

YERSINIA ENTEROCOLITICA BACTERAEMIA IN HAEMODIALYSIS

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Summary

Eight patients on haemodialysis developed a *Yersinia enterocolitica* bacteraemia. The infection occurred in two patients four months after the onset of desferrioxamine treatment. In all cases, cure was obtained with antibiotic therapy. One death was unrelated to the infection. All the patients had iron-overload, as evidenced by a history of iron administration (8/8), an elevated serum ferritin (in 7/7), an increased attenuation value of the liver on computed tomography (in 5/6) and positive bone marrow iron stain (4/4). Iron overload and possibly desferrioxamine therapy seems to predispose dialysis patients to *Y enterocolitica* bacteraemia.

Introduction

Three reports have mentioned the occurrence of a bacteraemia with *Y enterocolitica* in patients on maintenance haemodialysis [1-3]. Here we report a total of eight Belgian dialysis patients who developed this infection and the results of investigations on pathogenesis.

Methods

The iron status was investigated by the following parameters: the amount of iron given, the serum ferritin value, a computed tomography (CT) of the liver, the iron status of the bone marrow and HLA-typing. The amount of iron given prior to the bacteraemia was calculated on the basis that 1 ampoule of iron dextran (Imferon®, Fisons) contains 100mg of iron and 1ml of packed red cells contains approximately 1mg of iron. The serum ferritin concentration before the bacteraemia was measured radioimmunologically by means of the Becton-Dickinson Ferritin (¹²⁵I) Kit (Becton-Dickinson Immunodiagnostics, New York). Abdominal CT was performed without contrast with a Somatom DR2 (Siemens) using

125kV, 230 MAS and 480 projections. Measuring time was 3.2 seconds, slice thickness 4mm. The attenuation value of the liver was measured in a circle of at least 500 pixels, chosen as peripherally as possible in the right liver lobe, to avoid major portal branches. The attenuation coefficient of the liver has a normal value of 49.8 ± 9.2 Hounsfield Units [4]. Haemosiderin content of the reticulum cells of the bone marrow was evaluated semi-quantitatively (0 to 4+) after staining by the Prussian blue method. The HLA-A, B and C typing was performed by the NIH lymphocyte microcytotoxicity technique. Values are given as mean \pm SEM.

Results

Eight dialysis patients (6 males, 2 females, aged 47–69 years) from four different Belgium dialysis units developed a *Y enterocolitica* bacteraemia. The underlying nephropathy was chronic interstitial disease in three, chronic glomerulonephritis in four and polycystic disease in one patient. The patients were treated by maintenance haemodialysis for a mean of 6.6 years (range 2–10) before the *Y enterocolitica* bacteraemia developed. None had liver cirrhosis, malignancy, thalassaemia or diabetes nor was treated by immunosuppressive drugs. The infection never appeared during or immediately after blood transfusion. The bacteraemia manifested itself with high fever in all patients and with abdominal pain in four, which led to laparotomy in one patient. The *Y enterocolitica* serotype was 0:9 in six cases and 0:3 in two. Empiric antibiotic therapy was started in all patients. When the result of the positive blood cultures was known, a more appropriate antibiotic was chosen in half of the cases. All patients except one recovered. This patient became afebrile after one day of tobramycin therapy, but developed a cerebrovascular accident one week later, without evidence of a cerebral abscess. Necropsy was not obtained. Yersinia agglutinin titres were followed in four cases: in only one seroconversion developed a titre of 1:100.

Examination of the iron status of the eight patients gave the following results: a mean of 18.4 ± 4.8 g (range 6–48) of iron had been given parenterally, either by transfusion of packed red cells (in 5 patients) or as iron-dextran (in 1) or by both in combination (in 2). Desferrioxamine, dosed at 1 and 2g at each dialysis session, had been given to two patients for one and four months respectively prior to the *Y enterocolitica* bacteraemia. One or more 'haemochromatosis alleles' (HLA-A₃, B₇ and B₁₄) were present in four out of the seven examined patients. The mean serum ferritin, determined in the months preceding the *Y enterocolitica* bacteraemia was 2303 ± 972 ng/ml (range 629–8000). Only one patient had a mild elevation of the serum alanine aminotransferase. A liver CT was performed in six patients. Excepting the single patient with polycystic disease of kidneys and liver, the mean attenuation value of the liver was 71.6 ± 3.8 Hounsfield (range 60–82). A bone marrow iron stain was strongly positive (3+ to 4+) in the four cases examined.

Discussion

This is the first report of a group of dialysis patients who developed a *Y enterocolitica* bacteraemia. Systemic yersiniosis usually present as an opportunistic infection. Hepatic cirrhosis, aplastic anaemia, thalassaemia, malignancy, diabetes, malnutrition, immunosuppressive treatment and iron-overload all have been described as predisposing conditions [3,5]. Of the predisposing factors, only iron-overload was present in our patients. Indeed, a history of parenteral iron administration was found in all eight patients, due either to transfusion of packed red cells or to therapy with iron-dextran or to both. In one patient who died shortly after the infection, a history of iron-dextran administration was the only available evidence suggestive of haemosiderosis. The following indicate the existence of iron-overload in the seven remaining patients. First, 'haemochromatosis alleles' was found in 4/7 patients. These alleles are known to predispose dialysis patients to iron-overload [6]. Second, the serum ferritin level was elevated in all seven cases in whom it was determined. Third, a bone marrow iron stain was strongly positive in each of the four cases examined. Fourth, a liver CT showed an increased attenuation value in all but one of the six examined patients. The exception concerned a patient with polycystic disease of the kidneys and of the liver, which could have led to a falsely low attenuation value of the liver. Generalization of *Y enterocolitica* infection is well known to occur in states of haemosiderosis [2,7,8]. Indeed, iron-overload increases the virulence of *Y enterocolitica* [2,7,8] and decreases host defence, particularly phagocytosis [7].

In two of the eight patients, the *Y enterocolitica* bacteraemia developed within four months after starting desferrioxamine therapy. This chelating drug, by acting as a siderophore, also increases the virulence of *Y enterocolitica*, which is unable to synthesize iron-binding compounds [2,8]. In the two patients who had received this chelating agent, the respective roles of iron-overload and of desferrioxamine in triggering the bacteraemia is unknown. Treatment with desferrioxamine is also mentioned in one of the three previous reports of a dialysis patient with *Y enterocolitica* bacteraemia [2].

In conclusion, eight patients on maintenance dialysis developed a *Y enterocolitica* bacteraemia. Iron-overload is considered as the main predisposing factor. Treatment with desferrioxamine may play an additive role in triggering systemic yersiniosis.

References

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