Celiac Disease and Cancers in Morocco

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Abstract
Digestive cancers are the most severe complications of celiac disease (CD), which can lead to death. We can report 12 patients with CD associated with cancer. It is retrospective study of 12 patients with CD complicated by cancers, collected in the department of diseases of the digestive system "Medicine C", from 1995 to 2017. Six patients had lymphoma, three were gastric tumors, two were small intestine tumors, and one had liver tumor. The diagnosis of lymphoma was made at the same time as that of CD in one patient, three months later in two patients, 18 months later in two patients and 8 years later in one patient. Morphological and histological data were in favor of malignant non-Hodgkin's lymphoma with intestinal localization in four patients, with lymph node localization in one patient and one patient with refractory celiac disease type 2 with intraepithelial lymphoma. The treatment consisted of chemotherapy in four patients and corticosteroid therapy with parenteral nutrition in one patient. The evolution was marked by the death of 03 patients and 2 patients were lost without any idea about their evolution. The diagnosis of the gastric tumor was retained after the realization of a upper gastrointestinal endoscopy with biopsies. The histopathologic examination was in favor of a well-differentiated adenocarcinoma in two patients, and of an adenocarcinoma moderately differentiated in one patient. The treatment was palliative chemotherapy, with an abdominal scan three months later showed partial response. The hepatocellular carcinoma on healthy liver was diagnosed at the same time as CD on angio-CT scan data and liver biopsy with patient death at the time of diagnosis. Digestive cancers are severe complications of CD requiring early management and follow-up of patients to reduce the rate of death.

Keywords: cancers, celiac disease


1. Introduction
Celiac disease (CD) is an autoimmune inflammatory enteropathy secondary to the ingestion of gluten which can be complicated by cancers [1]. We report 12 patients with CD complicated by cancers and we will discuss this complication.

2. Patients and Methods
Retrospective study of 12 patients with CD complicated by cancers, collected in the department of diseases of the digestive system "Medicine C", from 1995 to 2017. All patients were hospitalized, biological, morphological and histological data were collected.

3. Results
Digestive cancers represented 6.34% of the 189 patients with CD in our training. The average age was 42 years. There are 06 women and 06 men. Six patients had lymphoma, three were gastric tumors, two were small intestine tumors, and one had liver tumor.

The diagnosis of lymphoma was made at the same time as that of CD in one patient, three months later in two patients, 18 months later in two patients and 8 years later in one patient. Morphological and histological data were in favor of malignant non-Hodgkin's lymphoma with intestinal localization in four patients, with lymph node localization in one patient and one patient with refractory celiac disease (RCD) type 2 with intraepithelial lymphoma. The treatment consisted of chemotherapy in four patients and corticosteroid therapy with parenteral nutrition in one patient.

The evolution was marked by the death of 03 patients and 2 patients were lost without any idea about their evolution. The diagnosis of the gastric tumor was retained after the realization of a upper gastrointestinal endoscopy with biopsies. The histopathologic examination was in favor of a well-differentiated adenocarcinoma in two patients, and of an adenocarcinoma moderately differentiated in one patient. The thoraco-abdomino-pelvic CT scan showed a large and metastatic gastric tumor classified as
T4 N2 M1 in a patient who was scheduled for palliative chemotherapy. A total curative gastrectomy with oesophageal anastomosis associated with lymph node dissection was performed in two patients.

The evolution was marked by the death of a patient in postoperative and 1 year later for the other patient. The diagnosis of the well-differentiated neuroendocrine tumor was carried out 30 years after that of CD. The patient underwent a resection of the first two duodenal portions with duodeno-jejunal anastomosis and a colonic resection with termino-terminal anastomosis.

The evolution was good with a 2 years follow-up. The second patient of intestinal cancer was a moderately differentiated adenocarcinoma of intestinal origin, the diagnosis was retained after an abdominal scan with mass biopsy. The treatment was palliative chemotherapy, with an abdominal scan three months later showed partial response. The hepatocellular carcinoma on healthy liver was diagnosed at the same time as CD on angio-CT scan data and liver biopsy with patient death at the time of diagnosis.

4. Discussion

Malignant disease is a serious concern in CD [2] and recently has been reviewed in detail [3,4]. Some patients may even present with lymphoma [5,6] or a small-intestinal adenocarcinoma [7], and the CD is only detected later. In others, malignancy, particularly lymphoma, complicates the clinical course of well-established CD, but may be especially difficult to diagnose [8]. The precise risk of malignant disease in adult CD is difficult to evaluate, but about 8%-10% with severe biopsy changes develop lymphoma [9], and this figure has remained remarkably constant over several years [10]. Age of first diagnosis of CD seems to be a critical factor. In those first diagnosed late in life (and presumably, initiating a protective gluten-free diet much later), detection of lymphoma may be much higher [11]. Lymphoma may be classified based on pathological and immunophenotypical features. B-cell and T-cell lymphomas both occur in CD. However, detection of a T-cell type more often leads to suspicion of underlying CD. Primary intestinal T-cell lymphoma is recognized under the WHO classification as enteropathy-associated T-cell lymphoma (ETL or EATL). They are very uncommon and represent an estimated 5% of all gastrointestinal lymphomas [11]. Previously, these were thought to be histocytic in origin (and labeled malignant histiocytosis) but their origin now appears to be from T cells, specifically intra-epithelial lymphocytes [11]. In CD (without lymphoma), the intra-epithelial lymphocytes express the following antigens (among others): surface CD3 and CD8. In a subset of patients that seem clinically refractory to a gluten-free diet, intra-epithelial lymphocytes have a different form of T-cell phenotypic expression: CD3 shows intra-cyttoplasmic expression while CD8 expression is absent. Some believe this may reflect a specific form of RCD (type 2) with a poor prognosis and a possible precursor lesion for the development of lymphoma [12,13,14]. Recent studies have also evaluated risk of lymphoma in CD. While the risk of lymphoma in CD, especially of the T-cell type, is increased, the risk appears not to be as significant. The relative risk has been estimated to be close to 3 and likely is lower in clinically silent disease [15]. Also intriguing are studies related to malignant disease elsewhere in the gastrointestinal tract. Small-bowel adenocarcinoma is increased in CD. Normally, this is a rare tumor. Some have suggested that this carcinoma may be related to an adenoma-carcinoma sequence but the risk of duodenal adenoma may not be increased in CD [16]. Most patients appear to present with proximal small-intestinal localization, usually with small-bowel obstruction or bleeding. If complete surgical resection of a small-intestinal adenocarcinoma can be accomplished, the prognosis is better than if lymphoma is present [17]. Treatment of lymphoma associated with CD to date has not substantially differed from lymphoma in the absence of CD, and generally involves a combination of surgical treatment, radiation and chemotherapy. Most believe that the best treatment results occur in those diagnosed early [18]. Biological agents are also being evaluated. In newly diagnosed lymphoma patients with chronic diarrhea and weight loss, underlying CD should be excluded, preferably prior to lymphoma treatment (since both radiation and chemotherapy may structurally alter the small intestine), because concomitant recognition of CD may have important nutritional implications.

5. Conclusion

Digestive cancers are the most severe complications of CD, hence the importance of early diagnosis and good observance of the gluten-free diet, which could decrease the risk of this complication especially lymphomas.

References


