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Intense fibroblast activation protein inhibitor localization around the site of embolized gastroduodenal artery in a patient with metachronous pancreatic adenocarcinoma: A potential pitfall in positron imaging

Ahmed Saad Abdlkadir[1], Hasan Alalawi[1] and Akram Al-Ibraheem[1,2]

Abstract

^{68}Gallium-Fibroblast activation protein inhibitor (^{68}Ga-FAPI) positron emission tomography/computed tomography (PET/CT) is increasingly used for evaluating various epithelial neoplasms. Despite addressing some pitfalls, many remain unacknowledged. This report details a 77-year-old man with suspected pancreatic malignancy who underwent a ^{68}Ga-FAPI PET/CT scan post-gastroduodenal coil embolization for upper gastrointestinal bleeding. The scan revealed intense ^{68}Ga-FAPI uptake in the pancreatic body and tail malignancy and around the embolized gastroduodenal artery, indicating a healing process. This highlights the importance of understanding FAPI expression in recent surgical sites for accurate radiologic interpretation.

Keywords

^{68}GA-FAPI, pitfall, gastroduodenal embolization, duodenal ulcer, unaddressed pitfalls, pancreatic cancer

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Introduction

Pancreatic ductal adenocarcinoma (PDAC) is the most common exocrine malignancy, accounting for more than 90% of pancreatic neoplasms.[1] According to the latest GLOBOCAN estimates, PDAC remains a significant global health burden. In 2020, there were approximately 495,773 new cases of pancreatic cancer globally, making it the 12th most common cancer worldwide.[2] Currently, the occurrence of PDAC is increasing, emphasizing the growing necessity for personalized management.[3]

Currently, many developed and developing countries rely on ^{68}Gallium-Fibroblast activation protein inhibitor positron emission tomography/computed tomography (^{68}Ga-FAPI PET/CT) to stage and monitor patients with PDAC. This novel diagnostic modality has shown unparalleled superiority over traditional ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET/ CT due to its high tumor-to-background ratios, theranostic potential, and improved sensitivity and detectability at primary and metastatic neoplastic sites.[4–6] However, the specificity of ^{68}Ga-FAPI is not perfect and can be affected by various non-oncologic conditions related to infection, inflammation, tissue repair, autoimmune disease, and fibrosis.[7] These factors

[1]Department of Nuclear Medicine and PET/CT, King Hussein Cancer Center (KHCC), Amman, Jordan
[2]School of Medicine, The University of Jordan, Amman, Jordan

Corresponding author:
Akram Al-Ibraheem, Department of Nuclear Medicine, King Hussein Cancer Center (KHCC), Queen Rania Street, Amman 11941, Jordan.
Email: akramalibrahim@gmail.com

highlight the importance of cautious interpretation when relying solely on FAPI-based imaging in clinical decision-making.

In this case report, we present a patient with a suspected pancreatic malignancy who exhibited intense ^{68}Ga-FAPI uptake at the sites of a recently embolized duodenal ulcer. This case also provides insights into the molecular and histopathological perspectives of this distinctive pattern of ^{68}Ga-FAPI expression.

Case report

Clinical history

A 77-year-old man with a complex medical history was suspected of having a pancreatic malignancy. His past medical history included longstanding hypertension, a recent duodenal ulcer, and benign prostatic hyperplasia. He is currently maintained on daily bisoprolol (2.5 mg), omeprazole (40 mg), and tamsulosin hydrochloride (0.4 mg) to control these conditions. His past surgical history included sigmoidectomy for a previous T3N0M0 stage IIa sigmoidal moderately differentiated adenocarcinoma. Following this, his oncologic history remained unremarkable for 3 years post-sigmoidectomy, which was performed to provide effective up-to-date care. The patient also reported a recent onset of upper gastrointestinal bleeding, which required interventional embolization of the gastroduodenal artery for bleeding control.

Imaging findings

During his emergency visit, an abdominal CT scan revealed an incidental pancreatic body and tail mass, necessitating further evaluation. After adequate control of the bleeding, the patient underwent comprehensive laboratory analysis for hematologic, hepatic, renal, and tumor marker profiling. These results were unremarkable except for markedly elevated cancer antigen 19-9 (CA 19-9) levels of 184 U/L. Additionally, a ^{68}Ga-FAPI PET/CT scan was ordered as part of the initial diagnostic workup (Figure 1). The scan revealed a large, intense ^{68}Ga-FAPI-avid pancreatic body and tail mass (Figure 1(a)–(d) and (f); arrowheads). A maximum standardized uptake value (SUVmax) of up to 18.9 was recorded (Figure 1(a), (c), and (f); arrowheads). Interestingly, nearby ^{68}Ga-FAPI localization within the second part of the duodenum (SUVmax up to 8.7) was also noted (Figure 1(a), (b), and (e)–(g); arrows). Notably, both findings were visualized in attenuation and non-attenuation corrected images (Figure 1(a) and (b); annotations). This focal duodenal ^{68}Ga-FAPI activity was found surrounding a metal coil artifact (Figure 1(a), (b), and (e)–(g); arrows), potentially correlating with the patient's recent history of an embolized gastroduodenal artery bleeding from duodenal ulcer. A direct call to the interventional radiologist in charge of the recent gastroduodenal artery embolization confirmed the site of the procedure and the methodology used. Apparently, embolization was performed using three 5 mm coils 10 days prior. Therefore, the duodenal ^{68}Ga-FAPI-avid focus was labeled as an ancillary finding related to recent gastroduodenal artery embolization. Given the intense ^{68}Ga-FAPI expression within the pancreatic body and tail mass, a provisional diagnosis of locally advanced PDAC was made. A multidisciplinary clinical discussion was held to determine the next course of therapeutic action. The MDC team decided to perform distal pancreatectomy and splenectomy. Subsequent histopathological evaluation of the resected tumor confirmed the presence of moderately differentiated T3N0M0 stage IIa PDAC. The postsurgical period was unremarkable. The patient's case will be rediscussed in a second MDC round to determine the best next plan.

Discussion

Upon retrospective review of the maximum intensity projection image for the ^{68}Ga-FAPI PET/CT, one might initially attribute the ^{68}Ga-FAPI-avid focus to multiple etiologies. However, each of these potential etiologies can be mitigated by referring to the axial fused PET/CT views, clinical history, and oncologic history. The patient's previous history of sigmoidal cancer might suggest a rare incidence of metastatic disease to the duodenum, which is seldom encountered in clinical practice.[8] Another possibility is metastatic or nodal attribution of this focus to a newly developed pancreatic malignancy, or a synchronous periampullary neoplasm.[9,10] All these entities should have associated morphologic evidence on the CT portion of the ^{68}Ga-FAPI PET/CT study. When referring to the fused PET/CT images, no morphologic evidence of irregular thickness, altered density, mass lesion, or pressure effect was noted, excluding these etiologies from the differential diagnosis.

Another potential and commonly encountered non-oncologic etiology is the possibility of involvement of this area by inflammatory bowel disease (mostly Crohn's disease). In fact, ^{68}Ga-FAPI PET/CT has shown promising potential for tracking the course of Crohn's disease by detecting areas involved by fibrosis.[11] However, such a disease would typically have a previous positive history and usually present with multiple segmental lesions.

Fibroblast activation is known to be present in various processes, including inflammation, tissue remodeling, tissue injury, postsurgical wound healing, and scar formation, and therefore these processes are known to cause ^{68}Ga-FAPI PET/CT imaging pitfalls. In the present case, the patient recently underwent surgical repair of an embolized bleeding gastroduodenal artery due to an ulcer, with the intervention occurring less than 10 days prior. Therefore, it is possible

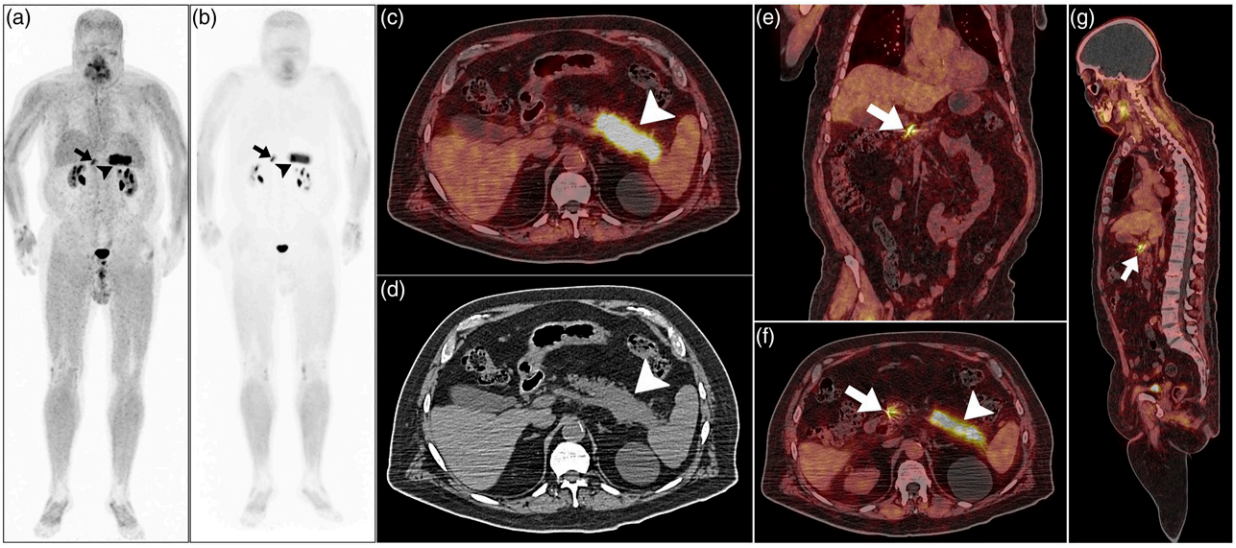

Figure 1. ^{68}Gallium-Fibroblast activation protein inhibitor (^{68}Ga-FAPI) positron emission tomography/computed tomography (PET/CT) was offered for a 77-year-old man to evaluate suspected pancreatic malignancy 10 days following recent gastroduodenal artery embolization. (a) Attenuation correction maximum intensity projection (MIP); (b) non-attenuation correction MIP; (c) axial PET/CT; (d) axial CT; and (e)–(g) coronal, axial, and sagittal PET/CT views exposed two foci of increased ^{68}Ga-FAPI uptake (annotations). (a–d, f) Images exposed an intensely ^{68}Ga-FAPI-avid pancreatic body and tail mass measuring about 7 cm in maximum dimensions (arrowheads). (a, b, e–g) Evidence of ^{68}Ga-FAPI expression surrounding metal coil artifact was observed correlating with the recent gastroduodenal arterial embolization (arrows).

that the observed FAPI-avid focus at the site of the recently treated ulcer can be attributed to ongoing wound healing, the recent surgical intervention, or a combination of both factors. Another potential cause of diagnostic misinterpretation in this area is related to technical artifacts. For example, attenuation correction artifacts at metal coil insertion sites can result in such an observation. This can be excluded by examining non-attenuation correction images; consistency in FAPI expression between these and attenuation correction images indicates true FAPI-related uptake rather than a technical artifact, as highlighted in our case. Furthermore, artifacts from breathing motion can also render false positive findings in the upper abdomen. In such context, evaluation of the fused image in sagittal views is most helpful to ensure precise radiotracer localization at the area of interest. In our case, we assessed the FAPI-avid duodenal focus in axial, coronal, and sagittal views to exclude such possibility.

Given the patient's recent history of coil gastroduodenal artery embolization to control upper gastrointestinal bleeding, paired with concomitant evidence of a metal coil artifact lying at the center of the second duodenal ^{68}Ga-FAPI-avid focus, a more detailed procedure briefing for the recent gastroduodenal artery embolization was needed. After confirming the site and technique of gastroduodenal artery embolization, which utilized metal coils at the site of the gastroduodenal bleeding source, the physician could confidently highlight this finding as ancillary evidence.

^{68}Ga-FAPI PET/CT represents a novel theranostic approach that offers comprehensive evaluation of epithelial neoplasms of pancreaticobiliary origin.[12–14] Compared to traditional ^{18}F-FDG PET/CT, ^{68}Ga-FAPI PET/CT demonstrates higher levels of sensitivity and specificity, making it a valuable tool in the staging of PDAC and the detection of early recurrence.[15] However, this is not applicable in all scenarios; for example, the reliability of ^{68}Ga-FAPI PET/CT tends to be underwhelmed by various pitfalls that become increasingly acknowledged over time. For instance, tumor-induced pancreatitis can sometimes mask the underlying pancreatic tumor, hampering accurate lesion depiction.[16] The same applies to stent-induced pancreatic ^{68}Ga-FAPI uptake, resulting in diffuse radiotracer expression throughout the pancreas.[17] In settings of inflammation and autoimmune disease processes, a similar pattern of diffuse ^{68}Ga-FAPI uptake has also been reported, overlapping with the previously mentioned etiologies.[18,19] All these benign causes can be effectively diagnosed upon clinical, biochemical, and multidisciplinary team evaluation.

A recent systematic review highlighted that ^{68}Ga-FAPI PET/CT pitfalls occur predominantly at vasculature, highlighting the potential of ^{68}Ga-FAPI PET/CT to monitor the vascular disease spectrum from ischemic to inflammatory and autoimmune etiologies.[20] However, this recent study did not mention embolized arterial ^{68}Ga-FAPI uptake as part of an observed non-oncologic pitfall. Moreover, our understanding of the time that will elapse until FAPI activity

fades from this embolized vessel is still unknown. Such a new paradigm is worth further exploration in later reports and studies to highlight the timing, duration, and uptake kinetics associated with these interventions. Finally, it remains most important to acknowledge the value of clinical history correlation, interdisciplinary communication for briefing, and differential diagnosis reasoning to optimize reporting of such unrelated etiologies when present.

Declaration of conflicting interests

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Ethical statement

Ethical approval

The study was conducted in accordance with the Helsinki declaration.

Informed consent

The patient signed an informed consent statement.

ORCID iDs

Ahmed Saad Abdlkadir https://orcid.org/0000-0002-2009-5110
Akram Al-Ibraheem https://orcid.org/0000-0002-0978-4716

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