Pseudo-appendicitis: Blame the Vikings!

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ABSTRACT

A 6-year-old Swedish boy presented with symptoms suggestive of appendicitis and with a mass in the right iliac fossa. Computed tomography of the abdomen showed ileal wall thickening with multiple retroperitoneal nodes. Biopsy of the lymph nodes showed necrotizing suppurative granulomatous lymphadenitis. *Yersinia enterocolitica* serotype 0:5 IgM was positive, suggesting a possible diagnosis of *Yersiniosis*. (J Infect Dis Antimicrob Agents 2004;21:17-20.)

INTRODUCTION

*Yersinia enterocolitica* is a well known cause of acute bacterial enteritis. It occurs most often in young children, who can present with high fever, diarrhea and vomiting. *Yersinia* infection may present as a pseudo-appendicular syndrome, which is frequently confused with appendicitis. We report a case of possible *Yersinia* infection, based on a positive serology test for *Yersinia enterocolitica* 0:5 in a child presenting with symptoms suggestive of appendicitis. The limitations of the serology test are also discussed.

CASE REPORT

A 6-year-old Swedish boy was referred from his local hospital to the Children’s Hospital at Westmead, Sydney, with a provisional diagnosis of appendicitis, after a one-week history of lower abdominal pain, fever, loose stools and reduced appetite. The abdominal pain was intermittent and worse during walking, but he was generally comfortable. Examination revealed a child who looked well. He had tenderness in the right iliac fossa, and on deep palpation a mass was felt in the area of the appendix.

The boy was born in Sweden, and the family moved to Australia 18 months before the present illness. He was a healthy child before this illness. He had no history of night sweats or weight loss. He had not eaten raw meat or drunk unpasteurized milk. He had no known contact with tuberculosis. At initial presentation, a full blood count was normal. The erythrocyte sedimentation rate was 103 mm/h and the serum C-reactive protein was 131 mg/L (normal <5 mg/L). Urinalysis, stool microscopy and blood cultures were negative. The blood urea, creatinine, electrolytes

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and liver function tests were normal.

Ultrasonography showed a multi-lobulated mass in the right iliac fossa, consistent with mesenteric adenopathy. There were also focal hypo-echoic lesions in the spleen. A small amount of fluid was reported in the Pouch of Douglas. Computed tomography of the abdomen demonstrated the presence of multiple nodes in the retroperitoneal space, in the right mid-abdomen, the pre-aortic region, and mesenteric root, as well as in the left inguinal area. There was also thickening of the ileal wall.

The patient was referred to the oncologists with a provisional diagnosis of lymphoma. A bone marrow biopsy was normal. Laparotomy was performed and the retroperitoneal mass was found to consist of a mass of matted lymph nodes. There was no abnormality in the appendix, caecum, small bowel and ascending colon. A frozen section of the biopsy of the lymph nodes showed enlarged, reactive lymph nodes filled with multiple, large granulomata with central necrosis, described as necrotizing suppurative granulomatous lymphadenitis. There was no evidence of lymphoma.

Cultures for bacteria and fungi were negative. The patient made a rapid recovery and appeared well.

Further history revealed that the family had kittens at home, and it was felt that the most likely diagnosis was cat scratch disease (CSD). Skin test with Mantoux and avian purified protein derivative (PPD) was negative. Lymph node specimens tested with acid-fast Ziehl-Neelsen (ZN) staining, culture and polymerase chain reaction (PCR) for *Mycobacterium* were negative. A nitroblue tetrazolium test was normal, excluding chronic granulomatous disease (CGD). Serum was sent for *Bartonella henselae* serology by indirect fluorescent antibody test (IFA), and one of the biopsied lymph nodes was retrieved to perform PCR for *B. henselae*. While awaiting these results, the patient was treated empirically for CSD rifampicin and ciprofloxacin.

At follow-up, the boy remained well. The abdomen was soft and no mass was palpable. Repeat abdominal ultrasonography, after three weeks of antibiotics, showed complete resolution of the lymphadenopathy. *Bartonella henselae* serology was negative, and DNA amplification of the biopsied tissue for *B. henselae* by PCR was also negative. CSD was excluded, and another diagnosis was sought.

The histopathology report was reviewed. The report stated that the necrotizing suppurative granulomatous lymphadenitis was likely of infectious origin, and that the differential diagnosis included CSD, mycobacterial infection and yersiniosis. Serum was retrieved and sent for *Yersinia* serology by enzyme-linked immunosorbent assay (ELISA). *Yersinia enterocolitica* 0:5 IgM was positive, while *Yersinia enterocolitica* 0:3 IgM was not detected. The elevated specific serum IgM suggested a possible diagnosis of *Yersinia enterocolitica* serotype 0:5 infection.

**DISCUSSION**

Our patient presented with symptoms mimicking appendicitis characterizing with fever, abdominal pain and right lower quadrant tenderness. A mass was found in the appendicular region, and radiological findings confirmed the presence of multiple nodes in the abdomen with thickening of the ileal wall. This was subsequently found on laparotomy to consist of a retroperitoneal mass of matted lymph nodes. The presentation and clinical studies supported a differential diagnosis of lymphoma or infectious mesenteric adenitis associated with *Y. enterolitica*, *Y. pseudotuberculosis*, *Salmonella*, *Campylobacter*, *Brucella*, *Francisella tularensis* or infection with *Mycobacterium tuberculosis* or non-tuberculous mycobacteria, or endemic fungi. Parvovirus B19 has been associated with pseudoappendicitis and infectious mononucleosis can cause mesenteric lymphadenopathy.1

The histology of the lymph nodes revealed a necrotizing suppurative granulomatous lymphadenitis. This distinctive but non-specific inflammatory reaction can be found in a variety of infections including CSD, yersiniosis, salmonellosis, tularaemia, brucellosis, lymphogranuloma venereum, mycobacterial infections and other more rare infections.2,3 In addition, rare
disorders of phagocyte function such as CGD, may also produce these microscopic features. A normal nitroblue tetrazolium test, however, excludes CGD. The clinical history and the site of involvement can exclude several infections in this case. Although CSD was initially suspected, serology and PCR for Bartonella henselae were negative. Mycobacterial work-up and fungal cultures were also negative.

Based on a relatively benign disease, generalized intra-abdominal lymphadenopathy, terminal ileitis, necrotizing suppurative granulomata of histopathology of lymph nodes and geographic data, a final differential diagnosis included Y. enterocolitica, Y. pseudotuberculosis, Salmonella spp., F. tularensis or C. fetus infection.

In our case, routine culture of both stool and biopsied specimens was negative, but special media and selective techniques were not used and these are especially important in isolating Yersinia and C. fetus. In addition to culture, serological tests are useful in diagnosing Yersinia but not in C. fetus infection, as in the latter serological diagnosis is still a research tool. In our patient, the IgM for Y. enterocolitica was positive, hence suggesting a possible diagnosis of Y. enterocolitica.

The serodiagnosis for yersiniosis has limitations. In Yersinia infection, specific IgM may persist for 6 to 8 months and sometimes for years after an infection, thus limiting the value of a single positive result. The reliability of serological diagnosis of Y. enterocolitica is tempered by the potential for cross-reactivity with other bacteria such as Brucella abortus, rickettsiae and with other members of the Enterobacteriaceae. High seroprevalence rates found in certain healthy population further limits the value of serology in diagnosis of yersiniosis. Although determination of serological responses has been used as evidence of infection in the presence of a compatible syndrome when culture results are negative, a diagnosis of Y. enterocolitica infection in this case is not conclusive. A four-fold rise in the titres of IgG or IgA against Y. enterocolitica would be a supportive diagnostic test, which was unfortunately not performed in this case.

Geographic differences in the frequency and distribution of Y. enterocolitica infection are apparent. The burden of disease attributed to Y. enterocolitica is highest in northern Europe, where sporadic infections are caused by serotypes 0:3 and 0:9 but outbreaks of disease are rare. In Japan, sporadic diseases are associated with serotype 0:3 while multiple serotypes are associated in the United States. In Australia, predominant serotypes causing sporadic infections are 0:3 and 0:5. This distribution may reflect geographic differences, different culinary practices, or may simply be a consequence of more intensive surveillance and the use of specialized culture techniques. The documented transmission of Y. enterocolitica to humans has occurred primarily by the ingestion of contaminated foods, water, and milk. Apparent transmission from dogs, cats, and pigs to humans has been reported, perhaps by the fecal-oral or oral-oral route, so it is possible that our patient caught Yersinia from his cats.

The organism is a fastidious, gram-negative, motile, aerobic bacterium belonging to the Enterobacteriaceae family. It grows slowly on all commonly used media, and its bacteriological identification can be difficult. Yield from stool cultures can be increased by using cold enrichment alkali treatment and selective culture media. However, stool culture for Yersinia from individuals with pseudo-appendicitis is often negative, suggesting that intestinal infection has preceded spread to mesenteric nodes. Culture of mesenteric nodes removed at operation can grow the organism.

Y. enterocolitica is usually susceptible to trimethoprim, aminoglycosides, chloramphenicol, tetracycline, third-generation cephalosporins and quinolones. It is resistant to most penicillins (including ampicillin and amoxycillin-clavulanic acid) and first-generation cephalosporins. Most patients with uncomplicated enterocolitis recover spontaneously, and treatment is only indicated for patients with septicemia, focal extra-intestinal infection and for immunocompromised patients with enterocolitis.
Quinolones are probably the treatment of choice for Yersinia infections, so it is fortunate that our patient was treated with a quinolone, even if for the wrong reason.

In conclusion, Yersinia should be considered in the differential diagnosis of acute appendicitis. Although a definite diagnosis cannot be made in this case due to the limitations of serological tests, the clinical context suggests the diagnosis of yersiniosis is probably correct. Serology for Yersinia can be clinically useful, especially if it is interpreted correctly in an appropriate clinical setting.

References


