Multiple hepatic abscesses following *Yersinia enterocolitica* septicemia

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ABSTRACT: Septicemia from *Yersinia enterocolitica* is unusual. Hepatic involvement occurring in this clinical setting is a rare complication. A case of a 64-year-old man who developed septicemia from *Y. enterocolitica* is reported. Abdominal ultrasound and computerized axial tomography scan revealed multiple defects in liver parenchyma compatible with abscesses. After treatment with intravenous aminoglycosides followed by trimethoprim-sulfamethoxazole, recovery was complete. General considerations regarding the manifestations and pathogenesis of *Y. enterocolitica* are discussed, with a review of the literature. *Can J Gastroenterol* 1990;4(5):179-183

Key Words: Hepatic abscesses, *Yersinia enterocolitica* septicemia

Abcès hépatiques multiples résultant d'une septicémie à *Yersinia enterocolitica*

RESUME: La septicémie provoquée par *Yersinia enterocolitica* est inhabituelle. L'atteinte hépatique se produisant dans ce cadre clinique est une complication rare. On rapporte le cas d'un homme de 64 ans atteint d'une septicémie due à *Y. enterocolitica*. L'échographie et la TDM ont révélé de multiples anomalies du parenchyme hépatique indiquant la présence d'abcès. Il y a eu guérison complète après un traitement aux aminosides intraveineux suivi de triméthoprime-sulfaméthoxazole. Les considérations générales relatives aux manifestations et à la pathogenèse d'*Y. enterocolitica* sont examinées et incluent une revue de la littérature.

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Received for publication July 20, 1989. Accepted January 31, 1990

YERSINIA ENTEROCOLITICA IS A Gram-negative organism becoming more frequently recognized in human infections. Seventeen serotypes and five biotypes have been identified (1). In Canada, 80% of infections are caused by serotype 0:3 biotype 4, although an outbreak in Montreal was caused by serotype 0:5,27 (2). In the United States, serotype 0:8 is predominant (3).

Y. enterocolitica infection produces a variety of clinical manifestations. The one most commonly encountered is acute gastroenteritis, found in all age groups. Mesenteric lymphadenitis and acute terminal ileitis are other well known entities associated with yersinia infections, especially in young people (4,5). Septicemia is a rare complication with approximately 100 cases reported in the literature (6). Few reports exist of hepatic abscesses; mortality from this complication is high (7). However, early recognition and appropriate antibiotic treatment may alter the prognosis.

Figure 1) Abdominal computerized axial tomography scan. Multiple hypodense lesions of variable size measuring up to 1 cm are scattered throughout the liver

Figure 2) Markedly increased hemosiderin pigment within the cytoplasm of hepatocytes. (Prussian blue A $\times 40$, B $\times 270$)

CASE PRESENTATION

A 64-year-old man from Bretagne in Northern France with no pertinent past medical history was admitted to hospital with a six month history of progressive weakness, 8 kg weight loss, polyuria and polydipsia. Twenty-four hours prior to admission the patient developed fever and was brought in in

a comatose state. Initial evaluation revealed a nonketotic hyperosmolar state (blood sugar 70 $\mu\text{mol/L}$) which improved with therapy. However, fever up to 40°C persisted and diarrhea developed. Three blood cultures drawn on admission later grew *Y enterocolitica* (serotype 0:3 biotype 4).

Cefoxitin 2 g intravenously every 6 h

was started. Clinical state improved and the patient was afebrile 72 h later. On the fifth day, jaundice and hepatomegaly developed. The patient was transferred to the authors' institution.

Physical examination disclosed an asthenic but nontoxic patient. Jaundice without hyperpigmentation was noted. Temperature was 37.2°C, pulse 88 beats/min and blood pressure 125/75 mmHg. Abdominal examination revealed a palpable liver 7 cm below the costal margin and 15 cm on percussion without evidence of splenomegaly. Laboratory tests revealed: hemoglobin 144 g/L; leukocyte count 27,920 with 87% neutrophils; aspartate aminotransferase 75 iu/L (normal 0 to 20); alanine aminotransferase 89 iu/L (normal 0 to 29); alkaline phosphatase 645 iu/L (normal 45 to 107); total bilirubin 55 $\mu\text{mol/L}$ (normal 0 to 17); direct fraction 24 $\mu\text{mol/L}$ (normal 0 to 10 $\mu\text{mol/L}$); ferritin 2754 $\mu\text{g/L}$ (normal 42 to 313); plasma iron 5.5 $\mu\text{mol/L}$ (normal 13 to 35); total iron binding capacity 21.14 $\mu\text{mol/L}$ (normal 44.75 to 71.60); and iron saturation 26.3%. Specific HLA-typing wasn't done.

Abdominal ultrasound was performed which confirmed hepatomegaly with multiple hypoechogenic lesions. Multiple hepatic abscesses were diagnosed. Cefoxitin was changed for gentamicin (4.5 mg/kg/day). Abdominal computerized axial tomography scan confirmed multiple hypodense lesions throughout the liver parenchyma consistent with liver abscesses (Figure 1). Repeat blood and stool cultures done after one week of antibiotic therapy failed to reveal *Y enterocolitica*. Upper and lower gastrointestinal series did not show evidence of ileitis.

After two weeks of treatment, a fine-needle liver biopsy (Figure 2) was performed in consideration of the occurrence of diabetes mellitus, *Y enterocolitica* septicemia and elevated ferritin in a patient of Breton origin. Histologic findings revealed diffuse increased parenchymal iron stores (grade 3 on a scale of 0 to 4) (8) without signs of tissue damage or any particular zonal distribution. No signs of cirrhosis were evident.

The patient's clinical status im-

TABLE 1
Yersinia enterocolitica and hepatic abscesses reported

Author	Year	Sex	Age (years)	Underlying condition	Treatment	Diagnosis	Outcome
Khanna (51)	1989	M	37	Diabetes	Gentamicin Clindamycin Trimethoprim-sulfamethoxazole	Computed tomography scan	Survived
Cauchie (52)	1987	M	47	Hemochromatosis	Cefuroxime Ampicillin	Ultrasound Biopsy	Survived
Leighton (6)	1987	F	71	Iron therapy	Gentamicin Trimethoprim-sulfamethoxazole	Ultrasound Biopsy	Survived
Abalain-Colloc (49)	1986	M	61	Diabetes	Thiamphenicol	Ultrasound Biopsy	Survived
Beeching (48)	1985	M	72	Hemosiderosis	—	Autopsy	Dead
Van Lier (47)	1983	M	38	Hemochromatosis	—	—	Dead
Fothergill (46)	1982	M	46	Diabetes	Gentamicin	Ultrasound Liver biopsy	Survived
Viteri (45)	1981	M	71	Diabetes	Cefoxitin & tetracycline	Gallium scan Laparotomy	Survived
Imhoof (44)	1980	M	48	Hemochromatosis	—	—	Dead
Ryan (43)	1979	M	3 months	—	Ampicillin	Technetium 99m scan & laparotomy	Survived
Mantse (42)	1978	M	64	Diabetes	Gentamicin	Gallium scan Laparotomy	Survived
Bottone (35)	1977	M	60	Cirrhosis	—	?	Dead
		M	69	Cirrhosis	—	?	Dead
Reinicke (41)	1977	M	59	Hemochromatosis	—	Autopsy	Dead
Rabson (23)	1975	M	55	Hemochromatosis	?	?	Dead
Rabson (22)	1972	F	57	Cirrhosis Hemochromatosis	Metronidazole Penicillin Tetracycline	Autopsy	Dead
Mollaret (40)	1971	F	69	Diabetes	Penicillin	Autopsy	Dead
Bloquiaux (39)	1968	M	40	None	Kanamycin Penicillin Ampicillin	Laparotomy	Survived
Hassig (38)	1949	M	60 69	Cirrhosis Cirrhosis	— —	Autopsy Autopsy	Dead Dead

M Male; F Female

proved following intravenous antibiotics for 21 days and oral trimethoprim-sulfamethoxazole (160 mg/800 mg bid) subsequently for two weeks. A subsequent visit revealed an improved clinical condition and a ferritin level returned to normal. Complete resolution of hepatic lesions was documented at the end of treatment by ultrasound study done at follow-up one month after the patient's discharge from the hospital.

DISCUSSION

Y enterocolitica infection may cause several clinical syndromes. Apart from the gastrointestinal manifestations, several extraintestinal symptoms are

known to occur in the weeks following acute infection. Erythema nodosum, Stevens-Johnson syndrome and arthritis have been described, especially in HLA-B27-positive individuals (5). Numerous other complications may occur. These include cellulitis (1), pyomyositis (9), pneumonia (10), pulmonary abscess (11), and endocarditis (12-14); rarely, neurologic (brachial plexus neuropathy and myelitis) (15), and nephrologic complications (glomerulonephritis) (16,17) and pharyngitis (18) have been reported.

Septicemia is a rare complication which carries a poor prognosis with a mortality ranging from 34 (1) to 50% (3). Certain predisposing factors seem

to favour septicemia. Children (19,20) and adults past the fifth decade (21,22) are more subject to septicemia. As in the present patient, diabetic individuals are at greater risk (1,4). Immunosuppressive therapy, blood dyscrasias and cirrhosis are other well known states favouring septicemia (1,4).

All patients with septicemia should be screened for iron overload. Rabson (23) first postulated an association between bacterial infections and the enhancing role of iron. Several large series (1,24) and case reports (8,25-27) have confirmed an association between septicemia due to *Y enterocolitica* and iron overload. Several hypotheses have been postulated. *Y enterocolitica*, which

has no iron-binding ligands, may proliferate if the exogenous supply of iron is increased (6). Furthermore, the growth of *Y enterocolitica* is enhanced in vitro (28) and its virulence increased strikingly in experimental (28) and probably human (30) infections with the use of desferoxamine which provides easily used iron for the bacteria. As well, iron appears to decrease the bactericidal and bacteriostatic activity of the serum and decreases host defence mechanisms (7). However, in Bouza's review (1), 22% of cases occurred in previously healthy individuals. Ferritin is a well known acute phase reactant, and the reversible increased level in the present case may be due to this fact.

This particular patient, however, had increased iron stores on liver biopsy, reflecting a degree of liver iron overload for which there was no clear explanation and which probably contributed to the occurrence of yersinia infection.

Hepatic complications from *Y enterocolitica* are of several types. Cholangitis has been reported (31) as well as cases of acute necrotizing hepatitis and granulomatous hepatitis (32-34). Few reports of liver abscesses exist in the literature (23,24,38-49) (Table 1). These may present in two

forms: solitary or multiple. Solitary abscesses present with nonspecific symptoms such as weight loss and right upper quadrant pain. Multiple liver abscesses usually follow septicemia and present with jaundice and hepatomegaly as in this case. Development of hepatic abscess due to *Y enterocolitica* infection is usually associated with a poor prognosis (7). However, cases reported from the past decade have shown a fall in the number of deaths associated with this condition. Several reasons may be postulated.

The advent of better imaging techniques is probably the greatest contributing factor. In earlier reports, diagnosis was usually done at autopsy. With recent developments in nuclear medicine and ultrasound, earlier diagnosis is now possible and appropriate therapy can be instituted. Microbiological studies have identified the antibiotic susceptibility of *Y enterocolitica*. The organism is usually susceptible in vitro to aminoglycosides, chloramphenicol, tetracycline, trimethoprim-sulfamethoxazole, the third generation cephalosporins (35,36) and the new quinolones (2,50). Better selection of antimicrobial regimen is thereby possible and may be an additional factor explaining the better outcome of patients. The drug of choice

for systemic infection has not yet been identified. Gentamicin 5 mg/kg/day intravenously, chloramphenicol 50 mg/kg/day or a third generation cephalosporin should be beneficial (36). Relapse may occur following treatment (6). Prolonged treatment (six weeks) may be continued on an outpatient basis using trimethoprim-sulfamethoxazole.

In conclusion, patients presenting with *Y enterocolitica* septicemia should be screened systematically for predisposing conditions, most notably diabetes and iron overload. Increased awareness of the several complications which may follow could lead to an earlier diagnosis. When hepatic abscesses are suspected, abdominal ultrasounds and computerized axial tomography scan will provide important diagnostic information. Treatment should be prolonged for hepatic abscesses — a minimum of six weeks or until complete radiologic resolution of abscesses. Earlier diagnosis and appropriate antibiotic selection will probably alter the prognosis of patients with *Y enterocolitica* abscesses.

ACKNOWLEDGEMENTS: The author thanks Mrs Isabelle Guyon for secretarial help.

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