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Case Report

Aeromonas veronii biovar veronii septicaemia and acute suppurative cholangitis in a patient with hepatitis B

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Gram-negative bacilli of the genus *Aeromonas* are widespread in aquatic environments and can be responsible for human infections. Although *Aeromonas* extraintestinal and systemic infections have been reported with growing frequency in recent years, *Aeromonas* septicaemia remains an uncommon finding, often associated with serious underlying disease and predominantly related to the species *Aeromonas hydrophila*, *Aeromonas veronii* biovar sobria and *Aeromonas caviae*. Here, a case of *A. veronii* biovar veronii septicaemia and acute suppurative cholangitis is reported in a patient with chronic hepatitis B.

Introduction

Members of the genus *Aeromonas* have been associated with a wide spectrum of enteric and non-enteric diseases, in both immunocompromised and immunocompetent patients (Janda & Abbott, 1996, 1998). *Aeromonas veronii* was originally described by Hickman-Brenner *et al.* (1987) as a novel species in the genus *Aeromonas* that had previously been referred to by the Centers for Disease Control as Enteric Group 77. Genetic studies have indicated that this species consists of two biovars, *A. veronii* biovar sobria, negative for aesculin hydrolysis and ornithine decarboxylase, and *A. veronii* biovar veronii, positive for these reactions (Altwegg *et al.*, 1990; Carnahan & Altwegg, 1996).

A. veronii biovar veronii has rarely been isolated from humans and little information is available regarding its occurrence in clinical specimens and its ability to cause infections. In the original study (Hickman-Brenner *et al.*, 1987), it was isolated from various non-sterile sites, such as wounds, faeces, sputum, maxillary sinus and endotracheal tube, in which its clinical significance remains unclear. Abbott *et al.* (1994) reported the first case of *A. veronii* biovar veronii bacteraemia, in a 77-year-old man suffering from multiple underlying diseases, including sigmoid colon cancer. In a subsequent report (Hsueh *et al.*, 1998), this species was responsible for bacteraemia and necrotizing fasciitis in a diabetic patient also affected by *A. veronii* biovar sobria urinary tract infection. To our knowledge, no other human bacteraemias caused by this micro-organism have been described.

Here, we report a case of *A. veronii* biovar veronii septicaemia and acute suppurative cholangitis in a patient with chronic hepatitis B.

Case report

A 76-year-old male who had been complaining of thoracic and abdominal pain for several days was admitted to the hospital after the onset of fever. He had a past history of cholecystectomy, due to gallstones 5 years earlier, diabetes and hepatitis B virus-related cirrhosis.

On examination, he had a temperature of 39·8 °C with shivers, abdominal pain with right-upper-quadrant discomfort and positive Murphy's sign. Laboratory investigation revealed a white blood cell count of 30 240 cells μl^{-1} (96 % neutrophils), erythrocyte sedimentation rate of 25 mm h^{-1}, 182 mU glutamic-oxaloacetic transaminase ml^{-1}, 212 mU glutamic-pyruvic transaminase ml^{-1}, 193 mU alkaline phosphatase ml^{-1}, 2·42 mg bilirubin dl^{-1}, 359 mU γ-glutamyl transpeptidase ml^{-1}, 2·17 mg creatinine dl^{-1} and 71 mg blood urea nitrogen dl^{-1}. Abdominal echography showed enlarged and thickened liver, absence of gall bladder, ectasia of intrahepatic and common bile ducts, multiple stones and sludge inside the common bile duct. Endoscopic retrograde cholangiopancreatography (ERCP), 6 days after admission, suggested infection of the biliary tract with purulent exudate at the level of the sphincter of Oddi, stenosis of the common bile duct in the third middle tract and marked ectasia upward. Moreover, there were multiple, possibly infected, stones inside the common bile duct.

Blood samples were collected immediately after the fever spikes on admission and 3 days later (temperature 38·4 °C) in BACTEC Standard 10 Aerobic and Lytic/10 Anaerobic bottles (Becton Dickinson). Bile was collected by a nasobiliary device, placed during ERCP, 6 days after admission. Blood and bile specimens yielded motile, Gram-negative,

oxidase-positive bacilli, growing on chocolate, blood, MacConkey and KF streptococcal agar. The isolates were identified as *A. veronii* by both the Sceptor and Phoenix identification systems (Becton Dickinson) (respective probability of 98·25 and 99 %) and showed positive Voges–Proskauer (API 20NE system; bioMérieux), ornithine decarboxylase and aesculin reactions and negative arginine dihydrolase reaction. The isolates did not grow in nutrient broth with NaCl (6 % w/v), were not susceptible to the vibriostatic agent O/129 and were string-test-negative. They were identified as *A. veronii* biovar veronii according to Abbott *et al.* (1994, 1998) and Janda & Abbott (1998). Antimicrobial susceptibility, determined by the Gram-negative breakpoint/ID panel Sceptor system (Becton Dickinson), showed that all isolates were susceptible to aminoglycosides, co-trimoxazole and quinolones and resistant to first- and second-generation cephalosporins (Table 1). The second blood isolate and the bile isolate were resistant to mezlocillin and piperacillin and showed intermediate susceptibility to some third-generation cephalosporins (Table 1). Antimicrobial susceptibility patterns were confirmed by the Kirby–Bauer disk diffusion method. On PFGE analysis after *Spe*I restriction enzyme DNA digestion, the second blood isolate was indistinguishable (Dice coefficient 1) from the bile isolate and closely related (Dice coefficient 0·8) to the first blood isolate. In particular, PFGE profiles of both the second blood isolate and the bile isolate yielded 30 well-resolved DNA bands ranging in size from approximately 10 to 400 kb, while that of the first blood isolate differed by two additional bands of approximately 50 and 170 kb (data not shown).

The patient was first treated intravenously with piperacillin (2 g die) and then, after isolation of the infectious agent, with ciprofloxacin (200 mg every 12 h) and ceftazidime (1 g every 8 h). Clinical and laboratory findings improved dramatically after antibiotic treatment and the patient was discharged 20 days after admission.

Table 1. *In vitro* susceptibility of *A. veronii* biovar veronii isolates to antimicrobial agents

Values are MIC breakpoints in μg ml^{-1}. R, Resistant; S, susceptible; I, intermediate.

Antimicrobial agent	First blood isolate	Second blood isolate and bile isolate
Penicillins		
Ampicillin	⩾32 R	⩾32 R
Mezlocillin	⩽16 S	⩾128 R
Piperacillin	⩽16 S	⩾128 R
***β*-Lactam/*β*-lactamase inhibitor combinations**		
Amoxicillin/clavulanic acid	⩾32/16 R	⩾32/16 R
Cephalosporins I		
Cephalothin	⩾32 R	⩾32 R
Cephalosporins II		
Cefamandole	⩾32 R	⩾32 R
Cefuroxime	⩾32 R	⩾32 R
Cefoxitin	⩽8 S	⩽8 S
Cephalosporins III		
Cefotaxime	⩽8 S	16–32 I
Ceftazidime	⩽8 S	⩽8 S
Ceftriaxone	⩽8 S	16–32 I
Cephalosporins IV		
Cefepime	⩽8 S	⩽8 S
Carbapenems		
Imipenem	⩽4 S	⩽4 S
Meropenem	⩽4 S	⩽4 S
Monobactams		
Aztreonam	⩽8 S	⩽8 S
Aminoglycosides		
Gentamicin	⩽4 S	⩽4 S
Amikacin	⩽16 S	⩽16 S
Tobramycin	⩽4 S	⩽4 S
Tetracyclines		
Tetracycline	⩽4 S	⩽4 S
Fluoroquinolones		
Ciprofloxacin	⩽1 S	⩽1 S
Ofloxacin	⩽2 S	⩽2 S
Pefloxacin	⩽2 S	⩽2 S
Folate pathway inhibitors		
Co-trimoxazole	⩽2/38 S	⩽2/38 S
Phenicols		
Chloramphenicol	⩽8 S	⩽8 S

Discussion

Of the numerous *Aeromonas* species, few have been related unquestionably to human extraintestinal infections, by virtue of their isolation in pure culture from sterile sites. Little is known about the exact role played by the newly described species in human infections, as underlined by the limited number of reports available in the literature (Janda & Abbott, 1998).

Septicaemia is perhaps the most relevant *Aeromonas* infection for severity and frequency and is associated predominantly with several underlying diseases, such as malignancy, hepatic disorders and diabetes (Janda & Abbott, 1998). *Aeromonas hydrophila*, *Aeromonas caviae* and *A. veronii* biovar sobria are the most frequently involved species (Hanninen & Siitonen, 1995; Janda *et al.*, 1994; Janda & Abbott, 1998; Ko & Chuang, 1995). Conversely, the role of *A. veronii* biovar veronii in human septicaemia has been described very rarely. In the first report (Abbott *et al.*, 1994), *A. veronii* biovar veronii was isolated from blood together with *Enterobacter aerogenes* and *Staphylococcus lugdunensis*, while, in the second case (Hsueh *et al.*, 1998), it caused monomicrobic bacteraemia in a patient with urinary tract infection by *A. veronii* biovar sobria.

In the present case, *A. veronii* biovar veronii was responsible for monomicrobic polyclonal bacteraemia, secondary to infection of the common bile duct and biliary tract, which could represent the primary infectious foci. In fact, the two isolates from blood showed limited differences in antimi-

crobial susceptibility and PFGE patterns, the second being identical to the bile isolate, possibly selected by the initial empirical antibiotic treatment. Indeed, a case of acute cholecystitis due to this species has been reported (Abbott *et al.*, 1998), but this was not followed by septicaemia, possibly because the patient underwent immediate cholecystectomy. Thus, it seems logical to speculate that the correlation between *Aeromonas* septicaemia and hepatic disorders (Janda *et al.*, 1994; Janda & Abbott, 1998) may be related in part to primary, undiagnosed, biliary infections. It has been reported that four of 30 patients with *Aeromonas* acute suppurative cholangitis developed septicaemia (Chan *et al.*, 2000). Moreover, the notion that hepatic lithiasis, as in the case described here, and biliary tract instrumentation are risk factors for *Aeromonas* septicaemia (Janda & Abbot, 1996; Ko & Chuang, 1995) suggests that the role of biliary tract infections in this pathology has been underestimated. Hepatic lithiasis and the presence of sludge in the bile could facilitate bacterial colonization and biofilm formation (Sung *et al.*, 1993), while biliary tract instrumentation could allow intestinal bacteria to cause ascending infections (Sung *et al.*, 1992).

The antimicrobial susceptibility patterns of recently recognized *Aeromonas* species are not completely known because of the small number of single-isolate cases reported, although a comprehensive susceptibility pattern of 12 *A. veronii* biovar veronii isolates has been described (Overman & Janda, 1999). In agreement with the above study, the *Aeromonas* isolates described here were susceptible to aminoglycosides, quinolones, co-trimoxazole and aztreonam but resistant to first- and some second-generation cephalosporins. Furthermore, the second blood isolate and the bile isolate were also resistant to piperacillin and showed intermediate susceptibility to some third-generation cephalosporins. This appears to be consistent with the view that *Aeromonas* species possess both constitutive and inducible β-lactamases responsible for resistance to β-lactamics (Rossolini *et al.*, 1996; Walsh *et al.*, 1997). In addition, the pattern of antimicrobial susceptibility of infectious agents can be related to their different geographical distribution, especially for those of environmental origin. *Aeromonas* strains from Taiwan have been shown to be more resistant to several antimicrobials than strains from the USA and Australia (Ko *et al.*, 1996); high resistance in environmental *Aeromonas* species has also been described in Europe (Goñi-Urriza *et al.*, 2000). This report confirms that the occurrence of drug resistance in *Aeromonas* species could be of clinical concern, also involving species generally thought to be susceptible.

In conclusion, this report describes a case of monomicrobic, polyclonal *A. veronii* biovar veronii septicaemia, secondary to acute suppurative cholangitis in a patient with liver disorders and lithiasis. Importantly, the clinical isolates were found to be resistant to different classes of antimicrobial agents, suggesting increased antibiotic resistance in this species and emphasizing that all clinical isolates may require antibiotic susceptibility testing.

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