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Second jejunal loop adenocarcinoma associated with celiac disease: the first case report

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SUMMARY: **Second jejunal loop adenocarcinoma associated with celiac disease: the first case report.**

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Introduction. *Jejunal adenocarcinoma is a very rare disease but the frequency of this rare carcinoma is higher in celiac patients. We report the first case report of a second jejunal loop adenocarcinoma associated with celiac disease.*

Presentation of case. *A 47-year-old woman, with a history of celiac disease. Computerized tomographic scans of the abdomen and pelvis demonstrated a severe retroperitoneal lymphoadenopathy, para-aortic, inter-aorto-caval, porto-caval, posterior pancreaticoduodenal space, celiac trunk, lesser gastric curvature, lymph node grouping. The patient underwent digiunal resection and regional lymphadenectomy. Diagnosis was poorly differentiated jejunal adenocarcinoma, infiltrating subserosal adipose tissue, metastasing in five out of eight regional lymph nodes. U.I.C.C. 2017 grading = pT3 pN2 G3 R0; Stage IIIB.*

Discussion. *The jejunum accounts for 11-25% of small bowel adenocarcinoma, that accounts for less than 5% of gastrointestinal cancer, notwithstanding that 90% of the mucosa surface area of the digestive tract is made by small intestine. To the best of our knowledge, this is the first report on a second loop jejunal adenocarcinoma complicating celiac disease.*

In our study, the diagnosis of cancer was made by computed tomography (CT) of abdomen and the patient was operated. For the diagnosis of small bowel tumour, CT enteroclysis has a sensitivity of 85-95% and a specificity of 90-96%. Complete resection (RO) of the jejunal adenocarcinoma, with regional lymph nodes resection and jejuno-jejunal anastomosis should be performed.

Conclusion. *After curative surgical resections of small bowel adenocarcinoma, adjuvant chemo-therapy has not shown a clear benefit in retrospective studies. Preoperative Chemo-Radio-therapy and careful Imaging Staging are the first steps to planning surgery.*

KEY WORDS: Jejunal adenocarcinoma - Celiac disease - Small bowel adenocarcinoma.

Introduction

Jejunal adenocarcinoma is a very rare disease but the frequency of this rare carcinoma is higher in celiac patients. Celiac disease is the most common autoimmune disease of small bowel in western countries. Its prevalence in the italian general population is 4,9 - 5,7 per 1000 (1). Its relative risk for small bowel adenocarcinoma ranges from 10 to 60 (2). In up to 73% of celiac disease patients with malignant small bowel complications has been shown poor mucosal healing despite a gluten-free regimen (3).

At our knowledge, this is the first case report of a second jejunal loop adenocarcinoma associated with celiac disease.

Case report

A 47-year-old woman, with a history of celiac disease, originally diagnosed with abdominal pain and anorexia. On physical examination she was afebrile, with a regular heart rate of 85/min, blood pressure 120/80, respiratory rate 16/min. The abdomen examination was negative, with normal bowel sounds, tenderness to deep palpation of the mesogastric region. The liver and spleen were not palpable.

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An admission laboratory test revealed a blood white cell count of 8.5 K/mm^3 (4.0-11.0 K/mm^3), hemoglobin of 10.7 g/dL (13.5-16.5 g/dL), platelet count of 252 K/mm^3 (150-450/mm^3), serum concentrations of alanine aminotransferase (ALT) of 32 IU/L (10-40 IU/L), aspartate aminotransferase (AST) of 38 IU/L (10-42 IU/L), total bilirubin of 1 (0.3-1.2 mg/dL), alkaline phosphatase of 78 (32-140 IU/L), total protein of 6,3 g/dL (5.7-8.2 g/dL), albumin of 4 g/dL (3.2-4.8 g/dL).

To further evaluate the virologic history, more laboratory studies were carried out, including antibodies for hepatitis B (HB) core IgG, HB core IgM, HBs, hepatitis C virus (HCV), hepatitis E IgM, hepatitis E IgG, cytomegalovirus CMV IgM, Epstein-Barr (EBV-EBNA) virus IgM, all of which were negative. Conversely, antibodies for cytomegalovirus CMV IgG and for Epstein-Barr EBV-VCA IgG and EBV-EBNA IgG were positive.

An upper endoscopy performed on September 5th, 2017, showed edema + erythema in the second portion of duodenum, with disappearance of mucosal pattern. Gastric biopsies showed non-H.pylori-related chronic inactive gastritis. Bulbar and second portion duodenal biopsies demonstrated severe atrophy of villi, increased lymphoplasmacellular infiltrate in the "lamina propria" and, in conclusion, type 3C after Marsh-Oberhuber celiac disease (PE-17-245, September 5th, 2017).

An abdominal ultrasound scan showed normal results, with alitiasic gallbladder, normal liver, not dilated biliary ducts, not dilated intestinal loops.

Computerized tomographic scans of the abdomen and pelvis demonstrated a severe retroperitoneal lymphoadenopathy, para-aortic, inter-aortocaval, porto-caval, posterior pancreaticoduodenal space, celiac trunk, lesser gastric curvature, lymph node grouping, lymph node diameter ranging from 1.2 to 4.5 cm (Figure 1). In the left adrenal gland, a 4-cm diameter solid mass was detected in the lateral arm of the gland.

On March 2018 the patient underwent digiunal resection and regional lymphadenectomy (Figure 2). The resected digiunal tract measured 12 cm in lenght and corresponded to the second digiunal loop (Figure 3). The digiunal wall contained a neoplastic proliferation, characterized by limited zones of different sized and branched glands, with fairly good structural complexity, lined with low column ep-

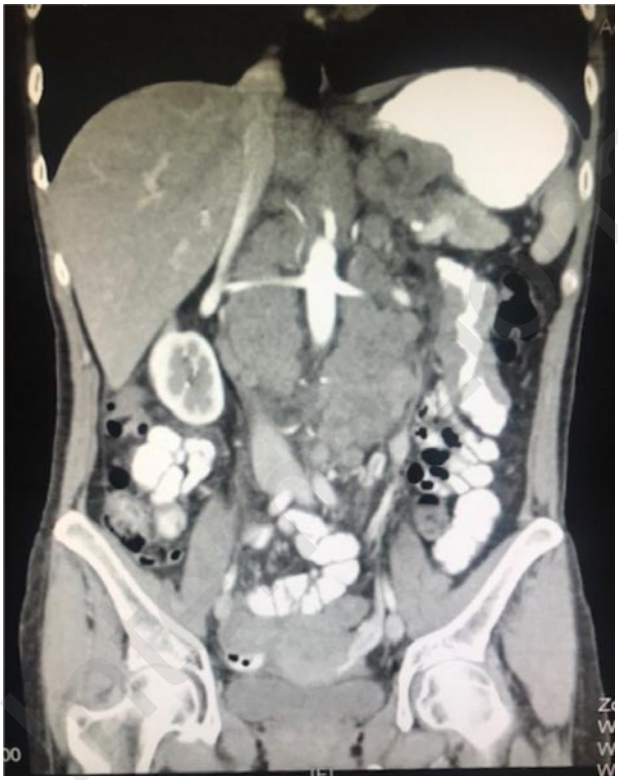

Figure 1 - Computed tomography scan showing severe retroperitoneal lymphoadenopathy.

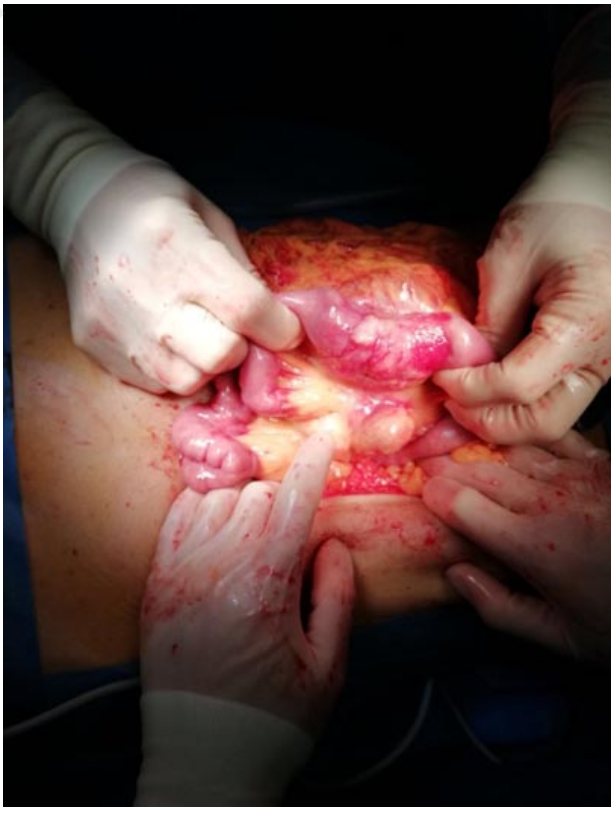

Figure 2 - Intraoperative image: second digiunal loop neoplasm.

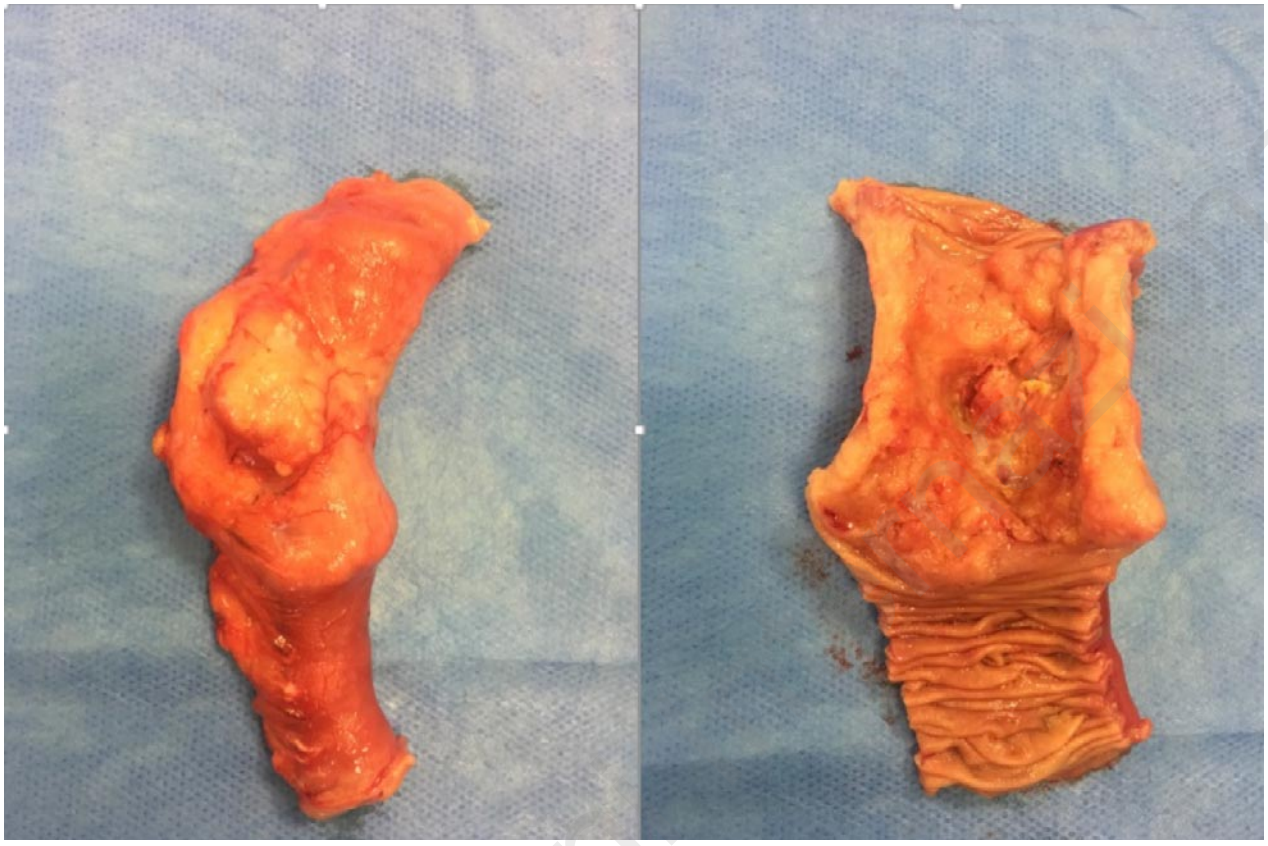

Figure 3 - Jejunal resection.

ithelium, with vesiculated nuclei, prominent nucleoli and a starting loss of polarity. It also presented wide solid zones composed of cells with polimorphic nucleus and scanty cytoplasm.

The tumoral cellular population was positive to anti-cytocheratin 20 antibodies (multifocal) and negative to anti-chromogranin, anti-CD56 and anti-CD45RB antibodies. Neoplasm develops in a penetrating fashion of growth and infiltrates the subserosal wall, without getting over the serosal membrane. Desmoplastic reaction is moderate, intra- and peri-tumoral lymphoplasmacellular inflammatory infiltrate is severe, necrosis is superficial. Proximal and distal resection margins are free from neoplastic infiltration. Five out of eight regional resected lymph nodes were metastatic and histopathologic features were the same as primitive tumour.

Diagnosis was poorly differentiated jejunal adenocarcinoma, infiltrating subserosal adipose tissue, metastasing in five out of eight regional lymph nodes. U.I.C.C. 2017 grading = pT3 pN2 G3 R0; Stage IIIB.

Discussion

The jejunum accounts for 11-25% of small bowel adenocarcinoma (4), that accounts for less then 5% of gastrointestinal cancer (5), notwithstanding that 90% of the mucosa surface area of the digestive tract is made by small intestine. In adults, the small bowel is 350 cm +-60 cm in average lenght (6). An 8% prevalence of small bowel adenocarcinoma was demonstrated in a cohort of 235 patients with celiac disease (2).

In a series of 395 cases of small bowel cancer, celiac disease was found in 13% of cases of small bowel adenocarcinoma, primarily localized in the jejunum (7).

To the best of our knowledge, this is the first report on a second loop jejunal adenocarcinoma complicating celiac disease. Celiac disease is a chronic immune-based reaction to dietery gluten which develops in genetically predisposed patients (8). In patients with celiac disease, the risk of small bowel adenocarcinoma is 60-80 fold increased as compared to controls (9).

In a review of 136 patients with adenocarcinoma in celiac disease, overall 74% of the cases were reported from Italy, United Kingdom and USA (10). The most frequently involved intestinal tract was the jejunum (11).

In patients with celiac disease, the mucosa adjacent to carcinoma shows no evidence of a premalignant lesion or dysplasia (12). For this reason, an adenoma-carcinoma sequence is considered the most likely mode of development of adenocarcinoma (13). In patients with long lasting celiac disease, the risk of carcinoma appears to be greatest (14). Gluten free diet seems to decrease the incidence of adenocarcinoma in celiac disease (15).

As shown in a large Swedish population based study, (16) small bowel adenocarcinomas was detected in patients diagnosed in adulthood (17). Proximal or estended bowel resections are sometimes necessary during emergency surgical operations (18).

In celiac disease, a malabsorpitive vitamin A and vitamin E deficiency and increased vulnerability to oxidative injury, would enhance oncogene sequence in a small bowel more permeable to carcinogen, due to mucosal damage (19). Long lasting celiac disease is associated with an increased risk of cancer (20). Celiac disease may be considered as a premalignant condition and in all patients with diagnosis of small bowel adenocarcinoma a subclinical or silent celiac disease should have been searched (15, 21).

In our study, the diagnosis of cancer was made by computed tomography/CT) of abdomen and the patient was operated. For the diagnosis of small bowel tumour, CT enteroclysis has a sensitivity of 85-95% and a specificity of 90-96% (22-25).

In symptomatic patients with celiac disease, in spite of a strict gluten free diet, multidetector computed tomography enteroclysis should be taken to detect an adenocarcinoma (22).

On CT enteroclysis, a small bowel adenocarcinoma appears as a polypoid lesion with regular margins or as a concentric limen structure with irregular edges (26).

In symptomatic patients with celiac disease, a video capsule endoscopy is advised as well (27).

The role of surveying patients with established celiac disease is controversial.

Complete resection (RO) of the jejunal adenocarcinoma, with regional lymph nodes resection and jejuno-jejunal anastomosis should be performed (28). After curative surgical resections of small bowel adenocarcinoma, adjuvant chemo-therapy has not shown a clear benefit in retrospective studies (29-32). Preoperative Chemo-Radio-therapy and careful Imaging Staging are the first steps to planning surgery (33).

Accurate preoperative imaging study of the level of tumour invasion is important because the risk of lymph node metastases rises with growing T stage (34-38).

Abdominal US is useful screening diagnostic exam in the cases with pain in upper abdomen, but computed tomography (CT) and magnetic resonance imaging (MRI) are mandatory to make an exact staging and preoperative planning of surgery (35).

An international randomized trial, BALLAD study (Benefit of Adjuvant Chemotherapy for Small Bowel Adenocarcinoma) will evaluate the benefit of adjuvant chemiotherapy (36). In the UK in August 2015 a phase III trial to evaluate adjuvant chemotherapy for small bowel adenocarcinoma was initiated by the International Rare Cancer Initiative (clinicaltrials.gov n. NCT02502370).

After R0 resected small bowel adenocarcinoma a randomized phase III trial was started in May 2017 to confirm the superiority of adjuvant chemotherapy with capecitaline and oxaliplatin (37).

Conflict of interest

None of the Authors has conflicts of interest to declare.

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