Clinical Usefulness of Fluoro-2-Deoxy-D-Glucose PET in a Case with Multiple Bone Metastases of Carcinoid Tumor after Ten Years

Yoshihiro Kobashi1, Hiroki Shimizu1, Keiji Mouri1, Tsutomu Irei2 and Mikio Oka1

Abstract

We report a peculiar case in an 80-year-old man with multiple bone metastases due to the recurrence of thymic carcinoid tumor after surgical resection and radiation therapy ten years earlier. He was admitted to our hospital with a complaint of lumbago. Fluoro-2-deoxy-D-glucose (FDG) PET was useful for recognition of multiple bone metastases due to the recurrence of thymic carcinoid tumor, while 201Tl-whole body scintigraphy and by 99mTc-methylene diphosphonate (99mTc-MDP) bone scintigraphy did not reveal the metastases. Finally, we performed a CT-guided bone biopsy from lumbar vertebra and could obtain the diagnosis of metastases of carcinoid tumor histologically. As evident in this case, it is important to consider the recurrence of carcinoid tumor even if a long time has passed after the surgical resection and radiation therapy; also FDG-PET may be a useful diagnostic imaging modality to detect metastases from thymic carcinoid tumor to other organs.

Key words: thymic carcinoid tumor, fluoro-2-deoxy-D-glucose (FDG) PET, multiple bone metastases


Introduction

Thymic carcinoid tumor was first reported in 1972 by Rosai and Higa (1) and over 150 cases of thymic carcinoid have been reported since then. Thymic carcinoid tumor is a neuroendocrine tumor arising from Kulchitsky cells of the thymus and histological criteria have been proposed by the World Health Organization (WHO) (2). The five-year survival rate ranges from 40% to 70% (3). Thymic carcinoid tumor has the potential for local and/or distant metastasis, frequently to the lymph nodes, liver, lung and bone (4). However, there are a few cases demonstrating multiple bone metastases due to the recurrence of thymic carcinoid tumor after surgical resection and radiation therapy ten years earlier as in this case.

Imaging techniques using not only CT, MRI, scintigraphy but also FDG-PET have recently been developed in order to detect primary and metastatic lesions of carcinoid tumors (5-7). We report a peculiar case of multiple bone metastases due to recurrence of thymic carcinoid tumor after surgical resection and radiation therapy ten years earlier. FDG-PET was useful to detect multiple bone metastases of thymic carcinoid tumor in this case.

Case Report

An 80-year-old man was admitted to our hospital with a complaint of lumbago. Although chest CT was performed every year in another hospital, the check of metastases was not performed before the occurrence of lumbago because there were no clinical symptoms suggestive of metastases. Ten years earlier, he had been diagnosed as having thymic carcinoid tumor histologically following surgical resection and received radiation therapy (January 1999). There were no abnormal laboratory findings, including tumor marker levels at that time. Chest radiograph showed left hilar swelling (Fig. 1). Chest CT demonstrated a mass lesion (50x50...
Figure 1. Chest radiograph (January, 1999) showed left hilar swelling (arrow).

Figure 2. Chest MRI (January 1999) demonstrated a mass lesion (50×50 mm) in the anterior mediastinum with a comparatively clear margin showing a low intensity on T1, high intensity on T2 and Gadolinium-DTPA enhancement (arrow).

mm) in the anterior mediastinum with high density enhancement. Chest MRI demonstrated a mass lesion with a comparatively clear margin showing a low intensity on T1, high intensity on T2 and gadolinium-DTPA enhancement (Fig. 2). Regarding metastases to other organs, there were no obvious metastases on ⁶⁷Ga whole body scintigraphy or ⁹⁹mTc-methylene diphosphonate (⁹⁹mTc-MDP) bone scintigraphy in January 1999.

Histological examination of the surgical specimen showed that the tumor consisted of diffuse cellular nests of polygonal tumor cells with oval to spherical hyperchromatic nuclei and scant cytoplasm, supported by abundant vascular stroma (Fig. 3). Immunohistochemical study confirmed that most tumor cells were positive for epithelial membrane antigen (EMA), chromogranin A and synaptophysin (Fig. 4), but negative for somatostatin receptor and serotonin. In the findings of electron microscopic examination, the cytoplasm of tumor cells had abundant mitochondria and multiple neuroendocrine granules were also recognized (Fig. 5).

Next, there were no abnormal laboratory findings including tumor marker levels on this admission (January 2009). Chest radiograph showed infiltration shadow in the left upper lung field due to the history of radiation pneumonitis (Fig. 6). Chest CT did not reveal new lesions in either lung field except for the finding of radiation pneumonitis in the left upper lobe, and also abdominal CT and brain MRI did not reveal any abnormalities.

Figure 3. Histological findings showing diffuse cellular nests of polygonal tumor cells with oval to spherical hyperchromatic nuclei and scant cytoplasm (Hematoxylin and Eosin staining, ×100).

Figure 4. Immunohistochemical findings showing a typical thymic carcinoid by positive staining for synaptophysin (×100)

Figure 5. Electron microscopic findings showing the cytoplasm of tumor cells had abundant mitochondria (arrow) and multiple neuroendocrine granules (arrowhead).
Figure 6. Chest radiograph (January 2009) showed infiltration shadow in the left upper lung field due to a history of radiation pneumonitis.

Figure 7. Bone scintigraphy using $^{99m}$Tc-MDP demonstrated any abnormal uptake.

Figure 8. FDG-PET showed increased uptake in multiple bones including cervical, thoracic, and lumbar vertebrae, ribs, pelvis and skull bones.

Figure 9. Bone metastases in the lumbar vertebrae were demonstrated by spinal MRI (arrow).

not detect any new lesions suspected to be metastatic lesions. Neither $^{201}$Tl-whole body scintigraphy nor bone scintigraphy using $^{99m}$Tc-MDP (Fig. 7) demonstrated any abnormal uptake. FDG-PET was performed in order to assess the staging of thymic carcinoid disease. There was diffuse intense FDG-PET uptake in various bones including cervical, thoracic and lumbar vertebrae, ribs, pelvis, skull bones (Fig. 8). Bone metastases in the thoracic and lumbar vertebrae were confirmed by spinal MRI (Fig. 9).

On histological examination of bone metastasis to the lumbar vertebrae, findings were the same as those of the thymic carcinoid tumor resected ten years earlier, including those on immunohistochemical study. Namely, the metastatic tumor of lumbar vertebrae consisted of diffuse cellular nests of polygonal tumor cells (Fig. 10). Most tumor cells were positive for EMA, chromogranin A and synaptophysin (Fig. 11), but negative for somatostatin receptor and serotonin in immunohistochemical study. Finally, we diagnosed the multiple bone lesions as histologically consistent with recurrence of thymic carcinoid tumor after ten years.

The patient refused treatment for the recurrence of thymic
carcinoid tumor.

Discussion

Because we could demonstrate that histological findings on biopsy of the lumbar vertebrae were consistent with those of the surgical specimen resected ten years earlier, multiple bone lesions showing intense FDG-PET uptake were proven to be recurrence of thymic carcinoid in this peculiar case. Carcinoid tumors arise from neuroendocrine cells. A carcinoid tumor of thymic origin is quite a rare neoplasm accounting for approximately 2% of intrathoracic tumors and has more malignant phenotypes than carcinoid tumors of the other organ origin (8, 9). The frequency of bone metastasis of carcinoid tumors has been described to range between 7% and 15% (10-12). The present case showed malignant phenotypes with multiple bone metastases. The interval from the diagnosis of carcinoid tumor to the appearance of bone metastases showed a wide range (0-239 months) in a previous report described by Meijer et al (13). The reason is probably related to the indolent course of the disease and the difficulty in diagnosis. In the present case, because there was no change excluding the lesion of radiation pneumonitis on chest CT and there were no clinical symptoms suggestive of the recurrence of carcinoid tumor, multiple bone metastases could not be detected until this patient consulted the hospital complaining of lumbago after ten years of the treatment for the primary lesion.

Concerning the radiological strategy, the optimal imaging modality has not been well defined and there is no optimal imaging technique that can identify both primary and metastatic sites. FDG-PET has recently been used to detect malignant lesions and several studies have reported the clinical usefulness for the detection of carcinoid tumors (14-18). Le Rest et al reported that FDG-PET identified more abnormal lesions in patients with carcinoid metastases than 123I-MIBG SPECT or somatostatin receptor scintigraphy (SRS) using 111In-octreotide (14). Fujishita et al also reported that FDG-PET was more useful to detect the primary and metastatic lesions due to thymic carcinoid than 123I-MIBG SPECT or 99mTc-MDP bone scintigraphy (15). Conversely, Jadvar and Segall reported that FDG-PET is inferior to SRS for detecting carcinoid tumors (16). In a previous report on the usefulness of FDG-PET in patients with thymic carcinoid (17), the imaging technique was successful in the detection of the primary site, but it failed to detect bone metastatic lesions in the vertebral. Namely, FDG-PET was less useful for detecting bone metastases than 99mTc-MDP bone scintigraphy and 123I-MIBG SPECT. In the present case, both FDG-PET and spine MRI showed positive findings for metastatic lesions at multiple bone sites, whereas neither 67Ga whole body scintigraphy nor 99mTc-MDP bone scintigraphy showed positive results. To our knowledge, our case is the second case report describing the usefulness of FDG-PET for detecting metastatic lesions in patients with thymic carcinoid tumor. The reason why FDG-PET showed positive results for primary and metastatic lesions in the present case in spite of the negative results of scintigraphy was not clear. Although Pasquali et al have speculated that FDG-PET may be more useful in neuroendocrine tumors that are characterized by rapid growth (18), the cytoplasm of tumor cells in our case had multiple neuroendocrine granules electromicroscopically (Fig. 5).

It is important to be aware of the possible recurrence of primary intrathoracic thymic carcinoid tumor even if a long time has passed after the first treatment; FDG-PET seems to be useful for the detection of bone metastasis of thymic carcinoid tumor.

References


2. World Health Organization International Histological Classification of Tumors: Histological Typing of Lung and Pleural Tumors. 3rd ed. Travis WD, Colby TV, Corrins B, Shimosato Y, Brambilla