Yersinia enterocolitica as a cause of intra-abdominal abscess: the role of iron

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Yersinia enterocolitica is gaining increasing attention as an important enteric pathogen. In many developed countries, it has surpassed *Shigella* and now rivals *Salmonella* and *Campylobacter* as a cause of acute gastroenteritis.[1] A number of characteristic factors related to virulence enable *Y. enterocolitica* to produce a wide spectrum of clinical manifestations, ranging from potentially fatal bacteremia and "pseudoappendicitis" to skin eruptions.[2] We report a case of *Y. enterocolitica* as a rare cause of intra-abdominal abscess in a young man having β-thalassemia and discuss how iron overload and therapeutic chelators may have contributed to the outcome.

Case report

A 21-year-old man of southeast Asian descent presented with a 1-week history of crampy abdominal pain and nonbloody diarrhea. He had thalassemia major for which he required monthly transfusions. He had received the last one 2 weeks before presentation. He had undergone a splenectomy at 5 years of age. His medications included penicillin as prophylaxis and an iron-chelating agent (Desferal; Novartis Pharmaceuticals Canada, Dorval, Que.). He was hemodynamically stable and had a body temperature of 39 °C. He had a large, firm, nonmobile mass on the right side of his abdomen, and there was localized tenderness. Otherwise no relevant physical abnormalities were noted. Laboratory tests revealed a microcytic anemia (hemoglobin 104 g/L) and an elevated leukocyte count (14.5×10^9/L [70% neutrophils, 20% lymphocytes, 10% monocytes]). Abdominal computed tomography confirmed a 9-cm complex mass in the right midabdominal region, beginning below the level of the hepatic flexure and extending along the medial aspect of the ascending colon. It was distinctly separate from the small bowel, appendix and colon (Fig. 1).

Intravenously adminstered antibiotics (cefotetan, 1 g every 12 hours) were started and a 12 French drain was placed percutaneously by interventional radiology under ultrasound guidance. A moderate amount of thick purulent material was aspirated. Over the next 24 hours, the patient continued to manifest increasing sepsis. He continued to have intermittent body temperatures in excess of 40 °C and his leukocyte count increased

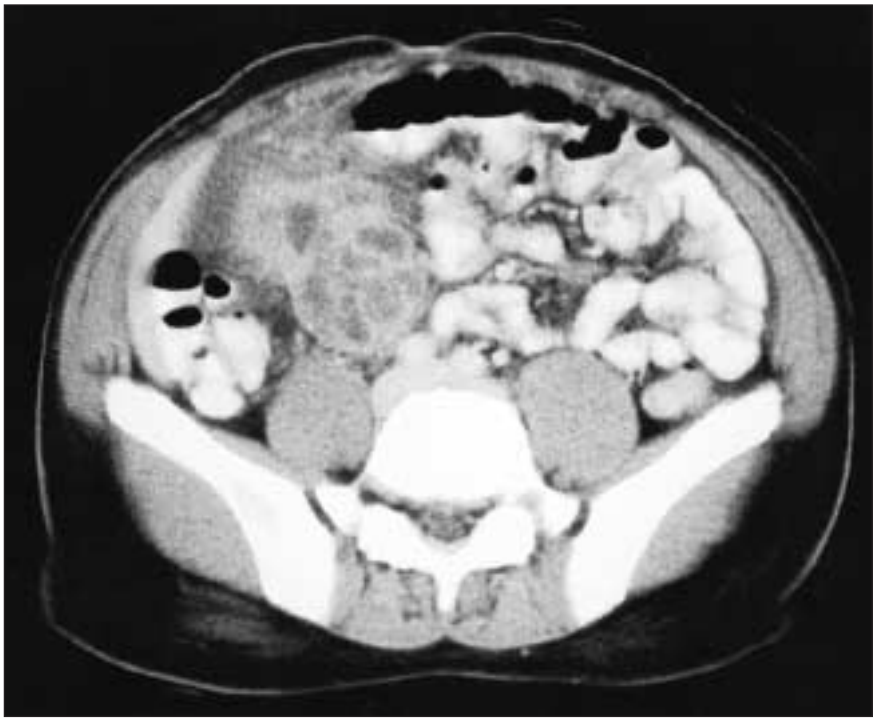

FIG. 1. Abdominal computed tomography scan showing a large complex mesenteric mass in a 21-year-old man who had thalassemia major.

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to 36×10^9/L. Blood and drainage fluid culture results were unavailable at this time. Because of presumed failure of percutaneous drainage, exploratory laparotomy was done to drain the abscess surgically. At laparotomy, a large mass of coalescent mesenteric lymph nodes containing areas of necrosis was found. It extended from the hepatic flexure to the paracecal area, medial to the colon. All other organs including the appendix, small and large bowel and gallbladder appeared normal. Postoperatively, he continued to have febrile episodes. Cultures from the drainage fluid grew *Y. enterocolitica*, so antibiotics were appropriately changed to trimethoprim-sulfamethoxazole (TMP-SMZ). His condition improved, drains were removed and he was discharged from hospital on postoperative day 8 to complete a 4-week course of TMP-SMZ. At 6-month follow-up, he remained clinically well and had not suffered any recurrence.

Discussion

Y. enterocolitica was first described by Pike and McIver in 1934.[3] They had isolated the small gram-negative coccobacilli from a facial abscess in a farmer. In that case the the infection ultimately resolved with X-ray therapy.

This enteric bacterium is widely distributed in nature in animals and in water reservoirs, with swine being the major source of human pathogenic strains. Of note is the fact that the majority of non-porcine isolates are avirulent.[4] Clinical infections occur after the ingestion of contaminated food or water but may also occur by direct inoculation through blood transfusions since *Y. enterocolitica* can grow at 4 °C, the temperature of stored blood.[5] However, for the microorganism to produce a clinical syndrome, it must possess several virulence factors, including multiple plasmid-encoded proteins, which allow invasion and establishment within a susceptible host.[6,7] The ingested microorganisms have a predilection for the terminal ileum where they are able to penetrate M cells within Peyer's patches. It is within these specialized phagocytic cells that they replicate and infect subjacent tissues. This process may result in microabscess formation and ulceration. Spread of the infection to mesenteric lymph nodes may produce mesenteric lymphadenitis with central necrosis and abscess formation. Occasionally, *Y. enterocolitica* becomes blood borne and spreads to other organs such as liver, spleen, lung and even brain.[8,9]

Systemic involvement is rare. Most patients with *Y. enterocolitica* infection have an underlying disease, commonly iron overload.[10] Iron is an essential growth factor for virtually all bacteria. In mammalian tissues, there normally exists a state of iron starvation because almost all iron is complexed with other molecules or is tightly bound to carrier proteins. Under these conditions, most bacteria produce chelators of low molecular weight, with high iron affinity known as siderophores. Because siderophores aid bacterial replication, they are regarded as virulence factors. Interestingly, *Y. enterocolitica* lacks siderophores,[11] explaining why it preferentially proliferates in states of iron overload. Further, the iron-chelating agent deferoxamine B paradoxically heightens the susceptibility of hemosiderotic patients to systemic yersiniosis.[12] This observation was first made when patients taking Desferal were noted to have higher rates of infection, with several bacterial species including *Klebsiella*, some strains of *Salmonella* and *Y. enterocolitica*.[13,14] This increase in infection results from the ability of these organisms to use feroxamine, the iron-containing form of Desferal, as a siderophore. Whereas in most instances, Desferal favours the host by binding iron and sequestering it from infecting microbes, it stimulates in-vivo replication of *Yersinia* by providing growth substrate. This is particularly needed in extraintestinal infections. While in the gut, *Yersinia* is able to utilize the abundant siderophores of other bacteria; in the tissues, feroxamine provides a means of obtaining sparse iron.

Thus, in patients with hemosiderosis taking iron chelating agents, the diagnosis of *Yersinia* lymphadenitis with necrosis should be considered in the differential diagnosis of complex intra-abdominal masses. Percutaneous aspiration for culture and initiation of appropriate antibiotics may avoid the morbidity resulting from surgical drainage.

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