

Intestinal lymphoma: a case report

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Abstract. – Primary intestinal lymphoma is rare representing about 0.5% of all colonic malignancies. It can be classified into two principal categories: follicular B cell lymphomas and intestinal T cell lymphomas. Other intestinal diseases are very important such as immunoproliferative small intestinal disease (IPSID), a prelymphomatous process, and MALT lymphomas, caused by infection of *Helicobacter pylori* (*H. Pylori*). We present a 79 years old male patient which presented with abdominal pain in the upper parts of abdomen of four months' duration, colic timpanists, tenderness, distention, weight loss. Sometimes the abdominal pain decreased expelling diarrheal dejections. Histological and immune-histochemical tests on bioptic piece helped to reach the diagnosis of lymphoma but only after histological investigation on operative piece was made the diagnosis of B-cell lymphoma. This case report shows that an accurate diagnosis, the evaluation of the extension and the presence of particular infections and/or co morbidities (*H. Pylori* positive, age, performance status) are fundamental to decide the therapeutic protocol.

Key Words:

Non-Hodgkin's lymphoma, Intestinal lymphoma, Chemotherapy.

Introduction

Primary small intestinal lymphoma is uncommon, comprising 0.2% to 0.65% of all colonic malignancies¹. The vast majority of these tumors are of B-cell origin but precedent studies have shown several cases of peripheral T-cell lymphomas of the intestine, often secondary to a celiac disease^{2,3}.

Intestinal T cell lymphomas are divided in enteropathy T cell lymphoma (EATCL), EATCL like lymphoma without enteropathy and non-EATCL

type of lymphomas⁴. EATL usually presents as multifocal, circumferential ulcers localized to the jejunum or proximal ileum^{5,6}. This type of lymphoma is generally associated with a history of celiac disease and reveals tumors cells that are CD3+, CD5-, CD7+, CD8-/+, CD4- and CD103+⁷.

Another particular form of non-Hodgkin lymphoma of the intestine, is adult T-cell leukemia/lymphoma (ATLL), a malignancy associated with retrovirus, human T-cell lymphotropic virus type 1 (HTLV-1)⁸⁻¹⁰. Although it has been demonstrated that ATLL attacks the gastrointestinal tract, colonic invasion has not been fully documented^{11,12}. Only Hokama et al showed a case of adult T-cell leukemia/lymphoma associated with HTLV1 presenting multiple lymphomatous polyposis¹³.

Case Report

A 79 years old male patient was admitted to our Hospital with abdominal pain in the upper parts of abdomen of four months' duration, colic timpanists, tenderness, distention, weight loss. Sometimes the abdominal pain decreased expelling diarrheal dejections. Two months before admission ultrasonography showed lithiasis of cholecyst not treated.

The local examination did not revealed any pathological signs and his body temperature was normal. His routine blood investigations showed a hypochromic anemia (5,400,000 GR, 10.8 g/d L Hb, HCT 34, 3% and MCV 63, 6 fl). The WBC, the platelet, blood chemistries and carcinoembryonic antigen were all within the normal limits. The patient was also subjected to serological blood tests looking for celiac disease, but anti-gliadin (AGA) and anti-endomysium (EMA) and anti-transglutaminase antibodies resulted negative.

Ultrasonography showed a moderate steatosis, absence of local lesions and lithiasis of gallbladder was confirmed.

Computed Tomography (CT) total body revealed a thickening involving the third distal part of esophagus and a bulky expansive mass in the proximal part of caecum. It has also been found a nodal mass near to ileo-colic artery with a diameter of 37 mm and liquid in the pouch of Douglas. To go into the diagnosis, the patients was subjected to a colonoscopy and biopsy that noted a modest diverticulosis and confirmed the presence of a growing villous adenomas taking up all circumference bleeding after biopsies.

The histological investigation showed a lymphoplasmocytoid and eosinophils infiltration CD20, CD10, bcl2, bcl6 positive CD3, CD5, ciclina D1 negative. After immunophenotyping and microbiological tests was made diagnosis of follicular B-cell lymphoma, *Helicobacter pylori* positive.

Right hemicolectomy was performed with ileo-transverse late-to-late anastomosis, lymphadenectomy and cholecystectomy. Successive histological investigation revealed a different tumor respect to bioptic result. In fact, it was found a ileal T-cell lymphoma, peripheral, small and medium-sized monomorphic cells (2 cm diameter), chronic idiopathic inflammatory disease, rich in epithelioid cells, and eosinophils with occasional foreign body giant cell type, predominantly in the ileum section of a rough surface, but extended to the ileum and colon cancer included in the surgical specimen. There were non-specific reactive lymphadenitis in sixteen ileocecal lymph nodes and a danger. Ileal and colonic resection margins were free and it was also found a fibrous obliteration of the appendix.

The immunophenotyping relived T-cell type CD3⁺ and CD20, CD79a, CD5, CD10, ciclina D1, CD15, CD30, bcl-2, bcl-6 negative. Pathologist confirmed the false positive of B cell lymphoma, probably obtained because of a biopsy in a inflammatory cellular population in a peripheral part of the tumor.

The patient was also subject to a therapeutic protocol to eradicate the *Helicobacter pylori* but he did not assume chemotherapy because of his age. He is today in good condition of life after five years of outset.

Discussion

Incidence of non Hodgkin lymphoma (NHL) increases with age and peaks in individual aged

80-90 years^{14,15}. In fact, an ageing population and occupational exposure have all been postulated to increasing incidence, that occurred in the elderly^{16,17}.

The most frequent primary intestinal lymphoma are follicular B cell lymphomas and intestinal T cell lymphomas.

Follicular lymphoma is a malignant group of B cells in the germinal centre as they approach the end of maturation at the centrocyte stage. It is the most common indolent lymphoma and, although many cases present late with and lymphonode involvement, patients with follicular lymphoma have a good outlook. Median overall survival is 9 years but most patients relapse several times and cure is very unlikely¹⁸.

Intestinal T cell lymphomas are divided in enteropathy T cell lymphoma (EATCL), EATCL like lymphoma without enteropathy and non-EATCL type of lymphomas⁴. Primary peripheral T-cell lymphomas of the intestine present several micromorphologic features and different topographic distribution that can be analyzed by an histopathological investigation of operative piece. Generally, in EATCL the lymphoma infiltration spreads within an atrophic mucosa. While in EATCL-LLWE the intramucosal lymphoma is limited to the tumors margins, in non-EATCL the lymphoma infiltration is strictly confined to the ulcerated lesion⁴. EATCL has been classified separately because of its primary T-cell morphology, close association with malnutrition and celiac disease, likelihood of being at an advanced stage at presentation and poor prognosis^{4,19-21}.

Another important intestinal disease, is immunoproliferative small intestinal disease (IPSID), a prelymphomatous process that occurs especially in young adults of low socioeconomic class²². The insurgence of this precancerous disease is due to a chronic stimulation from bacterial or parasitic antigenic particles that could cause an overproliferation of the intestinal lymphoid system, eventually developing into a monoclonal proliferation²³. It is now normally accepted that IPSID is a precursor of several types of high grade intestinal lymphomas such as histiocytic lymphoma, undifferentiated lymphoma and B cell immunoblastic sarcoma²³⁻²⁵. The particular etiology of this disease leads to approach it like an infection pain that can be cured by antibiotics (tetracycline)²⁶ while others think that is a cancer status that have to treat by chemotherapy.

The role of bacterial infection is also shown in MALT lymphomas. Infection by *Helicobacter*

pylori provides the antigenic drive for development of low grade MALT-type lymphoma and for this reason various studies investigated the possibility to use antibiotic therapy to eradicate *Helicobacter pylori* like first line treatment for patients with Malt-type lymphoma²⁷. Although the eradication of *Helicobacter pylori* has been demonstrated useful in the treatment of gastric lymphomas²⁸, we can remember a case report exposed by Raderer et al²⁹ that noted a total regression of a colonic low grade B cell lymphoma after successful eradication of *Helicobacter pylori* four months after initiation of antibiotic treatment. There was a case report of IPSID regression following eradication of *Helicobacter pylori* too³⁰.

Often, the clinical examination is aspecific and, for this reason is needless. The our patient presented abdominal pain in the upper parts of abdomen of four months' duration, colic timpanists, tenderness, distention, weight loss. All these symptoms do not indicate a non-Hodgkin's lymphoma but only a possible intestinal pathology. Therefore, CT scan and ultrasonography are really useful to obtain the diagnosis and to define the extension of intestinal non-Hodgkin lymphoma.

Endoscopic biopsy, that must be deep to include the sub mucosal tissue, is essential to establish a histological diagnosis. Studies of immunophenotype and molecular genetics makes possible to known the histotype. In fact, the immunophenotype varies between types of NHL just as it differs between B and T cells at different stages of differentiation.

In particular the case report presented small and medium T-cell type CD3⁺ and CD20, CD79a, CD5, CD10, ciclina D1, CD15, CD30, bcl-2, bcl-6 negative.

The most common type of peripheral T-cell lymphomas of the intestine usually presents tumor cells that are CD3⁺, CD5⁻, CD7⁺, CD8^{-/+}, CD4⁻ and CD130⁺. In tumors with a high proportion of small and medium-sized cells, the cells are CD3⁺, CD8⁺ and CD30⁻ (7). However, Chott et al (4) in immunophenotypes of 8 different peripheral T-Cell lymphomas of the intestine, found cells CD3⁺ in any cases and cells CD5⁻ in 7 on 8 patients.

Surgical resection, important for a correct diagnosis, is conformed for early stage intestinal lymphoma that has not infiltrated beyond the sub mucosa³¹. In case of regional lymph node invasion, the addition of abdominal radiation follow-

ing surgery contributes to improve the duration and the quality of life³². Although surgery is a mandatory step in the therapeutic treatment of lymphoma, it is rarely sufficient alone. In advanced stage patients is necessary a multidrug chemotherapy. Polychemotherapy includes CHOP (cyclophosphamide, doxorubicin, vincristin and prednisolone) or CHOP-like combination chemotherapy or MACOP-B-like regimens^{33,34}. In the treatment of B cell non-Hodgkin's lymphoma could be useful, a chimeric monoclonal anti-CD20, the rituximab. In 1997, it was the first monoclonal antibody to be approved by the US Food and Drug Administration (FDA) and today the combination of rituximab and chemotherapy is the standard treatment of follicular lymphoma and diffuse large B-cell lymphoma (35-38). It acts inducing programmed cell death by CD20 signal; for this reason is dependent on CD20 expression on B cells³⁹.

In this case report we did a surgical resection and an antibiotic therapy to eradicate *Helicobacter pylori*. The patient did not assume chemotherapy because of his age, but the surgery and the eradication of the *H. pylori* resulted sufficient. In fact, he is today in good condition after 5 years from diagnosis.

In conclusion an accurate diagnosis, the evaluation of the extension and the presence of particular infections and/or co morbidities (*H. Pylori* positive, age, performance status) should be considered to decide the therapeutic protocol.

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