Small Cell Carcinoma of the Gallbladder: ^{18}F -FDG PET/CT Imaging Features—A Case Report

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Received: 8 March 2010 / Revised: 21 April 2010 / Accepted: 28 April 2010 / Published online: 17 June 2010
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Abstract The diagnostic role of ^{18}F -fluorodeoxyglucose (^{18}F -FDG) positron emission tomography (PET)/computed tomography (CT) for gallbladder small cell carcinoma has not been reported. A knowledge of the imaging characteristic features of this malignancy can be useful. Here we report a rare case of a patient who had various diagnostic imaging modalities, including ^{18}F -FDG PET/CT.

Keywords Gallbladder · Small cell carcinoma · ^{18}F -FDG PET/CT

Introduction

Gallbladder small cell carcinoma is a rare disease with poor prognosis. Accurate preoperative evaluation of gallbladder tumors is essential for curative resection. ^{18}F -fluorodeoxyglucose (^{18}F -FDG) positron emission tomography (PET)/computed tomography (CT) is a well-established functional imaging technique for diagnostic oncologic imaging. We report a rare case of a small cell carcinoma of the gallbladder and its ^{18}F -FDG PET/CT imaging features.

Case report

A 58-year-old man presented with chronic intermittent right upper quadrant discomfort. Abdominal ultrasonography (US) was performed and multiple gallbladder stones were detected. Physical examination revealed only mild tenderness over the right upper quadrant, without definite Murphy's sign. There were no paraneoplastic endocrine manifestations. The results of initial laboratory evaluation were as follows: white blood cells, 7,420/ μl ; total bilirubin, 0.4 mg/dl; aspartate aminotransferase (AST)/alanine aminotransferase (ALT), 25/19 IU/l; C-reactive protein (CRP), 0.24 mg/dl. Initial abdominal sonography (Fig. 1a, b) showed not only multiple gallbladder stones with wall thickening (maximum diameter, 6.1 mm) but also a 2.4-cm-sized polypoid mass with heterogenous echogenicity in the gallbladder. Doppler study revealed internal vascular signals in this mass (Fig. 1c, d). For characterization of the mass lesion, contrast-enhanced abdomen CT was done. CT images showed a well-defined, heterogeneously enhancing polypoid mass (about 2.9×1.3 cm in size) in the left medial wall of the gallbladder body, and this mass was confined to the gallbladder (Fig. 2a, b). Another 1.8-cm-sized round nodular lesion with heterogenous enhancement was also noted in the pericholecystic area, which was suggestive of metastatic lymph node (Fig. 2c). These findings of CT scans were consistent with gallbladder carcinoma.

For the staging of the gallbladder cancer, ^{18}F -FDG PET/CT was done. PET/CT images showed a focally increased FDG uptake at the gallbladder mass (maxSUV=3.25) and another focal increased uptake (maxSUV=3.45) was noted in pericholecystic nodular lesion, inferiorly to the gallbladder (Fig. 3a–c). These findings suggested gallbladder cancer with regional lymph node metastasis.

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Fig. 1 **a** Abdominal US shows diffuse gallbladder wall thickening and multiple stones in the dependent portion (stone size, 0.8–1.3 cm; number, 10–20; wall thickness, 6.1 mm) **b, c, d** Transverse sonogram showing a 2.4-cm-sized, well-defined, sessile hypoechoic mass along the medial gallbladder wall with adjacent wall thickening and internal vascularity on color Doppler image

The patient was treated with open extended radical cholecystectomy and there was no evidence of intratumoral hemorrhage or necrosis. Histopathologic examination of the surgical specimen revealed tissue fragments, including dissected regional lymph node, consisting pure small cell carcinoma (Fig. 3d, e). Tumor had invaded perimuscular connective tissue without extension beyond the serosa or into liver. The tumor stage of this patient was IIb, T2N1M0. On immunohistochemical study, the tumor cells were positive

for neuroendocrine markers, such as synaptophysin, chromogranin, and CD 56.

Discussion

Approximately 90% of gallbladder carcinomas have an adenocarcinoma histology [1]. Other rarely seen histologic types include squamous cell, undifferentiated carcinoma, and

Fig. 2 Axial unenhanced (**a**), contrast-enhanced (**b**) CT scans show a smooth margined, heterogeneously enhancing luminal protruding polypoid mass (2.9×1.3 cm in size) located in the left medial wall of

gallbladder body. **c**. There is a 1.8-cm-sized, round-shaped, enhancing lymph node (*long arrow*) in pericholecystic area, and several 1-cm-sized stones (*short arrow*) in the extrahepatic duct

Fig. 3 **a** MIP of the PET/CT image shows two foci with increased uptake at the gallbladder and pericholecystic area. There are no other abnormal hypermetabolic foci except physiologic bowel uptakes. **b**, **c** ^{18}F -FDG PET/CT images show a polypoid mass lesion (max-SUV = 3.25, *arrow*) and pericholecystic nodular lesion (max-

SUV = 3.45). **d** Histological examination reveals a poorly differentiated endocrine carcinoma (H & E, $\times 40$). **e** Polygonal tumor cells with hyperchromatic pattern, indistinct nucleoli, frequent mitoses, and scanty cytoplasm, and some inflammatory cells (H & E, $\times 200$)

small cell carcinoma [1]. Among them, the prevalence of small cell carcinoma is reported to be up to 0.5% of cases [2]. There have been several reports of gallbladder small cell carcinoma since the first description in 1981 [3]. It was included as a variant of malignant epithelial tumors in the second edition of the World Health Organization histological classification of tumors of the gallbladder and extrahepatic bile ducts [4]. To our knowledge, only a few reports of the ^{18}F -FDG PET/CT imaging findings have been reported in the literature [5]. Therefore, we report a case to further clarify the imaging characteristics of this malignancy.

Neuroendocrine tumors of the gallbladder have been classified as carcinoid tumors and endocrine cell carcinomas or small cell carcinomas [3, 6]. They are histologically identical to small cell carcinomas of the lung and gastrointestinal tract [6]. Although small cell carcinoma of the gallbladder presents as a distinct histologic entity, it has many clinical characteristics similar to adenocarcinoma of the gallbladder, including comparable natural history and tendency for locoregional spread [1]. Small cell carcinoma has a predilection for elderly female patients, is frequently associated with cholelithiasis, shows occasional endocrine manifestation and a highly aggressive clinical course [1, 7]. It is highly lethal when demonstrating liver or lung metastases [7]. Aggressive multimodality therapy, such as postoperative adjuvant chemotherapy, has been reported to prolong survival [1, 4].

The usual imaging modalities, such as US, CT, and magnetic resonance imaging, are able to detect abnormalities of the gallbladder but are not always able to differentiate a malignancy from another common disease process, such as chronic cholecystitis or adenomyomatosis [5]. ^{18}F -FDG PET/CT is a well-established functional imaging technique for diagnostic oncologic imaging that provides information about glucose metabolism in lesions. Although ^{18}F -FDG uptake can be seen in both tumor cells and activated inflammatory cells [8], chronic cholecystitis in most patients do not reveal increased FDG uptake [2]. The correlation between CRP level and FDG uptake has been reported in gallbladder lesions. The specificity of PET for this malignancy was reported to be 80% in the group with a normal level of CRP [5]. In our case, as previously reported, relatively slightly increased ^{18}F -FDG uptake lesions (maxSUV=3.25 and 3.45) can be easily detected on maximum intensity projection (MIP) image of PET/CT due to normal CRP level. In order to minimize false-positive findings, patients with signs of acute inflammation, positive Murphy's sign, elevated inflammatory indicator, such as CRP, should be excluded from examination [5].

In conclusion, the role of ^{18}F -FDG PET/CT may prove to be useful in diagnostic imaging for the detection of small-sized small cell carcinomas of the gallbladder, underlying a non-inflammatory state of the gallbladder. And its imaging findings can help physicians make the

diagnosis and subsequently determine the appropriate treatment.

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