

A Rare Presentation of Extrahepatic Biliary Neuroendocrine Tumor Diagnosed using ⁶⁸Ga-DOTA-TOC Imaging, But Undetectable on ⁶⁸Ga-FAPI Imaging

Abstract

Neuroendocrine tumors (NETs) are commonly seen in the small intestine and rarely found within the bile ducts. This low incidence is due to a smaller number of Kulchitsky cells in the extrahepatic biliary tree, which predisposes to the disease. The diagnosis of biliary tree carcinoid preoperatively is very rare, with most cases in the literature being incidentally diagnosed during surgery or being identified on the histopathology report postoperatively. Here, we present an interesting case of an extrahepatic biliary NET which was diagnosed preoperatively.

Keywords: ⁶⁸Ga-DOTA-TOC, ⁶⁸Ga-FAPI-46, extrahepatic biliary neuroendocrine tumors

A 28-year-old female patient presented with complaints of jaundice, abdominal pain, and weight loss. Triphasic computed tomography (CT) of the abdomen showed a soft-tissue lesion probably arising from a common hepatic duct (CHD) and involving primary confluence, showing loss of fat planes with surrounding vascular structures, and suspecting intraductal cholangiocarcinoma. Subsequently, magnetic resonance cholangiopancreatography revealed a lesion at the hepatic hilum compressing biliary confluence, and dilated intrahepatic biliary radicles which is likely neoplastic in etiology. Later, USG-guided liver SOL biopsy and immunohistochemistry showed features of a well-differentiated neuroendocrine tumor (NET), grade-1. Overall, consistent with findings of NETs, the patient underwent whole-body ⁶⁸Ga DOTA-TOC positron emission tomography (PET) CT to look for other possible primary tumors and also for metastatic work-up revealed a high-grade ⁶⁸Ga-DOTA-TOC tracer avid lesion at the region of hepatic hilum involving neck of gallbladder, compressing CHD, primary biliary confluence causing upstream bilateral IHBRD [Figure 1]. The lesion is abutting left portal vein, right portal vein, and right hepatic artery without any obvious involvement—no other evidence of ⁶⁸Ga DOTA-TOC tracer avid disease in the rest of the scanned segment of the body.

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The following day, ⁶⁸Ga-FAPI-46 PET CT scan showed no abnormal increased tracer expression [Figure 2].

After a thorough discussion at a multidisciplinary tumor board, the final consensus was to proceed with surgical resection as the recommended course of action. The patient underwent left hepatectomy with extrahepatic bile duct resection and Roux-en-Y-hepaticojejunostomy-postoperative histopathological examination showing features of NET, grade-1. The patient had an uneventful postoperative course and was discharged.

We reported a sporadic case of preoperatively diagnosed extrahepatic biliary NET (EBNET) from biopsy and identified on ⁶⁸Ga DOTA-TOC PET/CT imaging. Modlin *et al.* demonstrated that the most common sites for primary NETs are the gastrointestinal tract (67.5%) and bronchopulmonary system (25.3%) with only 0.1%–0.4% occurring in the extrahepatic bile ducts.^[1] ⁶⁸Ga-DOTATATE PET/CT demonstrated a sensitivity of 97%, specificity of 95.1%, accuracy of 96.6%, positive predictive value of 98.5%, and negative predictive value of 90.4% in well-differentiated NETs.^[2] Although the ⁶⁸Ga-labeled somatostatin analogs used for diagnosing NETs have different affinities for the SSTRs, studies comparing the sensitivities and uptake

How to cite this article: Harini K, Jayanthi MR, Hari KS, Batchu S. A rare presentation of extrahepatic biliary neuroendocrine tumor diagnosed using ⁶⁸Ga-DOTA-TOC imaging, but undetectable on ⁶⁸Ga-FAPI imaging. *Indian J Nucl Med* 2024;39:155-7.

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Received: 25-12-2023

Revised: 22-02-2024

Accepted: 27-02-2024

Published: 29-05-2024

Access this article online

Website: www.ijnm.in

DOI: 10.4103/ijnm.ijnm_149_23

Quick Response Code:



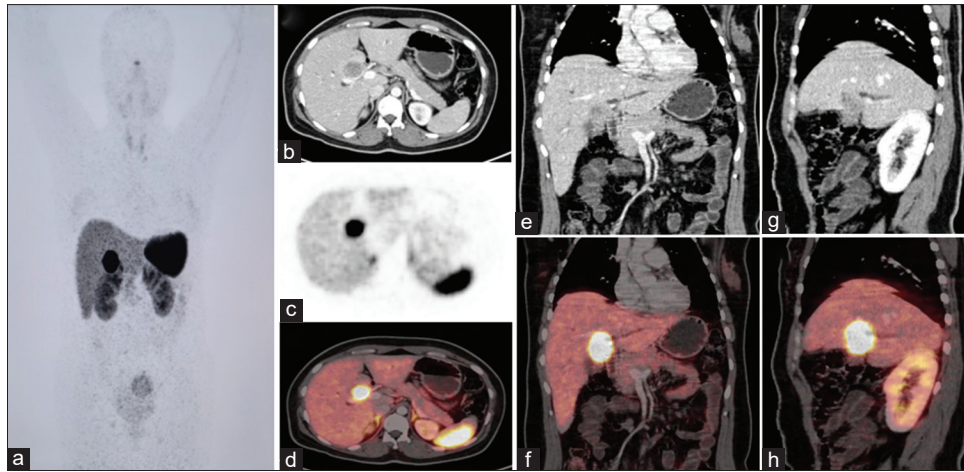


Figure 1: (a-h) Whole body Maximum intensity projection (MIP), corresponding sections of axial, sagittal, and coronal computed tomography (CT) and positron emission tomography-CT images of ^{68}Ga -DOTA-TOC showing well-defined heterogeneously enhancing intense SSTR expressing lesion at the hepatic hilum (represented by white solid arrow) compressing common hepatic duct with upstream bilateral IHBRD

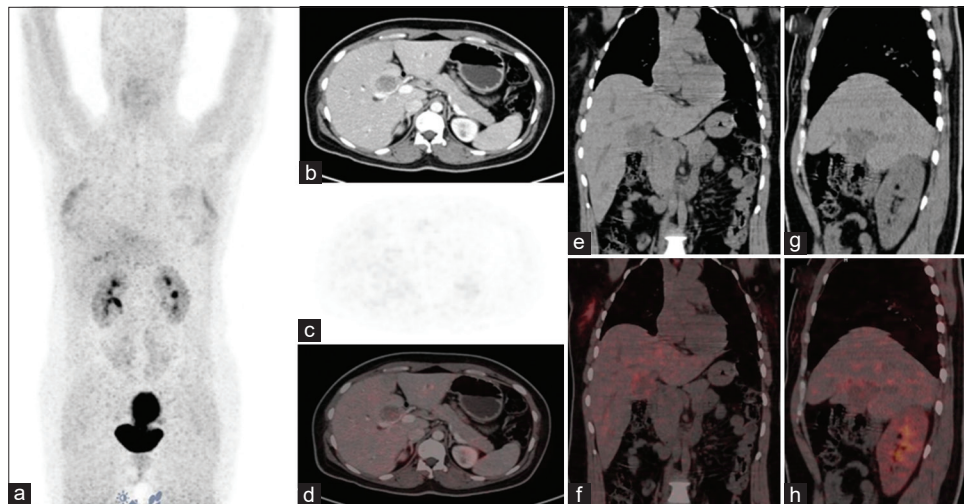


Figure 2: (a-h) Whole body Maximum intensity projection (MIP), corresponding sections of axial, sagittal, and coronal computed tomography (CT) and positron emission tomography-CT images of ^{68}Ga -FAPI-46 showing well-defined hypodense lesion (represented by white solid arrow) at hepatic hilum compressing common hepatic duct with upstream bilateral IHBRD, showing no abnormal increased FAPI expression

values of ^{68}Ga -DOTATATE versus ^{68}Ga -DOTATOC and ^{68}Ga -DOTATATE versus ^{68}Ga -DOTANOC have not identified any differences in diagnostic accuracy.^[3,4]

The target for the radiotracer ^{68}Ga -FAPI PET is fibroblast-activated protein, a transmembrane glycoprotein expressed on activated fibroblasts such as cancer-associated fibroblasts which are characterized by strong desmoplastic reaction. ^{68}Ga -labeled FAPIs rapidly bind and internalize into FAP-expressing cells, and undergo rapid renal clearance, resulting in high-contrast images.^[5]

Prior studies have reported that NETs are associated with the development of fibrosis.^[6] A positive finding of desmoplastic reaction in the context of gastroenteropancreatic NET is revealed by the employment of a ^{68}Ga -FAPI-46 PET/CT scan.^[7] The intention behind conducting this ^{68}Ga -FAPI-46 PET/CT imaging is to serve academic pursuits, specifically to identify the presence of desmoplastic reaction in EBNET.

In this case, the fact that ^{68}Ga -FAPI-46 PET/CT is negative suggests that EBNET does not demonstrate a desmoplastic reaction. For grade 1 EBNET, ^{68}Ga DOTA-TOC PET/CT positivity is sufficient; however, ^{68}Ga -FAPI-46 PET/CT imaging is performed to look for the presence of desmoplastic reaction as well as any added advantage over ^{68}Ga DOTA-TOC tracer in well-differentiated EBNET's.

We hope that our study sheds light on the fact that ^{68}Ga -FAPI-46 PET/CT is not particularly useful in EBNET. However, more studies are needed to support the claim that ^{68}Ga -FAPI-46 PET/CT is ineffective in EBNETs.

In summary, an accurate diagnosis of an EBNET can be made before surgery. Better preparation and condition management are made possible by this, which has important implications for treatment planning and patient care. For those with EBNET, a preoperative diagnosis can expedite the medical process and enhance results.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the patient has given her consent for her images and other clinical information to be reported in the journal. The patient understands that her name and initials will not be published and due efforts will be made to conceal her identity, but anonymity cannot be guaranteed.

Financial support and sponsorship

Nil.

Conflicts of interest

There are no conflicts of interest.

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