



# Extensive Skeletal Muscle Metastases in Malignant Pleural Mesothelioma Detected by FDG PET/CT

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World J Nuclear Med 2023;22:293–296.

## Abstract

Malignant pleural mesothelioma (MPM) is a rare but aggressive tumor originating from pleural mesothelial cells. Distant skeletal muscle metastasis is rare in MPM. A 54-year-old woman was diagnosed with epithelioid MPM and treated with surgery, chemotherapy, and radiotherapy 2 years ago. During follow-up, diffuse irregular pleural thickening with focal chest wall invasion in the right hemithorax and two small pleural thickenings in the left hemithorax were seen on control diagnostic contrast-enhanced computed tomography (CECT). Fluorine-18 fluorodeoxyglucose positron emission tomography/CT (FDG PET/CT) imaging was performed as part of restaging. PET showed diffusely increased FDG uptake in the recurrent right pleural tumor, and two hypermetabolic small metastatic foci in the contralateral pleura. In addition, multiple hypermetabolic areas of various sizes in various skeletal muscle localizations, suggestive of extensive muscle metastases were noted. Histopathologic study confirmed metastatic epithelioid MPM. FDG PET/CT revealed multiple muscle metastases which were not observed on earlier CECT and contributed to the visualization of more extensive metastatic involvements in the presented case with MPM. FDG PET/CT can detect rarely seen skeletal muscle metastases that are not visualized on diagnostic CT, and provides more accurate restaging of MPM.

## Keywords

- malignant pleural mesothelioma
- skeletal muscle metastasis
- FDG PET/CT
- contrast-enhanced CT

## Introduction

Malignant pleural mesothelioma (MPM) is an aggressive form of malignancy with a poor prognosis of fewer than 12 months from the time of diagnosis. It originates from mesothelial cells forming the pleural lining.<sup>1</sup> It is strongly associated with remote asbestos exposure. Histopathologically, MPM has major three subgroups, epithelioid, the predominant subgroup, less commonly sarcomatoid and biphasic subtypes.

Dissemination of MPM is generally local and regional lymph nodes are the major metastatic sites of MPM. Distant metastases are uncommon. However, distant metastases from MPM are

considered more common than previously reported and can involve the liver, spleen, lung, bone, adrenal, kidney, thyroid, and peritoneum, but more rarely the skeletal muscle and brain.<sup>2–5</sup>

Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) has been increasingly used for the presurgical characterization and staging, evaluation of the response to treatment, accurate detection of distant metastases, assessing recurrence, and selecting the site for tissue biopsy of MPM.<sup>6–8</sup>

Here, we report a case of MPM with extensive muscle metastases of various sizes in various skeletal muscle localizations detected by FDG PET/CT but not seen on diagnostic contrast-enhanced CT (CECT).

article published online  
December 4, 2023

DOI <https://doi.org/10.1055/s-0043-1774730>.  
ISSN 1450-1147.

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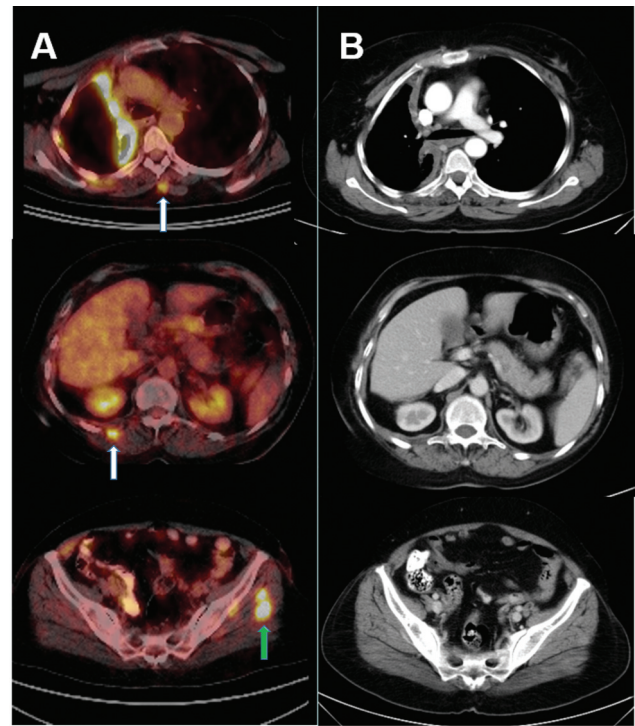
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## Case Report

A 54-year-old woman was diagnosed with epithelioid MPM 2 years ago and she was treated with right extrapleural pneumonectomy, hyperthermic intrathoracic chemotherapy, and radiotherapy. Because of her right-sided chest pain complaint, a control diagnostic CT scan of the chest, abdomen, and pelvis was obtained. Diffuse irregular pleural thickening with a focal chest wall invasion in the right hemithorax and two small pleural thickenings in the left hemithorax were seen on CT images. CT of the abdomen and pelvis did not show any abnormalities. Two weeks later FDG PET/CT imaging was performed as part of restaging. PET showed diffuse irregular high FDG uptake in the recurrent right pleural tumor, more prominent in the mediastinal side with maximum standardized uptake value (SUVmax) of 13.4, and also two hypermetabolic small foci in the left pleura, which suggest metastatic disease to the contralateral pleura (SUVmax: 2.7). In addition, PET/CT demonstrated multiple round, ovoid, or elongated hypermetabolic areas of various sizes in various skeletal muscle localizations, strikingly much more extensive in both legs, including the left medial pterygoid muscle, paraspinal muscles, both gluteal muscles, right biceps brachii muscle, and numerous muscles of both thighs and calves (SUVmax measured between 3.4 and 18.5) (►Fig. 1). On physical examination, the patient had only a slight swelling with mild pain in the lower part of the right biceps brachii muscle. Otherwise, she did not have any abnormal findings related to the skeletal muscles. After the FDG PET/CT findings, the CECT scan of the chest, abdomen, and pelvis was reviewed again, but no contrast-enhanced lesions were seen in the localizations corresponding to the hypermetabolic muscle lesions (►Fig. 2).

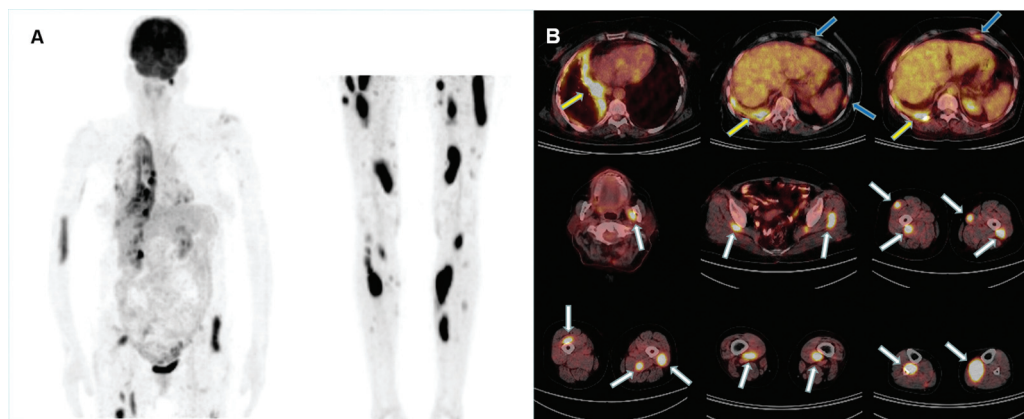
Biopsy from a relatively greater hypermetabolic muscle lesion located in the left calf and histopathology confirmed metastatic epithelioid MPM. Histopathologic examination demonstrated that invasion of the epithelioid neoplastic cells to the muscle tissue was present. The neoplastic cells stained positively for CK 5/6, WT-1, CK7, and CK20. Staining



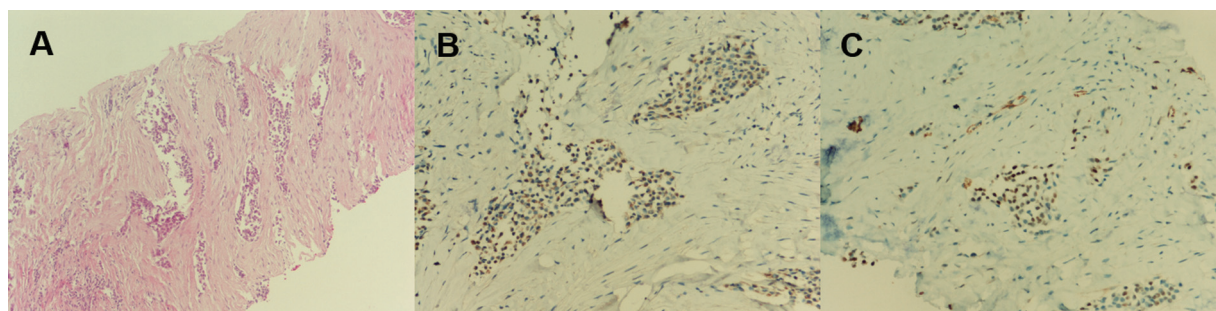
**Fig. 2** Fluorodeoxyglucose (FDG) avid metastatic lesions are clearly seen in the left and right paraspinal muscles (A, fused positron emission tomography/computed tomography [PET/CT] images, white arrows) and left gluteus medius muscle (A, fused PET/CT image, green arrow). No contrast-enhanced lesions are observed in the localizations corresponding to the hypermetabolic muscle lesions and muscle density of the metastatic foci is similar to normal muscles on contrast-enhanced computed tomography images, i.e., they are isodense muscle metastases (B).

was negative for calretinin, thyroid transcription factor-1, carcinoembryonic antigen, and CDX-2 in the immunohistochemical study (►Fig. 3).

In addition to local recurrence and contralateral pleural metastases, FDG PET/CT was able to detect multiple muscle metastases, which were not observed on diagnostic CECT,



**Fig. 1** Increased fluorodeoxyglucose (FDG) uptake in the recurrent right pleural tumor (A, maximum intensity projection [MIP] images; B, axial fused positron emission tomography/computed tomography [PET/CT] images, yellow arrows), and two metastatic hypermetabolic small foci in the left pleura (B, axial fused PET/CT images, blue arrows). Multiple FDG avid foci of variable sizes in different skeletal muscle groups, including left medial pterygoid muscle, paraspinal muscles, bilateral gluteal muscles, right biceps brachii muscle, and extensively in the muscle groups of both lower extremities (A, MIP images; B, axial fused PET/CT images, white arrows).



**Fig. 3** Histopathology of a hypermetabolic lesion biopsied from the left calf confirmed metastatic epithelioid malignant pleural mesothelioma (MPM). Invasion of the epithelioid neoplastic cells to the muscle tissue (A, hematoxylin and eosin,  $\times 100$ ). Immunohistochemistry demonstrated positive staining for CK 5/6 (B,  $\times 200$ ) and WT-1 (C,  $\times 200$ ).

and revealed more extensive metastatic involvements of the skeletal muscles in the presented case with MPM.

## Discussion

MPM is a rare cancer with increasing incidence and poor prognosis.<sup>9</sup> Presentation with metastasis is rare and cases with distant metastases are diagnosed more frequently during the clinical course of the disease.<sup>10</sup> Local metastatic spread is the major dissemination pattern. Distant dissemination is uncommon. However, distant metastases from MPM are considered more common than previously reported and can involve mostly the liver, spleen, lung, bone, adrenal, kidney, thyroid, and peritoneum.<sup>2,3</sup> Metastatic involvement of the skeletal muscle is rare among distant organ metastases in MPM. Not many but several MPM cases with distant muscle metastases have been reported in the literature.<sup>4-6,11-17</sup> It was also noted that the most common histological type of tumor in those cases was epithelioid MPM as observed in our patient.

FDG PET/CT imaging has been increasingly used for pre-surgical characterization and staging at presentation, for evaluation of response to treatment, and restaging during follow-up of patients with MPM.<sup>6-8</sup> Since FDG is a glucose analog, increased glucose use by malignant cells leads to high FDG uptake. Functional PET data, that is, increased FDG uptakes in malignant cells, along with anatomic CT data make FDG PET/CT a very useful and valuable imaging modality in most of malignant diseases.

Multiple skeletal muscle metastases from MPM detected by FDG PET/CT was first reported by Aukema et al.<sup>12</sup> FDG PET/CT was highlighted to be a superior and more effective imaging modality than CT alone in the evaluation of distant metastatic disease of MPM.<sup>2,3,6,12</sup> In the presented case, in addition to local recurrence and contralateral pleural metastases, PET/CT demonstrated extensive skeletal muscle metastases not suspected before, but there were no morphologic abnormalities on diagnostic CT corresponding to the hypermetabolic muscle lesions. As a result, FDG PET/CT provided more accurate restaging of our case with MPM.

The presence of skeletal muscle metastases are usually a rare entity with most malignancies; however, lung cancer has been reported as one of the most frequent causes of muscle metastases.<sup>18,19</sup> Due to the increasing use of hybrid imaging

using FDG PET with CT in recent times, an increase in the frequency of detection of skeletal muscle metastases has been observed.<sup>20</sup> The exact underlying causes are not known yet, but there are some hypotheses as to why metastatic involvement in muscles is so rare. Muscle motion and mechanical tumor destruction, inhospitable muscle pH, and the ability of the muscle to remove tumor-produced lactic acid that induces tumor neovascularization are considered to act as defensive factors against the spread of the tumor.<sup>21,22</sup>

## Conclusion

Rarely seen muscle metastasis in MPM may be missed on diagnostic CECT but FDG PET/CT can detect unusual or unexpected distant metastases such as skeletal muscle metastases and provides more accurate restaging of patients with MPM.

### Authors' Contributions

M.Y. has roles in acquisition, interpretation of PET/CT data, and writing the manuscript. O.K. has roles in analyzing of clinical data and writing the manuscript. E.T. has a role in reporting histopathological study and writing the manuscript. All authors have final approval of the manuscript to be published.

### Note

This paper was presented at the International Congress of Health Research (ICOHER 2022), Proceedings Book, October 12 to October 15, 2022, conducted online (<http://www.icoher.org>).

### Funding

None.

### Conflict of Interest

None declared.

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