

Simultaneous Gastrointestinal Infections in Children and Adolescents

Martin D. Fried, Martin E. Adelson and Eli Mordechai

Simultaneous infections were detected in the gastrointestinal tract of children and adolescents presenting with gastritis, duodenitis and/or colitis. Eighty-one consecutive patients presented with gastrointestinal complaints including abdominal pain (52/81), blood in the stool (16/81), gastroesophageal reflux (4/81), Celiac disease (3/81), Crohn's disease (3/81), duodenal ulcer, (2/81) and failure to thrive (1/81). Endoscopy confirmed the diagnoses of celiac disease and Crohn's disease, and assessed the gastrointestinal mucosa for inflammation. Biopsies were analyzed for *Borrelia burgdorferi*, *Bartonella* spp, *Mycoplasma fermentans*, and *Helicobacter pylori*. Pathogens were either absent (n = 26, 33%) or were detected as single (n = 30, 37%), double (n = 19, 24%), or triple infections (n = 6, 8%) associated with gastritis and duodenitis or colitis at the site of the biopsy.

INTRODUCTION

Gastrointestinal infections may present as abdominal pain, blood in the stool, and reflux or heartburn (1,2). The presence of multiple infections in the gastrointestinal tract may confound the clinical presentation. In a study completed at Jersey Shore University Medical Center, eighty-one consecutive pediatric patients (aged 8–21) were examined for infections associated with abdominal pain, reflux, heartburn and/or blood in the stool.

MATERIALS AND METHODS

All patients included in this study, were referred by their pediatricians to the Division of Pediatric Gastroenterol-

ogy and Nutrition at the Jersey Shore University Medical Center from January 2001 through April 2003 for evaluation of chronic abdominal pain, blood in the stool, gastroesophageal reflux with heartburn, Celiac disease, Crohn's disease and/or failure to thrive. Each evaluation included a history, physical examination, blood cell count, and a comprehensive metabolic panel including liver function tests, serum IgG and IgM titers for *Borrelia burgdorferi*, *Bartonella henselae*, and *Mycoplasma fermentans* (Quest and Labcorp). Eighty-one consecutive patients received esophagogastroduodenoscopy (EGD) or colonoscopy for diagnosis and were also tested for *Borrelia burgdorferi*, *Bartonella* spp., and *Mycoplasma fermentans* by polymerase chain reaction testing (PCR) (Medical Diagnostic Laboratories, Mt Laurel, New Jersey) and for *Helicobacter pylori* by light microscopy. The PCR procedures were used to detect the *B. burgdorferi* outer surface protein A (Osp A) and chromosomal Lyl gene, the *Bartonella* spp. and *Mycoplasma fermentans* 16S ribosomal RNA genes

Martin D. Fried, Division of Pediatric Gastroenterology and Nutrition, Jersey Shore University Medical Center, Neptune, NJ. Martin E. Adelson and Eli Mordechai, Medical Diagnostic Laboratories, Mount Laurel, NJ.

A SPECIAL ARTICLE

were performed as previously described (4,13). Completed reactions were electrophoresed through a 2% agarose gel containing 0.5 mg/mL ethidium bromide and were photographed with a Multi Genius BioImaging System (Syngene). A positive IgG Western blot contained the presence of 5 or more of the following *Borrelia burgdorferi* bands: 18, 23, 28, 31, 34, 39, 41, 45, 58, 66, and 93 kDa in accordance with the surveillance case definition of *B. burgdorferi* infection by the Centers for Disease Control and Prevention/Dearborn Criteria (3). Ultrasonography of the abdomen was performed when the history suggested a diagnosis of biliary tract disease, gallstones, or pancreatitis. CAT scan of the abdomen and pelvis was performed for suspected cases of appendicitis and mesenteric adenitis. Stool samples were examined for *Clostridium difficile* toxins A and B, and also for occult blood, *Salmonella*, *Shigella*, *Yersinia*, *Campylobacter*, *E. coli*, ova and parasites including giardia by ELISA antigen testing. Biopsy specimens were taken from areas of the gastrointestinal (GI) tract that appeared inflamed during EGD or colonoscopy testing. Biopsies were reported as acutely inflamed when polymorphonuclear cells were present in the mucosa and chronically inflamed if plasma cells and lymphocytes were present in the mucosa without polymorphonuclear cells in conjunction with a distortion of glandular architecture.

RESULTS

PCR testing of gastrointestinal biopsies from the stomach, duodenum and/or colon detected no infection in 26 of 81 patients (33%). Thirty of 81 (37%) had a positive GI biopsy PCR for a single pathogen infection, while 19 of 81 (24%) and 6 of 81 (8%) had PCR biopsies positive for two or three concurrent gastrointestinal infections, respectively. Of the thirty patients with a single infection, *Bartonella* spp (12), *H. pylori* (9), *M. fermentans* (6) and *B. burgdorferi* (3) were detected in decreasing frequencies of occurrence. Of the nineteen coinfections, *Bartonella* spp. and *M. fermentans* (10), *Bartonella* spp. and *B. burgdorferi* (6), and *B. burgdorferi* and *M. fermentans* (2) were documented in the gastrointestinal biopsies and associated with localized inflammation. Of the gastrointestinal biopsies with triple infections, *Bartonella* spp, *H. pylori* and *M. fermentans* were simultaneously detected in

four specimens, while *Bartonella* spp., *M. fermentans* and *B. burgdorferi* were simultaneously detected in two specimens. Overall, of 81 patients evaluated, 35 had a *Bartonella* spp infection, 24 had a *M. fermentans* infection, 14 had a *H. pylori* infection, and 13 had a *B. burgdorferi* infection. For the other testing performed, IgG and IgM *Bartonella* serology tests were negative. Stool analyses did not yield detectable infections. Ultrasonographies were not remarkable for gallstones, pancreatitis, or biliary tract disease.

DISCUSSION

Bartonella spp. were the most common pathogen detected in our patient population reporting abdominal pain. Previous pediatric reports have associated one of the members of the *Bartonella* genus, *Bartonella henselae*, with a vasculitis rash, abdominal pain, heartburn, gastritis and duodenitis (5). *B. henselae* has also been associated with cat scratch fever, lymphadenopathy, splenitis, and fevers of unknown origin. Only 5% of patients with cat scratch disease exhibit skin rashes. When present, the rash may present as violaceous in color and is associated with new blood vessel formation. Described as neovascularization, this rash may be observed near the armpits, on the breasts, buttocks, inner thighs, back of the knee, groin, and/or gluteal area. Neovascularization resembles the stretch marks, or striae distensae, seen in those patients who are obese, on steroid medications, or who gain weight rapidly. *Bartonella*-induced rashes differ from striae distensae, however, by exhibiting hard nodularity and persistence, which does not fade over time. Other rashes associated with *Bartonella* infections include erythema nodosum, thrombocytopenia purpura, erythema annulaire, and granulomatous skin lesions. The GI biopsies showed chronic inflammation with the presence of lymphocytes and plasma cells. Interleukins 2, 6, and 10, which are elicited by *Bartonella* infections, may account for the chronic inflammation. Interleukin-6, a multipotent cytokine, is associated with the formation of new blood vessels and may account for the observed neovascularization.

Borrelia burgdorferi has been shown to be associated with gastritis, duodenitis, and colitis in children. *B. burgdorferi* infections have also been detected in

children and were observed in the GI tract by Diertele stain of the spirochetes in the stomach, duodenum, and colon and by PCR of gastrointestinal biopsies (6-8). *Helicobacter pylori* is a known irritant to the stomach lining that predisposes individuals to gastric and duodenal ulcers. In pediatrics, abdominal pain, vomiting, and hematemesis are the most frequent presentations of *H. pylori* infection. In symptomatic patients, gastric biopsies are often inflamed due to *H. pylori*, and these organisms can be directly visualized by microscopy in the crypts and at the apex of affected tissue. Successful eradication of the organism requires two antibiotics for at least two weeks with concurrent use of a proton pump inhibitor medication (9).

Intracellular *Mycoplasma* infections are rarely detected in the blood. Due to their low abundance, *Mycoplasma* infections have been demonstrated to worsen the symptoms of other infections such as *Bartonella* and Lyme Disease and have also been associated with Chronic Fatigue Syndrome, rheumatoid arthritis, and Gulf War Syndrome (10,11). *Mycoplasma fermentans* stimulates proinflammatory cytokines Interleukin 1 and Interleukin 6 and tumor necrosis factor alpha which explains the inflammation associated with this infection. The chronicity of *Mycoplasma* infections may be attributed to the organism's surface antigenic variation, inability to suppress the host cell's immune response, intracellular localization, and slow growth rate.

CONCLUSION

Bartonella spp, *Borrelia burgdorferi*, *Helicobacter pylori*, and *Mycoplasma fermentans* were detected as single or multiple infections in the gastrointestinal tract of symptomatic patients. The association of these human pathogens with chronic gastritis, duodenitis and/or colitis warrants further evaluation. When gastrointestinal coinfections occur, the clinical presentation may include overlapping symptoms contributed by each infecting organism and the clinician

should consider the presence of all possible gastrointestinal pathogens and their possible relation to the endoscopic and biopsy findings and the formation of gastritis, duodenitis and ulcer disease before treating the patient (12). ■

References

1. Frank F, Stricker T, Stallmach T, Braegger P. *Helicobacter pylori* infection in recurrent abdominal pain. *J Pediatric Gastroenterol Nutr*. 2000; 31(4): 424-427.
2. Spencer MJ, Millet VE, Garcia LS, Rhee L, Masterson L. Parasitic infections in a pediatric population. *Pediatric Infectious Disease*. 1983; 2(2): 110-113.
3. CDC. Recommendation for test performance and interpretation from the 2nd National Conference on Serology, Diagnosis of Lyme Disease. *Mortality, Morbidity Weekly Report*. 1995; 44:590-591.
4. Eskow E, Rao RV, Mordechai E. Concurrent infection of the central nervous system by *Borrelia burgdorferi* and *Bartonella henselae*, evidence for a novel tick-borne disease complex. *Arch Neurol*. 2001; 58: 1357-1363.
5. Fried MD, Schairer J, Madigan G, Ball A. *Bartonella henselae* is associated with heartburn, abdominal pain, skin rash, mesenteric adenitis, gastritis and duodenitis. *J Pediatr Gastroenterol Nutr*. 2002; 35:3 Abstract 158.
6. Fried MD, Duray P, Pietrucha D. Gastrointestinal Pathology in children with Lyme Disease. *J Spirochetel and Tick-Borne Diseases*. 1996; 3:101-104.
7. Fried MD, Abel M, Pietrucha D, Yen-Hong K, Ball A. The spectrum of gastrointestinal manifestations in children and adolescents with Lyme disease. *J Spirochetel and Tick-Borne Diseases*. 1999; 6: 89-93.
8. Fried MD, Pietrucha D, Madigan G, Ball A. *Borrelia burgdorferi* persists in the gastrointestinal tract of children and adolescents with Lyme Disease. *J Spirochetel and Tick-Borne Diseases*. 2002; 9: 11-15.
9. Sherman P, Hassall E, Hunt RH, Fallone CA, Veldhuyzen Van Zanten S, Thomson AB. Canadian *Helicobacter* study group consensus conference on the approach to *Helicobacter pylori* infection in children and adolescents. *Can J Gastroenterol*. 1999; 13:553-559.
10. Nicolson GL, Berns P, Nasralla M, Haier J, Nicolson NL, Nass M. Gulf war illnesses: Chemical, biological and radiological exposures resulting in chronic fatigue illnesses can be identified and treated. *J Chronic Fatigue Syndr*. 2003; 11(1):135-154.
11. Nicolson GL, Nasralla M, Nicolson NL, Haier J. High prevalence of Mycoplasmal infections in symptomatic chronic fatigue syndrome family members of mycoplasma-positive gulf war illness patients. *J Chronic Fatigue Syndr*. 2003; 11(2):21-36.
12. Carpenter HA, Talley NJ. Gastroscopy is incomplete without biopsy. Clinical relevance of distinguishing gastropathy from gastritis. *Gastroenterology*. 1995; 108: 917-924.
13. Eskow E, Adelson ME, Rao RV, Mordechai E. Evidence for disseminated *Mycoplasma fermentans* in New Jersey Residents with Antecedent Tick Attachment and Subsequent Musculoskeletal Symptoms. *J Clin Rheumat*. 2003; 9: 77-87.

VISIT OUR WEB SITE AT
WWW.PRACTICALGASTRO.COM