1996;21:902-3.
11. Kageyama M, Seto H, Shimizu M, Nagayosh T, Watanabe N, Kamei T, Kakishita M. Thallium-201 single photon emission computed tomography in the evaluation of thymic carcinoma. *Radiat Med* 1994;12:237-9.
12. Campeau RJ, Ey EH, Varma GK. Thallium-201 uptake in a benign thymoma. *Clin Nucl Med* 1986;11:524.
13. Adalet I, Kocak M, Ece T, Yilmazbayhan D, Cantez S. Tc-99m MIBI and Tl-201 uptake in a benign thymoma. *Clin Nucl Med* 1995;20:733-4.

鉈-201核醫心肌灌注掃描意外偵測出侵犯性胸腺瘤

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鉈-201為一種氯化鉈的化合物，目前廣泛應用於核醫心肌灌注掃描檢查，但是鉈-201也被報告有搜尋腫瘤的功能。在許多的報告中，鉈-201可以被許多腫瘤組織吸收，包括甲狀腺瘤、肺癌、淋巴瘤、以及腦部、骨骼、肝臟和胸腺的惡性腫瘤。鉈-201也被報告使用於腫瘤治療反應的追蹤。在進行心肌灌注掃描攝影時，有時可意外發現胸腔腫瘤的例子。我們報告一個63歲的病人，罹患胸痛數週，臨床上懷疑患有缺氧性心臟疾病，因而安排進行鉈-201核醫心肌灌注掃描檢查。意外發現心臟外不正常的左前縱膈顯影。胸部電腦斷層進一步顯示為一6公分大小的左前縱膈腔腫瘤，病患接受縱膈腫瘤切除手術，病理報告證實為一侵犯性胸腺瘤，並已侵犯到左無名靜脈。術後病人接受放射線治療，病情穩定，繼續於門診追蹤。(長庚醫誌 2004;27:138-42)

關鍵字：鉈-201，前縱膈腔腫瘤，侵犯性胸腺瘤。