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Extraosseous accumulation of ^{99m}Tc-MDP in lymph node metastases of small cell carcinoma of the esophagus

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We report a case of esophageal carcinoma that showed extraosseous accumulation of ^{99m}Tc-MDP in lymph node metastases to the cervical and paracardial lymph nodes. There are few cases showing abnormal extraosseous accumulation of ^{99m}Tc-MDP in esophageal cancer lesion. The patient was a 53-year-old man with advanced esophageal cancer. Bone scintigraphy demonstrated extraosseous accumulations in left supraclavicular and paracardial lymph node metastases. The histopathological diagnosis was small cell carcinoma of the esophagus, which is a rare disease with aggressive behavior and poor prognosis. Our patient underwent 2 courses of systemic chemotherapy (CDDP + VP16), but died of rapidly growing systemic metastases 5 months after the initial treatment.

Key words: esophageal cancer, extraosseous accumulation, ^{99m}Tc-MDP, small cell carcinoma, lymph node metastasis

INTRODUCTION

IN VARIOUS KIND of tumors, extraosseous accumulations on bone scintigraphy have been reported. They can be seen in primary and metastatic malignant tumors such as lung cancer, breast cancer, gastric cancer, colon cancer, rectal cancer, and neuroblastoma.[1–5] However, there have not been any such cases reported among small cell carcimoma of the esophagus. Small cell carcinoma of the esophagus is a rare disease with aggressive behavior and poor prognosis.[6] We report a case of lymph node metastases from esophageal small cell carcinoma that showed extraosseous accumulation on bone scintigraphy.

CASE REPORT

A 53-year-old man presented with dysphagea and left supraclavicular lymph node swelling. Barium esophagogram demonstrated a Borrman II-like tumor (5 cm long in length) at the midthoracic esophagus (Fig. 1). Upper gastrointestinal endoscopy demonstrated an elevated lesion with ulceration on the wall of the midthoracic esophagus. He was referred to Saitama Medical Center. He had left supraclavicular lymph node swelling, and developed dysphagia and abdominal pain.

Chest CT demonstrated a midthoracic esophageal tumor, and lymph node metastases in the left supraclavicular area and mediastinum (Fig. 2). Abdominal CT showed a 9 × 7 cm mass with heterogeneous enhancement in the paracardial portion and paraaortic lymph node metastases (Fig. 3). No calcification was recognized in the tumor on chest and abdominal CT. ^{67}Ga scintigram showed abnormal accumulation in mediastinal, left supraclavicular, and paracardial regions (Fig. 4).

Biopsy specimen from an esophageal tumor was histopathologically diagnosed as small cell carcinoma. Laboratory data on admission showed that lactate dehydrogenase isozyme (LDH) was 1,069 IU/*l*. The tumor marker, gastrin-releasing peptide precursor (ProGRP), was elevated to 2,550 pg/m*l*, and carcinoembryonic antigen (CEA) and squamous cell carcinoma related antigen (SCC) were within the normal ranges.

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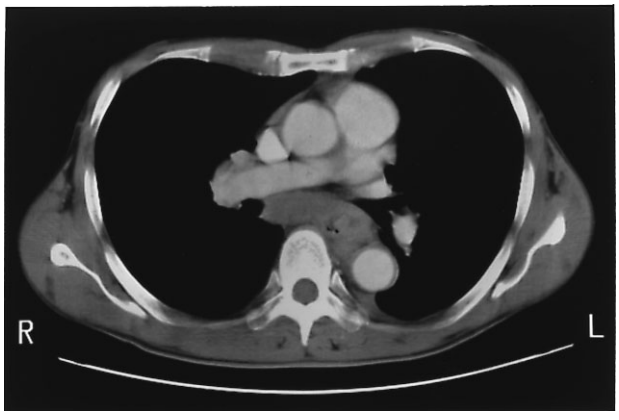
Fig. 1 Barium esophagogram showing elevated tumor with ulceration in the midthoracic esophagus.

A



B

Fig. 2 (A) CT scan showing left supraclavicular lymph node metastasis. (B) Chest CT scan showing midthoracic esophageal tumor and mediastinal lymph node metastases.

Fig. 3 Abdominal CT scan showing a tumor 9 × 7 cm in size in the paracardial region.

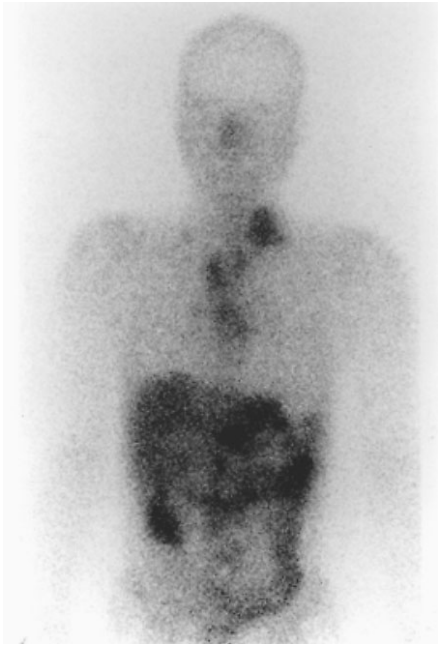


Fig. 4 ^{67}Ga scintigram showing abnormal findings in mediastinal, left supraclavicular, and paracardial regions.

The stage of esophageal cancer was confirmed as stage IV ($_{C}T_3N_1M_1$) based on the above examinations. Because histopathology was small cell carcinoma, systemic chemotherapy (CDDP + VP16) was performed. The regimen consisted of two cycles of CDDP (80 mg/m^2, day 1), and VP16 (100 mg/m^2, day 1–3) with appropriate granulocyte colony-stimulating factor support.

To examine bone metastases, whole body bone scan was performed 3 hours after intravenous injection of 740 MBq ^{99m}Tc-methylene diphosphate (MDP) 2 days after the beginning of the first course of chemotherapy. Slight uptake was noted in the left supraclavicular and paracardial lymph node regions (Fig. 5). These findings mainly corresponded in location to the necrotic area of the tumor on

Fig. 5 On bone scintigraphy with ^{99m}Tc-MDP, the metastatic left supraclavicular region and paracardial region are positively visualized as extraosseous accumulations.

CT. Extraosseous accumulation at the primary site was not recognized in planar image because of overlap with normal accumulation in the sternum. The sites of extraosseous accumulation agreed with the abnormal findings on ^{67}Ga scintigram except for the mediastinal region. Increased accumulation in both kidneys was also observed. Because severe hematopoietic toxicity and renal dysfunction occurred, the chemotherapy was terminated after completion of the second course. After chemotherapy, the primary lesion of the esophagus was diminished in size, but the systemic metastases grew rapidly, and the patient died of these 5 months after the initial treatment.

DISCUSSION

Extraosseous accumulation of ^{99m}Tc phosphate complex has been reported,[1,5] and can be observed in several tumors, and non-neoplastic lesions such as myoma of the uterus, infarction, inflammation, and ectopic calcification, and normal breast tissue.[5,7] Yasuda et al. found 43 cases of extraosseous uptake among 509 bone scintigraphies, two of which were extraosseous uptake in primary malignant tumors.[1] Yoshida noted that ectopic ^{99m}Tc-HMDP accumulation was found in 7.7% of primary lung cancers (34% squamous cell carcinoma, 21% adenocarcinoma, and 21% small cell lung cancer).[2] However, there have not been any previously reported cases of extraosseous uptake in small cell carcinoma of the esophagus. Wilkinson reported a case in which ^{99m}Tc-MDP concentrated in a hepatic metastasis from esophageal squamous cell carcinoma.[8] In our case, bone scintigraphy was performed to detect skeletal metastasis at the beginning of treatment and this image demonstrated that metastatic lymph nodes of esophageal cancer showed signs of extraosseous accumulation. Endo described a case of metastatic breast cancer with extraosseous accumulation of ^{99m}Tc-HMDP in the axillary lymph nodes.[3] She further reported that this patient had multiple lymph node metastases with atypical calcifications. However, our patient did not demonstrate calcification in the tumor on chest or abdominal CT or on biopsy specimen.

The mechanism for deposition of a ^{99m}Tc-HMDP in bone has been ascribed to chemoabsorption onto the calcium of hydroxyapatite.[4] Although the precise mechanism for extraosseous accumulation is unknown, there have been several explanations of the mechanism of extraosseous uptake including increased blood supply, capillary permeability, cellular alteration in calcium metabolism, binding of ^{99m}Tc phosphate agents to phosphate enzyme system, binding of ^{99m}Tc phosphate to collagen, and binding of ^{99m}Tc phosphate to tissue enzymes.[4,7,9–11] Yoshida noted that factors such as tumor size, calcification and tumor necrosis influenced the ectopic accumulation of ^{99m}Tc-HMDP.[2] It has been suggested that the mechanism of tumor calcification is related to tumor necrosis.[9] Zucker noted that the probable mechanism for ^{99m}Tc-MDP uptake in soft tissue was necrosis with subsequent neovascular hyperemia and microscopic calcium deposits.[12] The existence of necrosis in the tumor might have been a factor affecting extraosseous accumulation in our case.

Small cell carcinoma of the esophagus is a very rare disease with fewer than 200 such cases reported as of 1995.[13] It has characteristics similar to those of small cell carcinoma of the lung, and is associated with aggressive behavior and poor prognosis.[13] It is reported that the standard of treatment has not yet been defined.[6] A combined therapeutic approach is used based on data regarding small cell carcimona of the lung. Bennouna reported that optimal treatment seems to be the same as for small cell carcinoma of the lung, that is a multi-drug combination chemotherapy regimen used alone or with sequential radiation.[14] The median survival of primary small cell carcinoma of the esophagus was 8 months for patients with limited disease and 3 months for those with extensive disease.[15] Our patient died of systemic metastases 5 months after the beginning of chemotherapy.

It is worthy of note that bone scintigraphy showed extraosseous accumulation of ^{99m}Tc-MDP in lymph node metastases of small cell carcinoma of the esophagus.

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