CASE REPORT

Nodular lymphoid hyperplasia in endoscopic and FDG-PET/CT (18F-fluoro-2-deoxyglucose positron emission tomography/computerized tomography) imaging


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Abstract  Gastrointestinal nodular lymphoid hyperplasia is a rare lymphoproliferative state. In children, it is associated with familial immunodeficiency disease but most cases have no obvious etiology. In adults, nodular lymphoid hyperplasia is associated with immunocompromised status, including chemotherapy, acquired immunodeficiency viral infection, organ transplantation, and multiple polypoid lesions are noted in endoscopic findings and sometimes may be confused with family polypoid syndrome. We present a child with histological proof of focal intestinal nodular lymphoid hyperplasia that had a complete image study including negative results of 18F-fluoro-2-deoxyglucose positron emission tomography/computerized tomography analysis.

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Introduction

Nodular lymphoid hyperplasia (NLH) is a rare lymphoproliferative state that is not pathognomonic of a specific disease [1]. Its diagnosis is based on pathological findings of hyperplastic lymphoid follicles, mitotically active germinal centers with well-defined lymphocytic mantles, and lymphoid follicles localized at mucosa and/or submucosa. Its cause remains unknown but there is a hypothesis that it originates from proliferative plasma cell precursors which compensate for functionally inadequate intestinal lymphoid tissue due to a maturational defect in the development of B lymphocytes [2]. Because NLH is frequently associated with either several benign or malignant diseases in adults [3], it is important to elucidate between benign NLH and malignant lymphoma.

Case report

A 15-year-old boy consulted the emergency room of the Kaohsiung Medical University Hospital due to recurrent abdominal pain around the umbilical area for 2 weeks. The pain was characterized as dull and lasted for hours. There was no specific aggravating factor. The symptoms usually subsided after defecation or assuming a knee-to-chest position. The patient had an unremarkable past and family history. He was fully immunized.

At the emergency room, the patient’s body temperature was 36.5°C, pulse rate 93 beats/minute, respiratory rate 14/minute, and blood pressure 107/77 mmHg. Abdominal physical examination showed tenderness around the periumbilical area without rebound pain or muscle guarding. Complete blood count showed no leukocytosis (white blood cell count 6.98 × 10^9/L, 4.40 × 11.30 × 10^9/L) or anemia (hemoglobin 14.3 g/L, 14~17.5 g/L, and hematocrit 0.42, 0.42~0.50). Blood biochemistry was also unremarkable (asparate aminotransferase 23 U/L, 10~42 U/L; alanine aminotransferase 13 U/L, 10~40 U/L; blood ureas nitrogen 3.46 mmol/L, 2.85~7.14 mmol/L and creatinine 53.04 μmol/L, 53.04~114.92 μmol/L). Plain abdominal X-rays showed moderate gathering of bowel gas at the central lower abdomen, whereas abdominal computed tomography (CT) imaging disclosed enlarged lymph nodes in the right lower quadrant of the mesenteric space (Fig. 1).

Subsequent esophagastroduodenal endoscopy examination was unremarkable. Colonoscopy revealed numerous small nodular masses through the terminal ileum (Fig. 2). To further evaluate the extent of these lesions, follow-through series barium study of the small intestine was conducted, which showed nodular wall thickening of the terminal ileum, ileocecal valve, and cecum (Fig. 3).

Serial laboratory studies showed mildly elevated plasma levels of lactate dehydrogenase (LDH) 199 IU/L (normal range, 91~180 IU/L) and erythrocyte sedimentation rate (ESR) 15 mm/hour (normal range, 1~10 mm/hour). There was no fecal parasite found. Immunoglobulin (Ig) G level was 1210 mg/dL (normal range, 917.2~1891.2 mg/dL), IgA 115 mg/dL (normal range, 183.9~322.3 mg/dL), and IgM 138 mg/dL (normal range, 102.6~125.5 mg/dL). Plasma complement C3 and C4 levels were within normal limits at

Figure 1. Computed tomography of the abdomen with enhancement showing enlarged lymph nodes (size, 0.5~1.5 cm) in the right lower quadrant of the mesenteric space (as shown by the arrow).

106 mg/dL and 22.4 mg/dL, respectively. Antinuclear antibody (ANA) was negative.

Pathological findings of the biopsy specimen from the nodular mass in the terminal ileum via colonoscopy showed hyperplasia polyps with chronic inflammation over the terminal ileum.

To evaluate the nature of enlarged mesenteric lymph nodes found on the abdominal CT scan, 18F-fluoro-2-deoxyglucose positron emission tomography (PET) was performed (Fig. 4).

Repeated attacks of abdominal pain were noted and the patient was admitted to the pediatric ward 2 months later. A second examination session revealed similar findings as the previous colonoscopic examination in the terminal ileum. A laparoscopic intra-abdominal lymph node biopsy was performed (Figs. 5~7).

Figure 2. Colonoscopy showing multiple small nodular masses without ulceration or mucosal change at the terminal ileum.
Discussion

NLH is recognized in the pediatric population with more prevalence than the adult population with concomitant common variable immunodeficiency. The most common sites involved are the small bowel or colon in primary immunodeficiency syndrome, or the terminal ileum or colon in children without immunodeficiency [1]. Gastric involvement is rare. NLH is often an incidental finding, especially by endoscopic and histopathological confirmation without specific symptoms. Its diagnosis is based on characteristic pathological findings, with lymphoid infiltrates confined to the lamina propria and superficial submucosa. In differential diagnosis, lymphoid hyperplasia of the gastrointestinal tract can be distinguished from malignant lymphoma by the polymorphic nature of the infiltrates, absence of significant cytologic atypia, and presence of reactive follicles within the lesion [3].

Some patients may suffer from diffuse abdominal pain, intussusception, or gastrointestinal tract hemorrhage [4]. Rubio-Tapia et al. reported leading symptoms of duodenal NLH in 18 adults are diarrhea, involuntary weight loss, and abdominal pain [5]. In children, the clinical course of NLH is

![Figure 3. Small intestine series showing nodular wall thickening involving the terminal ileum, ileocecal valve, and cecum.](image3)

![Figure 4. PET showing no obvious FDG avid lesion in the gastrointestinal tract.](image4)

![Figure 5. Laparoscopic examination showing several enlarged lymph nodes around the terminal ileum and cecum.](image5)

![Figure 6. Multiple aggregations of lymphoid cells with germinal center formation.](image6)
usually benign with spontaneous gradual regression. By contrast, adult patients are often associated with immune deficiencies (e.g., common variable immunodeficiency, selective IgA deficiency) and giardiasis [6], and are predisposed to developing primary lymphoma of the gastrointestinal tract [7]. This case report was completely assessed with PET imaging and laparoscopic lymphectomy to exclude any malignant potential of enlarged lymph nodes located both in the intestinal mucosa and mesentery. 18F-Fluoro-2-deoxyglucose positron emission tomography (FDG-PET) is based on increased glycolysis of cancer cells. The agent is the radioactive glucose analog FDG, which is metabolically trapped within the cell after phosphorylation [8]. The degrees of uptake by PET imaging between benign and malignant lymphoma are variable. Metsers et al. reported on 33 patients with mucosa-associated lymphoid tissue lymphoma, and only 25% of patients had either suspected or proven malignancy demonstrating increased uptake. The lesions without FDG avid can be mistaken as benign lesions [9]. Some lymphomas, including Hodgkin’s lymphoma, diffuse large B cell lymphoma, and follicular lymphoma are routinely FDG avid [10]. In general, aggravating lymphoma usually shows high uptake; however, the indolent may be less FDG avid in PET imaging.

Lymphoma can be mimicked clinically by a broad range of disease entities and conditions, from infectious, inflammatory, and autoimmune conditions and drug reactions to benign lymphoproliferative disorders. In a systematic review of PET/CT studies performed in oncological patients during a 6-month period, there was benign non-physiological uptake of 18F-FDG in more than 25% of patients. In half of these, 18F-FDG uptake was moderate or marked in intensity, similar to that of malignant sites. A total of 73% of benign lesions were inflammatory in nature, with post-traumatic bone and soft-tissue abnormalities (including iatrogenic injury), whereas benign tumors accounted for the rest [10]. There is also a report on nodular lymphoid lesions mimicking low-grade malignant lymphoma in the liver [11]. Fusion imaging with PET/CT has been shown to improve not only the sensitivity of PET interpretation but also its specificity [12]. The gold standard is tissue biopsy to confirm the diagnosis. In the current concept, PET/CT is superior in following up the lesion instead of differential diagnosis of the malignant lesion. It is necessary to further investigate if PET or PET/CT can replace biopsy to differentiate between benign lymphoid hyperplasia and malignant lymphoma.

References