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CASE REPORT

Recurrent thymoma: radiological (CT and FDG-PET) and histological (WHO criteria) features

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Abstract A 66-year-old man, who had undergone surgical resection of a primary noninvasive thymoma (type B1) in the right anterolateral mediastinum 6 years before, underwent follow-up computed tomography (CT) scanning. The CT scan revealed a few nodules located at the posterior portion of the right thoracic base and just behind the right upper anterior chest wall. Subsequent fluorodeoxyglucose positron emission tomography (FDG-PET) scans showed multiple foci with high [standard uptake value (SUV) 4.3] and low (SUV 2.6) FDG uptake in the right lower posterior area and right upper anterior area of the chest, respectively. The fusion image of the CT and FDG-PET scans demonstrated that the areas of the increased FDG uptake corresponded to those of the nodules on the CT scan. All of the nodules were successfully removed surgically, and the histological features of the nodules indicated that they were type B1 or types B1 plus B2. We regarded the nodule located just behind the right upper anterior chest wall as a type B1 thymoma, whereas those in the posterior area of the right thoracic base as combined thymomas of types B1 plus B2. Our limited experience suggests that the degree of FDG uptake is a reflection of the subtype according to the World Health Organization (WHO) criteria. Furthermore, we showed the role of FDG-PET in the accurate assessment of recurrent thymoma and its therapeutic strategy.

Key words Thymoma · Recurrence · CT · FDG-PET

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Introduction

Thymomas are common primary neoplasms in the anterior mediastinum. They are usually slow-growing tumors. However, they include variable histologic features and heterogeneous oncologic behavior.[1] A small number of thymomas show invasive growth, pleural dissemination, and extrathoracic metastasis in the late clinical course even if they had shown noninvasive features macroscopically or microscopically (histologically) in the early clinical stage.[2]

In 1999, the World Health Organization (WHO) proposed a histological classification of thymic epithelial tumors that was based on the morphology of epithelial cells and on the lymphocyte-to-epithelial cell ratio. Thymic epithelial tumors are now classified into five thymoma entities: types A, AB, B1, B2, B3; all thymic carcinomas are called type C thymomas.[3,4]

We report here a patient who had undergone resection of a primary thymoma 6 years before but then

developed a recurrent thymoma with pleural dissemination. We describe the histological and radiological features of the primary and recurrent thymomas. Moreover, we discuss not only the probable correlation of fluorodeoxyglucose (FDG) uptake with the histological WHO criteria but also the role of FDG-positron emission tomography (PET) in the therapeutic strategy for the recurrent thymoma.

Case report

A 60-year-old man underwent chest radiography for his regular health checkup, and it showed a large nodular shadow at the right hilus. CT scans revealed a large mass at the right anterior-to-lateral mediastinum. However, there were no definitive pulmonary shadows and no mediastinal lymphadenopathy. The mediastinal mass was successfully resected. Macroscopically it looked like an encapsulated noninvasive thymoma. Histological examination demonstrated a lymphocyte-rich thymoma with no microscopic invasion to the capsule. It was retrospectively diagnosed as a type B1 thymoma according to the WHO criteria.

He underwent computed tomographic (CT) examination annually after the surgery. Six years later, the follow-up CT scan showed small nodular shadows with smooth contours and a homogeneous solid density in the right thoracic base located close to the diaphragm (Fig. 1). Moreover, we found a small nodule located just behind the right anterior chest wall (Fig. 2).

A PET study was scheduled to evaluate the grade of FDG uptake in the nodules. It was performed on a Biograph PET/CT scanner (Siemens, Hoffman Estates, IL, USA), which combines a dual-detector spiral CT scanner (Somatom Emotions; Siemens, Erlangen, Germany) and a high-resolution PET scanner with a resolution of 4.5 mm and three-dimensional image acquisition. Scans were performed 60 min after intravenous administration of 185 MBq of ^{18}F-FDG. PET images were corrected for attenuation on the basis of the CT data. Iterative algorithms (nonlinear Fourier rebinning and nonlinear attenuation-weighted ordered-subsets expectation maximization) with two iterations and eight subsets were used for image reconstruction. Data were filtered (3.0 mm in full width at half-maximum) and corrected for scatter. The computer displayed the average SUV of pixels in the region of interest (ROI) on the nodules.

The FDG-PET scan showed a few foci of increased uptake not only in the right lower chest but also in the right upper anterior chest, and the SUVs of the tumors in the right lower and right upper anterior chest were 4.3 and 2.6, respectively (Fig. 3). The fusion image of the CT and FDG-PET scans revealed that the areas of increased FDG uptake were just visible at the position of the nodules on the chest CT image (Fig. 4).

Open thoracic surgery demonstrated that the nodules at the right thoracic base were smooth, lobulated masses on the pleura underneath the right lung (Fig. 5). Histological features of the surgical specimen indicated that the nodules were type B1 thymoma or combined types

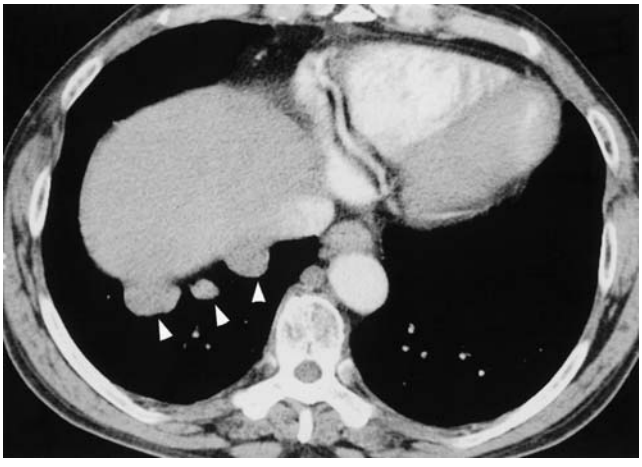

Fig. 1. Enhanced 5-mm collimation computed tomography (CT) scan 6 years after primary thymothymectomy obtained at the level of the intrahepatic inferior vena cava shows small nodular lesions (*arrowheads*) located at the border between the lung and the liver. The diameters of a few nodular components of the lobulated mass are 18–25 mm

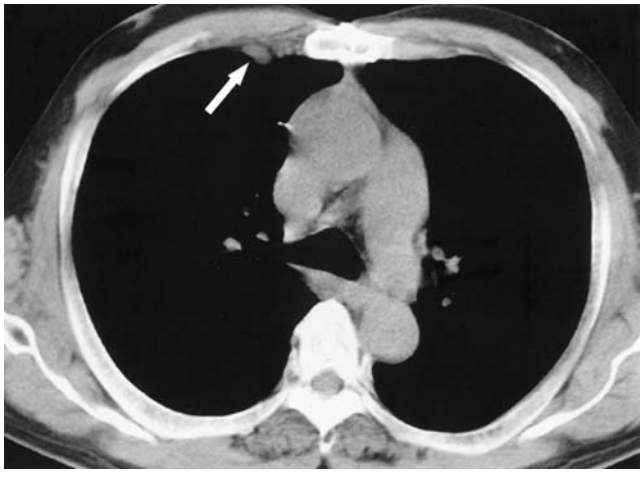

Fig. 2. A 10-mm collimation CT scan obtained at the level of the bronchial carina shows a small nodule (*arrow*) located at the border between the right anterior chest wall and the lung. The short and long diameters of the nodule are 8 mm and 13 mm, respectively

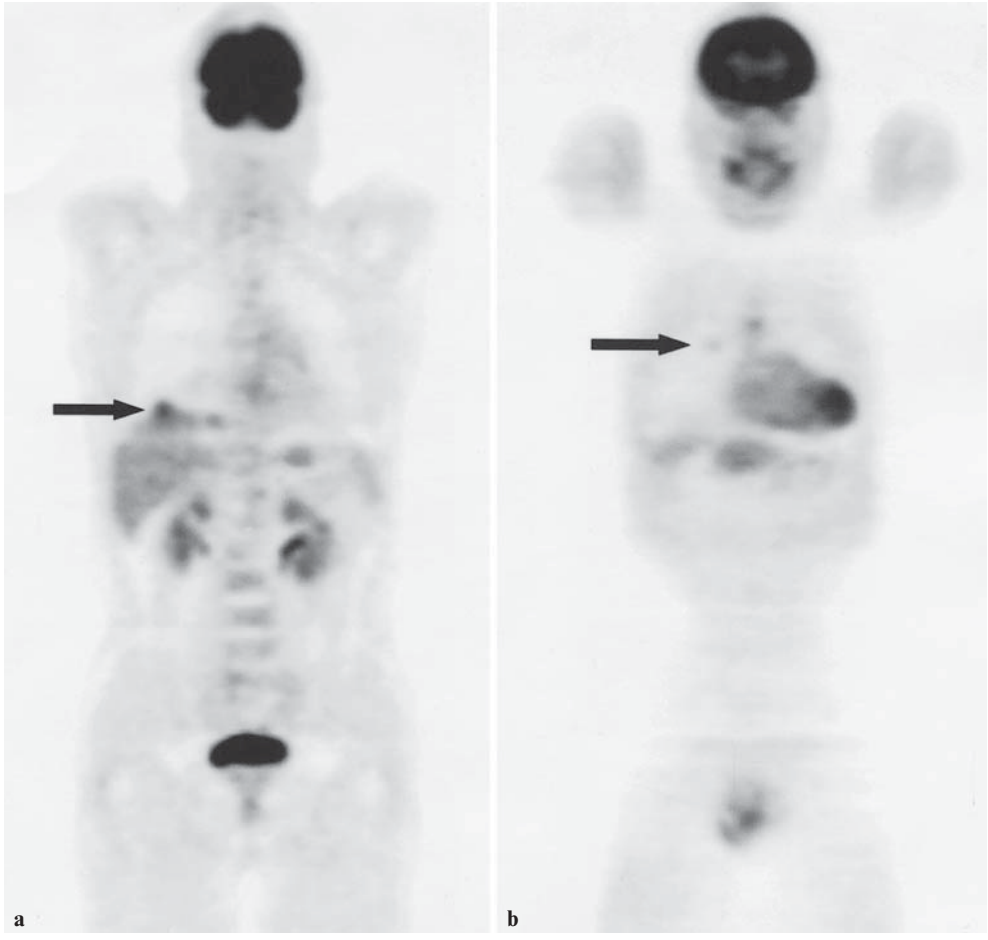

Fig. 3. **a** Fluorodeoxyglucose positron emission tomography (FDG-PET) shows high activity (*arrow*) at the right lower and posterior chest, the standard uptake value (SUV) of which was 4.6. **b** FDG-PET shows low activity (*arrow*) at the right upper anterior chest, the SUV of which was 2.4

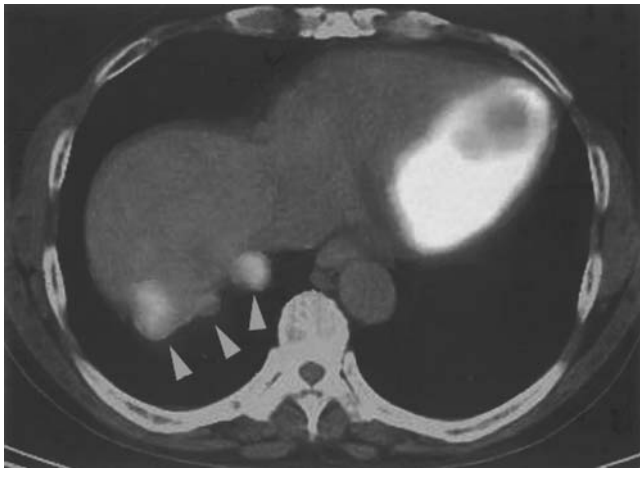

Fig. 4. Fusion image of FDG-PET and CT at the level of the intrahepatic inferior vena cava demonstrates that high uptake of FDG is visible in the nodules (*arrowheads*). High-level uptake is also seen in the myocardium of the left ventricle

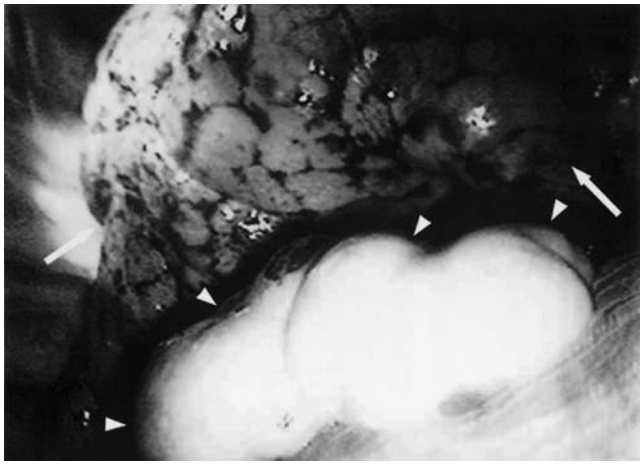

Fig. 5. Open chest surgery discloses that the large nodule (*arrowheads*) with a smooth and lobulated contour is located in the base of the right lower chest and is visible under the right lung (*arrows*). This photograph shows that the nodules on the CT image in Fig. 1 are part of the large lobulated mass

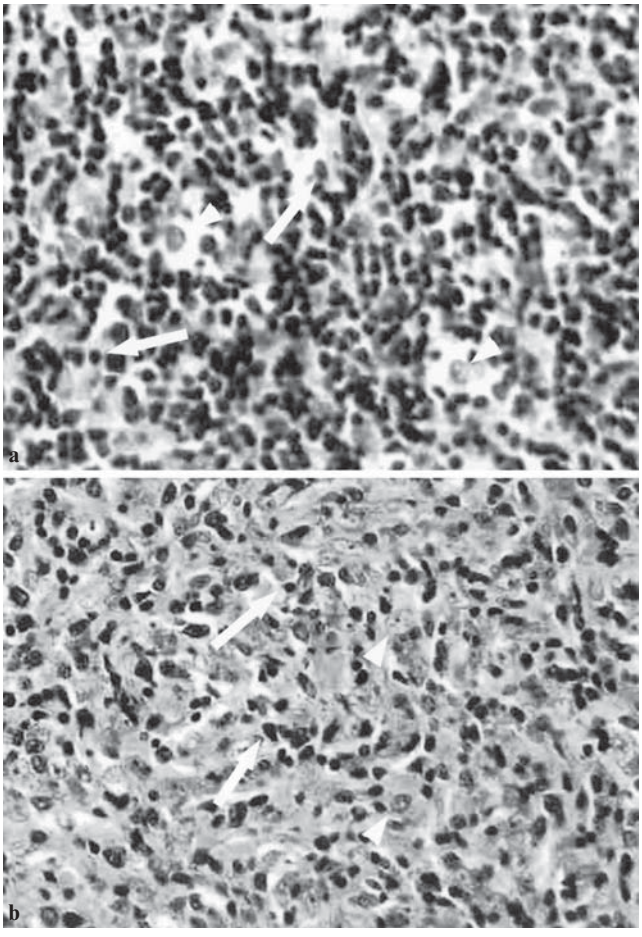

Fig. 6. **a** Microscopic histology shows a dense population of lymphocytes (*arrows*) and some epithelial tumor cells with large nuclei of pale chromatin and small nucleoli (*arrowheads*), which are features of type B1 thymoma. **b** Microscopic histology shows the combination of the features of Fig. 6a, which correspond to a type B1 thymoma; moderate lymphocyte infiltration (*arrows*), which is less abundant than is seen in type B1; and plump tumor cells with vesicular nuclei and distinct nucleoli (*arrowheads*), which correspond to the features of type B2 thymoma. **a**, **b** H&E ×200

B1 plus B2 thymoma. We regarded the small nodule just behind the right upper anterior chest wall as type B1 (Fig. 6a), whereas the nodules in the right lower thoracic base were a combined thymoma of types B1 plus B2 (Fig. 6b).

The patient has been well for half a year without definite signs of re-recurrence after the second surgery.

Discussion

Thymomas show variable histological features and heterogeneous oncologic behavior. Histological features include neoplastic epithelial cells with differing shapes and degrees of atypia and various degrees of nonneoplastic lymphoid cells in the tumors.[5] The histological features are now classified by the WHO criteria, which reflect the clinical features of the thymomas and correlate with their prognosis.[3,6] CT findings and histological features by WHO criteria have been compared in a recent study.[7] However, CT is of limited value in differentiating histologic types or subtypes according to the WHO criteria.[7,8]

The present patient underwent regular base CT examination annually after the first surgery, and 6 years later the CT scan revealed a few nodules with solid density and a smooth contour located at the posterior right thoracic base and just behind the right upper anterior chest wall. The CT features of the nodules located close to the pleura suggest pleural dissemination of the recurrent thymoma.[9]

FDG-PET scanning was performed to obtain further information about the nodules. The previous report indicated that the classification of thymomas by FDG-PET correlated with the clinical stage rather than the cytological classification (before the WHO criteria were established), and a high SUV usually reflected invasiveness of a malignant nature by the thymic tumor, whereas a low SUV reflected a less invasive malignant thymoma.[10] On the other hand, the behavior of type B1 thymoma differed from that of type B2, and the clinical stage and WHO histological subtype are both considered independent prognostic factors when predicting survival.[4] In contrast, to our knowledge, a comparison of FDG uptake and the WHO histological subtypes has not been described to date in the literature.

Primary thymomas are usually large enough to produce correct SUVs, whereas the nodules of recurrent thymoma with pleural dissemination often appear as multiple small nodules,[9] which makes it difficult to determine their actual SUVs because SUVs of the small nodules are frequently reduced by the partial volume effect of the PET scanner. The small nodule located just behind the right upper anterior chest wall of the present case was almost as large as twice the space resolution of the PET scanner. We eventually came to believe that the SUV of the nodule might be not greatly but only mildly reduced by the partial volume effect of the PET scanner.

We believe that the low or high level of the SUV is a reflection of thymomas of type B1 or of the combined types B1 plus B2, respectively, and that the classification of thymomas by FDG-PET probably correlates not only with the clinical stage but also with the WHO histological subtype. The validity of the correlation, however, should be addressed by further investigation with a large number of patients.

Referring to the simplified subgroups of the WHO histological criteria,[8] we think that the type B1 thymoma has a low risk of re-recurrence, whereas the combined

thymoma of types B1 plus B2, which has been described in a few patients with recurrent thymomas,[4,11] probably has a high risk of re-recurrence.

We wanted to determine if there were extrathoracic metastases in the present patient, although low-grade malignant thymomas usually invade contiguous structures and frequently cause progressive intrathoracic metastasis.[12] FDG-PET of the present patient eventually showed no extrathoracic abnormal uptake. Therefore, resection of recurrent thymomas is considered an appropriate therapeutic strategy because it usually improves the prognosis.[13]

Conclusion

We presented a patient who developed a recurrent intrathoracic thymoma a long time after resecting the primary thymoma. We also reported the radiological (CT and FDG-PET) and histological (WHO criteria) features. We believe that the different SUV levels for recurrent thymomas, determined by FDG-PET, are well correlated with the histological features classified by the WHO criteria. Moreover, we think that the FDG-PET study is useful for accurately demonstrating the position of the recurrence, with the resultant establishment of a therapeutic strategy for the recurrent thymoma.

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