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An unusual finding from fecal immunochemical testing: A case report

Endoscopic and histologic investigations following a positive fecal immunochemical test (FIT) result eventually led to the detection of a rare mucosa-associated lymphoid tissue (MALT) lymphoma.

ABSTRACT: This case report describes the presentation, workup, and management of a 73-year-old patient with multifocal extranodal mucosa-associated lymphoid tissue (MALT) lymphoma. The MALT lymphoma was identified through a process that began with routine fecal immunochemical testing, which is recommended in BC for screening average-risk patients for colorectal cancer. The fecal immunochemical test (FIT) used for screening requires the patient to submit a stool sample collected at home using a simple kit. The sample is then analyzed for the presence of blood. However, because bleeding can occur with benign pathologies such as hemorrhoids, inflammatory bowel disease, and vascular lesions, further investigation is required when certain pathologies are found on colonoscopy done in the colon screening program. In this case, investigation included esophagograstroduodenoscopy and CT imaging. The results from all investigations eventually led to the detection of a rare gastric cancer. Despite the patient being from a part of the world with high rates of endemic *Helicobacter pylori*, the MALT lymphoma identified was not associated with *H. pylori* and was probably related to a systemic inflammatory disorder.

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Case data

A 73-year-old female with average risk of colon cancer presented for routine fecal immunochemical testing. She had been screened in the past with the fecal immunochemical test (FIT). Her medical history was significant for a cerebrovascular accident, dyslipidemia, osteoporosis, and an inflammatory spondyloarthropahy with inflammatory sacroiliitis. Her medications included ASA, alendronate, and naproxen as needed. She was a nonsmoker with no alcohol consumption and had moved to Canada from Hong Kong. She had a second-degree relative diagnosed after age 60 with colorectal cancer.

After having negative FIT results in 2014 and 2015, the patient had a positive FIT result in July 2018 with a value of 171 ng/mL. When assessed prior to colonoscopy, she reported no hematochezia or melena and regular bowel movements with no change in her bowel habits. She had no early satiety, epigastric pain, nausea, or vomiting. Her weight was stable. She had no fevers, chills, or night sweats. Physical examination revealed no abdominal masses or peripheral lymphadenopathy.

Her colonoscopy revealed a 1-cm pedunculated polyp in the ascending colon and two 5-mm semi-pedunculated polyps in the transverse colon. Evidence of mild colitis was found in the rectosigmoid region and tissue was obtained for biopsy **[Figure 1]**. Retroflexion in the rectum revealed only internal hemorrhoids. The ascending colon polyp was a tubulovillous adenoma with low-grade dysplasia. The transverse polyps were a sessile serrated adenoma without dysplasia and a tubular adenoma with low-grade dysplasia.

Histologic sections of the rectosigmoid biopsies revealed an atypical lymphoid infiltrate that had expanded the lamina propria and replaced the glands **[Figure 2]**. Scattered lymphoepithelial lesions were identified. Immunohistochemistry demonstrates an atypical B cell population positive for CD20 and negative for CD3, CD5, CD10, and CD43. A lambda light chain restriction was observed. The findings were consistent with low-grade B cell mucosa-associated lymphoid tissue (MALT) lymphoma.

The patient underwent an esophagograstroduodenoscopy (EGD) that revealed atrophic gastric mucosa in the proximal stomach. Erythema with an abnormal mucosal pattern was seen from the mid-gastric body extending into the antrum, pylorus, and first part of the duodenum **[Figure 3]**. Biopsies of the gastric and duodenal mucosa again showed a clonal population of CD20 lymphocytes with lambda light chain restriction and confirmed the diagnosis

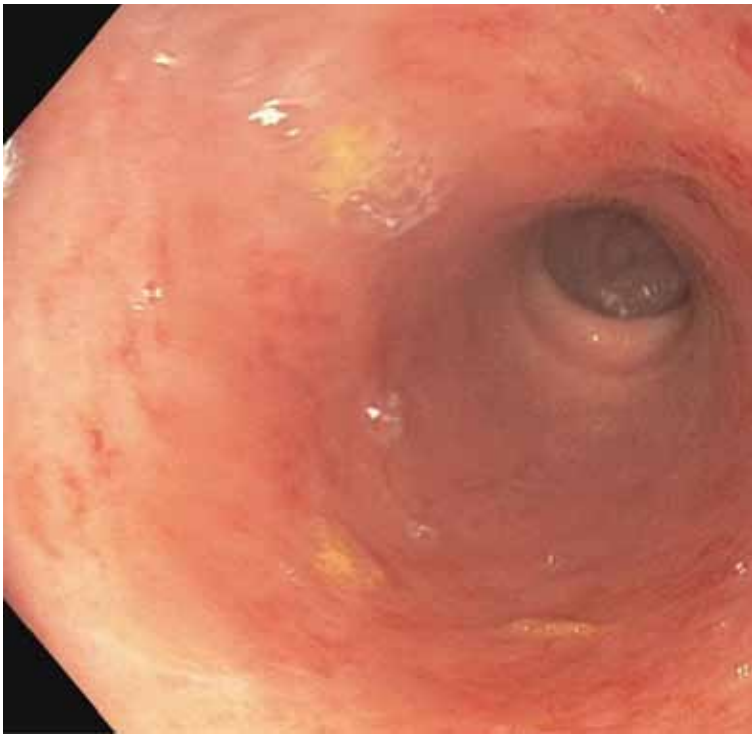

FIGURE 1. Visualization of the rectosigmoid by colonoscopy reveals an abnormal vascular pattern and hyperemia.

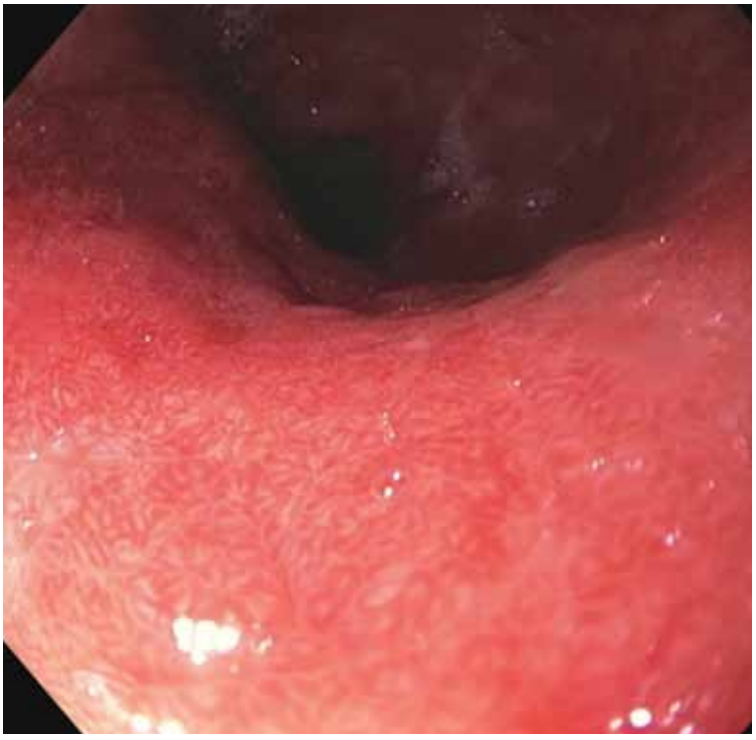

FIGURE 3: Visualization of the antrum by esophagograstroduodenoscopy reveals erythema with an abnormal mucosal pattern.

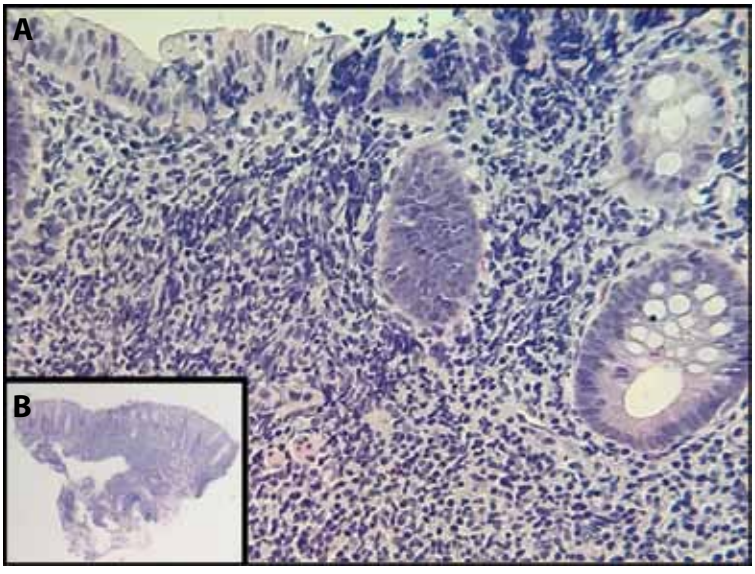

FIGURE 2. Immunohistochemistry findings. **A:** Hematoxylin and eosin staining of biopsied rectosigmoid tissue reveals an atypical polymorphous lymphoid infiltrate that expands the lamina propria and replaces the colonic glands. The majority of the atypical lymphoid cells are intermediate-size with centrocytic nuclei and variably abundant pale cytoplasm. Occasional larger lymphoid cells with vesicular chromatin and distinct nucleoli are also present (original magnification × 200). **B:** Hematoxylin and eosin staining shows that the atypical lymphoid infiltrate extends into the submucosa and is poorly circumscribed (original magnification × 40).

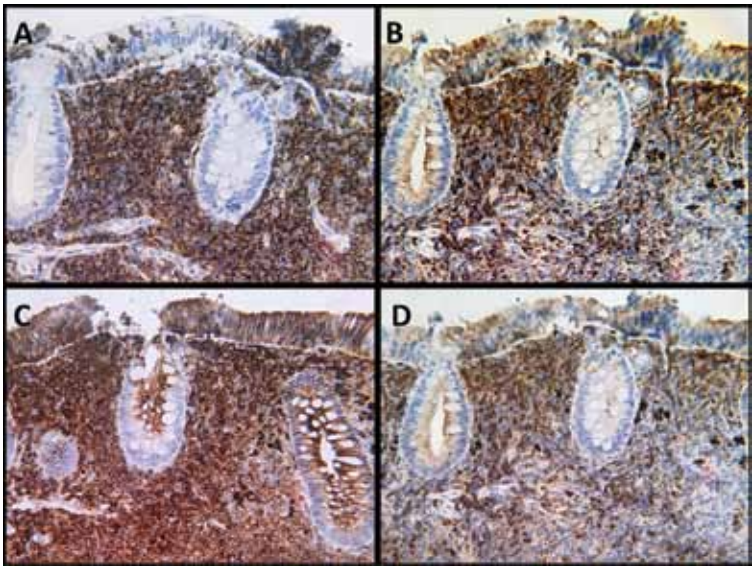

FIGURE 4. Immunohistochemistry findings. **A**: CD20 staining reveals a clonal B cell population in the deep lamina propria (see bottom right corner) and atypical lymphoid cells that are positive for CD20 (original magnification × 200). **B:** CD3 staining reveals scattered background reactive T cells (original magnification × 200). **C:** Lambda light chain immunohistochemistry shows lesional cells that exhibit monotypic reactivity for immunoglobulin (original magnification × 200). **D:** Kappa light chain immunohistochemistry highlights a few non-neoplastic plasma cells (original magnification × 200).

of extranodal marginal zone MALT lymphoma **[Figure 4]**.

Other investigations revealed the patient's hemoglobin level was 117 g/L, her WBC was 3.5 x 10^9/L, and her platelet count was 163 x 10^9/L. The patient was also found to have a lactate dehydrogenase (LDH) level of 187 IU/L, creatinine of 74 µmol/L, and beta-2 microglobulin of 2.4 mcg/mL. Her serum protein electrophoresis showed a monocloncal IgM lambda band in the beta 2 region. *Helicobacter pylori*, bacteria endemic in the patient's area of origin and typically associated with this lymphoma, were not identified by biopsy or by a urea breath test. A bone marrow biopsy showed no bone involvement. A CT scan showed abnormal wall thickening in the gastric antrum, proximal duodenum, and lower rectum **[Figure 5]**. There were prominent subcentimetre lymph nodes near the stomach and rectosigmoid.

The patient was followed by her oncologist and a repeat EGD and colonoscopy were done at 6 months and found to show no endoscopic or histologic changes. Currently the patient remains on an active surveillance schedule and is receiving no therapy as she is asymptomatic and has a good performance status.

Discussion

Extranodal mucosa-associated lymphoid tissue lymphomas are induced by chronic inflammation,[1] with MALT lymphoma being the most common of marginal zone B cell lymphomas.[2] The prototypical infection for MALT involvement of the stomach is *H. pylori*. A study published in 2010 found the incidence of *H. pylori*-associated MALT lymphoma has declined[3] compared with an earlier study that found *H. pylori* infection in 92% of all gastric MALT lymphomas considered.[4]

US data indicate that extranodal marginal zone lymphoma is rare, with 18.3 cases per 1 million person years, and that the median age at diagnosis is 66 years.[5] The stomach is the most frequent site of involvement, but MALT can also involve the colon, salivary glands, ocular adenexa, lungs, thyroid, breast, and liver.[6] Symptoms can include reflux, epigastric pain, anorexia, weight loss, and gastrointestinal bleeding.[7] Monoclonal gammopathy is found in 27% to 36% of patients.[8]

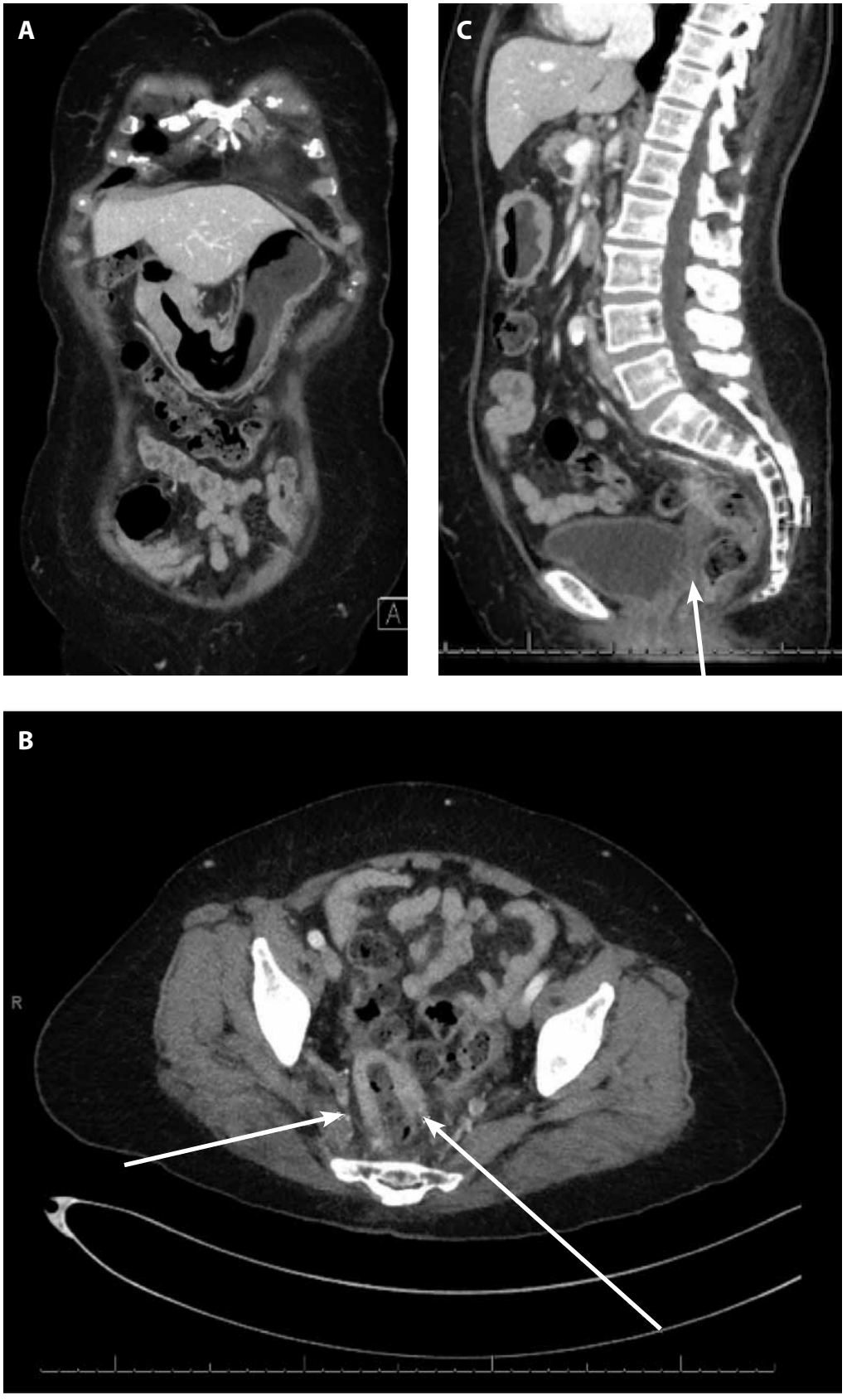

FIGURE 5. CT findings. **A:** Coronal view shows diffuse thickening of the gastric antrum. **B:** Transverse view shows thickening of the rectosigmoid (arrows). **C:** Sagittal view shows fat stranding (arrow) associated with colonic involvement.

This case is interesting because the diagnosis was made with the help of the BC Cancer Colon Screening Program, which identifies those at risk of colon cancer using the FIT—a simple test that requires patients to provide a stool sample for analysis. If blood is detected, follow-up procedures are ordered. This case is also interesting because the patient had multifocal disease with involvement of the stomach, small bowel, and rectosigmoid, yet had no evidence of *H. pylori* infection. Besides *H. pylori* infection, autoimmune diseases such as systemic lupus erythematous, Sjögren's syndrome, Hashimoto disease, and relapsing polychondritis have been associated with MALT.[1,9,10] This patient had inflammatory spondyloarthropahy with inflammatory sacroiliitis. The mechanism postulated in cases such as this is that chronic inflammation leads to the local accumulation and proliferation of antigen-dependent B cells and T cells. B cell clones will remain that still depend on the antigen-stimulated immune response for growth and survival. With acquisition of additional mutations, the tumor becomes antigen-independent and capable of systemic spread.[11]

Historically, the Lugano staging system was used for gastrointestinal lymphomas, but models such as the Paris Staging System[12] can also be used. This patient was designated stage IV as she had disseminated extranodal involvement in multiple areas of the gastrointestinal tract.

In *H. pylori*-associated cases, bacteria eradication therapy should be prescribed regardless of disease stage.[1,12] Eradiation of the bacteria should then be documented with a breath test.[13] The decision to use rituximab, chemotherapy, or radiation is dependent on symptoms and disease distribution.[12] Long-term follow-up with physical examinations, blood testing (including a CBC), cross-sectional imaging, and endoscopy should be implemented to monitor for progression and transformation.[12]

Summary

In the case described here a 73-year-old female was diagnosed with mucosa-associated lymphoid tissue lymphoma after a process that began with routine fecal immunochemical testing. A positive FIT result led to the patient undergoing colonoscopy, esophogastrodenoscopy, blood testing, and CT imaging. Although the patient was not found to have *H. pylori*-associated disease, she did have inflammatory spondyloarthropahy with inflammatory sacroiliitis. Her systemic inflammatory disorder may have been a factor in her MALT diagnosis, since extranodal mucosa-associated lymphoid tissue lymphomas are known to be induced by chronic inflammation.

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The stomach is the most common site affected, but MALT lymphoma can also involve the colon, salivary glands, ocular adenexa, lungs, thyroid, breast, and liver. Symptoms may include reflux, epigastric pain, anorexia, weight loss, and gastrointestinal bleeding. Once identified, treatment of MALT lymphoma may include *H. pylori*-eradication therapy, chemotherapy, or radiation. In this case, the patient is currently asymptomatic and remains on an active surveillance schedule without therapy. The patient was referred for a radiation oncology opinion for symptom management or to delay the need for systemic therapy. She was offered radiation to the gastric lesion, but declined treatment due to lack of symptoms and concern around the side effects of radiation. ■

Competing interests

None declared.

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