

CASE REPORT

Diffuse polypoid lesions of the digestive tract in severe hypogammaglobulinemia

C. JURCUȚ¹⁾, MARIANA JINGA¹⁾, RALUCA COSTACHE¹⁾,
FLORINA VASILESCU²⁾, ALINA STĂNESCU-POPP³⁾, I. COPACI¹⁾

¹⁾Department of Internal Medicine

²⁾Department of Pathology

"Dr. Carol Davila" Central University Emergency Military Hospital, Bucharest

³⁾Clinic of Pediatrics,

"Carol Davila" University of Medicine and Pharmacy, Bucharest

Abstract

We present a case report of diffuse polypoid lesions of the digestive tract in which multiple endoscopic techniques (upper endoscopy, colonoscopy, and capsule endoscopy) were performed in order to complete and refine the diagnosis in a patient with severe hypogammaglobulinemia with recurrent infections, bronchiectasies and diffuse nodular lymphoid hyperplasia of the digestive tract. In patients with hypogammaglobulinemia, the endoscopic evaluation of the digestive tract might be mandatory, even in asymptomatic patients. The complete assessment should include the upper endoscopy and colonoscopy with multiple biopsies and, if possible, capsule endoscopy.

Keywords: hypogammaglobulinemia, polypoid lesions, capsule endoscopy.

■ Introduction

Gastrointestinal involvement was previously reported in patients with immune deficiencies (i.e. hypogammaglobulinemia). However, in daily clinical practice, the diagnosis of these digestive lesions might be challenging and could benefit from both gastroenterology and pathology departments expertise.

Currently, endoscopic examination is considered the best method for the visualization of digestive tract lesions. Recently, the endoscopic armamentarium was completed by the capsule endoscopy, making possible the complete examination of the digestive tract.

We present a case report of diffuse polypoid lesions of the digestive tract in which multiple endoscopic techniques (upper endoscopy, colonoscopy and capsule endoscopy) were performed in order to complete and refine the diagnosis.

■ Patient, Methods and Results

A 20-year-old man was referred to our department for fever and cough. The diagnosis of acute pneumonia was made and an antibiotic treatment was started with complete remission of the symptoms after several days. Few months before, the standard thoracic radiography and computed tomography revealed the multiple polyadenopathies (mediastinal and hilar) and bilateral basal bronchiectasies. The biopsies performed by mediastinoscopy were negative for any infectious or neoplastic diseases and showed the reactive nature of this polyadenopathies. Moreover, the bronchoscopic examination was negative for any specific lesion. The diagnostic of tuberculosis was carefully excluded.

Taking into account the history of recurrent upper airways and pulmonary infections, we performed a complete evaluation of the patient in order to find a condition predisposing to these repeated infections. A severe hypogammaglobulinemia (0.17 g/dL) with complete absence of IgA and severely reduced levels of IgG and IgM was revealed. As the ultrasound examination of the abdomen revealed a moderate splenomegaly, we ordered an abdominal computed tomography, which revealed an unusual thickening of the digestive tract wall and perimesenteric mild polyadenopathies.

Consequently, we performed the endoscopy and colonoscopy, which revealed diffuse polypoid lesions from the stomach (Figure 1), duodenum (Figure 2) to terminal ileum (Figure 3) and large bowel (Figure 4). For a better evaluation of the extent of the lesions, we performed the capsule endoscopy examination that revealed multiple and diffuse polypoid lesions in the small bowel wall (Figure 5).

Multiple biopsies were done that showed lymphoid follicular hyperplasia (Figure 6), with lymphoid germinal centers. In order to have an accurate diagnosis, the immunohistochemistry stain was also performed (Figures 7 and 8).

Moreover, celiac disease, parasitic infections (including *Giardia lamblia*) and an acquired cause for this immunodeficiency were excluded. No specific somatic malformations were revealed at the clinical examination. It is important to note, that the patient did not report any history of chronic diarrhea or abdominal pain.

The final diagnostic was severe hypogammaglobu-

linemia with recurrent infections, bronchiectasies and diffuse nodular lymphoid hyperplasia of the digestive tract.

A treatment with intravenous immunoglobulin was planned and a careful future screening for lymphoma is mandatory.



Figure 1 – Gastric nodular lesions at upper endoscopy.



Figure 2 – Diffuse polypoid lesions visible in duodenum at upper endoscopy.



Figure 3 – Polypoid lesions in terminal ileum at colonoscopy.



Figure 4 – Small polypoid lesions at large bowel examination by colonoscopy.

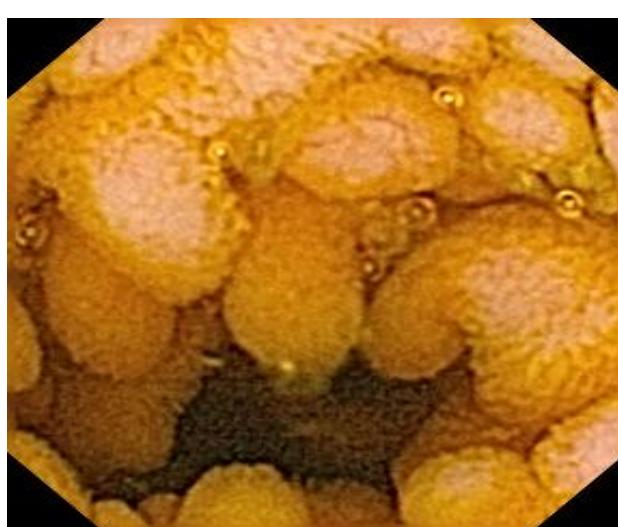


Figure 5 – Capsule endoscopy examination showing multiple polypoid lesions in the small bowel's wall.

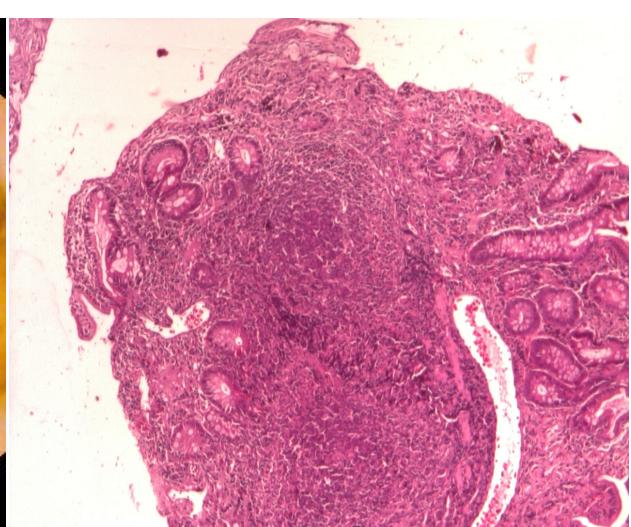


Figure 6 – Lymphoid follicular hyperplasia with germinal centers in the small bowel (HE stain, $\times 40$).

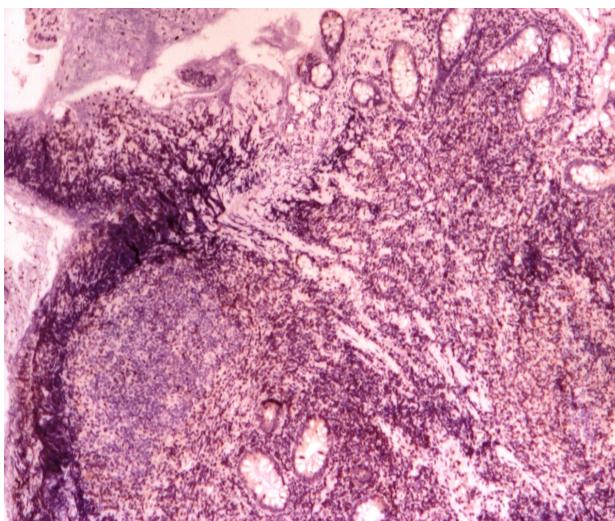


Figure 7 – Immunohistochemistry stain for *bcl-2* was negative into the germinal centers and positive in the interfollicular lymphoid infiltrate, excluding the follicular lymphoma and confirming the reactive lymphoid hyperplasia, $\times 40$.

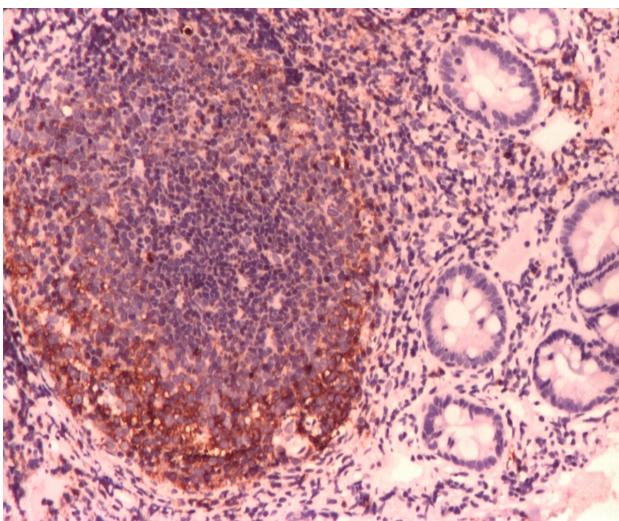


Figure 8 – Immunohistochemistry stain for L26 (CD20) was positive into the germinal centers, showing the presence of B-lymphocytes in germinal centers, $\times 100$.

Discussion

The digestive manifestations in patients with hypogammaglobulinemia were already reported several decades ago [1, 2]. Several studies tried to link these abnormalities with celiac disease [3], inflammatory bowel diseases [4] and *Giardia lamblia* infection [5]. Some authors designated the digestive tract abnormalities in these patients as “enteropathy associated with hypogammaglobulinemia” [6]. The nodular lymphoid hyperplasia of the small intestine was also described and a high risk for the development of intestinal lymphoma was suggested [7–9]. The case reports [10, 11] and the small series that evaluated the presence of digestive tract lesions in patients with immune deficiencies were based mainly on upper endoscopy, colonoscopy, radiological-based investigation, ¹¹¹Indium leukocyte scintigrams showing intestinal inflammation and biopsies techniques [6]. Until now, there is no standardized diagnostic approach of the digestive lesions in patients with primary immunodeficiencies. Moreover, it is still unclear which might be the correct evaluation workup in asymptomatic patients.

There are some reports concerning the utility of the capsule endoscopy for the diagnosis of the lymphoid hyperplasia in patients with hypogammaglobulinemia. Postgate A *et al.* reported a case of diffuse intestinal nodular hyperplasia in a patient with selective immunoglobulin A deficiency [12]. The capsule endoscopy might be one of the most important imaging techniques in patients with immune deficiencies, being able to characterize the extension of the disease.

Taking into account the risk for developing lymphoma, an endoscopic surveillance with repeated examinations and biopsies was proposed. The role of the pathology laboratories for the correct diagnostic is therefore essential. However, this screening for further lymphoma is not standardized and the utility of endoscopic capsule in this process needs further prospective studies.

It is also important to underline the need for correct diagnosis in patients with diffuse polypoid lesions of the digestive tract. In these patients, a screening for the immune deficiencies might be important along with histopathological examinations.

Finally, the optimal treatment of these patients with digestive lesions is not clearly established, especially in asymptomatic patients. Taking into account the history of infections, our patient will receive an intravenous immunoglobulin treatment according to current recommendations. A complete examination of the digestive tract is planned after one year of treatment. However, the evolution of the digestive lesions after immunoglobulin treatment need further studies in order to have valid conclusions, especially in asymptomatic patients.

Conclusions

In patients with hypogammaglobulinemia, the endoscopic evaluation of the digestive tract might be mandatory, even in asymptomatic patients. The complete assessment should include the upper endoscopy and colonoscopy and, if possible, capsule endoscopy.

References

- [1] Ammann AJ, Hong R, *Selective IgA deficiency: presentation of 30 cases and review of the literature*, Medicine (Baltimore), 1971, 50(3):223–236.
- [2] Hermans PE, Huizenga KA, Hoffman HN, Brown AL, Markowitz H, *Dysgammaglobulinemia associated with nodular lymphoid hyperplasia of small intestine*, Am J Med, 1966, 40(1):78–89.
- [3] Webster AD, Slavin G, Shiner M, Platts-Mills TAE, Asherson GL, *Celiac disease with severe hypogammaglobulinaemia*, Gut, 1981, 22(2):153–157.
- [4] Fillit H, Bernstein L, Davidson M, Brandt L, Bezhaher G, Cohen M, *Primary acquired hypogammaglobulinemia and regional enteritis*, Arch Intern Med, 1977, 137(9):1252–1254.
- [5] Ochs HD, Ament ME, Davis SD, *Giardiasis with malabsorption in X-linked agammaglobulinemia*, N Engl J Med, 1972, 287(7):341–342.
- [6] Teahan K, Webster AD, Price AB, Weston J, Bjarnason I, *Studies on the enteropathy associated with primary hypogammaglobulinaemia*, Gut, 1994, 35(9):1244–1249.

- [7] Bästlein C, Burlefinger R, Holzberg E, Voeth C, Garbrecht M, Ottenjann R, *Common variable immunodeficiency syndrome and nodular lymphoid hyperplasia in the small intestine*, Endoscopy, 1988, 20(5):272–275.
- [8] Castellano G, Moreno D, Galvao O, Ballestín C, Colina F, Mollejo M, Morillas JD, Solís Herruzo JA, *Malignant lymphoma of jejunum with common variable hypogamma-globulinemia and diffuse nodular hyperplasia of the small intestine. A case study and literature review*, J Clin Gastroenterol, 1992, 15(2):128–135.
- [9] Aguilar FP, Alfonso V, Rivas S, López Aldeguer J, Portilla J, Berenguer J, *Jejunal malignant lymphoma in a patient with adult-onset hypo-gamma-globulinemia and nodular lymphoid hyperplasia of the small bowel*, Am J Gastroenterol, 1987, 82(5):472–475.
- [10] Joo M, Shim SH, Chang SH, Kim H, Chi JG, Kim NH, *Nodular lymphoid hyperplasia and histologic changes mimicking celiac disease, collagenous sprue, and lymphocytic colitis in a patient with selective IgA deficiency*, Pathol Res Pract, 2009, 205(12):876–880.
- [11] Piaścik M, Rydzewska G, Pawlik M, Milewski J, Furmanek MI, Wrońska E, Polkowski M, Butruk E, *Diffuse nodular lymphoid hyperplasia of the gastrointestinal tract in patient with selective immunoglobulin A deficiency and sarcoid-like syndrome: case report*, Adv Med Sci, 2007, 52:296–300.
- [12] 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)*, Gastrointest Endosc, 2009, 70(1):168–169; discussion 169.

Corresponding author

Ciprian Jurcuț, MD, PhD student, Internal Medicine Department, "Dr. Carol Davila" Central University Emergency Military Hospital, 88 Mircea Vulcănescu Street, 010816 Bucharest, Romania; Phone +4021–319 30 51, Fax +4021–319 30 79, e-mail: cjurcut@gmail.com

Received: March 13th, 2010

Accepted: January 15th, 2011