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Case Report
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Ileal MALT-Derived Lymphoma Causing Small Bowel Obstruction - A Case Report and Literature Review

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Abstract

Mucosa-Associated Lymphoid Tissue (MALT) is a rare type of Marginal Zone Lymphomas (MZLs) that can affect the small bowel; it usually present with vague symptoms, but sometimes it can occur with complications such as perforation, bleeding or obstruction. We present a case of a male patient presented with sudden abdominal pain and vomit; the abdominal CT scan showed a stenosing lesion of the small bowel. A segmental intestinal resection was performed and the histological specimen revealed the presence of an ileal MALT lymphoma; the control CT scan at 1 year did not show recurrence of the disease. Even if antibiotic therapy, chemotherapy and radiotherapy are the first treatment option for gastrointestinal lymphoma, surgery still has a role in case the first clinical presentation is represented by a severe complication.

Case Presentation

A 51 years-old man presented to the emergency room for the onset of abdominal pain and vomit within a few hours. There was no history of previous abdominal discomfort, diarrhea, fever, weight changes, or melena. He had no significant other past medical history. Physical examination revealed tenderness localized at the superior quadrants, bowel sounds were hypoactive, and no abdominal mass could be palpated; the patient had another episode of vomit during the visit. Laboratory results showed leukocytosis with a WBC count of 12.68 × 10^3/uL HI with 91.1% of neutrophils and increased LDH level (997 U/L, normal value 210 to 400 U/L) with normal CPK level. Other laboratory results were unremarkable. Abdominal ultrasound scan study was difficult to carry out because of the intestinal meteorism but it revealed ileal distension with a moderate quantity of free abdominal fluid; the abdominal CT scan demonstrated fluid distension of the small bowel loops with a sudden narrowing in the distal part corresponding to a stenosing lesion extended for about 5 cm, with no enlargement of mesenteric lymph nodes (Figures 1a-1c). The patient underwent to an explorative laparotomy that showed a neoformation of 6 cm of diameter localized in the middle ileum causing small bowel occlusion so an intestinal resection was performed. The post-operative course was uneventful, the patient recovered well and he was discharged in VIII post-operative day. Histological specimen was composed of a 25 cm portion of distal ileum which contained a 5 cm stenosing lesion. On microscopic examination, an extensive transmural atypical and diffuse lymphoid infiltrate was present. The atypical lymphoid cells were positive for CD20, CD79a, and negative for CD3, CD5, CD10, CD21, CD23, cyclin D1, and CD56. Rare lymphoepithelial lesions were also present. The proliferation rate of the lesion was low, with a Ki-67 percentage of 5%. One lymph node specimen was identified in the mesentery but it was reported to be tumor-free. The ileal mass was consistent with a diagnosis of extranodal marginal zone (MALT) lymphoma. No other lesions were found at the whole body CT scan; bone marrow biopsy was not effectuated. The presentation was consistent with a clinical stage I_2 of the Lugano lymphoma classification system [1]. No additional therapy was given and the patients were referred to the oncology department for further treatment. The control CT scan at 1-year showed no recurrence of the disease.

Discussion

Small bowel rarely develops malignant tumor. This finding can be explained by some hypotheses such as the higher motility rate by the peristaltic contraction that reduces the time of exposure of the intestinal wall to the carcinogenic agents, and the lower bacterial population that results in reduced formation of carcinogens from bile acid breakdown [2]. Risk factors for small bowel tumor can be divided into three groups. The first concerns medical conditions such as inflammatory bowel disease, coeliac disease, gallstone disease, small intestine adenomas or familial adenomatous polyposis. The second involves malignant cancer such as hereditary nonpolyposis colorectal cancer,

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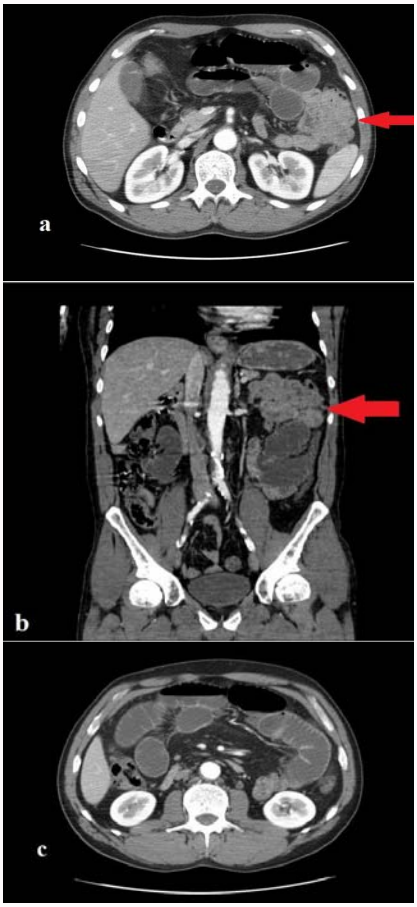

Figure 1: Computer tomography scan in patient with small bowel obstruction showing stenosing lesion (a, b. red arrow) and proximal intestinal fluid distension (c).

sporadic colorectal cancer, or multiple endocrine neoplasia type 1. The latter includes life-style factors as alcohol consumption, cigarette smoking, a diet rich in red meat, and high BMI [2,3]. Marginal Zone Lymphomas (MZLs) are a group of B-cell lymphomas that arise from memory B cells normally present in the 'marginal zone' of secondary lymphoid tissues [4]. MZLs account for 5% to 17% of all non-Hodgkin Lymphoma (NHLs) [5] and comprise over 50% of primary gastrointestinal NHLs [6]. MZLs include three subtypes: Mucosa-Associated Lymphoid Tissue (MALT), splenic MZL and nodal MZL that account for 70%, 20% and 10% respectively of all marginal zone lymphomas. MALT lymphoma comprises around 8% of all B cells lymphomas; most cases occur in adults with a median age of 60 years. The stomach is the most common location for MALT lymphoma, accounting for about one-third of cases [7], but it has been described in several non-gastric sites, such as salivary gland, thyroid, skin, conjunctiva, larynx, lung, breast, kidney, liver, prostate, small and large bowel, and also intracranial dura [8]. Bone marrow infiltration is described in up to 20% of the cases and it is associated with a worse prognosis [9]. MALT lymphoma is associated with chronic antigenic stimulation that causes lymphocytes invasion in mucosal sites and their subsequent proliferation and transformation. In consequence of this, B cells, by interacting with T cells that are triggered by the antigens, proliferate and may acquire genetic abnormalities [8]. These abnormalities lead to neoplastic mutation with loss of dependency from antigenic stimulation and with histological mutation [10,11]. Cytogenetic alterations include trisomy of chromosome 3 or 18, the 6q23.3 deletion, and four translocations (t11;18) (q21;q21); t(1;14) (p22;q32); t(14;18) (q32;q21); t(3;14) (p14.1;q32)); some of these alterations converge to the activation of the NF-κB pathway that exerts a role in immunity, inflammation, and apoptosis [12]. The chronic antigenic stimulation arises from infectious agents or autoimmune diseases. Regarding the first group, *Helicobacter pylori* is strictly linked with the development of gastric MALT lymphoma, but also in other sites an etiopathogenetic association with other microbial agents has been implicated. These associations are *Chlamydophila psittaci* for ocular adnexal lymphomas, *Borrelia Burgdoferi for* cutaneous lymphomas, *Achromobacter xylosoxidans* in pulmonary MALT lymphomas [13], and also *Campylobacter jejuni* for the small intestine lymphomas, notably in the subtype of MALT lymphoma named Immunoproliferative Small Intestinal Disease (IPSID) [14]. Concerning the autoimmune diseases, Sjogren syndrome is related to an increase risk for the development of salivary or lacrimal gland MALT lymphoma, whereas Hashimoto thyroiditis is linked with thyroid MALT lymphoma. Hepatitis C Virus (HCV) infection is related to an increased risk for all types of MZLs, but the closest association is with splenic MZL. MALT lymphoma has different and variable macroscopic presentation, namely localized or multiple polypoid lesions [15,16], ulcerative (including structuring, non-stricturing, and aneurismal forms), diffuse-infiltrating or mixed type; the most frequent presentation is the ulcerative type [17]. Intestinal lymphomas commonly present with vague and a specific symptoms, including abdominal pain or discomfort, lack of appetite, diarrhea, melena or hematochezia, and weight loss [18]; in some cases the first clinical presentation is represented by a severe complication as bowel obstruction, bleeding or perforation. We considered a literature review searching on PubMed for unusual presentation of small bowel MALT lymphomas; in one case-report MALT lymphoma was associated with protein-losing enteropathy that caused the onset of lower leg edema and severe hypoalbuminemia [19]. Two case-reports reported intussusceptions of the small bowel in correspondence of the MALT lymphoma mass. Intussusceptions are more frequent in young people [20], but they can occur also in elderly patients [21]. In one patient MALT lymphoma presented as a large aneurysmal dilatation of the small bowel with an ulcer causing anemia and tarry stools [22]. We found only two cases of MALT-derived lymphoma presenting with small bowel obstruction. In both cases the onset of the symptoms initiated long before the admission to the hospital (2 months and 1 week earlier) but the subsequent investigations, made before the hospitalization, did not find any abnormalities expect for mild lymphadenopathy at the CT scan [23,24]. Conversely, our patient had a sudden onset of symptoms. After staging evaluation one was consistent with a clinical stage II_E, so no additional therapy was given, while the second resulted in a clinical stage III_E and underwent to therapy with single agent rituximab (monoclonal antibody against CD20) for two years. When a marginal zone lymphoma is presumed or confirmed, extensive staging valuation is necessary and it includes laboratory tests (blood cell counts, renal and liver function, basic biochemical studies, LDH and β2-microglobulin levels, serum protein immunofixation, Human Immunodeficiency Virus (HIV), Hepatitis B (HBV), and C Virus (HCV) serologies), radiological examination (CT scan of the chest, abdomen and pelvis; the value of Positron Emission Tomography (PET) scan is still unclear so its use is not routinely recommended), bone marrow aspirate and biopsy. In the event of small bowel lymphoma, further diagnostic procedures are advised and they may include endoscopy, double contrast X-ray and *Campylobacter jejuni* search in the tumor biopsy. Another useful tool

is oral Double Balloon Endoscopy (DBE) that can be employed in a non-emergent setting to completely explore the small bowel and to obtain histopathological samples [25]. MALT lymphoma therapy can include antibiotic therapy, radiotherapy, chemotherapy or a combination of them. Due to the etiologic association with bacterial chronic infections, first line therapy for localized *H. pylori* positive gastric MALT lymphoma comprise triple therapy (proton pump inhibitor plus clarithromycin and amoxicillin) for *H. pylori* eradication. This can lead to MALT lymphoma regression in 60% to 100% of the cases. There are cases of regression after antibiotic therapy in *H. pylori* negative patients as well, possibly due to a false-negative test or to infection by other Helicobacter species. Antibiotic therapy must not be taken into account merely in the presence of (11; 18) translocation, because this genetic alteration is associated with antibiotic resistance. The management of patients with non-gastric MALT lymphoma is less outlined. Antibiotic therapy is used for small bowel IPSID, cutaneous or ocular adnexal lymhpomas owing to their etiological relationship with infectious agents. Radiotherapy is considered in patients with stage I/II gastric *H. pylori* negative MALT lymphoma, or as second line therapy in case of persistent lymphoma after antibiotic treatment, and in non-gastric localized presentations [26]. Lymphomas of the small and large bowel are not usually amenable to radiotherapy because of their variable location and spread [27]. Chemotherapy is advisable in more advanced stages, but there is no consensus of the best schedule choice to use. Rituximab plus chemotherapy appears the most appropriate choice, but enrollment in controlled clinical trials is also advisable. In localized diseases, surgery can be a sufficient therapy and further treatment may not be needed [28-30].

Conclusion

We report a case of MALT-derived lymphoma causing small bowel obstruction with an acute onset of symptoms. In literature, we found only two cases comparable to our patient, even if in both case-reports the symptoms initiated long before the admission to the hospital. Antibiotic therapy, chemotherapy and radiotherapy are the best option for GI lymphoma. In small intestinal lymphoma, complications such as perforation, obstruction or bleeding are more common, so surgical excision may be required before establishment of the correct diagnose.

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