

# <sup>18</sup>F-fluorodeoxyglucose imaging of primary malignant pericardial mesothelioma with concurrent pericardial and pleural effusions and bone metastasis: A case report

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**Abstract.** Primary malignant pericardial mesothelioma (PMPM) is an aggressive tumor that originates from the mesothelial cells of the pericardium. PMPM with extensive atrial infiltration and bone metastasis is extremely rare. The diagnosis and staging of PMPM based on anatomical imaging may be difficult when concurrent pericardial and pleural effusions are present. A 28-year-old man presented with progressive chest pain. Concurrent pericardial and pleural effusions were identified on computed tomography. On echocardiography, mild thickening and adhesions of the pericardium with the right ventricle and atrium were observed. <sup>18</sup>F-fluorodeoxyglucose (FDG) metabolism imaging revealed increased accumulation in the pericardium and adjacent right atrium. Ring-shaped radioactivity aggregation and bone destruction in the sacrum were demonstrated on <sup>18</sup>F-FDG and <sup>99m</sup>Tc-methyl diphosphonate imaging. The diagnosis of PMPM was subsequently confirmed by pathology. The patient survived for >1.5 years with comprehensive treatment.

## Introduction

Primary malignant pericardial mesothelioma (PMPM) is extremely rare, with an estimated incidence of <0.0017%, as reported in a large autopsy study of ~50,000 cases (1). PMPM is an aggressive tumor that originates from the mesothelial cells of the pericardium and is generally diagnosed following

surgical excision. Tumor diagnosis and staging (including myocardial infiltration) with anatomical imaging methods, such as computed tomography (CT), echocardiography and magnetic resonance imaging (MRI), may be particularly challenging in PMPM due to its diffuse pattern of growth. Early diagnosis, staging (including assessment of myocardial infiltration) and response evaluation are crucial for determining treatment. We herein report our experience with <sup>18</sup>F-fluorodeoxyglucose (FDG) metabolism imaging in a PMPM patient for early diagnosis, staging and response evaluation.

## Case report

In May 2010, a 28-year-old man was admitted to the Nanjing First Hospital due to progressive left-sided chest pain and breathlessness for 4 months, which had worsened over the last 1 h. The patient had a 10-year history of smoking (1 pack/day). There was no history of tuberculosis or asbestos exposure. Two months prior to admission, the patient had been hospitalized with the same symptoms in another hospital. Physical examination, chest radiography, computed tomography (CT) and enhanced CT revealed widening of the myocardial boundary, concurrent large pericardial effusion and little-to-moderate pleural effusion (Fig. 1B). A total of 1,800 ml of pericardial fluid were evacuated. Cytological examination of the pericardial fluid only found reactive mesothelial cells, without acid-fast bacilli or tumor cells. Echocardiography revealed thickening of the free wall of the right ventricle (RV), with adhesions to the adjacent pericardium and uneven thickening of the right atrium (RA) to 0.8-1.4 cm. The thickened pericardium near the output of the RV has also restricting myocardial motion. A liquid anechoic area was detected in the pericardial cavity and pericarditis was highly suspected (Fig. 1A). Experimental antituberculosis treatment was refused when the Mantoux test was found to be strongly positive. The patient was referred to our hospital due to worsening shortness of breath and was tentatively treated with antituberculous agents (isoniazid and rifampin), with a poor therapeutic effect and increasing volume of the pericardial effusion. <sup>18</sup>F-FDG imaging was performed to rule out malignancy; it revealed highly increased uptake of

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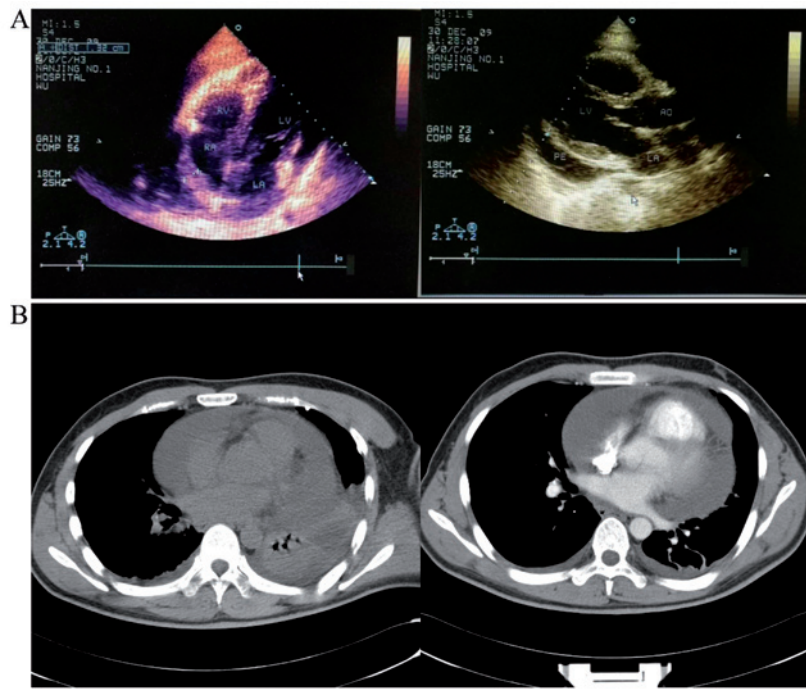


Figure 1. (A) Echocardiogram and (B) chest computed tomography (CT) images (left, unenhanced; and right, enhanced CT scan). Echocardiography revealed thickening of the pericardium and adjacent right ventricle and right atrium. CT images revealed concurrent pericardial and pleural effusion.

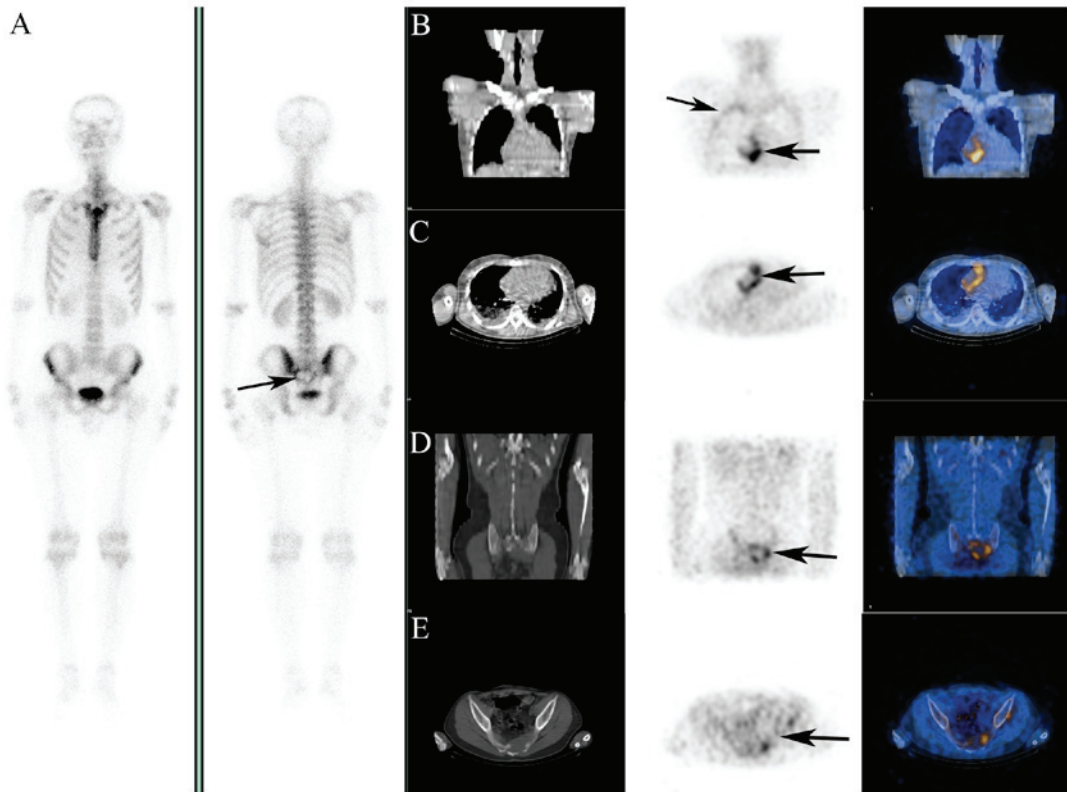


Figure 2. <sup>18</sup>F-FDG images and <sup>99m</sup>Tc-MDP bone scan images. (A) <sup>99m</sup>Tc-MDP whole-body scan showing a sacral osteolytic metastasis (arrow) (left, anterior view; right, posterior view). (B and C) Highly increased uptake of <sup>18</sup>F-FDG was observed in the right atrium and the pericardium adjacent to the right ventricle and atrium, with mild increase in the inner wall of the thoracic cavity (arrows). (D and E) Ring-shaped radioactivity aggregation and osteolytic bone metastasis in the sacrum were visualized on <sup>18</sup>F-FDG coincidence imaging (arrows). B-E: Left panel, CT; middle panel, <sup>18</sup>F-FDG PET; and right panel, PET-CT fusion images. FDG, fluorodeoxyglucose; MDP, methyl diphosphonate; CT, computed tomography; PET, positron emission tomography.

<sup>18</sup>F-FDG in the RA, the pericardium adjacent to the RV and RA (Fig. 2B and C, arrows), and mildly increased uptake

along the inner thoracic wall (Fig. 2B, arrows). Ring-shaped radioactivity aggregation and bone destruction in the sacrum

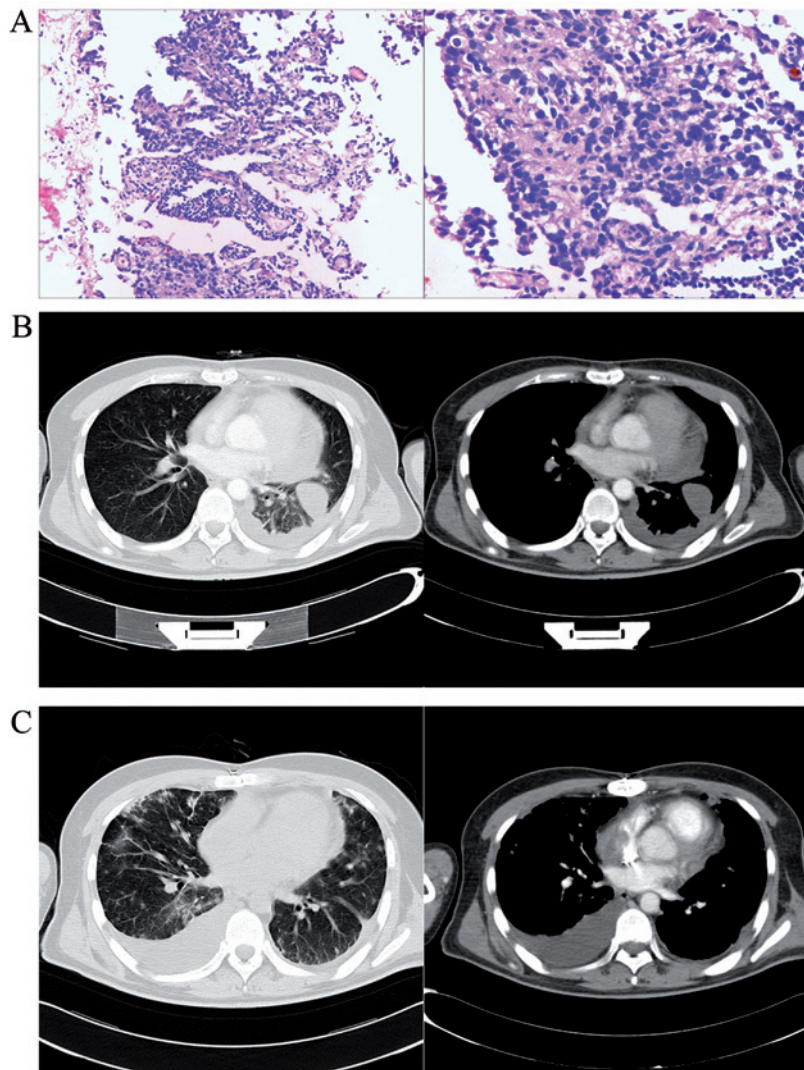


Figure 3. Pathology of pericardium and computed tomography (CT) images at 4 months and 1 year after surgical resection. (A) Tissue from the pericardium and adjacent atrium stained with hematoxylin and eosin staining (original magnification: left panel, x50; and right panel, x100) revealed diffuse infiltration of the pericardium by epithelioid cells in papillary arrangements. The tumor cells were characterized by abundant cytoplasm, prominent nuclei and cytoplasmic vacuoles. (B) No pericardial effusion and little pleural effusion were observed at 4 months after the operation on contrast-enhanced CT (left panel, lung window; and right panel, mediastinal window). (C) Multiple lung metastases and a large pleural effusion were found at 1 year postoperatively (left panel, lung window; and right panel, mediastinal window).

were visualized on  $^{18}\text{F}$ -FDG imaging (Fig. 2D and E, arrow) and  $^{99\text{m}}\text{Tc}$ -methyl diphosphonate (MDP) whole-body scan (Fig. 2A, arrow). PMPM with RA infiltration and bone metastasis was highly suspected. An incisional pericardial biopsy was performed and pathological examination of the samples obtained by biopsy confirmed the diagnosis of PMPM with atrial infiltration (Fig. 3A) (cytokeratin5/6<sup>+</sup>, D2-40<sup>+</sup>, calretinin<sup>+</sup>, carcinoembryonic antigen<sup>-</sup>, thyroid transcription factor 1<sup>-</sup>). Following surgery, a doublet chemotherapy regimen (pemetrexed 500 mg/m<sup>2</sup> + cisplatin 75 mg/m<sup>2</sup> were administered on the first day of each 3-week cycle, for a total of six cycles) was introduced immediately after definitive diagnosis. During follow-up, CT imaging revealed little pericardial effusion at 4 months postoperatively (Fig. 3B), but lung metastasis and large pleural effusion were observed 1 year after the operation (Fig. 3C). The patient survived for >1.5 years after the diagnosis and succumbed to severe pericardial effusion and cardiac tamponade in September 2012.

## Discussion

Malignant mesothelioma usually occurs in the peritoneum or pleura, while it rarely occurs in the pericardium. Primary malignant pericardial mesothelioma (PMPM) is an extremely rare occurrence with a low incidence (<0.0022%) and a poor prognosis (2).

Without a definitive etiology or specific clinical manifestations (3), early diagnosis and staging of PMPM may be difficult, particularly in the presence of concurrent pericardial and pleural effusions (4-9). Asbestos exposure is less frequently associated with pericardial mesothelioma compared with pleural mesothelioma, and it is not necessarily considered a risk factor for the development of pericardial mesothelioma. Pericardial effusion/tamponade or constrictive pericarditis is common, and its causes may be infectious (tuberculosis, viral or bacterial infection) or non-infectious diseases (tumor, rheumatism, endocrine and metabolic diseases).



The clinical misdiagnosis rate of PMPM is extremely high due to its non-specific symptoms, ranging from cough, dyspnea and dysphagia to chest pain, as in the present case. The clinical signs are often misdiagnosed as other conditions, such as coronary heart disease, tuberculous pericarditis, atrial myxoma and cardiomyopathy. In the present case, tentative antituberculosis treatment was introduced due to a misdiagnosis based on a positive PPD test. Aspiration and evaluation of pericardial fluid was inconclusive, as it is difficult to differentiate malignant mesothelioma cells from reactive cells.

The characteristic feature of PMPM is focal or diffuse uneven solid growth of the mesothelium, with atypical cavities surrounded by fibrous stroma (10). Among anatomical imaging tools, echocardiography is the one most commonly used. CT and MRI may not clearly delineate the mass and the boundary of PMPM, particularly when adjacent myocardium is infiltrated. <sup>18</sup>F-FDG metabolism imaging is an alternative tool for the diagnosis and accurate staging of most malignant tumors, although it is rarely reported for pericardial mesothelioma (11). Increased tumor <sup>18</sup>F-FDG metabolism may be evident prior to the appearance of anatomical changes. When increased FDG aggregation is demonstrated in the pericardium of patients presenting with recurrent or unexplained pericardial effusion, PMPM should be suspected (12). Multimodal imaging and clinical data are important, while pathology remains the gold standard for the definitive diagnosis of PMPM (13).

The prognosis of PMPM is extremely poor, with a median survival of ~6 months (13,14). Early and systemic therapy, such as surgical resection, radiotherapy and chemotherapy, are required to prolong patient survival. A doublet chemotherapy regimen (pemetrexed + cisplatin) with pemetrexed maintenance was administered to our patient immediately after surgical resection (14,15). Multiple metastases in the lungs were diagnosed 1 year after the operation and the patient survived for >1.5 years after the diagnosis. <sup>18</sup>F-FDG imaging may be a particularly useful tool for early diagnosis, staging and response evaluation in patients with PMPM (7,11,15).

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