

Yersinia Enterocolitis Mimicking Crohn's Disease in a Toddler

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ABSTRACT. A 3½-year-old girl presented with persistent abdominal pain, fever, vomiting, and diarrhea accompanied by rash, oral ulceration, anemia, and an elevated sedimentation rate. Initial evaluation revealed no pathogens and was extended to include abdominal ultrasound and computed tomography showing marked ileocecal edema and mesenteric adenopathy. Colonoscopy revealed focal ulceration from rectum to cecum with histology of severe active colitis with mild chronic changes. Enteroclysis demonstrated a nodular, edematous terminal ileum. Because of the patient's clinical deterioration despite antibiotics, these features were construed consistent with Crohn's disease, and glucocorticoid therapy was begun. By the ninth hospital day, admission cultures grew *Yersinia enterocolitica*, and trimethoprim/sulfamethoxazole was begun followed by prompt clinical improvement. The delay in diagnosis afforded an unusually comprehensive clinical description of the presentation and diagnosis of *Yersinia enterocolitica* in childhood. *Pediatrics* 1999;104(3). URL: <http://www.pediatrics.org/cgi/content/full/104/3/e36>; *Yersinia enterocolitica*, Crohn's disease, child, radiology, colonoscopy.

ABBREVIATION. CT, computed tomography.

Yersinia enterocolitica is a well known cause of acute bacterial enteritis. Outbreaks have been reported as a result of contaminated milk, water, and animal products (particularly pork). Acute infection is characterized by high fevers, diarrhea, and vomiting. It is seen frequently in infants and young children who can present with severe, often life-threatening symptoms. *Yersinia enterocolitica* may resemble other gastrointestinal ailments including inflammatory bowel disease and appendicitis, thus leading to delay in diagnosis and appropriate therapy. We describe a patient whose presentation of severe inflammatory bowel disease with initially negative stool cultures prompted extensive diagnostic studies and intervention. This case demonstrates the clinical, radiographic, and histologic manifestations of severe *Yersinia enterocolitica* and provides an opportunity to discuss clues to diagnosis.

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CASE REPORT

A previously healthy biracial (black and white) female toddler presented in January 1998 with a 1-week history of severe abdominal pain, tenderness, nonbloody vomiting and diarrhea, and daily fevers up to 41°C followed by an erythematous exanthem resembling erythema multiforme. The onset of these symptoms was preceded by the appearance of a sublingual oral ulcer. Forty-eight hours after the onset of her illness, she was treated by her pediatrician with benzathine penicillin G for a positive rapid group A *Streptococcus* latex agglutination pharyngeal swab without improvement. A barium enema ordered by a surgeon to exclude appendicitis or intussusception was normal before admission.

Medical history revealed a developmentally normal 3½-year-old girl who was reportedly healthy but considered small for age. She weighed 2.67 kg at 37 weeks gestation after a normal spontaneous vaginal delivery. She had a history of a ventricular septal defect that had closed spontaneously in the first year of life. There was no history of sickle cell disease or trait, past transfusion, sick contacts, animal exposure, recent travel, or immunocompromise. Family history revealed Crohn's disease in a maternal aunt as well as irritable bowel syndrome in the mother. She had the recent history of ingestion of a bite of raw hamburger.

Physical examination revealed a small, ill-appearing, dehydrated child. Temperature was 39.8°C, respiratory rate 38 breaths per minute, heart rate 132 beats per minute, and blood pressure 97/66 mm Hg. Her height of 90 cm and weight of 10.7 kg both were below the fifth percentile for age. Her weight was 82% of ideal body weight for height, and her height was 83% of expected for age. A small yellow sublingual erosion measured 2.0 mm in diameter. Funduscopic examination was normal, and there was no conjunctivitis. Lung and heart examinations were normal. Her abdomen was distended moderately and diffusely tender with diminished bowel sounds. She had no hepatosplenomegaly, masses, rebound tenderness, or guarding. Rectal and perianal examinations were normal. Skin examination revealed a violaceous reticular rash over her entire body including trunk, face, palms, and soles, resembling erythema multiforme, although no target lesions were present.

Laboratory findings included an initial erythrocyte sedimentation rate of 92 mm/hour peaking at 103 mm/hour by her sixth hospital day; C-reactive protein of 13 mg/dL; hematocrit of 30% dropping to 20%; and white blood cell count of 13 000/μL with 0% bands, 83% neutrophils, 13% lymphocytes, and 4% monocytes. Serum albumin was 3.0 g/dL, potassium 2.5 mmol/L, and she had a normal blood urea nitrogen and urinalysis. Purified protein derivative for tuberculosis was negative. Stool cultures were negative for *Escherichia coli* O157:H7, *Salmonella*, *Shigella*, and *Campylobacter*. *Yersinia* cultures on selective media were pending. Serology for *Entamoeba histolytica* was negative. Stool enzyme-linked immunosorbent assay for Shiga-like toxins was negative. Stool examinations for ova and parasites were repeatedly negative.

Total parenteral nutrition and fluid support were initiated while diagnostic studies were performed. Abdominal ultrasound showed markedly enlarged lymph nodes in the right lower quadrant and a thickened gallbladder wall. Computed tomography (CT) of the abdomen (Fig 1) confirmed the mesenteric lymphadenopathy and revealed thickened bowel wall without abscess or mass. Colonoscopy (Fig 2) demonstrated a regular array of light yellow oval aphthae (round 2- to 3-mm erosions) from rectum to cecum. Although there were no pseudomembranes, these findings, in conjunction with the history of bicillin therapy, raised the suspicion of *Clostridium difficile* colitis and prompted early initiation of metronidazole therapy. Subsequently, assays for *C difficile*

Fig 1. CT image demonstrates mesenteric lymphadenopathy (solid arrow) and the thickened bowel wall (open arrow).

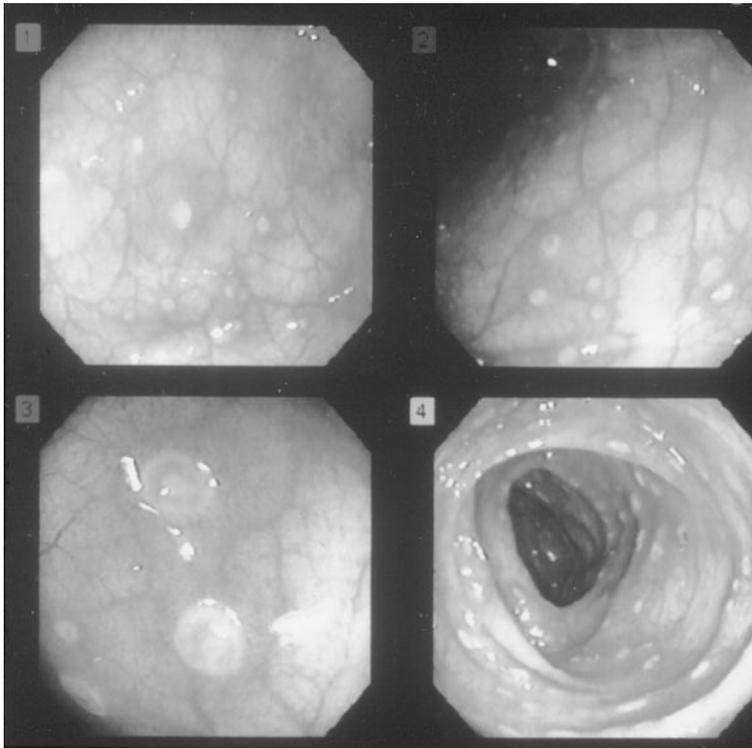
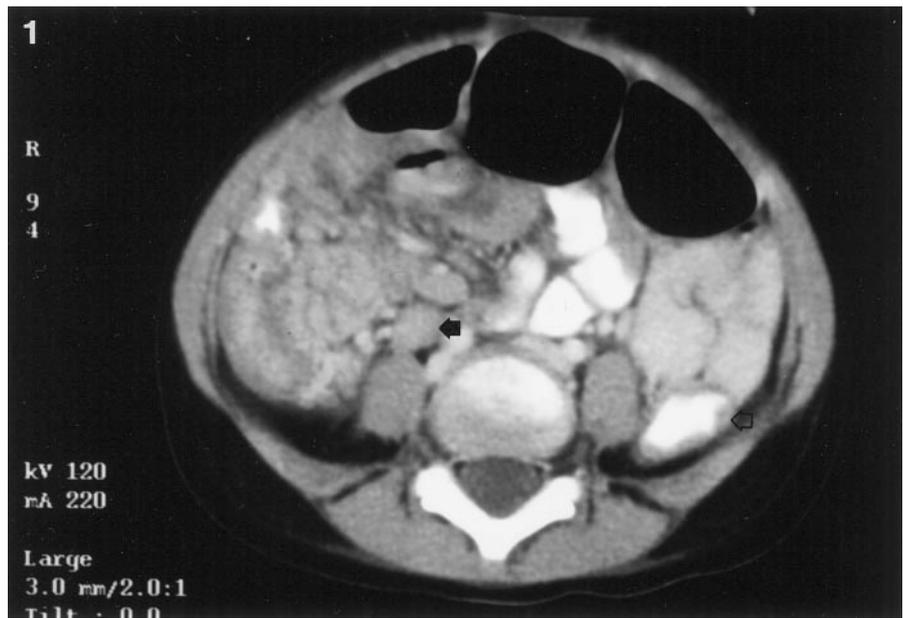


Fig 2. Colonoscopic photographs at various locations throughout the colon reveal multiple mucosal aphthae.

toxin A by enzyme-linked immunoadsorbent assay and cytotoxin B were negative. Histologic studies from colonoscopic biopsies revealed severe active colitis with cryptitis, crypt abscesses, and acute ulceration. In addition, there were the chronic features of mild crypt distortion with abnormal budding of the crypts. Intravenous piperacillin-tazobactam was added after 3 days for concern of evolving peritonitis and deteriorating clinical course. After no significant clinical improvement ensued, an enteroclysis demonstrated a nodular, edematous terminal ileum that was consistent with Crohn's disease. A slit-lamp examination of the eyes was normal. Intravenous methylprednisolone (2 mg/kg) was added on hospital day 4. Shortly after beginning the methylprednisolone, she developed bloody diarrhea and leukocytosis to 25 000 per μ L. She also began to complain of joint tenderness at her knees, ankles, and wrists on palpation as well as with movement, although no

joint erythema, edema, or warmth could be detected. She had gradual reduction in abdominal pain and bloody stools, return of appetite, and a drop in erythrocyte sedimentation rate to 40 mm/hour.

On the ninth hospital day, stool cultures on cefsulodin-irgasanovobiocin (CIN) agar (Becton-Dickinson) became positive for *Y enterocolitica* with serology revealing serotype O:8. The metronidazole and piperacillin-tazobactam were discontinued, steroids tapered, and trimethoprim/sulfamethoxazole initiated for a 14-day course. Clinical improvement was seen within 48 hours, and the patient was discharged from the hospital. Both the 1-month and 8-month follow-up encounters confirmed that she remained asymptomatic, and her 1-month follow-up stool culture was negative for *Yersinia*. Her weight had improved to 12.3 kg (88% of expected weight for height).

DISCUSSION

Our patient underwent extensive diagnostic evaluation because of the severity of her presentation and delayed diagnosis of *Yersinia* infection because of slow growth in stool culture. The delay in diagnosis led us to compile an unusually comprehensive view of the radiologic, colonoscopic, and histologic manifestations of *Yersinia* enterocolitis. The presentation and clinical studies supported a differential diagnosis of: *C difficile* enterocolitis, Crohn's disease, appendicitis, lymphoma, as well as infectious mesenteric adenitis caused by *Y enterocolitica*, *Y pseudotuberculosis*, and *Mycobacterium tuberculosis*. Abdominal ultrasound evidence of striking mesenteric adenopathy and thickened loops of bowel was confirmed by abdominal CT. Colonoscopy and biopsy histology supported an inflammatory process with both acute and chronic features consistent with Crohn's disease or *C difficile* enterocolitis. Enteroclysis revealed a nodular, edematous, and relatively nonpliable terminal ileum. These radiologic findings, combined with the history of oral and colonic aphthous lesions, growth parameters indicating acute and chronic undernutrition, hypoalbuminemia, and hypokalemia, led to a diagnosis of Crohn's disease. Finally, 9 days into her hospital course admission stool cultures revealed *Y enterocolitica*. In retrospect, the constellation of exposure to uncooked meat, young age of the patient, extremely high sedimentation rate, and marked mesenteric adenitis was more consistent with *Yersinia* enterocolitis than with chronic inflammatory bowel disease. Indeed, later questioning of the family revealed some potential exposure to home-prepared pork chitterlings during the recent holiday.

Y enterocolitica is a Gram-negative motile aerobic bacterium belonging to the Enterobacteriaceae family. *Y enterocolitica* first was identified as a distinct organism isolated from the stool of human cases of diarrhea by Schleifstein and Coleman^{1,2} in 1939. It was recognized for its tendency toward pathogenicity isolated in 2.8% of infectious diarrhea cases. Since that time, it has become identified more commonly as an enteric pathogen with a variety of clinical manifestations. It can be detected via several methods. Diagnosis by culture (cold enrichment) is 56% sensitive and by serology is 84% sensitive within 1 week of symptoms. Selective media such as CIN agar may be more sensitive. Combined culture and serology testing is 88% sensitive for disease.³

Y enterocolitica is distributed worldwide with a higher frequency of isolation in cooler climates⁴ and typically is seen most frequently during the winter.⁵ It can be characterized by biochemical testing, phage typing, plasmid analysis, or serotyping. Serotyping of *Y enterocolitica* is based on specific somatic O antigens.⁶ The most common serotype responsible for outbreaks in the United States is O:8, although serotypes O:3 and O:9 are recognized as virulent in other areas of the world.⁷ Geographic differences are apparent in the frequency and distribution of *Y enterocolitica*. In Europe, sporadic cases are common,

whereas in the United States, sporadic disease is unusual and outbreaks usually are seen.⁸

Symptomatic *Yersinia* infection is more common in children, although adults are still susceptible. In the prospective study by Marks et al,⁹ the median age for presentation was 24 months with documented cases in infants as young as 2 months. The male to female ratio is 1.7:1, and the incubation period is usually 4 to 6 days ranging from 1 to 14 days with initial symptoms of prodromal listlessness, anorexia, and headache. Typically in younger children, the infection progresses to an enterocolitis characterized by vomiting, diarrhea, fever, and abdominal pain. In older children, a pseudoappendicitis-like picture may be encountered with fever, abdominal pain, right lower quadrant tenderness, arthritis, and leukocytosis, similar to those in the present case.^{7,10-15} Atypically, *Y enterocolitica* may cause a pharyngitis with cervical adenopathy.⁷ This may have been the case in our patient, along with concurrent group A β -hemolytic streptococcal infection or pharyngeal streptococcal carrier status resulting in the positive rapid strep test. Extraintestinal features of disease may include cellulitis, pyomyositis, osteomyelitis, pneumonia, lung abscess, meningitis, or glomerulonephritis.^{7,16-22} Postinfectious complications include reactive arthropathy and erythema nodosum.^{11,14,19-22}

This case demonstrates the importance of requesting stool cultures specifically for *Yersinia* in patients with abdominal pain and diarrhea when excluding infectious sources. Most clinical microbiology laboratories do not use selective techniques routinely to isolate *Yersinia* on stool cultures unless ordered. Specific *Yersinia* culture and serologic titers should be considered when evaluating a patient for inflammatory bowel disease (ie, Crohn's disease) or in a patient suspected to have inflammatory bowel disease who fails to respond to steroid therapy before electing more aggressive immunosuppressive therapy. Patients and their families must be queried for risk factors leading to *Yersinia* infection. Specifically, they should be questioned about any exposure to pork products, especially chitterlings, often prepared and/or consumed during the holiday season.^{23,24} Finally, our case demonstrates that *Yersinia* enterocolitis may present with the constellation of terminal ileitis, mesenteric adenitis, features of appendicitis, protracted abdominal symptoms with fever, chronic active colitis with aphthous lesions, pharyngitis, and rash.

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