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Case Report

Intestinal Lymphoid Hyperplasia and Chronic Giardiasis Secondary to Immune Common Variable Immunodeficiency. Case Report

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Abstract

We present a male of 25 years old with clinical history of 9 years of chronic diarrhea who was managed with multiple treatments for giardia and antibiotics with outcome of the diarrhea but reappearance of it in the meantime. We study his case with laboratory tests, image and endoscopic procedures where the diagnosis was of a common variable immunodeficiency with chronic giardiasis, nodular lymphoid hyperplasia of the entire small intestine surface observed by endoscopy capsule and associated with a suspicious of bacterial overgrowth, because of the low serum B12 vitamin and his response to rifaximin initial treatment. The patient had also pylori helicobacter, lymphocytic microscopic colitis and mesenteric lymphopathies.

Keywords: *Lymphoid Hyperplasia; Giardiasis; Common Variable Immunodeficiency*

Introduction

The common variable immunodeficiency (CIVD) is characterized by an alteration in the differentiation of B cells that produce defects in the production of immunoglobulins. It is defined by a marked reduction of immunoglobulin G in combination with low levels of immunoglobulin M and immunoglobulin A with a poor response to immunizations and in the absence of other immunodeficiency diseases [1].

CIVD is a rare disease that can occur in 1 in 25,000 individuals [2]. The presentation in adulthood is between 20 to 45 years, but can be diagnosed in 30% in patients under 20 years and even children [3]. Patients may have manifestations in the respiratory system in which infections are characteristic. It can be associated with autoimmune diseases such as hemolytic anemia, rheumatoid arthritis, pernicious anemia, autoimmune thyroiditis and vitiligo. It may also be related to allergies, lymphadenopathies, splenomegaly and non-Hodgkin lymphoma.

The CIVD can have a 20% of alterations in the gastrointestinal system such as nodular lymphoid hyperplasia, pernicious anemia, bacterial overgrowth, protein losing enteropathy, malabsorption, microscopic colitis, inflammatory bowel disease and infections caused by cytomegalovirus, norovirus, *Salmonella, Campylobacter, Cryptosporidium* and chronic giardiasis [4,5]. 10% of patients may have impaired liver profile such as alkaline phosphatase and may be accompanied by liver diseases such as hepatitis C, primary biliary cholangitis and nodular regenerative hyperplasia [6].

Five distinct phenotypes have been delineated for the CIVD that are one with no complications, autoimmunity related disease, polyclonal lymphocytic infiltration, enteropathy, and lymphoid malignancy [7].

We present an interesting case of CIVD with gastrointestinal affection.

Presentation of the Case

It is a 25-year-old male patient with no clinical history of respiratory or digestive infections in childhood. The clinical picture of the patient begins at 16 years of age characterized by chronic diarrhea in the number of 5 to 15 fluid stools per day, of episodic appearance and that gave way with the treatment of antibiotics or antiparasitics. In the last year he remains 3 months without diarrhea. The patient throughout his illness removed gluten from the diet without improvement of the symptoms and consumption of dairy products for some years. It was managed by multiple doctors who on several occasions identified giardiasis in stool tests and received multiple schemes, of which nitazoxanide and metronidazole stand out.

In the evaluation of the physical examination, it is a patient with a muscle mass index of 20, without skin alterations or lymphadenopathy, and the lower border of the spleen is palpated in the evaluation of the abdomen.

The diagnostic behavior was initially directed with basic studies of haemogram, renal function, coproparasite serial, nutritional status tests, HIV, TSH and celiac disease investigation. In the examinations the blood count was normal, it discarded acquired immunodeficiency syndrome, hepatitis C, hepatitis B and thyroid disorders. The tests for celiac disease were negative (anti-transglutaminase IgA, anti-endomysial IgA and IgA antigliadin). In the faecal study, calprotectin was studied, which was negative with a value of 40 and positive coproparasitic giardia antigen was detected.

For the nutritional evaluation, ferritin, folic acid with normal values, vitamin B12 low in 163 (reference range 180 to 900) and serum albumin levels normal in 5 g/dl, but the level of low globulins in 1.1 g/dl are requested for which a study of partial immunoglobulins is requested.

In the study of immunoglobulins the IgA, IgM and IgG values were very low IgG 103 (800 to 1700), IgM 9 (50 to 330), IgA 6 (85 to 450) and IgE 0.53 and was assessed by hematology and diagnosis of Common Variable Immunodeficiency.

Imaging studies are performed and in the ultrasound the enlarged spleen of size 14 cm is identified. In addition, computed tomography with contrast of the abdomen determines the presence of adenopathies throughout the mesentery of up to 1 cm in diameter and the spleen of 14 cm.

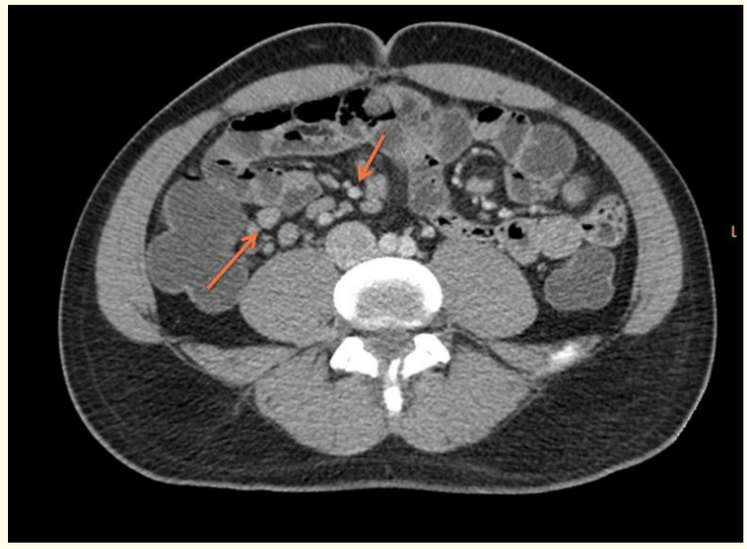

Figure 1: *Contrast tomographic study of the abdomen with the presence of adenopathies up to 1cm in the entire mesentery, mild splenomegaly. Computed tomography demonstrating multiple adenopathies in the mesentery. Image courtesy of the Image Service of the Metropolitan Hospital.*

The patient underwent upper gastrointestinal endoscopy in which the nodular duodenal mucosa was identified. Histopathological corroboration revealed severe duodenal lymphoid hyperplasia with giardiasis and chronic gastritis with *Helicobacter pylori*.

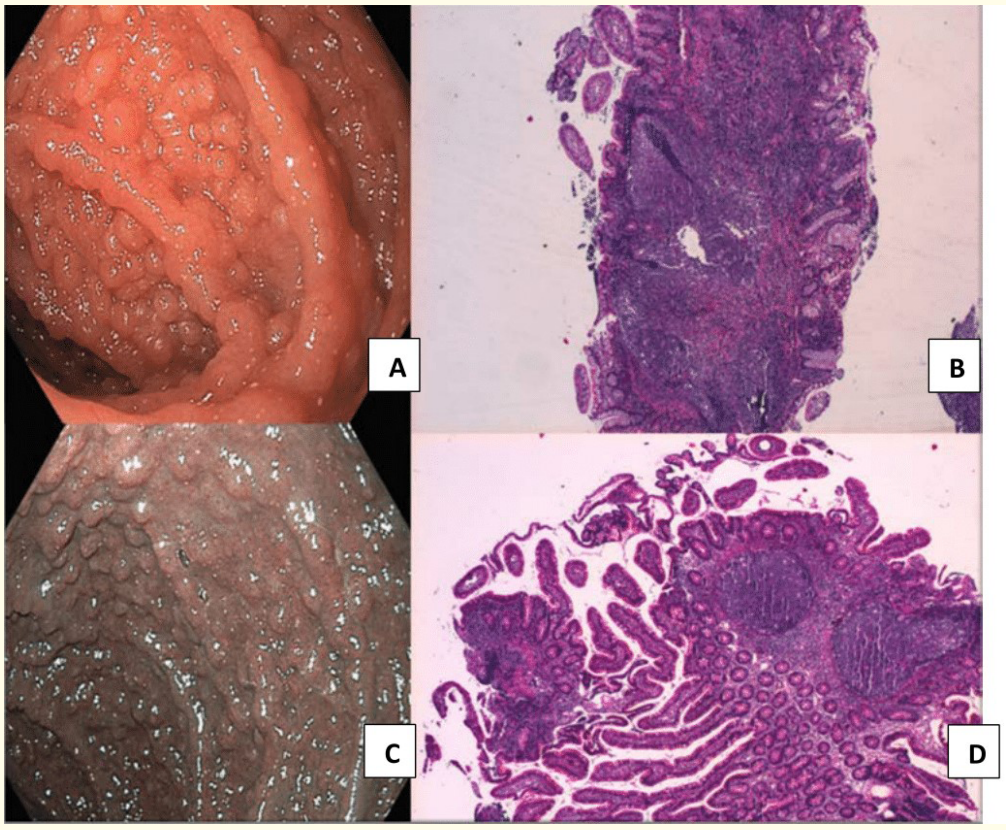

Figure 2: *Endoscopic image of the duodenum with white light and NBI with its histopathological correlation.*

A and C: Images of the nodular duodenum mucosa, B and D images of hematoxylin-eosin with presence of lymphoid hyperplasia, normal villi and presence of guard between the villi.

Images courtesy of Dr. Gustavo Ayala and the Pathology Service of the Metropolitan Hospital of Quito.

In the colonoscopy the colon mucosa was normal and in the terminal ileum again multiple nodules. In the histopathological result, the mucosa of the colon demonstrates the presence of microscopic lymphocytic colitis and lymphoid hyperplasia of the ileum.

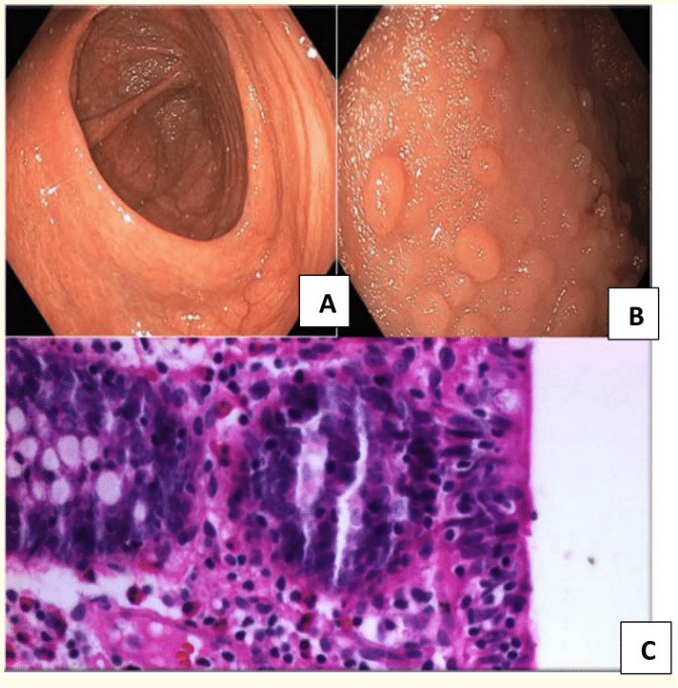

Figure 3: *Colonoscopic images of the cecum and terminal ileum and the histopathological correlation of the colon.*

A: Blind, B: Terminal ileum mucosa with the presence of multiple nodules and C: Hematoxylin-eosin staining of the colon in which intraepithelial lymphocytes are identified and is classified as lymphocytic colitis.

Images courtesy of Dr Gustavo Ayala and the Pathology Service of the Metropolitan Hospital.

Due to the findings and the association of variable immunodeficiency common to lymphoproliferative diseases, studies to rule out intestinal lymphoma with determination of uric acid, lactic dehydrogenase; which were normal, and B2microglobulin which was slightly elevated with a value of 2.84 mg/dl. This finding in the context of severe lymphoid hyperplasia was not a strong determinant for lymphoma, therefore an endoscopic capsule study is performed, which reveals the presence of nodulations in the entire mucosa of the small intestine with a size of 5 to 8 mm.

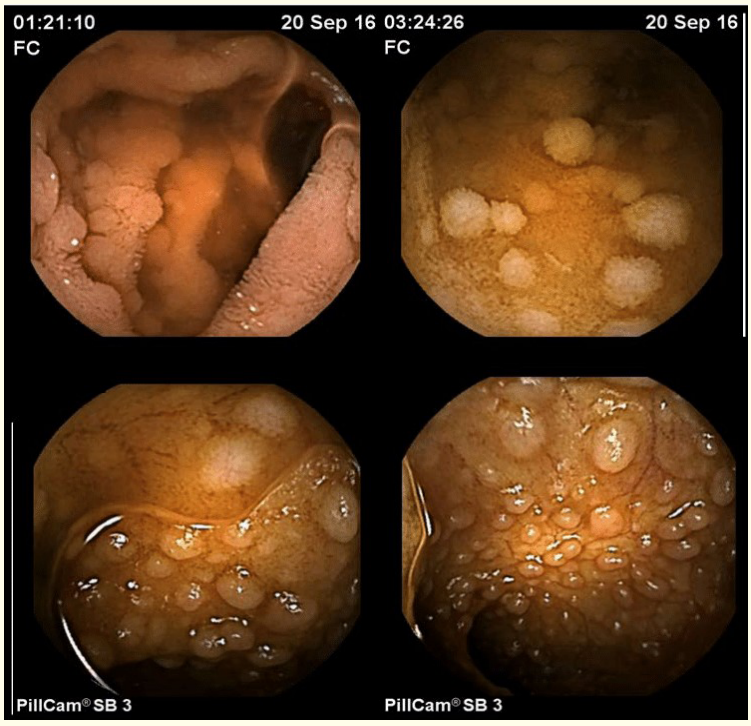

Figure 4: *Images of the small intestine by endoscopic capsule. Photos of several segments of small intestine with nodular mucosa in the endoscopic capsule. Images courtesy of Dr Gustavo Ayala.*

The final diagnosis of the patient was a Common Variable Immunodeficiency with a unique affection to the gastrointestinal system. The patient was treated with rifaximin for the first 5 days with a good response to treatment, after the histopathological report starts ornidazole, bismuth, parenteral vitamin B12 and intravenous immunoglobulin.

In addition, *Helicobacter pylori* treatment was given after the aforementioned treatment and revaluation of lymphadenopathies was scheduled in 6 months without any changings in the adenopathies. In the follow up of the patient we tried to eliminate the giardia with different antibiotics as albendazole, ornidazole, nitazoxanide, metronidazole and chloroquine with longer days of treatment but without success. The use of immunoglobulin was maintained for 8 months, but the patient stopped it without any changes in his evolution.

Discussion

This case of chronic diarrhea was cause for a genetic immunopathology that for an unknown reason its symptomatic presentation begins in the adolescence. In the common variable immunodeficiency numerous of immune abnormalities had been reported but the most common is the defective differentiation of the antibodies. Both humoral and cell-mediated lymphocytic responses are affected [8].

The chronic intestinal infection lead to the lymphoid hyperplasia of the gastrointestinal tract is characterized by nodules ranging from 2 to 10 mm that can be distributed in any organ of the gastrointestinal tract but that is more frequent in the small intestine. The most frequent sites are ileon and recto [9]. It is often seen in common variable immunodeficiency syndrome or in selective IgA deficiency associated with infections by giardia and even *Helicobacter pylori*. The lymphoid hyperplasia is a condition that is usually asymptomatic or can present with diarrhea, constipation, abdominal pain, bacterial overgrowth and occasionally with bleeding. The association of immunodeficiency, giardiasis and lymphoid hyperplasia is known as Herman's syndrome [10]. The relationship between celiac disease and lymphoid hyperplasia is rare (missing reference).

The treatment for lymphoid hyperplasia is directed to the etiology that is causing it, so that for CIVD as well as for lymphoid hyperplasia, guard determination is essential [11]. In the case of the patient, lymphoid hyperplasia of the small intestine may be due to giardiasis, but there are publications that describe that although the eradication of this infectious agent is achieved, no regression is achieved in the number or size of the nodules [12].

The treatment for CIVD is the immunoglobulin to reduce the cycle of recurrent infections and improve physical functioning. The use of immunoglobulin is limited in patients with enteropathy affectations in several studies [13]. In this case the suspension of the immunoglobulin did not changed the evolution of the patient. The patient improved his diarrhea with the rifaximin. At the moment he has a few episodes of diarrhea that are well controlled with the use of antibiotics as tetracycline. Also, in this case the resistance in the treatment of the giardia has been a problem.

The most important follow-up in this type of patients is in search of the transformation to lymphoma, so the study with endoscopic capsule is important [14]. Another diagnostic method that has an effective role is positron emission tomography (PET-FDG) since this study has the capacity to determine the malignancy or benignity of the lesions found and their stratification [15-18].

Conclusion

The patient had as final diagnoses common variable immunodeficiency with chronic resistance giardiasis, nodular lymphoid hyperplasia of the entire small intestine surface observed by endoscopy capsule and associated with a suspicious of bacterial overgrowth, because of the low serum B12 vitamin and his response to antibiotic initial treatment. The patient had also pylori helicobacter, lymphocytic microscopic colitis and mesenteric lymphopathies.

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