Incidentally Detected Celiac Disease with Splenomegaly on 18F FDG PET/CT: A Potential Lymphoma Mimic

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ABSTRACT

Celiac disease is an immune-mediated disorder triggered by hypersensitivity to gluten occurring in genetically susceptible individuals. A high-index of suspicion is needed for diagnosis as patients can be asymptomatic or present with atypical symptoms or extra-intestinal manifestations. Typical 18F-Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET)/Computed Tomography (CT) gastrointestinal manifestations of celiac disease include increased multifocal or diffuse jejunal and ileal uptake; focal duodenal uptake is less common. Splenomegaly with increased splenic FDG uptake is also uncommon in celiac disease in the absence of portal hypertension; small-sized spleen and functional hyposplenism are more typical. We report a case of celiac disease diagnosed after PET/CT showed FDG uptake in the duodenum and enlarged spleen. Follow-up after gluten-free diet showed complete metabolic resolution and regression of splenomegaly. The combination of focal bowel and splenic uptake is unusual in celiac disease and may be mistaken for a lymphoproliferative disorder. Awareness of this entity may avoid misdiagnosis and guide appropriate management.

Introduction

Celiac disease is an autoimmune disorder triggered by immune reaction to gluten in genetically predisposed individuals. While enteropathy and gastro-intestinal symptoms (e.g. chronic diarrhea, malabsorption, and abdominal pain) are the typical manifestations of this disease, various extra-intestinal symptoms have been reported such as multi-factorial anemia, metabolic bone disorders due to vitamin D deficiency, neurological symptoms due to vitamin B12 deficiency and co-existence with other autoimmune conditions (1). Patients can also be asymptomatic despite specific questioning about gastrointestinal symptoms. Therefore, a high-index of suspicion is needed for diagnosis in asymptomatic patients or in those with atypical symptoms and extra-intestinal manifestations (1, 2). Familiarity with less common manifestations of celiac disease on 18F-Fluorodeoxyglucose (FDG) Positron Emission Tomography (PET)/Computed Tomography (CT) can avoid diagnostic pitfalls. The purpose of this report is to describe a case of celiac disease diagnosed in an asymptomatic patient based on findings on FDG PET/CT scan and discuss the pertinent clinical and FDG PET imaging features of celiac disease. We also discuss the clinical significance of incidental bowel uptake and the causes of increased splenic uptake on FDG PET imaging.

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Case Report

A 56 year old Caucasian never-smoker man underwent whole body FDG PET/CT for staging of newly diagnosed lung cancer. The initial PET/CT showed expected FDG uptake in lung mass and incidental focal FDG uptake in proximal duodenum ($SUV_{max}=7.3$), splenomegaly with increased splenic uptake ($SUV_{max}=5.8$) and diffuse bone marrow uptake ($SUV_{max}=3.1$) relative to the liver ($SUV_{max}=2.8$) (Figure 1). The spleen measured 16.5 cm in craniocaudal dimension (normal spleen size <13 cm). Differential considerations for splenic and duodenal uptake in this patient included concomitant lymphoproliferative disorder and inflammatory/reactive uptake.

![Baseline FDG PET/CT](image)

Figure 1. Baseline $^{18}$F-FDG PET/CT images performed for lung cancer staging show expected FDG uptake in lung mass (dotted black arrow on whole body maximum intensity projection image) and incidental focal FDG uptake in proximal duodenum ($SUV_{max}=7.3$), splenomegaly with increased splenic uptake ($SUV_{max}=5.8$) and diffuse bone marrow uptake ($SUV_{max}=3.1$) relative to liver ($SUV_{max}=2.8$). The spleen measured 16.5 cm in craniocaudal dimension.

On subsequent workup, the complete blood count, peripheral blood smear and serum erythropoietin level were within normal range. Specifically, the hematological workup did not show abnormalities commonly seen in celiac disease such as anemia, thrombocytopenia, leukopenia and Howell-Jolly bodies on blood smear (a marker for functional hyposplenism). Serum biochemistry showed findings consistent with vitamin D and iron malabsorption such as low serum vitamin D level (value 16 ng/ml, normal reference range 20-50 ng/mL) and elevated serum ferritin (patient value 434 mcg/mL, normal reference range: 24-336 mcg/mL).

Esophagogastroduodenoscopy showed diffuse atrophic duodenal mucosa compatible with celiac disease. This was subsequently confirmed on duodenal biopsy pathology that showed villous atrophy and increased intra-epithelial lymphocytes (Figure 2). Splenic biopsy was normal without findings to suggest lymphoproliferative disorder (Figure 2). The serological test for celiac disease diagnosis showed elevated serum tissue transglutaminase (TTG) IgA levels > 100 U/ml (normal < 4 U/ml). These collective findings were diagnostic of celiac disease.
On specific questioning, the patient only complained of vague abdominal fullness. No other gastrointestinal symptoms were present. The patient was initiated on a gluten-free diet. Subsequent PET/CT performed 8 months after gluten-free diet showed complete resolution of FDG uptake in duodenum, spleen and bone marrow and decreased spleen size (Figure 3). New FDG uptake was demonstrated in lower anterior left sided rib fractures in a pattern suggestive of osteoporotic fractures. Serum TTG IgA decreased to 52 U/ml consistent with favorable celiac serological response. Subsequent to the diagnosis of celiac disease in our index patient, one of his children was also diagnosed with celiac disease; another grandchild had symptoms suggestive of celiac disease and is currently undergoing further evaluation.
Discussion

This report describes a case of celiac disease diagnosed after incidentally detected duodenal FDG uptake and splenomegaly on PET/CT with complete metabolic resolution after gluten free diet. While imaging manifestations of celiac disease on FDG PET imaging have been described previously (3, 4), this case presents several unique features such as the lack of specific patient symptoms and the presence of concomitant splenomegaly at the time of initial presentation. To our knowledge, there have only been two case reports describing FDG PET/CT manifestations of celiac disease; both of these described symptomatic patients with diffuse FDG uptake in small bowel and small bowel thickening and jejunalization of ileum on CT (3, 4). While concomitant FDG avid mesenteric lymph nodes were described in one report raising the question of lymphoma (3), there was no splenomegaly, splenic or bone marrow uptake. In our case, focal uptake was only seen in the second part of duodenum. A literature review of incidentally detected focal small bowel uptake on FDG PET revealed that this is uncommon. For instance, in a large retrospective study of 41,358 FDG PET/CT exams, bowel uptake was demonstrated in only 0.7% (303) exams and small bowel uptake was seen in only one exam (5). Similarly, in another study of 4,390 patients, incidental bowel uptake was demonstrated in 1.3% (58 patients) and only two cases demonstrated small bowel uptake (6). Thus it is recommended to follow-up incidentally detected focal small bowel uptake with further endoscopic and radiological imaging (7). The duodenal FDG uptake in celiac disease is attributed to mucosal inflammation and intraepithelial lymphocytes, as demonstrated on pathology (4).

Secondly, celiac disease is typically associated with functional hyposplenism and small sized spleen. The functional hyposplenism is characterized by Howell-Jolly bodies on peripheral blood smear (8). Splenomegaly with splenic and bone marrow uptake in association with celiac disease has not been reported, to our knowledge. This combination of splenic and bone marrow FDG uptake can also be seen in severe anemia, after administration of granulocyte-macrophage colony-stimulating factors, extramedullary hematopoiesis and granulomatous conditions. Splenomegaly in celiac disease has been described secondary to portal hypertension induced by antigenic stimulation of splenorenal axis and non-cirrhotic portal fibrosis (9-13). In our case, all of these conditions were excluded after appropriate investigations. While malignancies, including lung cancer can also induce diffusely increased splenic and bone marrow uptake due to anemia and systemic inflammation (14, 15), the complete metabolic resolution of splenomegaly after gluten-free diet suggests that the splenic and bone marrow uptake was due to celiac disease. While the exact mechanisms for FDG uptake in bone marrow and spleen in celiac disease are not known, these may be attributed to cytokine-induced activation of humoral immunity triggered by gluten (16).

Lymphoproliferative disorder is often the chief differential consideration when encountered with this spectrum of findings; i.e. bowel, splenic and bone marrow uptake (2). However, the combination of villous atrophy and intraepithelial lymphocytes on duodenal biopsy and elevated serum TTG-A is considered the gold standard for celiac disease diagnosis, as shown in this case (1). Elevated serum TTG IgA can be particularly helpful in asymptomatic patients due to its high sensitivity. Anti-endomysial antibody is a more specific serological marker but also a more expensive test and may be considered in symptomatic patients with a clinical suspicion of celiac disease but with normal TTG Ig-A (1).

Follow-up FDG PET/CT after gluten-free diet is useful as the resolution of FDG uptake combined with favorable serological response can help exclude the possibility of non-responsive or refractory celiac disease (2, 3). Rarely celiac disease can be further complicated by enteropathy-associated T-cell lymphoma, characterized by intestinal FDG uptake and lymphadenopathy (17). Lastly, while celiac disease has been associated with increased risk of other malignancies including gastrointestinal adenocarcinomas and B-cell Non-Hodgkin’s lymphoma (18, 19), the risk of lung cancer is reportedly decreased in these patients (1, 20). Thus, the presence of lung cancer in this case was unrelated to celiac disease.

In conclusion, celiac disease should be considered as a diagnostic possibility when encountered with focal small bowel uptake on FDG PET/CT. Activation of immune response may lead to concomitant splenic and bone marrow FDG uptake, with expected resolution after a gluten-free diet.

References

FDG PET/CT of Celiac Disease with Splenomegaly

Panda A et al


