Spontaneous *Yersinia enterocolitica* septicemia in a patient with iron overload

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**ABSTRACT:** *Yersinia enterocolitica* septicemia is described in a patient with transfusional iron overload and a myelodysplastic syndrome. The organism was biotype 1 serotype 0:5,27 and carried a virulence-encoding plasmid. It was calcium-dependent, autoagglutinating and virulent to orally challenged mice, but not resistant to the bacteriocidal activity of serum. The patient had depressed neutrophil chemotaxis and bactericidal activity. In this case, both host and microbial factors were present to select out this particular bacteremic disease. Patients with iron overload states should be recognized as compromised hosts and potentially susceptible to spontaneous sepsis due to *Y enterocolitica*. *Can J Infect Dis* 1990;1(2):57-60

**Key Words:** Iron, Septicemia, *Yersinia*

**YERSINIA ENTEROCOLITICA IS A COMMON CAUSE OF**
enterocolitis, but a very uncommon cause of septicemia. The pathogenesis of enteric disease is often ascribed to the carriage of a virulence plasmid (1), while the pathogenesis of bacteremic disease is more often linked to the iron overload (2-13). The virulence characteristics of most bacteremic strains are not well described. The following reports a case of sepsis in an adult immunocompromised male with combined problems of iron overload and neutrophil dysfunction, in which the bacterial strain was examined for virulence characteristics.

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**CASE PRESENTATION**

A 55-year-old male presented with a one week history of fever, anorexia and malaise. He denied a history of diarrhea. There was a 14 year history of an evolving myelodysplastic syndrome characterized primarily by ineffective erythropoiesis with spontaneous remissions and exacerbations requiring blood transfusions totalling in excess of 500 units. He had developed transfusion hemosiderosis with hyperpigmentation, cardiomyopathy, diabetes mellitus and impaired hepatic function. He had used alcohol heavily until 12 years previously. Examination revealed him to be darkly pigmented and chronically ill with a temperature of 38.2°C, tachycardia, hepatosplenomegaly and mild epigastric tenderness. There were no significant joint findings. A heart murmur was not detected and no cutaneous lesions were seen. Fundoscopic examination was normal.

**Laboratory values:** Hemoglobin 118 g/L, platelet count 51 x 10^9/L, leukocyte count 6.5 x 10^9/L with 5.135 x 10^9/L neutrophils, 0.585 band cells, 0.488
lymphocytes, 0.260 monocytes and 0.033 reactive lymphocytes x 10^9/L. Serum iron was 132 μg/dL (normal 65 to 165); total iron binding capacity 159 (normal 245 to 420); iron saturation 83%; ferritin 2540 ng/mL (normal 10 to 320); alkaline phosphatase 145 iu/L; aspartate aminotransferase 47 iu/L; gamma-glutamyl transferase 67 iu/L; and hepatitis B surface antigen positive.

Chest roentgenogram was normal. Abdominal ultrasound confirmed hepatosplenomegaly but no intra-abdominal abscess was seen. Bone marrow biopsy demonstrated panhypoplasia and increased iron stores marked by prominent, iron-laden histiocytes. Cytogenetic studies were normal. Neutrophils were tested for chemotactic response and phagocytic and bactericidal capacity against Staphylococcus aureus and this strain of Y enterocolitica (14). Chemotaxis was not impaired; however phagocytosis and bactericidal capacity were both reduced more than 50% compared to the normal control. No differences were noted between results with Staph aureus and Y enterocolitica. Differences in either test of 20% or greater were considered significant.

**Microbiologic studies:** Three of six sets of blood cultures (Bactec NR6A Tryptic Soy Broth aerobic, NR7A Tryptic Soy Broth anaerobic and Dupont Isolator system) drawn in the first 12 h yielded Y enterocolitica sensitive to amikacin, gentamicin, netilmicin, tetracycline, trimethoprim-sulfamethoxazole, tobramycin and piperacillin, and resistant to ampicillin and cephalothin. All subsequent blood cultures were negative. No pathogens were isolated from sputum or urine. Three fecal cultures using a combination of CIN medium (Oxoid) and cold enrichment for 14 days yielded no Y enterocolitica. The strain of Y enterocolitica was identified as being biotype 1 serotype 0:5,27, and this strain of Y enterocolitica. Differences in either test of 20% or greater were considered significant.

**Clinical course:**

On admission, intravenous tobramycin 80 mg every 8 h and cefazolin 1 g every 6 h were started. On day 2, therapy was modified to tobramycin 140 mg every 8 h and piperacillin 3 g every 6 h because of failure to improve and a preliminary report of a Gram-negative organism in the blood cultures. The patient gradually improved, becoming afebrile on the sixth hospital day, and was discharged three weeks after admission. Antibiotics were continued for a total of 14 days. After six months, there was no recurrence of infection.

**Discussion:**

Y enterocolitica in humans primarily causes an acute gastroenteritis with fever, abdominal pain, nausea and diarrhea, but is also associated with mesenteric adenitis, polyarteritis nodosa and post infectious arthritis. Y enterocolitica infections are commonly found in Europe and less commonly in Africa, Japan, Australia and the United States. Y enterocolitica has been recovered from most provinces in Canada, and in one Vancouver, British Columbia hospital, yersinia organisms were isolated from the stools of up to 15.9% of patients presenting with gastrointestinal symptoms (15).

A recent review of the literature found over 100 reports of Y enterocolitica septicemia (2-12,16). It is a relatively rare occurrence in the absence of a focus of infection. Thirty per cent of the patients had disorders of iron metabolism including Bantu hemosiderosis, primary and secondary hemochromatosis, and thalassemia. Eighty per cent of the patients had underlying disease such as cirrhosis, diabetes mellitus, renal failure or malignancy. Over 60% had an evident focus of infection such as diarrhea, liver abscess or lung infiltrate, but no such focus was found in the present patient. Bouza (2) reported that 22% of cases occur in previously healthy individuals.

Cases have been reported of transmission of Y enterocolitica by transfusion of refrigerated blood (3,7,8). Although the present patient had received multiple blood transfusions, he had not received any blood products for two months prior to this admission, making transfusion an unlikely source of his infection. Studies have shown that normal human serum does not inhibit the growth of plasmid-infected Y enterocolitica (10,17,18) and that iron overload impairs leukocyte function with enhancement of bacterial virulence (19-23). Iron overload particularly predisposes to septicemia with Y enterocolitica and Y pseudotuberculosis since these organisms rely on exogenous iron to facilitate extraintestinal infection (24,25).

The interactions between Y enterocolitica and human defence mechanisms have been previously studied. Pai and DeStephano (26) observed that strains of Y enterocolitica that were virulent in either a rabbit or mouse model were not killed when grown at 37°C in Hanks' balanced salt solution with 0.1% gelatin and 10% normal human serum, while avirulent strains were killed. They speculated that this was similar to serum resistance seen with certain Escherichia coli (27) and due to an altered outer membrane protein en-
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REFERENCES


