Liver Metastasis of Lung Cancer Detected with Similar Uptake Pattern on Bone Scintigraphy and Fluorine-18 Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography: What’s the Pathophysiologic Mechanism?

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Abstract

Bone scintigraphy with ⁹⁹ᵐTc diphosphonates may exhibit extraosseous lesions in addition to metastatic lesions. Multiple factors can affect extraosseous ⁹⁹ᵐTc methylene diphosphonate (MDP) uptake. Similar uptake pattern of ⁹⁹ᵐTc MDP and fluorine-18 fluorodeoxyglucose (¹⁸F FDG) in hepatic metastasis was not already notified. In our case, initial tumor necrosis and subsequent intracellular calcification resulted in similar ⁹⁹ᵐTc MDP and ¹⁸F FDG accumulation in the metastatic area.

Keywords: Bone scintigraphy, fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography, hepatic metastasis, lung cancer

Introduction

Fluorine-18 fluorodeoxyglucose positron emission tomography/computed tomography (¹⁸F FDG PET/CT) is used to determine primary disease or for staging most of the malignant disease, like lung cancer. FDG is a glucose analogue undergoes the same uptake as glucose. This uptake in neoplastic tissue is called “metabolic trapping.”

In lung cancer, the most common sites of metastasis are the adrenal gland, bones, brain, lung, and liver. Bone scintigraphy with ⁹⁹ᵐTc diphosphonates is considered to be the most practical and the most widely used technique for assessing entire skeleton. It is also noninvasive and effective technique. ⁹⁹ᵐTc methylene diphosphonate (⁹⁹ᵐTc MDP) accumulation is rare in liver metastasis of lung cancer, and its uptake was previously reported.[1-4]

Here, we presented a case of similar uptake pattern with ⁹⁹ᵐTc MDP and ¹⁸F FDG in the metastatic area, and we identified underlying pathophysiologic mechanism.
Case Report

A 65-year-old male patient was admitted due to a headache. On the neurological examination, right sixth nerve involvement was determined. At the clivus neighborhood, contrast diffuse holding 2 cm × 1.5 cm lesion on magnetic resonance imaging has been identified. To determine the unknown primary PET/CT scan was performed. In PET/CT imaging; middle lobe of the right lung was likely primary tumor with centrally located intense \(^{18}\text{F} \text{FDG}\) uptake foci; also, multiple bone and liver metastases were determined. In upper abdominal images of the PET/CT annular, \(^{18}\text{F} \text{FDG}\) uptake was seen in liver segment 4A (77 mm × 70 mm) and segment 2 (33 mm × 34 mm) [Figure 1]. In addition, conventional abdominal CT images showed lower density in the center of the lesions in the liver, indicating central necrosis. Patient’s histopathology confirmed squamous-cell carcinoma of the lung. Separation of potential skeletal metastases with bone scintigraphy has been proposed. In bone scan addition to metastatic regions, the annular \(^{99m}\text{Tc} \text{MDP}\) uptake in liver was observed the same as described in \(^{18}\text{F} \text{FDG}\) uptake [Figure 2].

Discussion

Some of the factors influencing glucose utilization and hence \(^{18}\text{F} \text{FDG}\) accumulation in neoplastic cells are glucose transport and hexokinase enzyme activity. It is reported that hypoxia-inducible factor-alpha is activated to promote the transcription of some enzymes such as glucose transporters and glycolysis when tumor cells are exposed to a hypoxic environment due to insufficient blood supply.\[^5\] To increase glucose metabolism, anaerobic glycolysis is induced by tissue hypoxia. Thus, the more increase in hexokinase and GLUT activity is manifested as the more increased \(^{18}\text{F} \text{FDG}\) uptake in the hypoxic metastatic liver tumor.

Liver localized focal uptake of diphosphonate has been reported in various malignancies.\[^1-4\] Multiple factors can affect extra-osseous MDP uptake: (1) Technical factors, (2) primary malign and metastatic lesions, (3) soft tissue, (4) amyloidosis, (5) infraction, (6) hypercalcemia, (7) inflammation, (8) chemotherapy and (9) radiotherapy.\[^5-8\] MDP accumulates, especially within calcified hepatic metastasis. However, in the present case, liver metastasis not showed calcification in CT examination. It is reported that many pathophysiological ways affect MDP accumulation such as serum Ca elevation, −PO\(_4\) ion, tissue pH and the factors disrupting cell integrity like infection or radiotherapy and expansion of the extracellular fluid.\[^6,7,9,10\] The liver with high blood flow and dual blood supply is an extensive vascular bed. MDP may accumulate in the calcific regions in necrotic or proliferating fibrous tissue. The necrotic metastatic mass initially leads passive congestion and enlargement of affected organ. Then, developing infarction cause tissue hypoxia and hemosiderin and calcium depositions forms which relate to MDP affinity. When ischemic damage disrupts cell integrity, calcium influx intracellular region, calcium precipitates as salt within the mitochondria and over denatured proteins. It is reported that MDP localizes in irreversibly damaged or dying cells if some residual blood flow about 10% of normal perfusion is present.\[^9\]

The similar uptake pattern of \(^{99m}\text{Tc} \text{MDP}\) and \(^{18}\text{F} \text{FDG}\) in hepatic metastasis was not already notified. In our case, initial tumor necrosis and subsequent intracellular calcification resulted in similar \(^{99m}\text{Tc} \text{MDP}\) and \(^{18}\text{F} \text{FDG}\) accumulation in the metastatic area.

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Conflicts of interest
There are no conflicts of interest.

References
1. Ikehira H, Furuichi Y, Kinjo M, Yamamoto Y, Aoki T. Multiple extra-bone accumulations of technetium-99m-HMDP. J Nucl Med Technol 1999;27:41-2.
2. Baumert JE, Lantieri RL, Horning S, McDougall IR. Liver metastases of breast carcinoma detected on 99mTc-methylene diphosphonate bone scan. AJR Am J Roentgenol 1980;134:389-91.
3. Shih WJ, Han JK, Magoun S, Wierzbinski B. Bone agent localization in hepatic metastases. J Nucl Med Technol 1999;27:38-40.
4. Peller PJ, Ho VB, Kransdorf MJ. Extrasosseous Tc-99m MDP uptake: A pathophysiologic approach. Radiographics 1993;13:715-34.
5. Takebayashi R, Izuishi K, Yamamoto Y, Kameyama R, Mori H, Masaki T, et al. [18F] Fluorodeoxyglucose accumulation as a biological marker of hypoxic status but not glucose transportability in gastric cancer. J Exp Clin Cancer Res 2013;32:34.
6. Kaye J, Hayward M. Soft tissue uptake on 99mTc methylene diphosphonate bone scan imaging: Pictorial review. Australas Radiol 2002;46:13-21.
7. Loutfi I, Collier BD, Mohammed AM. Nonosseous abnormalities on bone scans. J Nucl Med Technol 2003;31:149-53.
8. Al-Katib S, Al-Faham Z, Balon H. Liver uptake on bone scanning: A diagnostic algorithm. J Nucl Med Technol 2015;43:135-6.
9. Caobelli F, Paghera B, Pizzocaro C, Guerra UP. Extrasosseous myocardial uptake incidentally detected during bone scan: Report of three cases and a systematic literature review of extrasosseous uptake. Nucl Med Rev Cent East Eur 2013;16:82-7.
10. Charkes ND, Makler PT Jr. Studies in skeletal tracer kinetics. V: Computer-simulated Tc-99m (Sn) MDP bone-scan changes in some systemic disorders: Concise communication. J Nucl Med 1981;22:601-5.