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CASE REPORT

Gastric cancer in a patient with IgG4-related disease: Importance of diligent interpretation of [^{18}F]FDG PET/CT

Amin Saber Tanha[1,2], Farid Jafari Zarrin Ghabaei[1,2], Amirreza Khorasanchi[3], Ramin Sadeghi[1]

[1]*Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran*

[2]*Student Research Committee, Mashhad University of Medical Sciences, Mashhad, Iran*

[3]*Cancer Research Center, Razavi Hospital, Imam Reza International University, Mashhad, Iran*

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*Corresponding Author:
Dr. Ramin Sadeghi
Address: Nuclear Medicine Research Center, Mashhad University of Medical Sciences, Mashhad, Iran.
Email: sadeghir@mums.ac.ir

ABSTRACT

IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory disorder that can involve multiple organs, including the retroperitoneum. We report the case of a 58-year-old man with IgG4-related retroperitoneal fibrosis (IgG4-RPF) diagnosed a decade earlier and initially managed with corticosteroids and azathioprine. Over the years, he developed a range of symptoms that ultimately led to the diagnosis of gastric cancer following complaints of dyspepsia. This case underscores both the diagnostic value and limitations of [^{18}F]FDG PET/CT in IgG4-RD, particularly its inability to reliably distinguish inflammation from malignancy. Although [^{18}F]FDG PET/CT is commonly used to monitor the inflammatory activity of IgG4-RD, this case highlights its potential role in detecting concurrent malignancies. It also emphasizes the critical importance of vigilant screening and long-term follow-up in this patient population.

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INTRODUCTION

IgG4-related disease (IgG4-RD) is a systemic fibroinflammatory disorder characterized by infiltration of IgG4-positive plasma cells and storiform fibrosis. Retroperitoneal fibrosis is a recognized manifestation of IgG4-RD, and [^{18}F]FDG PET/CT serves as a valuable tool for assessing disease extent, although it has limited specificity in differentiating inflammation from malignancy. IgG4-RD has been reported to be associated with an increased risk of malignancy, particularly involving the gastrointestinal tract. Although the precise mechanisms underlying oncogenesis remain unclear, general risk factors-such as male sex, advanced age, smoking, occupational exposure, and disease recurrence-highlight the importance of maintaining vigilant follow-up in affected individuals [1]. We present a case of IgG4-related retroperitoneal fibrosis (IgG4-RPF) complicated by subsequent gastric adenocarcinoma, underscoring the importance of careful imaging interpretation and long-term surveillance.

CASE PRESENTATION

A 58-year-old man was diagnosed with IgG4-RPF ten years earlier following evaluation for abdominal pain, which culminated with a diagnostic laparotomy. The fibrosis was predominantly located around the right ureter, right common iliac artery and the inferior vena cava near its bifurcation. Hisotopathological examination revealed fibrosis with an increased ratio of IgG4-positive plasma cells, confirming the diagnosis of IgG4-RPF. He was initially treated with prednisolone and azathioprine; however, treatment was discontinued due to abnormal liver function tests. He remained asymptomatic for approximately eight years, after which he developed bilateral lower-extremity paresthesia accompanied by onychodystrophy and nail shedding affecting both the hands and feet. Given these findings, an [^{18}F]FDG PET/CT scan was performed as part of a malignancy workup for suspected paraneoplastic syndrome. The scan revealed limited retroperitoneal fibrosis with intense hypermetabolism (Figure 1A), primarily surrounding the bilateral common iliac vessels and inferior vena cava (Figure 1B). Subsequent investigations, including upper endoscopy, colonoscopy, and electromyography/nerve conduction velocity (EMG-NCV) testing, were unremarkable. However, he did not complete further evaluation due to noncompliance. Approximately one year later, he developed deep venous thrombosis in the left lower extremity, complicated by pulmonary embolism. Several weeks thereafter, he presented with dyspepsia, prompting repeat endoscopic evaluation. This revealed a gastric mass and biopsy confirmed gastric adenocarcinoma. A repeat [^{18}F]FDG PET/CT scan (Figure 1D) demonstrated intense hypermetabolism within the gastric tumor (Figure 1E), along with multiple cervical, mediastinal and retroperitoneal lymphadenopathies as well as metastases involving the left adrenal gland and intraperitoneal deposits (Figure 1E & 1D), consistent with Stage IV gastric adenocarcinoma. Notably, the retroperitoneal fibrosis identified on the initial [^{18}F]FDG PET/CT performed 18 months earlier (Figure 1B), had completely resolved on follow-up imaging (Figure 1C).

Systemic IgG4-RD is an immune-mediated condition that predominantly affects middle-aged to elderly males and may involve multiple organs [2]. [^{18}F]FDG PET/CT is an effective modality for assessing disease extent, guiding interventional procedures and evaluating therapeutic response in IgG4-RD [3–7]. While [^{18}F]FDG PET/CT demonstrates high sensitivity and can facilitate early disease detection, it lacks adequate specificity for distinguishing inflammatory activity from malignancy [4,8-10]. More recently, [^{68}Ga]Ga-FAPI has been reported to offer additional value in the evaluation of IgG4-RD, potentially improving sensitivity; however, it does not significantly enhance specificity compared with [^{18}F]FDG PET/CT[8, 9, 11-16]. Furthermore, [^{68}Ga]Ga-FAPI may serve as a predictor of relapse-free survival [17]. The limited specificity of both [^{18}F]FDG and [^{68}Ga]Ga-FAPI PET/CT is clinically relevant, as it may lead to underdiagnosis of concurrent malignancies [18] or, conversely, overstaging of known malignant disease [19-22] This issue is particularly important given reports suggesting an increased incidence of malignancies—such as colorectal and gastric cancers—among patients with IgG4-RD [1, 23]. In a recent observational study by Keller-sarmineto et al., both solid and hematologic malignancies were more frequently observed in patients with pancreatobiliary IgG4-RD. The standardized incidence ratio (SIR) for malignancy in patients with IgG4-RD was 2.54 compared with the general Italian population, suggesting a potential paraneoplastic association. Based on these findings, the authors recommended close oncologic surveillance, particularly during the first 36 months following the diagnosis of IgG4-RD [24].

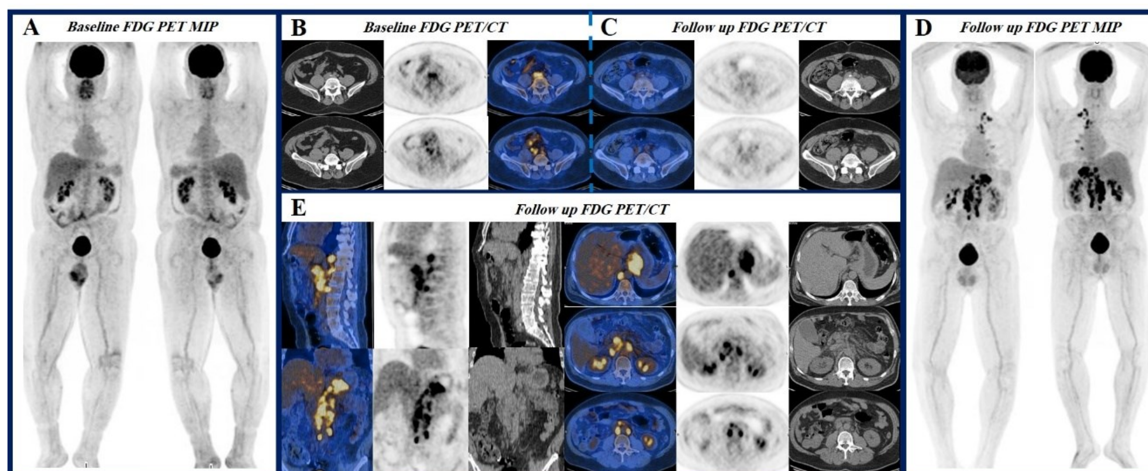

Figure 1. (A) Maximum intensity projection (MIP) image from the baseline [18F]FDG PET/CT demonstrates a λ-shaped region of increased [18F]FDG uptake in the mid-abdominal area extending toward the right side. (B) Corresponding baseline axial images localize the hypermetabolic activity to fibrotic tissue surrounding the right ureter, right common iliac artery, and inferior vena cava near its bifurcation. (C) Follow-up [18F]FDG PET/CT performed approximately 18 months later shows resolution of the previously noted fibrotic changes following treatment. (D) MIP image from the follow-up scan illustrates the distribution of hypermetabolic lymph nodes. (E) Follow-up [18F]FDG PET/CT axial and sagittal images demonstrate intense metabolic activity in a gastric tumor, accompanied by multiple hypermetabolic retroperitoneal, retro-pancreatic, and celiac lymph nodes

CONCLUSION

These observations underscore the necessity of rigorous screening and long-term follow-up in patients with IgG4-RD. While sensitive modalities such as [18F]FDG PET/CT are invaluable, clinicians must remain vigilant regarding their limitations. Our experience suggests that serial [18F]FDG PET/CT follow up in IgG4-RD can reveal concurrent malignancies, enabling earlier diagnosis. Imaging findings suggestive of disease progression or new hypermetabolic lesions should prompt comprehensive clinical correlation and, when appropriate, histopathological confirmation to avoid misclassification of malignancy as inflammatory activity or vice versa.

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