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CASE REPORT

The Superiority of ^{68} Ga-FAPI-04 over ^{18}F-FDG in a Case of Gallbladder Cancer

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Abstract

A 56-year-old man presented with vague upper abdominal pain for more than 4 months. His abdominal ultrasound and MRI showed thickening of the neck and base of the gallbladder and nodule formation at the base of the gallbladder. ^{18}F-FDG PET/CT revealed intense FDG uptake in the base of the gallbladder and multiple lymph nodes. ^{68} Ga-FAPI-04 PET/CT not only showed intense FAPI uptake in the above mentioned FDG-avid lesions but also showed intense FAPI uptake in the neck lesion of the gallbladder and some other additional lymph nodes. Finally, histopathological examination confirmed poorly differentiated tubular adenocarcinoma of the neck and base of the gallbladder. Our case illustrated that ^{68} Ga-FAPI-04 PET/CT may outperform ^{18}F-FDG PET/CT in the detection of gallbladder cancer primary and metastatic lesions.

Keywords Gallbladder cancer · ^{18}F-FDG · ^{68} Ga-FAPI-04 · PET/CT

Introduction

Gallbladder cancer is the most common bile duct malignancy, and epidemiological studies have shown that the global incidence of gallbladder cancer is about 2/100,000 [1]. The onset of gallbladder cancer is insidious, and most patients have developed to an advanced stage when they are treated, with a poor prognosis. Therefore, early diagnosis and early treatment are the keys to improve the prognosis of patients with gallbladder cancer. ^{18}F-fluorodeoxyglucose (FDG) PET/CT is a useful diagnostic imaging method for gallbladder cancer, but there were also positive results (such as inflammatory gallbladder disease) and false negative results (such as small size and/or low-grade tumors) that need attention [2–4]. Many studies have shown that ^{68} Ga-labelled fibroblast activation protein inhibitor (FAPI) is a promising PET tracer that has shown a superior diagnostic efficacy than ^{18}F-FDG for the diagnosis of primary and metastatic lesions in patients with various types of cancer [5–8]. Here is a case report which demonstrates the superiority of ^{68} Ga-FAPI-04 PET/CT over ^{18}F-FDG PET/CT.

Case Report

A 56-year-old man presented with vague upper abdominal pain for more than 4 months, which was persistent and slightly worse after eating and drinking. Physical examination revealed slight tenderness in the upper abdomen. Gastrointestinal tumor markers showed elevated ferritin (418.70 ng/ml), CA19-9 (43.51 U/ml), and CA50 (28.60 IU/ml). His abdominal ultrasound showed thickening of the gallbladder wall. MRI showed thickening of the neck and base of the gallbladder, nodule formation at the base of the gallbladder, and isointensity on T1-weighted image (T1WI), and hyperintensity on T2-weighted image (T2WI), diffusion-weighted imaging (DWI), and SPAIR, and inhomogeneous enhancement on enhanced scans. He was referred to perform ^{18}F-FDG PET/CT scan and then recruited in our ^{68} Ga-FAPI PET/CT trial (AHSWMU-2020–035) approved by the institutional review board at our hospital. A written informed consent was signed by the patient. ^{18}F-FDG PET/CT revealed intense FDG uptake (SUVmax 11.0) at the base of the gallbladder and multiple lymph nodes (SUVmax 14.9) in

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the hepatic hilar region, retroperitoneal region, and para-abdominal aorta areas (Fig. 1). ^{68} Ga-FAPI-04 PET/CT showed intense FAPI uptake not only in the above FDG-avid lesions, including the base of the gallbladder (SUVmax 12.0) and multiple lymph nodes (SUVmax 18.0) in the region described above, but also in the neck lesion of the gallbladder (SUVmax 12.0) and some other lymph nodes (SUVmax 12.2) in the above region (Fig. 2). Therefore, cancer of the gallbladder neck and gallbladder base with lymph node metastases was considered. The patient had a surgical indication, was in fair health, and the patient and his family had a strong desire for surgery and prolonged survival. The patient then underwent laparoscopic radical cholecystectomy for gallbladder cancer, i.e., cholecystectomy, lymph node dissection, wedge resection of the liver, and tissue biopsy of the gallbladder duct. Tumor tissues were observed at the base of the gallbladder and the neck of the gallbladder, respectively, measuring approximately 2.7 cm × 2.2 cm × 1.5 cm and 0.8 cm × 0.5 cm × 0.7 cm, and histopathological examination confirmed poorly differentiated tubular adenocarcinoma of both the neck and base of the gallbladder (Fig. 3). After surgery, the patient underwent chemotherapy.

Discussion

^{18}F-FDG, an analogue of glucose, reflects the glucose metabolism and the expression of glucose transporter protein of the lesion [9], but ^{68} Ga-FAPI-04 reflects the expression of the fibroblast activation protein (FAP) in the tumor stroma [10]. In our case, gallbladder neck lesions with strong FAPI uptake did not have increased uptake of FDG. The false negative result for gallbladder neck tumor on ^{18}F-FDG PET/CT may be associated with small size and/or low-grade tumors [2–4]. FAP is highly expressed on CAFs (cancer-associated fibroblasts) present in > 90% of human epithelial tumors [11]. The uptake of FAPI was higher in gallbladder neck tumors due to the possibility of a significant degree of fibrosis and high expression of FAP. Compared with ^{18}F-FDG PET/CT, the ^{68} Ga-FAPI-04 PET/CT detected more primary and metastatic lesions and delineated these lesions more clearly, illustrating

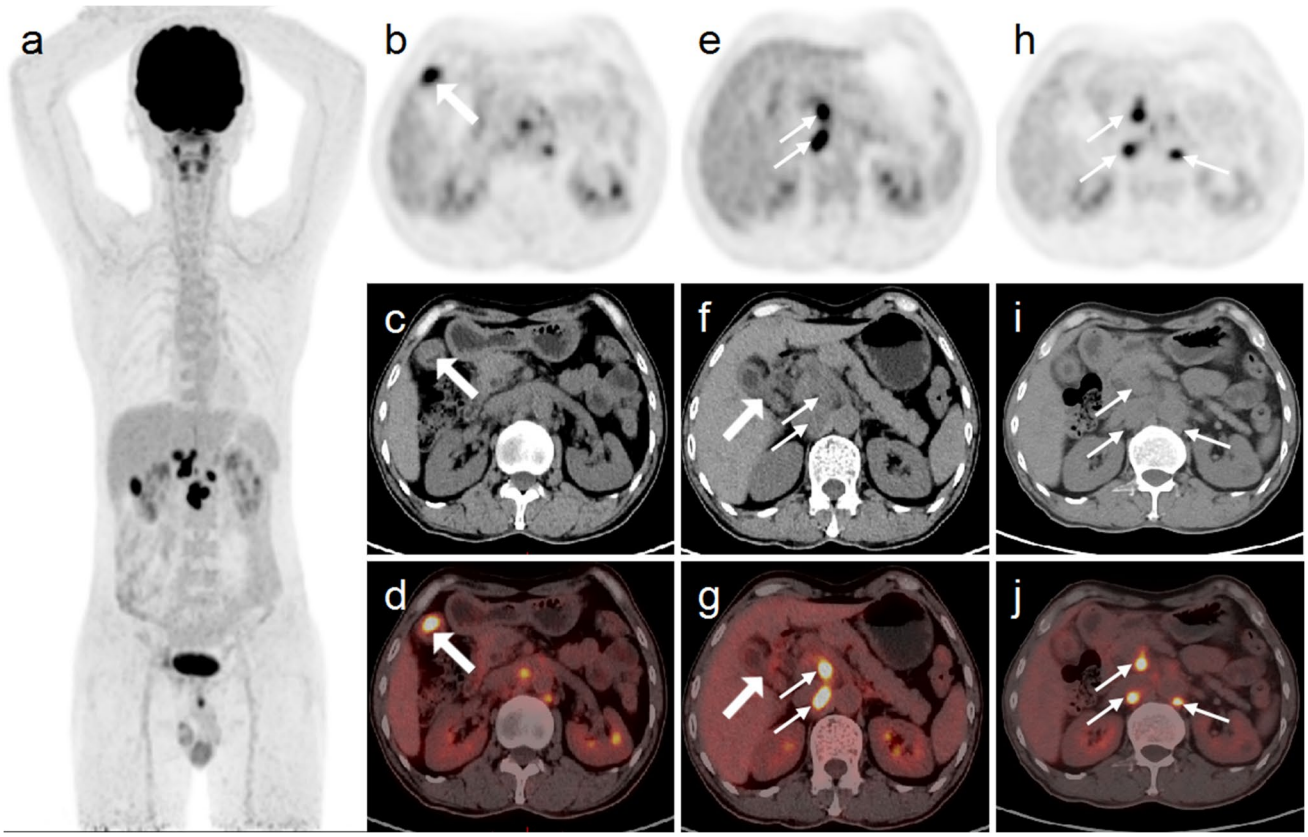

Fig. 1 The MIP of ^{18}F-FDG PET (**a**) showed multiple hypermetabolic lesions in the upper abdomen. Abdominal axial images (**b**–**d**) showed thickening of the base of the gallbladder with nodule formation and intense ^{18}F-FDG uptake (thick arrows). Abdominal axial images (**e**–**g**) showed thickening of the neck of the gallbladder without increased ^{18}F-FDG uptake (thick arrows). Additionally, there were multiple hypermetabolic lymph nodes (thin arrows) in the hepatic hilar region, retroperitoneal region, and para-abdominal aorta areas (**a**–**j**)

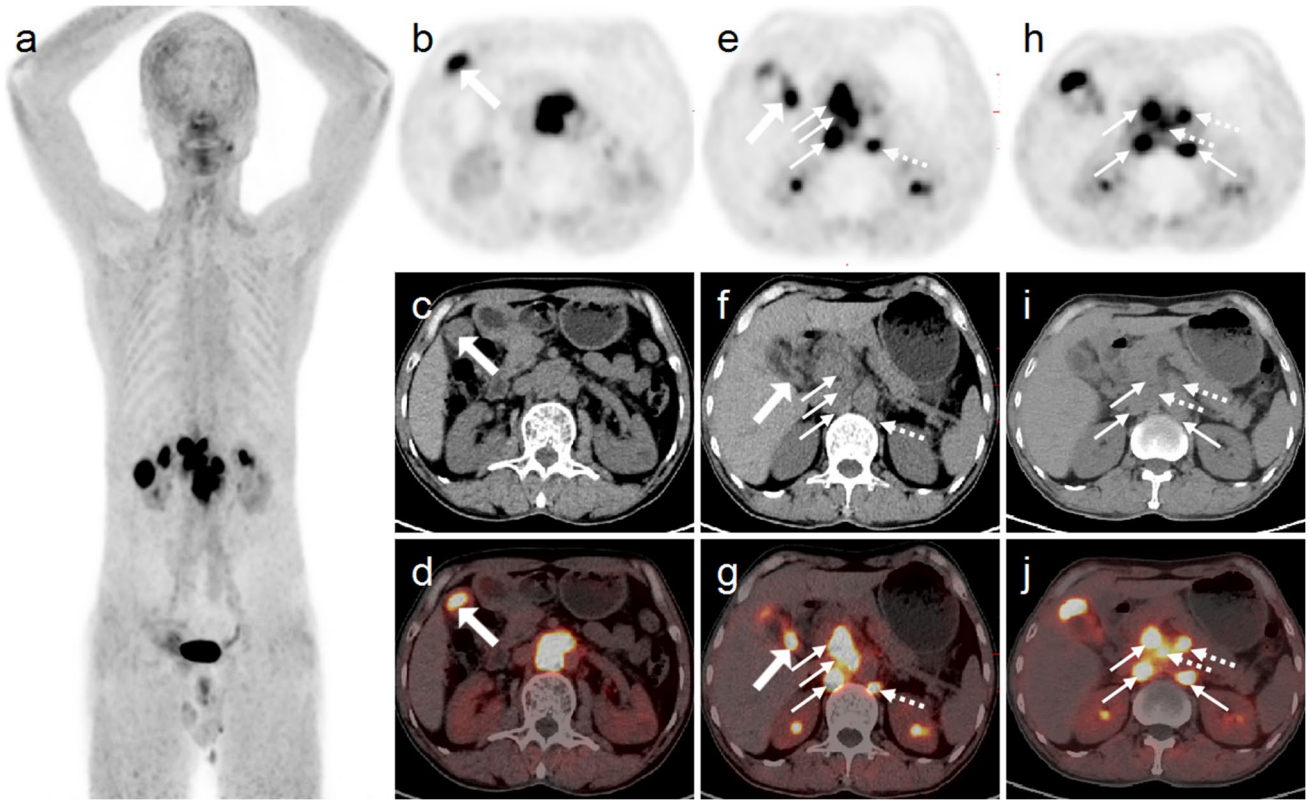

Fig. 2 In ^{68} Ga-FAPI-04 PET/CT, the MIP of PET (**a**) showed more lesions with high uptake of FAPI in the upper abdomen than ^{18}F-FDG PET/CT. In the corresponding axial fusion images (**b**–**j**), intense ^{68} Ga-FAPI-04 uptake was also noted in the above FDG-avid lesions. In addition, gallbladder neck lesions without increased ^{18}F-FDG uptake showed strong ^{68} Ga-FAPI-04 uptake (**e**–**g**, thick arrows) in abdominal axial images and showed more lymph nodes with high FAPI uptake (**e**–**j**; dotted arrow)

that ^{68} Ga-FAPI-04 may outperform ^{18}F-FDG in the detection of gallbladder cancer lesions. ^{68} Ga-FAPI-04 PET/CT provides a more comprehensive and clearer understanding of the site of lesion involvement and could guide intraoperative surgical maneuvers such as avoiding clamping of tumors in the neck of the gallbladder, and intraoperative tumor suppression has been reported to increase the number of circulating tumor cells (CTCs), which can lead to recurrence [12–14]. In addition, ^{68} Ga-FAPI-04 PET/CT can be used for prognostic assessment, and usually high expression of FAP is associated with poor prognosis [10], as well as for postoperative efficacy monitoring, which may be more sensitive than ^{18}F-FDG PET/CT. Further investigations should be done for the potential of ^{68} Ga-FAPI-04 PET/CT in the diagnosis of gallbladder cancer.

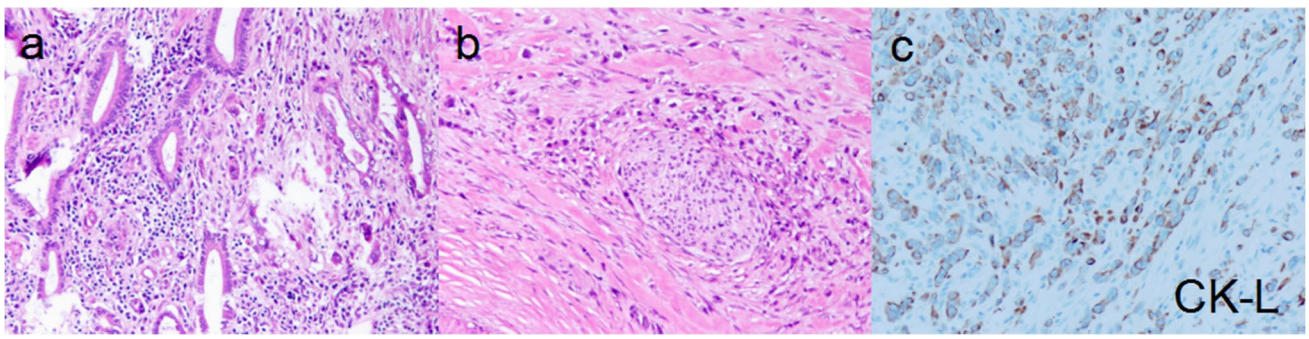

Fig. 3 Figures **a** and **b** were stained by HE, and figure **c** was stained by ELPS, with CK-L being the low molecular CK. Histopathological examination revealed poorly differentiated tubular adenocarcinoma of the neck and base of the gallbladder

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Author Contribution Zhanwen Huang collected this case. Chunmei Guo and Dengsai Peng make the same contribution. Ya Liu and Liming Chen made comments on this case.

Data Availability Data sharing not applicable to this article as no datasets were generated or analyzed during the current study.

Declarations

Conflict of Interest Chunmei Guo, Dengsai Peng, Ya Liu, Liming Chen, and Zhanwen Huang declare no conflict of interest.

Ethical Approval and Consent to Participate The study was approved by the institutional review board of the Affiliated Hospital of Southwest Medical University (AHSWMU-2020–035), and informed consent was obtained from all individual participants included in the study. All procedures performed in studies involving human participants were in accordance with the Helsinki declaration as revised in 2013 and its later amendments.

Consent for Publication The participants signed consent regarding publishing their data and photographs.

References

1. Hori M, Saito E. Gallbladder cancer incidence rates in the world from the Cancer Incidence in Five Continents XI. Jpn J Clin Oncol. 2018;48:866–7.
2. Annunziata S, Pizzuto DA, Caldarella C, Galiandro F, Sadeghi R, Treglia G. Diagnostic accuracy of fluorine-18-fluorodeoxyglucose positron emission tomography in gallbladder cancer: a meta-analysis. World J Gastroenterol. 2015;21:11481–8.
3. Ramos-Font C, Gómez-Rio M, Rodríguez-Fernández A, Jiménez-Heffernan A, Sánchez Sánchez R, Llamas-Elvira JM. Ability of FDG-PET/CT in the detection of gallbladder cancer. J Surg Oncol. 2014;109:218–24.
4. Moradi F, Iagaru A. The role of positron emission tomography in pancreatic cancer and gallbladder cancer. Semin Nucl Med. 2020;50:434–46.
5. Kratochwil C, Flechsig P, Lindner T, Abderrahim L, Altmann A, Mier W, et al. 68Ga-FAPI PET/CT: tracer uptake in 28 different kinds of cancer. J Nucl Med. 2019;60:801–5.
6. Chen H, Pang Y, Wu J, Zhao L, Hao B, Wu J, et al. Comparison of [68Ga]Ga-DOTA-FAPI-04 and [18F] FDG PET/CT for the diagnosis of primary and metastatic lesions in patients with various types of cancer. Eur J Nucl Med Mol Imaging. 2020;47:1820–32.
7. Chen H, Zhao L, Ruan D, Pang Y, Hao B, Dai Y, et al. Usefulness of [68Ga]Ga-DOTA-FAPI-04 PET/CT in patients presenting with inconclusive [18F]FDG PET/CT findings. Eur J Nucl Med Mol Imaging. 2021;48:73–86.
8. Sharma P, Singh SS, Gayana S. Fibroblast activation protein inhibitor PET/CT:a promising molecular imaging tool. Clin Nucl Med. 2021;46:e141–50.
9. Boellaard R, Delgado-Bolton R, Oyen WJ, Giammarile F, Tatsch K, Eschner W, et al. FDG PET/CT: EANM procedure guidelines for tumour imaging: version 2.0. Eur J Nucl Med Mol Imaging. 2015;42:328–54.
10. Loktev A, Lindner T, Mier W, Debus J, Altmann A, Jäger D, et al. A tumor-imaging method targeting cancer-associated fibroblasts. J Nucl Med. 2018;59:1423–9.
11. Imlimthan S, Moon ES, Rathke H, Afshar-Oromieh A, Rösch F, Rominger A, et al. New frontiers in cancer imaging and therapy based on radiolabeled fibroblast activation protein inhibitors: a rational review and current progress. Pharmaceuticals (Basel). 2021;14
12. Gall TM, Jacob J, Frampton AE, Krell J, Kyriakides C, Castellano L, et al. Reduced dissemination of circulating tumor cells with no-touch isolation surgical technique in patients with pancreatic cancer. JAMA Surg. 2014;149:482–5.
13. Hashimoto M, Tanaka F, Yoneda K, Takuwa T, Matsumoto S, Okumura Y, et al. Significant increase in circulating tumour cells in pulmonary venous blood during surgical manipulation in patients with primary lung cancer. Interact Cardiovasc Thorac Surg. 2014;18:775–83.
14. Li X, Liu S, Li H, Guo L, Zhang B, Lin Z, et al. Proper hepatic pedicle clamping during hepatectomy is associated with improved postoperative long-term prognosis in patients with AJCC stage IIIB hepatocellular carcinoma. Oncotarget. 2016;7:24623–32.