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Single Case

Multilocular Hepatic Abscess Formation and Sepsis due to *Yersinia enterocolitica* in a Patient with Hereditary Hemochromatosis and Type 2 Diabetes Mellitus

Matthias Sauter^{a, f} Stephan R. Vavricka^{a, f} Pascal Locher^b
Benjamin Preiswerk^c Dominik Weishaupt^d Christoph A. Meier^{b, e}
Benjamin Misselwitz^{a, f}

^aDivision of Gastroenterology, Department of Internal Medicine and Specialties, Triemli Hospital, Zurich, Switzerland; ^bClinic for Internal Medicine, Department of Internal Medicine and Specialties, Triemli Hospital, Zurich, Switzerland; ^cDivision of Infectious Diseases, Department of Internal Medicine and Specialties, Triemli Hospital, Zurich, Switzerland; ^dInstitute of Radiology and Nuclear Medicine, Triemli Hospital, Zurich, Switzerland; ^eUniversity Hospital Basel, Basel, Switzerland; ^fDivision of Gastroenterology and Hepatology, University Hospital Zurich, Zurich, Switzerland

Keywords

Hepatic abscess · *Yersinia enterocolitica* · Sepsis · Hemochromatosis · Iron overload

Abstract

Infection with *Yersinia enterocolitica* (YE) typically presents with mild gastroenteritis without systemic infection. However, systemic YE infection has been described in states of iron overload. We present the case of a patient with sepsis with hepatic abscesses due to YE infection. Workup revealed a past diagnosis of diabetes mellitus and hemochromatosis which had been untreated for the previous 5 years due to patient refusal. This case highlights risk factors for systemic infection with YE. A high degree of suspicion for YE infection is warranted in patients with iron overload, diabetes mellitus, or immunosuppression.

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Introduction

Infection with *Yersinia enterocolitica* (YE), a gram-negative bacillus belonging to the family of Enterobacteriaceae, typically presents with enterocolitis or gastroenteritis accompanied by fever and abdominal pain [1, 2]. The incubation period for yersiniosis typically lasts 4–6 days (range 1–14). Infection usually remains self-limiting without systemic spread. However, systemic YE infection has been described in states of iron overload, immunocompromised patients, and infants [3–5], as well as in transfusion-transmitted sepsis [6]. Here, we present the case of hepatic abscess formation and sepsis due to YE in a patient with untreated hereditary hemochromatosis and type 2 diabetes mellitus.

Case Presentation

A 65-year-old male was referred to our emergency department with fever, confusion, and somnolence for several days. On admission, the patient reported alcohol abuse and a past diagnosis of type 2 diabetes mellitus, gastroesophageal reflux disease, and arterial hypertension. A further history could not be obtained on admission. During examination, the patient was somnolent and tachycardiac, but afebrile and with normal blood pressure. A physical examination revealed moderate tenderness in the right upper abdomen. Laboratory tests showed a blood glucose level of 45 mmol/L (normal range, fasting: 4.6–6.4), elevated liver function test results (alanine aminotransferase 165 IU/L, normal <41; aspartate aminotransferase 247 IU/L, normal <40; γ -glutamyltransferase 500 IU/L, normal <61), and an elevated C-reactive protein level (230 mg/L, normal <5) with a normal leukocyte count. The patient was admitted to the ICU, and antibiotic therapy with ceftriaxone and metronidazole, as well as i.v. insulin therapy, was started. CT scanning of the abdomen revealed signs of liver cirrhosis and multiple hypodense hepatic lesions with a size of up to 3 cm, consistent with either abscesses or malignancy. MRI (Fig. 1) and abdominal ultrasound confirmed liver lesions consistent with an infectious diagnosis but could not rule out malignancy. Blood cultures unexpectedly yielded growth of YE in 2 out of 4 samples, resistant to amoxicillin plus clavulanic acid but susceptible to all other antibiotics tested.

Two days after admission, after the weekend, the patient's primary care physician was contacted to complete the personal history. The patient had been diagnosed with hereditary hemochromatosis (homozygous C282Y mutation) 5 years previously but had refused treatment up to now. Further laboratory work confirmed the untreated hemochromatosis with profoundly increased ferritin levels (4,874 μ g/L, normal 30–400) and a transferrin saturation of 94% (normal 16–45).

Under antibiotic therapy – initially with ceftriaxone followed by ciprofloxacin p.o. and correction of hyperglycemia, secondary to both infection and lack of adequate insulin therapy – the patient improved. The patient was discharged after 19 days and oral antibiotic treatment was continued for a total of 6 weeks. The etiology of the diabetes was considered to be a combination of hemochromatosis-associated insulin deficiency and peripheral insulin resistance. Further investigation revealed no additional signs of hemochromatosis-related organ damage, and phlebotomy was initiated. Follow-up MRI after 6 weeks and 18 months showed regression of the abscesses with stable residual cystic changes.

Discussion

The availability of iron is crucial for all living beings including bacteria. Sequestering iron (and other nutrients) from pathogens is a defense strategy referred to as “nutritional immunity.” In the human host, iron is therefore stored either intracellularly, within the heme ring or the iron storage protein ferritin [7]. In addition, free iron is rapidly bound by the high-affinity iron sequester transferrin with an association constant of 10^{36} [8]. Together, these factors render the human body a hostile environment for microorganisms.

Siderophores are iron-binding proteins synthesized by bacteria which bind iron even more strongly than transferrin, enabling microbial iron uptake. Virulent *Yersinia* species such as *Y. pestis*, *Y. pseudotuberculosis*, and YE biotype 1B are capable of synthesizing yersiniabactin [9], a functional endogenous siderophore iron uptake system (Fig. 2). In contrast, low-virulence (biotypes 2–5) and apathogenic YE strains (biotype 1A) are unable to synthesize siderophores, limiting YE pathogenicity in iron-scarce states such as a healthy human host.

However, an iron-rich environment (e.g., in untreated hemochromatosis) leads to breakdown of nutritional immunity. Low-virulence YE strains or other *Yersinia* species can restore their virulence by amplified bacterial iron uptake [10]. The bacterial strategies in this situation have not been fully clarified but might include uptake of heterologous siderophores from other bacteria in the gut. A more efficient metabolism also of siderophore-lacking *Yersinia* strains results in an increased bacterial load and virulence, enabling systemic infection and abscess formation in various organs.

Systemic YE infection including sepsis and abscess formation in organs such as the liver, spleen, or bones has rarely been reported in iron overload states such as primary hemochromatosis or secondary iron overload [2, 4, 9]. A previous summary of the literature from 1945 to 2001 identified only 45 case reports (many of which are only available as abstracts) with documented YE hepatic abscesses [4]. Of these cases, 64% had underlying hemochromatosis and 29% had diabetes mellitus, which is considered to be a risk factor due to its well-known immunocompromising effects. Our patient suffered from both predisposing factors.

This case demonstrates the strong link between systemic YE infection, hemochromatosis, and diabetes mellitus. A high degree of suspicion regarding iron storage diseases and immunosuppression is warranted in patients with systemic YE spread, and we recommend screening of all patients with confirmed YE bacteremia or abscess formation. On the other hand, in patients with known hemochromatosis and signs of infection, systemic YE infection should be excluded.

Statement of Ethics

There is written informed consent of the patient for this case to be published in anonymized form.

Disclosure Statement

None of the authors have any conflict of interest pertaining to this publication, and none have any competing interests to declare.

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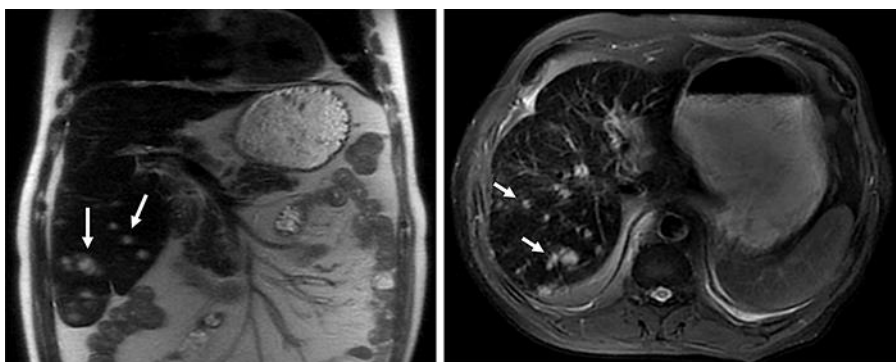


Fig. 1. Coronal (left) and transverse (right) T2-weighted MR images of the upper abdomen demonstrating multiple hyperintense hepatic lesions (white arrows), which turned out to be abscesses due to *Yersinia enterocolitica* infection. Note the dark signal of the liver parenchyma consistent with iron overload. Image source: Institute of Radiology, Stadtspital Triemli, Zurich, Switzerland.

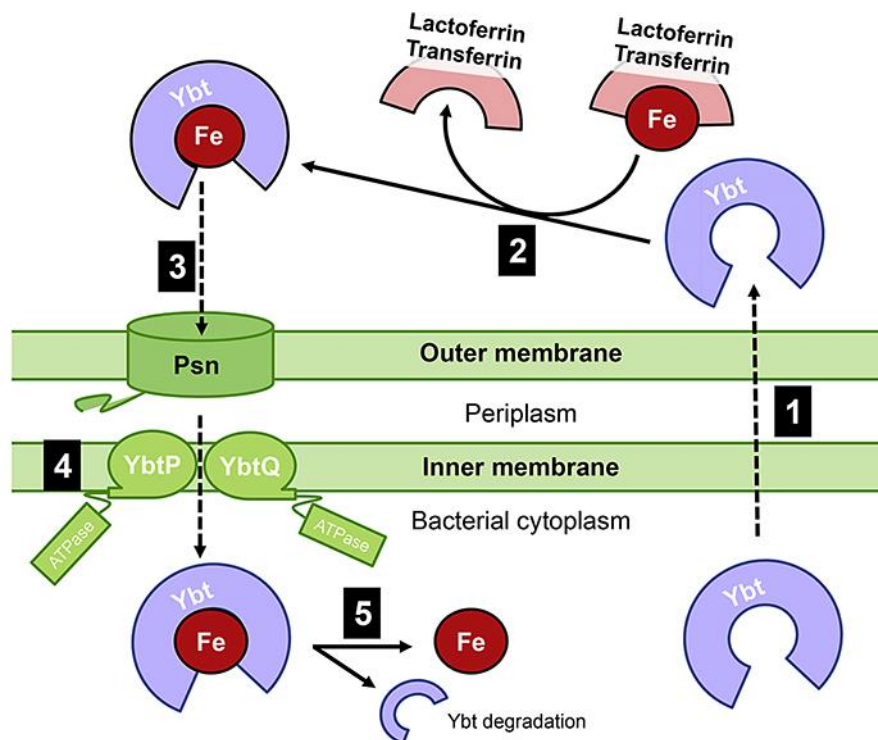


Fig. 2. Yersiniabactin (Ybt)-dependent Iron (Fe) uptake in *Y. pestis*, adapted from Perry and Fetherston [9]. Step 1: Ybt biosynthesis, transport via the bacterial inner membrane and outer membrane and release (by an unknown mechanism). Step 2: Ybt competes with human transferrin and lactoferrin for iron binding; due to its higher affinity, iron preferentially binds Ybt. Step 3: uptake of the Fe-Ybt complex into the bacterial periplasm by the receptor Psn. Step 4: Fe-Ybt is subsequently transported to the cytoplasm by the ATPases YbtP and YbtQ. Step 5: release of Fe and degradation of Ybt.