

Lymphoid Nodular Hyperplasia Associated with Ulcerative Colitis: Case Study and Literature Review

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Abstract

Lymphoid nodular hyperplasia is a pathology of the gastrointestinal tract that rarely occurs among adults. It is characterized by growth of submucosal lymphoid tissue and mucosal response to different types of noxious stimuli. It has been described in association with other diseases such as HIV/AIDS, giardiasis, *Helicobacter pylori* infections, celiac disease, and very rarely with inflammatory bowel disease. At present, there is no specific clinical presentation or treatment.

Keywords

Ulcerative Colitis, lymphoid nodular hyperplasia, gastrointestinal endoscopy.

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INTRODUCTION

Nodular lymphoid hyperplasia (NLH) is a rare lymphoproliferative condition that is not pathognomonic of any disease. It has most often been described in children under 10 years of age and in immunosuppressed and immunocompetent subjects with immune system disorders. (1) It is macroscopically characterized by multiple nodules that are two to ten millimeters in diameter, that are located in the mucosa and/or submucosa of the stomach, small intestine, colon and/or rectum, and that resemble polypoid lesions. Microscopically marked lymphoid hyperplasia can be seen with mitotically active germinal centers and well-defined mantles in the lamina propria and/or in the superficial part of the submucosa of these bodies. (2) Its incidence in adults is unknown, but it is considered to be rare. (1) This may be because of endoscopic underreporting or because it really is a rare condition. (3) Some patients have associated diseases such as giardiasis. (4) In a few cases, NLH has been associated with inflammatory bowel disease (IBD). (5, 6)

This article presents the case of a male patient with ulcerative colitis who was diagnosed endoscopically with NLH.

CASE DESCRIPTION

The patient was a 33 year old man who had suffered from bloody diarrhea for one month. Associated symptoms included rectal tenesmus, pushing, and weight loss. At the time of the physical examination the patient was generally in good condition. Palpation of the abdomen produced no pain, and the abdomen was soft and without masses or organomegaly. Feces and blood tests were normal, and the patient tested negative on a urease test. An esophago-gastroduodenoscopy revealed erythematous gastritis in the antrum and corpus. The diagnostic impression was that he suffered from bleeding secondary to either hemorrhoids or colorectal neoplasia. A total colonoscopy showed ulcerated proctitis with lesions compatible with ulcerative colitis located 15 cm from the dentate line and multiple benign-appearing polypoid lesions distributed throughout the

mucosa of the distal ileum (Figure 1). Pathological study of biopsy samples taken from the colon and distal ileum revealed fragments of colonic mucosa some of which were coated with columnar epithelium with a conserved pattern of tubular crypts surrounded by lamina propria with moderate chronic inflammatory infiltrate mediated by lymphocytes and plasma cells. Other fragments had irregular crypts without mucin, cells with enlarged nuclei and large amounts of mitosis surrounded with abundant neutrophils and formation of cryptic microabscesses.. Multiple secondary lymphoid follicles with well-defined mantles and active germinal centers were observed in the lamina propria of the distal ileum (Figure 2). The final diagnosis was nodular lymphoid involving Peyer's patches and associated with findings of inflammatory bowel disease suggestive of ulcerative colitis.



Figure 1. Endoscopic appearance of distal ileal mucosa with multiple nodular, polypoid lesions, 2 to 10 mm in diameter

DISCUSSION

NLH presents in two forms, diffuse and focal. The focal form most often compromises the terminal ileum, but it can also be found in the stomach, colon and rectum. (2) The most common site is in the small intestine. Although

its pathogenesis is not well understood, it has been proposed that in immunocompromised persons it may represent a countervailing mechanism to poor immune response in the digestive tract, (7) while in immunocompetent patients it could be secondary to overstimulation of the digestive tract's lymphoid tissue by stimuli that are harmful to the mucosa. One example is the case of IBD, for which it has been proposed that NLH develops as a result of upregulation of the immune system associated with immune disorders. (7) Some authors consider NLH to be a transitional stage and a risk factor for the occurrence of intestinal and extra intestinal lymphomas, although the latter are rare. (8-10) Associations between NLH and non-exophytic colonic neoplasms, adenomas and adenocarcinomas have also been suggested. (10)

It has been associated with several diseases including common variable immunodeficiency, selective IgA deficiency, HIV/AIDS, *Helicobacter pylori* infections, and giardiasis. (11) In children it has also been described in relation to food allergies. (2, 7) NLH is usually asymptomatic or has gastrointestinal symptoms that do not follow any specific pattern and range from mild abdominal pain to complete bowel obstruction and to heavy bleeding. (12) One cohort study of 283 children described diarrhea as the most frequent symptom, followed by weight loss and abdominal pain. (1)

NLH can be detected by endoscopy, barium enema studies and others such as MRIs. (2, 14) Classic endoscopic findings include nodular lesions with erythematous halos and/or reddish macules that are generally less than 5 mm in diameter. However, the similarity of NLH's macroscopic lesions to those of other entities such as polyposis syndromes make pathological studies of biopsy samples from the lesions necessary for diagnosis. In cases that compromise the small bowel, barium enemas and video capsule endoscopy (VCE) are extremely useful for excluding compli-

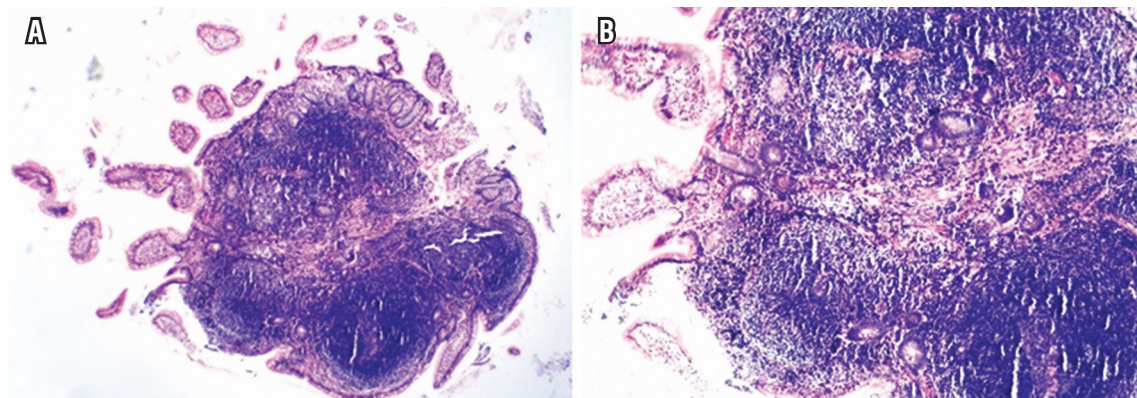


Figure 2. Fragment of the ileum with hyperplastic lymphoid follicles with active germinal centers and well-defined mantles located in the mucosa and superficial submucosa (HE, 2a: 40X, 2b: 100X)

cations and determining the extent of the disease. (13) Nevertheless, suspicion of NLH does not formally indicate diagnosis or follow up with VCE. We should add that the NLH can be indistinguishable from Crohn's disease in magnetic resonance imaging. (14)

A definitive diagnosis is established by a histopathological finding of hyperplastic lymphoid follicles with mitotically active germinal centers and well defined lymphocyte mantles immersed in the mucosa and submucosa. (2) The polymorphic nature of the infiltrate and absence of atypical cytology combined with the presence of reactive lymphoid follicles differentiate nodular lymphoid hyperplasia from lymphoma. In some cases the using immune system markers and molecular studies are required in order to make a definitive diagnosis. (15)

Treatment is often directed at an associated condition. The eradication of giardiasis is usually accompanied by resolution of symptoms, but the majority of cases do not report on whether or not there are recurrences of lesions. (16) Some authors suggest regular monitoring of patients with endoscopic video capsules and biopsies of any rapidly growing lesions to rule lymphomatous transformation (17).

CONCLUSIONS

NLH is a rare condition in adults that has various clinical manifestations. Its etiology has been linked to immune system disorders. Although there are few reported cases associated with IBD, this could represent over-regulation by response mechanisms of lymphoid tissue associated with the digestive tract. Because of its endoscopic appearance, differential diagnosis requires histopathology.

REFERENCES

1. Rubio-Tapia A, Hernández-Calleros J, Trinidad-Hernández S, Uscanga L. Clinical characteristics of a group of adults with nodular lymphoid hyperplasia: a single center experience. *World journal of gastroenterology:WJG*. 2006;12(12):1945-8.
2. Albuquerque A. Nodular lymphoid hyperplasia in the gastrointestinal tract in adult patients: A review. *World J Gastrointest Endosc*. 2014;6(11):534-40.
3. Colarian J, Calzada R, Jaszewski R. Nodular lymphoid hyperplasia of the colon in adults: is it common? *Gastrointestinal endoscopy*. 1990;36(4):421-2.
4. Ward EM, Wolfsen HC. Review article: the non-inherited gastrointestinal polyposis syndromes. *Alimentary pharmacology & therapeutics*. 2002;16(3):333-42.
5. Kokkonen J, Karttunen TJ. Lymphonodular hyperplasia on the mucosa of the lower gastrointestinal tract in children: an indication of enhanced immune response? *Journal of pediatric gastroenterology and nutrition*. 2002;34(1):42-6.
6. Iacono G, Ravelli A, Di Prima L, Scalici C, Bolognini S, Chiappa S, et al. Colonic lymphoid nodular hyperplasia in children: relationship to food hypersensitivity. *Clinical gastroenterology and hepatology: the official clinical practice journal of the American Gastroenterological Association*. 2007;5(3):361-6.
7. Lin C SH, Kuo C et al. Nodular lymphoid hiperplasia in endoscopic and FDG-PET/CT. *Kaohsiung J MED SCI*. 2013;29(7):396-9.
8. Monsanto P, Lérias C, Almeida N, Lopes S, Cabral JE, Figueiredo P, et al. Intestinal nodular lymphoid hyperplasia and extraintestinal lymphoma-a rare association. *Acta gastroenterológica, Bélgica*. 2012;75(2):260-2.
9. Chiamonte C GS. Nodular lymphoid hyperplasia of the small bowel complicated by jejunal lymphoma in a patient with common variable immune deficiency syndrome. *Am J roentgenol*. 1994;163(5):1118-9.
10. CA R. Nonprotruding colorectal neoplasms: epidemiologic viewpoint. *World J Surg*. 2000;24(9):1098-103.
11. Khuroo MS, Khuroo NS, Khuroo MS. Diffuse duodenal nodular lymphoid hyperplasia: a large cohort of patients etiologically related to *Helicobacter pylori* infection. *BMC Gastroenterology*. 2011;11:36.
12. Garg V, Lipka S, Rizvon K, Singh J, Rashid S, Mustacchia P. Diffuse nodular lymphoid hyperplasia of intestine in selective IgG 2 subclass deficiency, autoimmune thyroiditis, and autoimmune hemolytic anemia: case report and literature review. *Journal of gastrointestinal and liver diseases. JGLD*. 2012;21(4):431-4.
13. Said-Criado I, Gil-Aguado A. Nodular lymphoid hyperplasia in common variable immunodeficiency. *The Lancet*. 2014;383(9911):e2.
14. Plumb AA, Pendse DA, Mc Cartney S, Punwani S, Halligan S, Taylor SA. Lymphoid nodular hyperplasia of the terminal ileum can mimic active Crohn disease on MR enterography. *AJR American journal of roentgenology*. 2014;203(4):W400-7.
15. Tomita S, Kojima M, Imura J, Ueda Y, Koitabashi A, Suzuki Y, et al. Diffuse nodular lymphoid hyperplasia of the large bowel without hypogammaglobulinemia or malabsorption syndrome: a case report and literature review. *Int J surg pathol*. 2002;10(4):297-302.
16. Luzzi G, Zullo A, Iebba F, Rinaldi V, Sanchez Mete L, Muscaritoli M, et al. Duodenal pathology and clinical-immunological implications in common variable immunodeficiency patients. *The american journal of gastroenterology*. 2003;98(1):118-21.
17. Postgate A, Despott E, Talbot I, Phillips R, Aylwin A, Fraser C. An unusual cause of diarrhea: diffuse intestinal nodular lymphoid hyperplasia in association with selective immunoglobulin A deficiency (with video). *Gastrointestinal endoscopy*. 2009;70(1):168-9.