Case Report: Two Cases of B Lymphoma Indicative of Celiac Disease


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Abstract

Celiac disease (CD) is a chronic immune mediated enteropathy induced by the ingestion of gluten in genetically predisposed individuals. In cases of long term evolution and poor adherence to gluten-free diet (GFD), the outcome of CD may be the development of malignant diseases mainly lymphomas that can be responsible of a higher mortality rate. In some rare cases, the diagnosis of CD is made upon the discovery of the lymphoma. The main histological type is the enteropathy-associated T-cell lymphoma but can also be a B-cell kind. We report here the case of 02 patients with lymphomas revealing a CD.

Keywords: Lymphoma Indicative Celiac disease genetically.

CASE 1

First case is about a 48 years old male with no medical history who presented with ascites and lower limb oedema with the presence of fever, drenching night sweats and weight loss within the previous two months. Examination demonstrated a fever, cervical, left axillary and bilateral inguinal swollen nodes. The laboratory investigations showed an iron deficiency anaemia with inflammatory syndrome (high C reactive protein). Investigations for infections and tuberculosis were negative. Upper gastrointestinal endoscopy was performed and showed multiple ulcerations and nodules of the pylorus with a scalloping of the duodenal folds. Histology showed total villous atrophy with lymphoid proliferation, immunohistochemistry (IHC) was compatible with low-grade non Hodgkin B lymphoma. The abdominal CT scan revealed the presence of a suspicious ileal thickening with intra- and retro-peritoneal lymph node suggesting lymphomatous disease. Ileocolonoscopy was normal. Patient then received chemotherapy based on R-CHOP protocol (Rituximab, cyclophosphamide, hydroxydaunorubicin, oncovin and prednisolone) and the fellow-up for the coming year was marked by a remission.

Fig-1: Ulcerated stenosis of the proximal jejunum with spontaneous bleeding

CASE 2

We report for the second case the findings in a 27 years old male with history of intermittent greasy loose stools and vomiting associated with abdominal discomfort. He was admitted to the emergency departement with melena with no hematesis, altered general condition, fever and drenching night’s sweats. Examination showed fever and inguinal bilateral swollen nodes. Biology showed an iron deficiency anemia. Investigations for infections and tuberculosis were also negative. Upper gastrointestinal endoscopy showed a reduction of duodenal folds. Ileocolonoscopy was normal except the presence of melena. An upper gastrointestinal enteroscopy was performed and showed an ulcerative mass of the proximal jejunum responsible of a passable stenosis that extends over 20 centimeters (Figure 1). IHC was compatible with low-grade non Hodgkin B lymphoma with staining patterns of CD20. The computed tomography showed an intraperitoneal effusion and jejunal wall thickening. Upon these findings, the diagnosis of malignant complication of CD was retained. Patient was then transferred to an onco hematology unit and started chemotherapy.
The mortality of a celiac population is significantly increased compared to the general population. The criteria associated with this increased risk are late diagnosis of the disease, non-compliance with GFD, the severity of the malabsorption syndrome and certain complications such as malignancies [3]. The prevalence of malignant lesions in untreated CD is approximately 10%. Non-Hodgkin lymphoma (NHL) of the small intestine is the most well-known malignant complication, but there are other visceral neoplasms associated with CD [4]. These neoplasms are in order of frequency: carcinomas of the esophagus and oropharynx (standardized incidence ratio [SIR] of 2.3 and 4.2, respectively), adenocarcinoma of the small intestine, colon cancer (SIR 1, 5) and pancreatic adenocarcinoma (SIR 2.7). Lymphoma is a general term used to refer to more than 50 related cancers. There are two general categories of lymphoma: Hodgkin lymphoma and non-Hodgkin lymphoma (NHL). The difference between these two is whether or not the Reed-Sternberg cells are present (a cell derived from a B lymphocyte and is only present in the case of Hodgkin lymphoma). If there are no Reed-Sternberg cells in the lymphatic tumor, the diagnosis is likely to be NHL. Of all lymphoma diagnoses, 85% are NHL. Primary lymphomas of the digestive tract are NHL), derived by definition from MALT (Mucosa Associated Lymphoid Tissue) [5]. They correspond to 1% of gastrointestinal tumors. The stomach is the most frequent site, followed by the small intestine and colon. B lymphomas (90%) are more common than T lymphomas (10%). Digestive T lymphomas are rare, accounting for less than 1% of NHL. In addition to the intestinal locations of vireo-induced T lymphomas (linked to HTLV1 or EBV), those linked to immune deficiencies, or CD4 + T lymphomas of the chorion [6], the relative risk in the event of celiac disease is increased from 3 to 80 according to studies [16]. This can be explained by the local inflammatory process secondary to the ingestion of gluten and by the antigenic stimulation of B and T lymphocytes in a persistent way which promotes the development of lymphoma in this location [19]. Note that in one out of two cases, lymphoma is indicative of a silent celiac disease and manifests itself as a surgical complication such as hemorrhage, intestinal perforation or obstruction [15]. On imaging, lymphoma may be responsible of a narrow intestinal lumen, a thickened intestinal wall, the presence of nodules, an intraluminal mass, ulceration, lymphadenopathy or even lesions of the omentum [17]. Lymphoma is only slightly enhanced on CT scan [18]. There are three types of lymphoma: non-Hodgkin's B lymphoma, refractory sprue and intestinal T lymphoma EATL (Enteropathy-Associated T cell Lymphoma). Non-Hodgkin's B lymphoma can be localized in the intestine and a strong genetic involvement has been suggested to explain its development [16]. In patients with celiac disease, the relative risk has been reduced to 6 according to recent studies [15]. Enteropathy-associated T lymphoma (EATL) is a very rare type of rapidly growing (aggressive) NHL. It is most common in Europe and in humans. It most commonly affects people between the ages of 60 and 70 years old. EATL most often occurs in the jejunum. It can also start in other parts of the small intestine and in the colon. EATL type I is associated with celiac disease or gluten sensitivity, whereas EATL type II is not associated with celiac disease or gluten sensitivity. It is less common than type I EATL [7-10]. LTAE type I can be diagnosed during a surgical emergency and reveal celiac disease. Conversely, when celiac disease is known, lymphoma should be looked for in the case of resistance to the GFD and its diagnosis can be difficult. It is based on enteroscopy, thoraco-abdominal computed tomography, positron emission tomography or even laparotomy.

Prof. Cellier's team highlighted refractory clonal sprue, known as type II (RS II), which is considered to be a low degree of malignancy, intraepithelial lymphoma, associated with celiac disease and characterized by an expansion of small intraepithelial lymphocytes of abnormal phenotype (no surface expression of the CD3-T receptor complex, but CD3 + intracellularly in IHC and CD8-, CD103 +) [11]. It is complicated by T lymphoma of high degree of malignancy in 30 to 50% of cases at 5 years and its prognosis is poor with less than 45% of patients alive 5 years after diagnosis [12]. Its diagnosis is difficult and requires in particular specialized IHC, phenotypic and molecular biology (PCR Multiplex) studies.

When CD is diagnosed in childhood, there is no observed increased risk of cancer, most likely due to early initiation of GFD [13]. In symptomatic adults, a well-monitored and prolonged GFD for at least 5 years significantly reduces the overall risk of cancer (carcinomas and lymphomas combined), but the difference mainly concerns the lymphomas [14]. In general, the therapeutic strategies for gastrointestinal lymphomas are based on chemotherapy and are specific to the histological type and their location in the digestive tract. The poor prognosis of RS type II is linked to the lack of effective treatment since those usually used (corticosteroids and immunosuppressants) only have a partial and temporary effect (12). Two new therapeutic strategies for RS type II: 1 - a classic treatment by chemotherapy-autograft, 2- a therapy targeted by the use of inhibitors of the intra-lymphocyte signaling pathway of IL-15 (inhibitors of JAK 3, in project). The goal is to cure patients with RS type II and prevent the onset of high degree of malignancy T lymphomas (EATL).

CONCLUSION

In case of a symptomatic celiac patient despite a correctly followed gluten-free diet, the various possible malignant complications of celiac disease, mainly digestive cancers and lymphomas, should be excluded. More specifically concerning the malignant
digestive complications of celiac disease involving the small intestine, it will be remembered that they are essentially adenocarcinoma and lymphoma for which we distinguish non-Hodgkin B lymphoma, refractory sprue and intestinal T lymphoma.

REFERENCE


In Neoplastic Diseases of the Blood (pp. 867-918). Springer, New York, NY.