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Case Report

Small Bowel Lymphoma Associated with Celiac Disease: 2 Cases Report

Jihane Sabar[1, 2*], Moustapha Traore[1, 2], Jalil Medarheri[1, 2]

[1]Digestive Surgical Department B, Ibn Sina University Hospital, Rabat, Morocco
[2]Faculty of Medicine and Pharmacy, Mohammed V University in Rabat, Morocco

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***Corresponding Author:** Jihane Sabar
Digestive Surgical Department B, Ibn Sina University Hospital, Rabat, Morocco

Abstract

Small bowel lymphoma associated with celiac disease is rare. The annual incidence varies from 0.5 to 1 per million inhabitants. We report two cases of small bowel lymphoma associated with celiac disease. The first case is a 50-year-old patient, treated for celiac disease since 2010 and whose tumor was revealed on abdominal CT as part of the etiological assessment of abdominal pain with an anemic syndrome. In the other case, it was a 52-year-old patient presenting the same symptomatology, in whom endoscopy revealed total villous atrophy, indicating the diagnosis of celiac disease, and CT showed a small bowel tumor. Both patients underwent segmental resection with single-stage anastomosis. The anatomopathological study concluded to a small lymphoma. Adjuvant chemotherapy was administered in both cases, and their evolution was favorable.

Keywords: Celiac disease, lymphoma, segmental resection, chemotherapy.

INTRODUCTION

Celiac disease (CD) is a chronic autoimmune inflammatory enteropathy caused by a gluten peptide, gliadin, in genetically predisposed subjects [1].

Celiac disease, treated or not by a gluten-free diet, can progress to malignant lesions. These are most often malignant non-Hodgkin lymphoma (NHL), of type T. They represent 10 to 25% of primary intestinal lymphomas and mainly affect patients in their sixth decade, with a slight male predominance [2].

We report two cases of malignant lymphoma occurring in celiac disease. These cases were collected in the surgery department B of the Ibn Sina university hospital in Rabat between 2010 and 2022.

FIRST CASE

Mrs. MF, 50 years old, is originally from Oujda and living in Salé with a history of iron deficiency anemia since childhood. She had been followed since 2010 for celiac disease on a strict gluten-free diet. She came to the service in October 2011 for an anemic syndrome associated with abdominal pain.

The history of the disease went back to one month by the installation of diffuse abdominal pain without particular irradiation, intense, accentuated by food intake, associated with an anemic syndrome made up of tachycardia, dizziness, dyspnea on effort (stage three of NYHA) without signs of exteriorized digestive or extra digestive hemorrhages. The examination on admission found an asthenic patient, discolored conjunctivae, with a body mass index of 15.2 kg/m² and blood pressure of 100/70 mm Hg. The clinical examination found abdominal tenderness sitting in the peri -umbilical and left flank, no palpable mass or hepatosplenomegaly. Furthermore, there were no peripheral adenopathies. The rest of the somatic examination was unremarkable.

Biologically, the blood count showed microcytic hypochromic anemia with hemoglobin at 8 g/dl. C-reactive protein was slightly elevated at 26.40 mg/l, liver function tests were normal. The renal assessment and blood ionogram were normal. Abdominal ultrasound was unremarkable.

CT-enteroclysis showed regular circumferential intestinal thickening (8 millimeters), extending over 12 cm and associated with mesenteric lymphadenopathy not exceeding seven millimeters,

possibly suggesting lymphomatous or tuberculous transformation.

Esogastroduodenal fibroscopy showed erythematous antral and fundic gastritis with rarefaction and flattening of the duodenal mucosa. Colonoscopy showed erythematous rectosigmoid and colonic mucosa.

The patient was operated, the approach was a median above umbilical laparotomy. Exploration found two stenosing tumors 70 and 80 cm from the duodenojejunal angle with dilatation of the hail upstream. The surgical procedure consisted of segmental hail resection, with immediate restoration of digestive continuity by end-to-end hail and hail anastomosis.

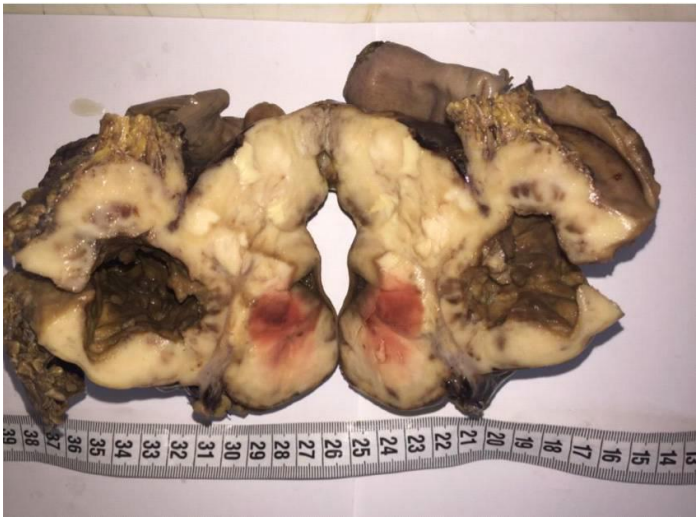

Figure 1: Resected tumor

The postoperative course was simple. The anatomopathological study of the surgical specimen showed a histological appearance and the immunohistochemical profile of a large T-cell lymphoma associated with enteropathies. The patient was referred to oncology for adjuvant chemotherapy, with good evolution.

SECOND CASE

Mrs. MH, aged 52 and treated for microcytic hypochromic anemia, presented to the service in September 2018 for the treatment of an ileal tumor discovered radiologically as part of the etiological assessment of her anemia.

The history of the disease went back one month, with abdominal pain localized at the level of the periumbilical region, of moderate intensity, paroxysmal, without particular irradiation, accompanied by melena and abdominal meteorism. This pain was associated with an anemic syndrome consisting of asthenia and dizziness, which motivated the patient to consult. The examination on admission found a patient asthenic, pale and afebrile.

Abdominal examination found tenderness on palpation of the hypogastric region, no palpable mass or hepato-splenomegaly.

Biologically, the blood count showed hypochromic microcytic anemia with hemoglobin at 9 g/dl and ferritin at 2 ng/ml and C-reactive protein was high at 58.90 mg/l.

Abdominal CT revealed a large tumoral process occupying the wall of one of the last ileal loops, very extensive over about ten by seven centimeters. Pre-aortic formations evoking macro-adenopathies measuring three centimeters in the major axes for the largest, with some peri-aortico-cellar adenopathies.

Colonoscopy showed erythematous ileocolic mucosa with, on histological examination of the biopsies of the last loop, total villous atrophy, suggesting celiac disease.

The patient was operated. Exploration found a whitish tumor about 40 cm in large diameter, oblong at the expense of the small intestine about 35 cm from the ileocecal valve. The surgical procedure consisted of a segmental resection of the small bowel removing the tumor and the facing mesentery with immediate restoration of digestive continuity with latero-lateral anastomosis using automatic forceps.

The postoperative course was simple with discharge of the patient on D+6.

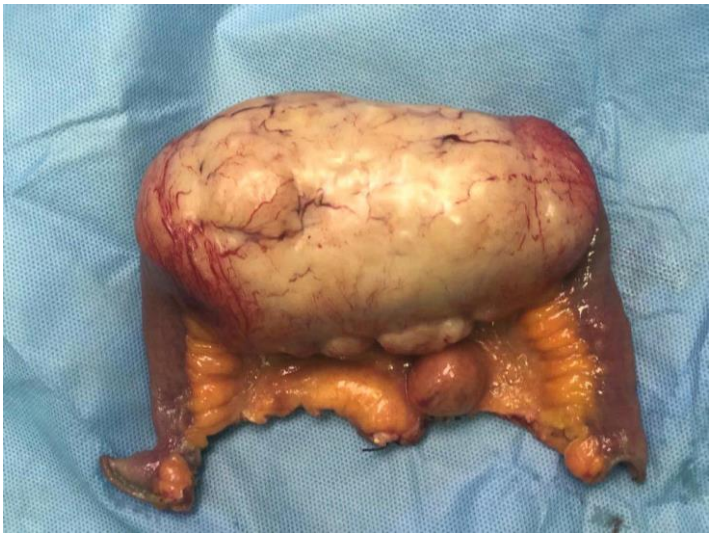

Figure 2: Resected tumor

The anatomopathological examination of the specimen concludes with a diffuse and undifferentiated malignant tumoral process with large cells evoking a lymphomatous origin infiltrating the entire small wall with lymph node localization.

An immunohistochemical complement was performed, showing the appearance of a diffuse large B-cell lymphoma.

The patient was referred to oncology for adjuvant chemotherapy. After a follow-up of 30 months, the evolution was deemed satisfactory with no recurrences or other secondary localizations.

DISCUSSION

The relative risk of malignant lymphoma is increased by three to 80 in the celiac population, according to studies [3, 4]. Enteropathy-associated T-cell lymphomas (ETAL) are rare tumors, accounting for less than 1% of non-Hodgkin's lymphomas and constituting 5.4% of all peripheral T-cell lymphomas [5]. The incidence of EATL increases considerably with age, with a clear male predominance [6]. Depending on the series, the average age at the time of diagnosis varies between 50 and 64 with extremes ranging from 20 to 92 years. AETL is a more common condition in men than in women with an incidence of 2.95 per 100,000 men/year versus 1.09 per 100,000 women/year in the population over 50 [7]. In our study, the age of our patients was respectively 50 and 52 years and both are female. Malignant lymphoma associated with celiac disease usually occurs in the jejunum. Cases of colonic and gastric localizations have been reported in the literature [2].

The extension is most often locoregional with mesenteric lymph node involvement and involvement of neighboring organs. Bone marrow involvement is exceptional [8].

Enteropathy-induced small bowel lymphoma usually presents in an adult with CD, previously diagnosed and properly treated with a previously effective strict gluten-free diet, with a resurgence or exacerbation of classic CD symptoms [9]. In the majority of studies, the main symptoms observed are abdominal pain (50 to 84% of cases), diarrhea (30 to 50% of cases), nausea/vomiting (30 to 40% of cases) as well as the presence of B symptoms (in 30 to 40%) including fever, night sweats and weight loss greater than 10% of body mass) [2]. On the other hand, the diagnosis is difficult in the absence of known CD. Symptoms are not very specific and mix +/- with those related to enteropathy [10].

Esogastroduodenal fibroscopy and colonoscopy are effective screening methods for gastrointestinal lymphomas. The advantage of endoscopy over radiology for the diagnosis of malignant tumors developed in the mucosa is obvious. In addition to the certainty provided by the direct visualization of the tumour, it is notably possible to perform multiple biopsies using all the modern techniques of staining, immunohistochemistry and molecular biology. Nevertheless, conventional endoscopy can explore, at best, only the first 30 to 40 centimeters from the jejunum and the last 20 to 30 centimeters from the ileum [11].

In our case, esophagogastroduodenal endoscopy was performed on the patient. She objectified erythematous antral and fundic gastritis associated with rarefaction and flattening of the duodenal mucosa with, on histological examination of the biopsies, stage III villous atrophy.

Colonoscopy was requested in our two patients; it showed erythematous colonic and rectosigmoid mucosa in the first case, and erythematous ileo-colonic mucosa with, on histological examination

of the biopsies of the last loop, total villous atrophy in the second case.

Recent reports have demonstrated relatively low sensitivity of capsule video compared to CT-enteroclysis in our setting. Therefore, in patients with a clinical suspicion of small bowel tumour, CT-enteroclysis should precede video-capsule endoscopy [12].

Abdominal ultrasound can sometimes detect the tumor and can guide percutaneous fine needle aspiration. The hepatosplenic invasion is well objectified. Our first case benefited from an abdominal echography, returned without particularity.

The interest of CT scans lies in the positive diagnosis, the assessment of the extra-intestinal development of the lymphoma, the differential diagnosis with a nearby tumor invading the hail, the staging assessment and the performance of percutaneous cytopuncture for lesions of the more than 2cm, as well as post-operative follow-up. CT was performed in the second patient. She objectified a right ileocolic tumoral process with some pre-aortic lymphadenopathy and peri-aortic-cava lymphadenopathy.

On CT-enterology, intestinal lymphoma represents 20 to 30% of digestive localizations and can appear in two forms:

- The aneurysmal form is the most characteristic, presenting as a bulky, incompressible ileal mass, associated with an enlargement of the digestive lumen.
- The infiltrating form is more difficult to identify, requiring good unfolding of the jejunal and ileal loops by enteroclysis. It results in a more or less extensive thickening of the small intestine with rigidity of the folds and sometimes multiple nodular formations protruding into the intestinal lumen.

Often voluminous locoregional adenopathies, which can form real tumoral masses, are present in both cases.

CT-enterology was requested in the first patient and showed regular circumferential intestinal thickening associated with mesenteric lymphadenopathy.

The staging assessment must be systematic, looking for visceral or remote associated lymph node involvement. The evaluation of the remote extension must include the search for peripheral or deep lymph node involvement (thoracic and abdominopelvic CT), and upper and lower digestive endoscopy.

There is no validated standard treatment for intestinal lymphoma in patients with celiac disease. The low incidence of this malignancy, the broad spectrum of its clinical presentation, its complex diagnosis, and the poor performance status of the host due to undernutrition, hamper the development of prospective controlled or randomized clinical trials [1].

The therapeutic role of surgery lies in the local reduction and resection of tumor masses at high risk of obstruction, hemorrhage or perforation, which could become higher during chemotherapy or radiotherapy. A possible disadvantage of intestinal surgery is the delay of chemotherapy, in particular in postoperative fistulas or infections or healing problems. Data from single case reports or a few patients suggest a better prognosis and lower risk of perforation in patients with complete resection compared to those with residual disease [10].

Laparoscopic resection of small bowel tumors follows the same principles as open surgery, starting with exploration for secondary locations and characterization of the tumor, then resection in one piece of the tumor and of the opposite mesentery, in a healthy zone, respecting sufficient resection margins.

The treatment of EATL is essentially based on chemotherapy. It must be systematic and early with or without prior surgery. Complete remission is more common in stage I/II patients: 50 to 80% complete remission for the best published series, vs 0 to 11% for stage III/IV [9].

Very few data have been reported in the literature to illustrate the impact and efficacy of radiotherapy in the treatment of EATL. Radiotherapy is rarely indicated in this case [10].

Monitoring should be closer during the first two years, then less frequent thereafter. Endoscopic controls must be performed every four months during the first year, then every six months during the following 2 years, these patients will be subject to annual clinical and endoscopic follow-up with biopsies for at least ten years. Our patients have a good evolution at 10 years.

CONCLUSION

Celiac disease is very rarely complicated by small bowel lymphoma. T-cell lymphoma associated with enteropathy is the most common and best characterized form.

The clinical symptomatology of EATL is nonspecific and highly variable, ranging from malabsorption and abdominal pain to surgical emergencies (peritonitis, intestinal obstruction, gastrointestinal bleeding).

Technical advances in explorations over the past few years, including video capsule endoscopy, double-balloon enteroscopy and CT-enteroscopy, make it possible to visualize the entire small intestine and detect intestinal lymphoma at an earlier stage. His diagnosis is confirmed by histological and immunohistochemical examination.

The therapeutic decision must take into account the age, the general state of the patient as well as the degree of extension of the disease.

There is no validated and standardized therapeutic protocol for intestinal lymphoma in celiac disease, but the best current therapeutic strategy includes systemic chemotherapy preceded by optimization of nutritional status and surgical resection.

Thanks to the new therapeutic recommendations, we can hope for better results in terms of survival.

Data Availability Statement

The data that support the findings of this article are available from the corresponding author upon reasonable request.

Conflicts of interest: Drs Jihane Sabar, Moustapha Traore and Jalil Medarheri declare no conflict of interest.

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