Al^{18}F-NOTA-FAPI-04 outperforms ^{18}F-FDG PET/CT in imaging for intrahepatic metastasis of hepatocellular carcinoma

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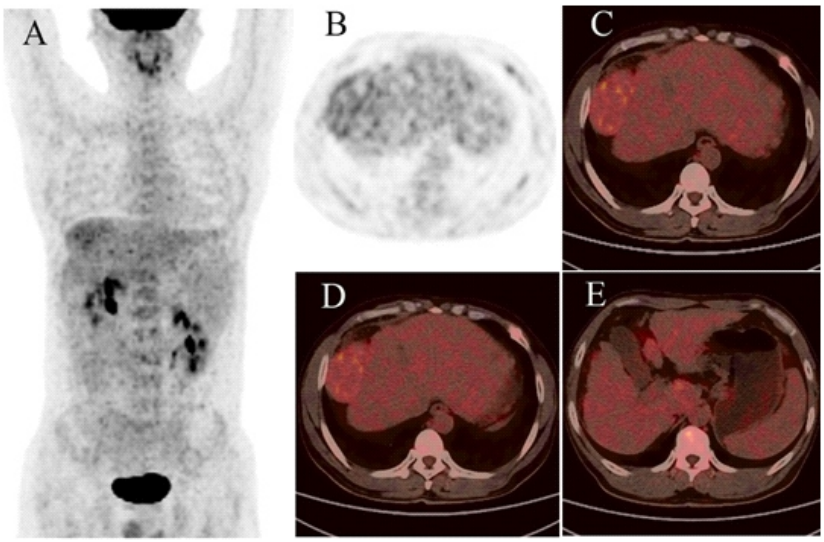

Figure 1. A 46-year-old male presented with repeated abdominal pain for more than 3 months.The patient showed abdominal pain without obvious inducement, no diarrhea or abdominal distension. Abdominal plain CT showed cirrhosis and several low-density hepatic lesions, and further examination was recommended to determine the nature of the hypodensity lesions. The patient underwent fluorine-18-fluorodeoxyglucose (^{18}F-FDG) positron emission tomography/computed tomography (PET/CT) examination twice before surgery for biopsy. There was medium ^{18}F-FDG uptake (SUVmax:4.7) in the segment VIII of the liver on PET/CT imaging (size: 4.1cm×7.7cm), with no otherhypermetabolic foci observed in the rest of liver. Nodular moderate hypermetabolism of ^{18}F-FDG was seen in the liver right lobe on maximum intensity projection (MIP) (A). Massive moderate ^{18}F-FDG uptake was seen in segment VIII of the right liver lobe on axial PET (B) and fusion PET/CT (C, SUVmax:4.7). No ^{18}F-FDG uptake was seen in segment II and segment V of the liver (D-E).

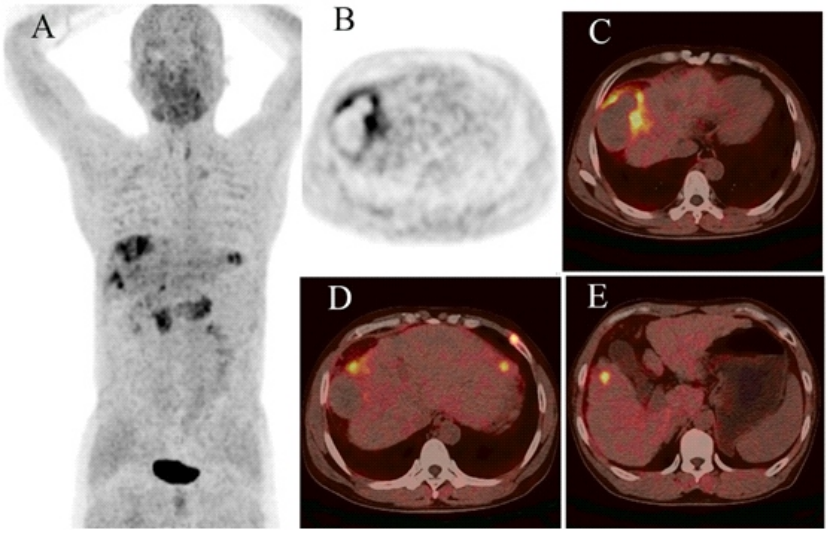

Figure 2. To determine any correlation to malignancy and to determine the extent of the disease, aluminum fluoride complex-1,4,7-triazacyclononane-1,4,7-triacetic acid-fibroblast activating protein alpha inhibitor-04 (Al^{18}F-NOTA-FAPI-04) was performed two weeks later as part of a clinical trial approved by our institutional review board. Nodular hypermetabolism of Al^{18}F-NOTA-FAPI-04 was seen in the right and left liver lobes on MIP(A). Elevated arc-shaped Al^{18}F-NOTA-FAPI-04 uptake was seen in segment VIII of liver on axial PET image(B) and fusion PET/CT image (C, SUVmax:7.4). Nodules of elevatedAl^{18}F-NOTA-FAPI-04 uptake in segment II and segment V on axial fusion PET/CT image(D-E, SUVmax:9.0,5.7).

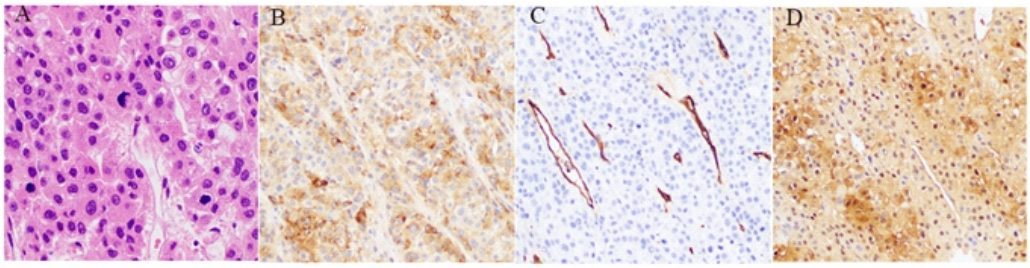

Figure 3. The patient underwent surgery, intra-operative exploration revealed that the tumor was located in the segment VIII of the liver and with exophytic growth and surrounded by a dense tumor capsule. Severe nodular sclerosis of the liver and a small amount of ascites could also be seen. Intra-operative ultrasound imaging suggested that segment V and segment II were mixed with hypo-echo which also revealed hypermetabolism on Al^{18}F-NOTA-FAPI-04 imaging. Considering the severe cirrhosis and the high risk of further liver resection, microwave curing was performed for the above-mentioned two liver lesions. Postoperative pathological results of segment VIII lesion indicated moderately differentiated hepatocellular carcinoma with hemorrhage and necrosis, Edmondson Steiner grade II. The tumor size was about 8.5cm× 6.5cm×3.0cm invading the liver capsule, but not breaking through the capsule. No satellite nodules were observed and the microvascular invasion was grade 1. The tumor cells were large and polygonal in size, with eosinophilic cytoplasm, vacuolar nuclei and pathological mitosis, and clear nucleoli arranged in beam-like or acinous shape (A). G1ypican-3, CD34, and arginase-1 were positive on Immunohistochemical examination (B-D).

Primary liver cancer (PLC) refers to malignant tumors that occur in hepatocytes or intrahepatic bile duct epithelial cells and can be divided into hepatocellular carcinoma (HCC), intrahepatic bile duct carcinoma and mixed liver cancer according to the cell origin [1]. In our case a histologically confirmed moderately differentiated hepatocellular carcinoma, showed on ^{18}F-FDG one lesion in the right lobe of the liver with moderate increased homogeneous ^{18}F-FDG uptake, while no ^{18}F-FDG uptake was observed in the rest of the liver. The feature of HCC on ^{18}F-FDG uptake is similar to literature reports [2]. However, on Al^{18}F-NOTA-FAPI-04 PET/CT imaging 2 weeks later, the lesion in the right lobe of the liver showed arc-shaped Al^{18}F-NOTA-FAPI-04 uptake and the focal Al^{18}F-NOTA-FAPI-04 hypermetabolism were suspected asintrahepatic metastatic sites. This suggests that Al^{18}F-NOTA-FAPI-04 imaging is superior to ^{18}F-FDG imaging in detecting primary hepatocellular carcinoma and intrahepatic or extrahepatic metastases. Although there have been previous reports about gallium-68 (^{68}Ga)-FAPI-04 PET/CT in the diagnosis and staging of hepatocellular carcinoma [3-5], ^{68}Ga-labeled tracers have a relatively short half-life of ^{68}Ga ($t_{1/2}$=67.7min) and are limited in the availability of radionuclide from ^{68}Ge/^{68}Ga-generators. Considering the long half-life of ^{18}F ($t_{1/2}$ = 109.8 minutes) and the availability of ^{18}F from cyclotrons that are owned by many medical centers, Al^{18}F-NOTA-FAPI-04 is more convenient for clinical use. Since there are currently no reported literature reports about Al^{18}F-NOTA-FAPI-04 imaging of hepatocellular carcinoma, our case is the first described Al^{18}F-NOTA-FAPI-04 PET/CT imaging in hepatocellular carcinoma.

The authors declare that they have no conflicts of interest.

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