Functional asplenia and microscopic (collagenous) colitis

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Asplénie sans anomalie organique et colite microscopique (collagénique)

BRIEF COMMUNICATION

HJ FREEMAN. Functional asplenia and microscopic (collagenous) colitis. Can J Gastroenterol 1996;10(7):443-446. A 54-year-old female presented with a pulmonary infection that resolved completely with antibiotic treatment. Peripheral blood films showed features characteristic of splenic hypofunction, and radiolabelling studies confirmed an absence of splenic reticuloendothelial cell activity, which is typical of functional asplenia. The patient had a remote history of watery diarrheas but no clinical and laboratory features of malabsorption. Extensive upper and lower gastrointestinal tract biopsy studies revealed histopathological features of collagenous colitis without gastric or small intestinal inflammatory changes or epithelial lymphocytosis. Hyposplenism has been associated with different gastrointestinal disorders, particularly celiac disease. This is the first report of functional asplenia and microscopic collagenous colitis.

Key Words: Celiac disease, Collagenous colitis, Functional asplenia, Hyposplenism, Malabsorption syndrome, Microscopic colitis, Watery diarrhea syndrome

I mpaired splenic function has frequently been recognized in several clinical disorders (1), including diseases causing malabsorption, such as celiac disease (2-5), as well as tropical sprue (6), Whipple's disease (7) and intestinal lymphangiectasia (8). Hyposplenism has been associated with other chronic diarrheal disorders, usually involving the large intestine, including both ulcerative colitis and Crohn's disease (9-11). In some patients hyposplenism has been associated with more widespread atrophy of the lymphoreticular system in celiac disease (12). In others it has been linked to some rare disorders associated with celiac disease, including cavitation necrosis of mesenteric lymph nodes (13,14) and lymphoma-associated necrosis of hepatic, splenic and lymph node tissues (15). Collagenous colitis was initially reported in 1976 in two patients, one with celiac disease (16,17). It is an unusual, but increasingly recognized, colonic mucosal inflammatory disease process usually occurring in middle-aged to elderly females with a watery diarrhea syndrome. Colorectal biopsies typically reveal subepithelial collagen-containing deposits in the lamina propria. Some pathologists have classified collagenous colitis and lymphocytic colitis as types of microscopic colitis (18), and both occasionally may be associated with celiac disease (19-22).

In the patient reported here, presentation with a pulmonary infection led to detection of hyposplenism. Because of the frequent association of hyposplenism with specific gas-
CASE PRESENTATION

A 54-year-old female presented with malaise, anorexia, cough, fever and chest pain for two days. Although physical examination was normal, the normal hemoglobin value of 140 g/L appeared with a mild leukocytosis of 12,200/mm$^3$ and chest radiograph revealed a left lower lobe pneumonic infiltrate. Ampicillin was given and the symptoms resolved.

Follow-up radiographs of her chest confirmed resolution of the pulmonary infiltrate.

During the initial evaluation hemogram (hemoglobin, red blood cell indexes, white blood cell count and differential, and platelet count) was normal but peripheral blood smear revealed irregular contracted cells with Howell-Jolly bodies and large platelets, typical of hyposplenism (Figure 1). An abdominal ultrasound showed a small spleen, estimated to be 8 cm. A liver-spleen scan with radiotagged technetium ($^{99m}$Tc) sulphur colloid (Figure 2) showed hepatic extraction of the radiopharmaceutical but no splenic activity. SPECT imaging demonstrated an absence of functioning splenic tissue, consistent with functional asplenia. Because of the latter findings and her presentation with a respiratory tract infection, she was administered polyvalent pneumococcal vaccine.

Additional history revealed no prior abdominal trauma, skin rash or other symptoms suggestive of a collagen vascular disease (23), hematological disorder, coagulopathy (24-26) or prior surgery. There was a remote history of intermittent
watery, nonbloody diarrhea during the previous two decades but this was never severe enough that the patient sought medical assessment or used antidiarrheal medications.

Other laboratory investigations were normal including urea nitrogen, red blood cell folate, serum creatinine, alkaline phosphatase, glucose, aspartate aminotransferase, alanine aminotransferase, electrolytes, carotene, calcium, total proteins, albumin, immunoglobulins, thyroid-stimulating hormone, free thyroxine, cortisol, vitamin B₁₂, iron and iron binding capacity. Antinuclear antibodies, antineutrophilic cytoplasmic antibodies and rheumatoid factor were negative. Urinalysis was normal.

Because of the reported association between celiac disease and inflammatory bowel disease, fibroptic endoscopic biopsies of the stomach, and the small and large bowel were done. Colonic biopsies showed characteristic features of collagenous colitis (Figures 3,4) (16,17). Gastric biopsies were normal, without epithelial lymphocytosis or collagen deposits (27, 28). Multiple small intestinal biopsies from different sites in the proximal small intestine were also normal. Amyloid stains were negative (29).

**DISCUSSION**

This is the first description of functional asplenia associated with microscopic (collagenous) colitis. While this observation may only reflect the presence of two separate and uncommon conditions in the same patient, the frequent association of both conditions with celiac disease and the occasional reports of hyposplenism in other forms of chronic inflammatory bowel disease (ie, ulcerative colitis, Crohn’s disease) (9-11) suggest that the two conditions are more directly related and that a more generalized – possibly immunologically related disorder – exists in the present patient.

At least three lines of evidence indicated that the patient’s splenic function was significantly impaired. First, the splenic reticuloendothelial cells normally remove particulate matter and abnormal elements from the circulation, including damaged or abnormally shaped structures and antibody-coated cells. In disorders such as celiac disease, physiological or functional impairment of these splenic cells may occur. This often results in a bizarre blood smear containing red blood cells with whole nuclei, nuclear fragments (Howell-Jolly bodies), precipitated hemoglobin masses (Heinz bodies) and pitted or distorted cell membranes, as occurred in our patient. Second, ⁹⁹ᵐTc, a radiopharmaceutical agent normally removed from the circulation by reticuloendothelial cells, may be detected by abdominal scanning over the liver and spleen. In our patient, hepatic, but not splenic, uptake was seen. Finally, clinical evidence of impaired splenic function may result in susceptibility to bacterial infections, particularly pneumococcal infections. Initial presentation in our patient was due to clinical features of pneumonia. Although a reduction in splenic reticuloendothelial cells may be present, a qualitative reduction in phagocytic function may also develop. Although the mechanisms involved in or responsible for this functional impairment, such as in celiac disease or ulcerative colitis, are very poorly understood, significant enteric loss of lymphocytes (30) and raised levels of circulating immune complexes (31) have been hypothesized to contribute to the splenic hypofunction that appears to be very isolated, rather than a reflection of a more generalized abnormality in lymphoreticular function (32).

**CONCLUSIONS**

The frequency of hyposplenism in patients with collagenous colitis is unknown but needs to be explored. Failure to recognize this association may reflect, in part, the limited sensitivity of the peripheral blood film for general assessment of splenic function, particularly splenic reticuloendothelial function. Other researchers, particularly those studying celiac disease patients, have used the clearance of isotopically labelled heat-damaged red blood cells (3) or differential interference contrast microscopy to detect pits and craters in the erythrocyte membrane (33). In a previous report on elderly celiac patients (4), for example, a review of peripheral blood films led to the recognition of hyposplenism in 13%. In contrast, studies using the clearance of isotopically labelled red blood cells or pitted red blood cell counts have shown that up to 75% of patients with celiac disease may have hyposplenism (5,34). Therefore, it can be predicted that the frequency of hyposplenism in different colonic inflammatory bowel disorders, such as collagenous colitis, is much greater than is appreciated.

The potential clinical significance of this association may be more than academic, particularly for the typically elderly individual with collagenous colitis, especially if this predisposes to a serious bacterial infection. Additional studies, possibly using more sensitive methods for the evaluation of splenic function, are needed in patients with microscopic forms of colitis.