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Mucosa-associated lymphoid tissue lymphoma in the terminal ileum: A case report

MALT lymphoma in the terminal ileum

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Abstract

BACKGROUND

The lymphoma of the mucosa-associated lymphoid tissue (MALT) is predominantly found in the stomach. The few cases reported in the literature of MALT lymphomas affecting the ileum are in patients who are already symptomatic and with clear advanced endoscopic findings. We present the first case of an asymptomatic female patient, who underwent colonoscopy as a routine examination with the finding of an ulcer in the distal ileum region, which histopathological examination associated with immunohistochemistry revealed the diagnosis of MALT lymphoma.

CASE SUMMARY

A 57-year-old asymptomatic female patient underwent a colonoscopy exam for screening. The examination revealed an ulcer, of medium depth, with well-defined borders, covered by a thin layer of fibrin and with a halo of hyperemia in the distal ileum portion. Findings are nonspecific but may signal infections by viruses, protozoa, and parasites or inflammatory diseases such as Crohn's disease. Biopsies were taken. The anatomopathological result revealed an atypical diffuse lymphocytic infiltrate of small cells, with a characteristic cytoplasmic halo of marginal zone cells. The immunohistochemical study was performed which the results demonstrated a negative neoplastic infiltrate for the expression of cyclin D1 and cytokeratin AE1/AE3 and positive for BCL60 in the germinal center. The test also revealed CD10 positivity in the glandular epithelium and germinal center of a reactive follicle with dual-labeling of CD20 and CD3 demonstrating the B lymphocyte nature of the neoplastic infiltrate. In BCL2 protein labeling, the neoplastic infiltrate is strongly positive with a negative germinal center. The findings are consistent with immunophenotype B non-Hodgkin's lymphoma, better classified as extranodal marginal zone lymphoma (MALT). The patient was treated with chemotherapy and showed complete regression of the disease, as evidenced by colonoscopy performed after treatment.

CONCLUSION

MALT lymphomas in the terminal ileum¹ are extremely rare and only 4 cases have been reported in the literature. Given the low sensitivity and specificity of endoscopic images in these cases, the pathology can be confused with other important differential diagnoses such as inflammatory diseases or infectious diseases, which makes the biopsy, even in asymptomatic patients, with anatomopathological analysis and performing immunohistochemistry, the gold standard for correct diagnosis.

Key Words: MALT lymphoma; ileum; colonoscopy; diagnosis; biopsy

de Figueiredo VLP, Ribeiro IB, de Moura DTH, Oliveira CC, de Moura EGH. MALT Lymphoma in the terminal ileum: A rare case report and review of literature. *World J Gastrointest Endosc* 2021; In press

Core Tip: Mucosal-associated lymphoid tissue lymphoma (MALT) are predominantly found in the stomach. Only a few cases of MALT lymphomas affecting the ileum have been published in the literature and these patients already had clear symptoms and endoscopic findings. We present a rare case of MALT lymphoma in the terminal ileum in an asymptomatic patient who underwent the examination for age screening.

INTRODUCTION

Mucosal-associated lymphoid tissue lymphoma (MALT) is a low-grade B-cell neoplasm of the extranodal marginal zone, characterized by a lymphoid infiltrate in the mucous layer of hollow organs and glandular tissues^[1,2]. The gastrointestinal tract is involved in about 50% of cases^[2,3], with the stomach accounting for 85% of all cases and strongly related to the presence and infection by *Helicobacter pylori*^[1,4]. Other, less usual regions can also be affected, such as salivary glands, lungs (14%), head and neck (15%), ocular attachments (12%) and skin (11%)^[5].

MALT lymphomas in the ileum ¹are extremely rare and few cases have been reported in the literature^[5-9]. In these, all patients already presented with an advanced degree of involvement, with important symptoms and with lesions dispersed throughout the ileocecal region^[5,6].

This is the first reported case of a terminal ileum MALT lymphoma in an asymptomatic patient reported in the literature.

CASE PRESENTATION

Chief complaints

Asymptomatic.

History of present illness

A 57-year-old asymptomatic female patient underwent a colonoscopy exam for screening. The examination revealed an ulcer, of medium depth, with well-defined borders, covered by a thin layer of fibrin and with a halo of hyperemia in the distal ileum portion (Figure 1). Findings are nonspecific but may signal infections by viruses, protozoa, and parasites or inflammatory diseases such as Crohn's disease. Biopsies were taken.

The anatomopathological result revealed an atypical diffuse lymphocytic infiltrate of small cells, with a characteristic cytoplasmic halo of marginal zone cells. The infiltrate presented with nodular and poorly delimited areas, with dissection of collagen fibers and the muscular layer of the mucosa. There was no clear distinction regarding germinal centers. Signs of cellular atypia were also observed, with enlarged nuclei. In the most superficial portion, there was focal erosion, epithelial reactivity, and eosinophilia (above 15 per high-power field) (Figure 2). No granulomas were found and there were no signs of infection by parasitic agents. An immunohistochemical study was requested to investigate lymphoproliferative disease.

The immunohistochemical study was performed by the EnVision FLEX Visualization System kit AGILENT (DAKO) method, which the results demonstrated a

negative neoplastic infiltrate for the expression of cyclin D1 (figure 2B) and cytokeratin AE1/AE3 (figure 2C) and positive for BCL60 in the germinal center (figure 2D). The test also revealed CD10 positivity in the glandular epithelium and germinal center of a reactive follicle (figures 3A and 3B) with dual labeling of CD20 and CD3 demonstrating the B lymphocyte nature of the neoplastic infiltrate. (Figure 3C and 3D) In BCL2 protein labeling, the neoplastic infiltrate is strongly positive with a negative germinal center (Figure 4A and 4B).

History of past illness

Nothing noteworthy.

Personal and family history

Nothing noteworthy.

Physical examination

Without changes.

Laboratory examinations

Without changes.

Imaging examinations

Without changes.

FINAL DIAGNOSIS

The findings are consistent with immunophenotype B non-Hodgkin's lymphoma, better classified as extranodal marginal zone lymphoma (MALT). The identification of lymphoid proliferation with atypical limits, in a nodular and infiltrative pattern with foci of epithelial aggression, was crucial for the diagnosis. Since MALT lymphomas are always negative for BCL6 and CD10 and positive for BCL2 with

a negative germinal center, it was possible to rule out the differential diagnosis of follicular lymphoma.

TREATMENT

The patient was referred to the oncology team and treated with chemotherapy.

OUTCOME AND FOLLOW-UP

Upon completion of treatment, the patient showed complete regression of the disease, as evidenced by colonoscopy performed after treatment (Figure 5)

DISCUSSION

Extranodal marginal zone lymphoma (MALT lymphoma) is characterized by the proliferation of small B lymphocytes^[10]. The stomach is the most common site of involvement, where the main etiology is *H. pylori* infection^[1]. In these cases, the endoscopic findings are varied and involve polyps, ulcerations, erythematous lesions, nodules and other non-specific findings^[11]. Extranodal marginal zone lymphomas that affect the ileum region are extremely rare and only a few cases have been reported in the literature^[5-9]. None of the previous studies showed *H. pylori* infections, so the etiology of the disease remains unknown.

Endoscopic findings of primary small bowel lymphoma can be classified into 5 patterns: mucosal fold thickening; nodular pattern, defined by the presence of nodules and micronodules of variable sizes; infiltrative pattern, where the bowel wall is immobile, not distended by insufflation, and firm over forceps; ulcerative pattern with ulcers of variable sizes and depths, and mosaic pattern^[12].

Among the four cases published in the literature on ileum MALT lymphomas, all presented endoscopic findings with multiple protuberances: Two^[5,7] cases with ulcerations and two^[6,8] cases with smooth mucosa. In one case, the presence of a single mass in the intestine was demonstrated, without erosions in the mucosa^[6].

The treatment of MALT lymphoma is initially made with the eradication of *H. pylori*, in cases of involvement by the bacteria. If there is no concomitant *H. pylori* infection or no tumor remission after *H. pylori* treatment, radiotherapy, chemotherapy, or immunotherapy with anti-CD20 monoclonal antibodies should be considered. Radiotherapy has an excellent prognosis when used in cases where the disease is localized. In the presence of disseminated or more advanced disease, the use of radiotherapy or immunotherapy is indicated. Treatment must be individualized according to the stage of the disease and symptoms, as well as the patient's preference^[13]. Although MALT lymphoma has a favorable prognosis and is responsive to systematic therapy, especially when identified early, when patients are symptomatic, unfortunately they already have a more advanced degree of involvement.

Terada *et al*^[5] reported the case of a 34-year-old patient with abdominal pain and melena, whose colonoscopy revealed multiple nodules and ulcers scattered throughout the ileum. Endoscopic images were suggestive of ileitis, mesenchymal tumor, or lymphoma.

Hasegawa *et al*^[6] described two cases of oligosymptomatic patients, abdominal pain being a common symptom. Colonoscopy in the first case found multiple whitish nodules in the region close to the ileocecal valve, which had a smooth and polished appearance. In the second case, a colonoscopy revealed an ileocecal valve with an enlarged, soft appearance and areas of enanthema.

Makino *et al*^[7] discussed a case of a patient with initial complaints of postprandial epigastric pain. Colonoscopy examination revealed multiple protruding lesions in the terminal ileum with an erosive surface covered by swollen mucosa.

In the report by Ohashi *et al*^[8] colonoscopy identified multiple polyposis lesions in the terminal ileum, with an absence of villi.

In all cases, biopsy with histological evaluation concurrently with immunohistochemical analysis was crucial for the diagnosis of MALT lymphoma.

The uniqueness of the case presented in this study is due to the fact that the patient was asymptomatic and her endoscopic findings had a more discrete and

nonspecific pattern compared to other studies, which makes the diagnosis even more challenging.

CONCLUSION

Given the low sensitivity and specificity of endoscopic images in these cases, the pathology can be confused with other important differential diagnoses such as inflammatory diseases (such as Crohn's disease) or infectious diseases, which makes the biopsy, even in asymptomatic patients, with anatomopathological analysis and performing immunohistochemistry, the gold standard for correct diagnosis^[14].

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