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Case Report

Duodenal-type follicular lymphoma in ^{18}F-FDG PET/CT imaging: a case report

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Abstract: Follicular lymphoma (FL) is a subtype of non-Hodgkin lymphoma (NHL) that is typically characterized by a slow-growing course. Duodenal-type follicular lymphoma (D-FL) was recently reclassified as a distinct variant. This subtype exhibits unique clinical and biological characteristics, which set it apart from other forms of FL. We report a case of a 36-year-old male patient with multiple, small, gray polypoid lesions in the descending duodenum which were detected by esophagogastroduodenoscopy. The pathological diagnosis was low-grade D-FL. ^{18}F-FDG PET/CT was performed for staging and revealed the pancreas and peripheral lymph nodes were involved by FL, with a clinical IV stage. The patient underwent a bone marrow smear cytology, which revealed no bone marrow abnormalities, and excluded bone marrow involvement. He was treated with six cycles of chemotherapy using the R-CHOP regimen and reached complete remission.

Keywords: Follicular lymphoma, duodenal-type, ^{18}F-FDG, PET/CT, case report

Introduction

Follicular lymphoma (FL) is a subtype of non-Hodgkin lymphoma (NHL) that is typically characterized by a slow-growing course [1]. FL accounts for approximately 20-25% of NHL cases worldwide, making it the second most common subtype of NHL [2]. Duodenal-type follicular lymphoma (D-FL) was recently reclassified as a distinct variant of FL in the 2017 World Health Organization classification. This subtype exhibits unique clinical and biological characteristics, which set it apart from other forms of FL. FL and diffuse large B-cell lymphoma (DLBCL) exhibit contrasting progression-free and overall survival outcomes, with discernible differences in their respective survival curves. Notably, DLBCL represents the most frequently encountered aggressive lymphoma subtype [3, 4]. FL is characterized by a slow growth rate, with approximately 80% of patients being diagnosed at clinical stage III or IV [5]. In contrast, D-FL is typically diagnosed at an early stage and can arise in various locations within the duodenum, with the descending portion being the most frequent site of involvement [6-8].

Here, we present a report on the imaging presentation and treatment modality of a patient with D-FL using ^{18}F-FDG PET/CT. The patient was successfully treated with six cycles of chemotherapy using the first-line rituximab plus cyclophosphamide, doxorubicin, vincristine, and prednisone regimen (R-CHOP), resulting in complete remission of the lesion. Furthermore, we discuss the advantages and usefulness of ^{18}F-FDG PET/CT examination in accurate staging, assessing treatment response, and predicting prognosis in FL patients.

Case presentation

A 36-year-old male patient presented with symptoms of acid reflux and heartburn one month ago. He came to our hospital for a physical examination and carbon-13 breath test which did not reveal any abnormality. Laboratory

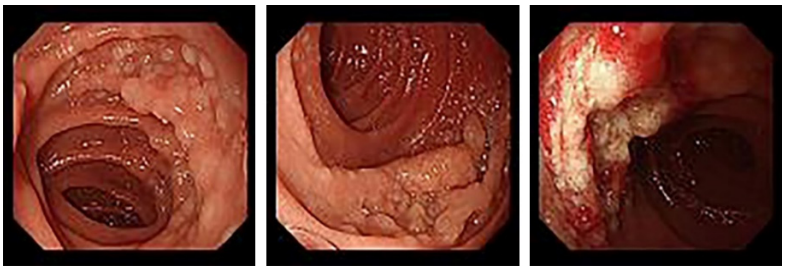

Figure 1. Esophagogastroduodenoscopy revealed multiple small gray polypoid lesions in the descending duodenum. The surface mucosa appeared smooth and the lesions ranged in size from 0.2 cm × 0.2 cm to 0.5 cm × 0.5 cm.

tests showed reduced gastrin-17 at 4.56 pg/mL (normal range 35 to 105 pg/mL). As shown by esophagogastroduodenoscopy, multiple small gray polypoid lesions were observed in the descending duodenum. The surface mucosa appeared smooth and the lesions ranged in size from 0.2 cm × 0.2 cm to 0.5 cm × 0.5 cm (**Figure 1**). To obtain a pathological biopsy, larger polyps were removed using traps. Pathological microscopy revealed nodular and diffusely proliferating lymphocytes densely arranged in the lamina propria of the mucosa. Immunohistochemical staining revealed CK (-), CD20 (+), CD79a (+), Cyclin D1 (-), CD3 (-), CD43 (-), CD21 (FDC+), CD23 (FDC+), CD10 (+), Bcl-6 (+), Bcl-2 (+), CD5 (-), CD30 (-), MUM-1 (-), and Ki-67 (15%+), consistent with a diagnosis of D-FL (**Figure 2**).

To accurate stage, the patient subsequently underwent an ^{18}F-FDG PET/CT scan, which revealed a localized thickening of the descending duodenum with moderately increased FDG uptake, and its maximum standardized uptake value (SUVmax) was 5.5. Lesions of increased FDG uptake were also observed in the body of the pancreas (SUVmax = 3.9), along with FDG-avid lymph nodes in the hepatogastric space, peripancreatic, mesenteric, and retroperitoneal areas (SUVmax = 3.8) (**Figure 3**). He underwent a bone marrow smear cytology, which revealed no bone marrow abnormalities, and excluded bone marrow involvement. The clinical stage of the patient was stage IV, and after excluding contraindications to chemotherapy, the patient was treated with six cycles of chemotherapy using the R-CHOP regimen. Subsequent ^{18}F-FDG PET/CT examination showed a significant reduction in metabolically active lesions in the descending duodenum and body of the pancreas, with no observed metabolic increase in the hepatogastric space, peripancreatic, mesenteric areas, and small retroperitoneal lymph nodes (**Figure 4**). Pathological biopsy confirmed complete remission of the lesions. The patient has been in stable condition and followed up for one year without any recurrence.

Discussion

Most cases of D-FL manifest as nonspecific upper gastrointestinal symptoms, although asymptomatic cases are also frequently encountered [9]. The presence of clinical indicators such as weight loss, anemia, or fever is only occasionally related to lymphoma [10]. D-FL is frequently identified incidentally during esophagogastroduodenoscopy [11]. The most commonly observed endoscopic features include white granular or multiple nodular, polypoid lesions located in the descending portion of the duodenum, with dimensions typically ranging between 1 and 5 mm. In cases where these lesions become ulcerated, it is imperative to obtain biopsy specimens from the surrounding tissue to enhance diagnostic yield [12, 13]. Furthermore, a comprehensive evaluation of the gastrointestinal tract using colonoscopy, double-balloon endoscopy, and capsule enteroscopy may reveal jejunal or ileal lesions of D-FL cases, thereby facilitating a more accurate determination of the disease distribution [12, 14].

The diagnosis of D-FL relies on the results of pathological histology and immunohistochemistry. The histopathological examination of affected tissues reveals the presence of neoplastic follicles comprised of small to medium-sized cleaved cells in the lamina propria. Furthermore, an examination of neoplastic follicles shows a unique pattern of follicular dendritic cells (FDCs) that bears a resemblance to some cases of gastric mucosa-associated lymphoid tissue (MALT) lymphoma [12]. Immunohistochemical staining reveals the presence of positive B-cell markers, accompanied by the expression of Bcl-2, Bcl-6, CD10, and CD20. D-FL is characterized by the presence of genetic translocations involving the *t(14;18) (q32; q21)* region, as well as aberrations in the usage of heavy chain variable (VH)

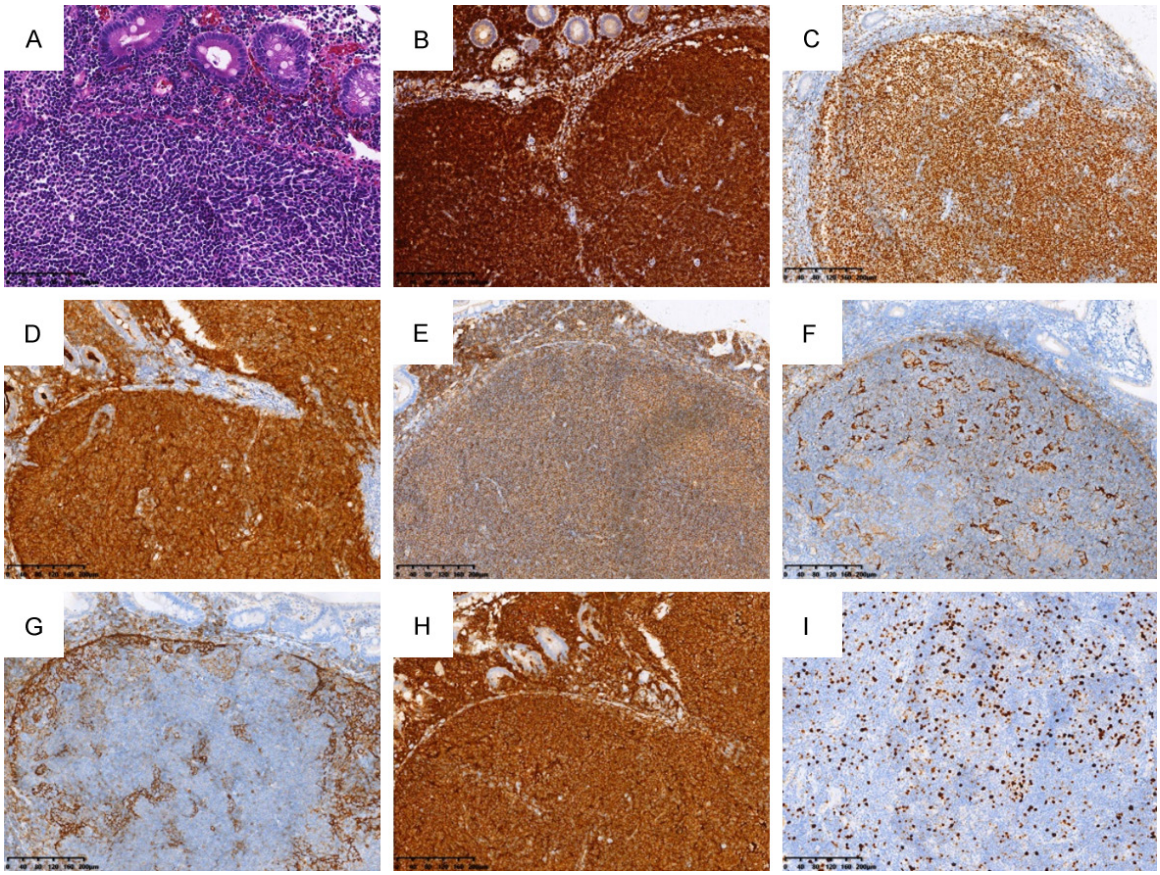

Figure 2. Pathological and immunohistochemical staining images. (A) Hematoxylin-eosin (HE) staining (magnification ×200). Immunohistochemical staining of Bcl-2 (B), Bcl-6 (C), CD10 (D), CD20 (E), CD21 (F), CD23 (G), and CD79a (H). In addition, Ki67 (I) was observed to be positive in 15% of the tumor cells [Envision (B-H) ×100].

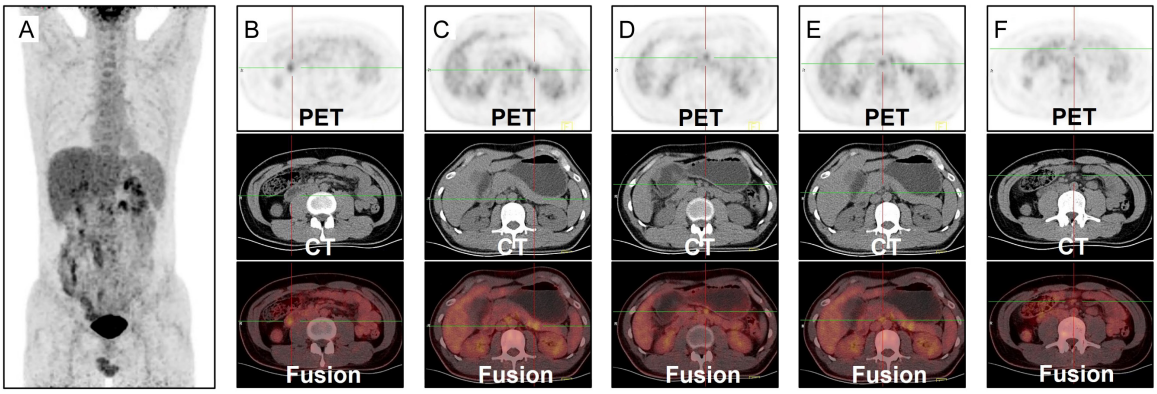

Figure 3. ^{18}F-FDG PET/CT images of duodenal-type follicular lymphoma before treatment. A. Multiple FDG-avid lesions in the duodenum and peripancreatic were found by PET MIP image [Liver uptake (SUVmax = 2.7) and mediastinal blood pool uptake (SUVmax = 1.3)]. B. The transverse images showed localized thickening of the descending duodenum with moderately increased FDG uptake (SUVmax = 5.5). C. The transverse images showed foci of increased FDG uptake in the body of the pancreas (SUVmax = 3.9). D-F. The transverse images showed multiple FDG-avid lymph nodes in the hepatogastric space, peripancreatic, mesenteric, and retroperitoneal areas (SUVmax = 3.8).

genes, particularly in VH4-34 and VH5 [5, 8, 12]. In addition, the number of mitotic figures and the expression of Ki67 in neoplastic cells are exceedingly low [5]. Pathologists categorize

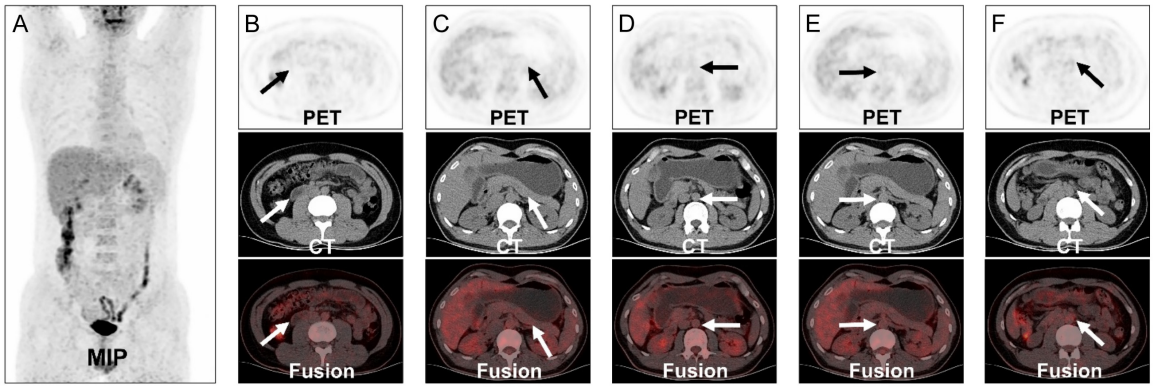

Figure 4. ^{18}F-FDG PET/CT images of duodenal-type follicular lymphoma after treatment. (A) PET MIP images revealed no increase in metabolism within the previous FDG-avid lesions [Liver uptake (SUVmax = 3.0) and mediastinal blood pool uptake (SUVmax = 1.4)]. The transverse images showed no increase in FDG uptake (long arrows) of the descending duodenum (B), body of the pancreas (C), lymph nodes in the hepatogastric space, peripancreatic, mesenteric, and retroperitoneal areas (D-F).

FL into grades 1, 2, and 3 based on the number of centroblasts. However, it is important to note that the pathologic grade alone cannot predict the clinical outcome of FL [5, 15]. Bende et al. [16] observed that surface IgA expression, which is typically absent in nodal FL, is a distinguishing feature of D-FL cells located in the intestinal mucosa. Additionally, they noted the presence of α4β7 integrin expression, which is believed to facilitate the "mucosal homing" of lymphocytes. Accurate diagnosis of D-FL requires differentiation from intra-nodal FL involving the duodenum, reactive follicular hyperplasia, and MALT lymphoma.

In the past few years, there has been a growing interest in using ^{18}F-FDG PET/CT as a diagnostic tool for FL patients. This imaging technique has proven to be particularly useful for staging, restaging, and evaluating treatment responses in these patients. When it comes to staging, PET/CT has demonstrated a greater sensitivity compared to the standard CT scan. This increased sensitivity improves outcomes for these patients. Two parameters that are particularly relevant for predicting FL outcomes are the total metabolic tumor volume (MTV) and the pre-treatment SUVmax [17-20]. Our case involved the pancreas and peripheral lymph nodes, with a clinical stage of IV. The follow-up PET/CT examination showed that the metabolically active foci had largely disappeared, corresponding to a complete remission of the pathology.

Some studies have suggested that the baseline ^{18}F-FDG PET/CT scan can serve as a valuable predictor of progression-free and overall survival in patients with high tumor burden FL following frontline treatment [21, 22]. According to Yang et al. [1], the prognostic value of ^{18}F-FDG PET/CT imaging may aid in identifying patients who could potentially benefit from a "watch-and-wait (W&W)" approach, as well as in more effectively selecting patients who require early treatment with rituximab monotherapy to delay disease progression. Li et al. [23] conducted a study to assess the effectiveness of a novel baseline PET parameter, which quantifies both lesion dissemination and metabolic parameters by predicting progression-free survival and pathologic grade in patients with FL. FL commonly presents with bone marrow involvement (BMI), making it a critical factor to consider during upfront staging [24]. Accurate assessment of BMI is essential, as it can impact patient management decisions. Ródenas-Quiñonero's study demonstrates that both bone marrow biopsy and PET/CT should be incorporated into the diagnostic evaluation of FL [25]. The combined use of these modalities provides independent prognostic value and enhances the predictive power of the most commonly employed clinical scores. FL may undergo histologic transformation (HT) during its course, with an estimated 10-year cumulative incidence of 8% confirmed by biopsy [26]. Early detection of HT is crucial since it is associated with a poor prognosis. Rajamäki et al. [27] reported that the repeat biopsy guided by a

high SUVmax in diagnostic ^{18}F-FDG PET/CT scan is a valuable approach in identifying clinically undetected HT of FL.

Radiomics uses automated or semi-automated quantitative analysis of high-dimensional images to improve characterization, diagnosis, and prognosis. In recent years, a rapid increase has been shown in radiomics applications in nuclear medicine. Several radiomics studies have been applied to FL. According to de Jesus et al. [28], the application of machine learning analysis to radiomic features may have diagnostic value in discriminating between FL and DLBCL tumor lesions, surpassing the predictive power of SUVmax alone. In their study, a logistic regression model based on SUVmax achieved an AUC of 0.79 and an accuracy of 70%. However, the Gradient Boosting classifier demonstrated significantly higher AUC and accuracy values compared to the SUVmax-based logistic regression model ($P \leq 0.01$). Faudemer et al. [29] conducted a study to evaluate the efficacy of ^{18}F-FDG PET/CT radiomics in diagnosing BMI in patients with FL. A total of 66 patients were included in the study and a ROC analysis was performed. The optimal cutoff for the diagnosis of BMI using PET pred.score was found to be -0.190, with the corresponding sensitivity, specificity, positive predictive value, and negative predictive values of 70.0%, 83.3%, 77.8%, and 76.9%, respectively.

D-FL can be treated using various therapeutic strategies, including W&W, chemotherapy, immunochemotherapy, rituximab alone or in combination with other chemotherapies (Rituximab-chemo, R-chemo), radiotherapy, autologous stem cell transplantation, and novel immunomodulatory agents [5, 18, 30-33]. For patients with asymptomatic low tumor burden FL, a reasonable initial management approach is to utilize W&W until disease-related symptoms emerge [1, 5, 34]. The R-chemo approach is favored by some clinicians due to observations of FL transformation into more aggressive forms, such as DLBCL or Burkitt-type lymphoma. Our patient was anxious about the W&W approach and was treated with 6 cycles of chemotherapy using the R-CHOP regimen, which resulted in complete remission of the lesion. Although the clinical course of patients with Stage IV advanced D-FL has been elucidated, the long-term outcome remains uncertain as the longest follow-up cases have been reported to reach the 20-year [11]. As such, establishing clear criteria for treating advanced D-FL will be crucial in the future.

In summary, D-FL is a clinically rare disease with unique biological features and a good prognosis. Long-term follow-up is necessary to monitor the possibility of recurrence. ^{18}F-FDG PET/CT examination can comprehensively show the site and extent of the lesion, provide a basis for clinical staging of the tumor, and aid in treatment monitoring and follow-up.

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Disclosure of conflict of interest

None.

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