Ochrobactrum anthropi Bacteremia in a Child with Inborn Error of Mitochondrial Fatty Acid Oxidation

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Key Words

Ochrobactrum anthropi • Bacteremia • Mitochondrial fatty acid oxidation

Abstract

Objective: To report an incident of bacteremia caused by *Ochrobactrum anthropi*. **Case Presentation and Intervention:** The case of a female child aged 2 years and 10 months with a known history of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase deficiency who developed *O. anthropi* bacteremia during hospital stay is presented. Patient's history, clinical findings, laboratory and radiological investigations were thoroughly reviewed. The cultured organism was identified using MicroScan WalkAway 96 SI (Dade Behring) as well as by conventional techniques. Imipenem resistance was confirmed by the conventional Kirby-Bauer disk diffusion technique on Muller-Hinton agar with no zone of inhibition around a 10-μg imipenem disk (Hi Media) using the 0.5 McFarland standard. **Conclusion:** This report shows *O. anthropi* as a rare nosocomial pathogen that affected a patient who was immunocompromised. The *O. anthropi* showed multidrug resistance. Copyright © 2007 S. Karger AG, Basel

Introduction

Ochrobactrum anthropi, formerly known as *Centers for Disease Control and Prevention* group Vd or *Achromobacter* group Vd, is a nonfastidious, Gram-negative, motile, nonfermenting bacillus with strict oxidative metabolism that possesses a very active urease [1]. The organism has been isolated from different human clinical sources leading to its specific epithet *anthropi* [2]. However, nonhuman sources exist and include soil, hospital water sources, indwelling catheters, retained foreign bodies, and contaminated pharmaceuticals [3]. Although *O. anthropi* is an opportunistic pathogen in immunocompromised patients, it is increasingly being recognized to be a causative agent in healthy hosts [4]. Incidents of nosocomial bacteremia in children caused by this organism are very infrequent.

We report a case of *O. anthropi* bacteremia in a child from Kuwait with an inborn error of mitochondrial fatty acid oxidation.

Case Report

The patient was a female child aged 2 years and 10 months with a known history of long-chain 3-hydroxyacyl-coenzyme A dehydrogenase (LCAD) deficiency, an inborn error of mitochondrial

fatty acid oxidation. She was born to first-degree-related parents with a sibling who died at the age of 5 months and found to have LCAD deficiency.

The patient was admitted to the hospital on January 6, 2006. She had a fever, dyspnea, cough and a wheezy chest. On examination, she was conscious and responded to commands. Heart rate was 110 beats/min, blood pressure 120/80 mm Hg, temperature 38.5°C, and respiratory rate 70/min. Cardiac examination revealed cardiomegaly. Chest examination showed diminished air entry, expiratory wheezes and widespread scattered crackles. Abdominal examination revealed abdominal distension and hepatomegaly. Chest X-ray showed a picture of bronchopneumonia.

Laboratory investigation showed white blood cells $9.2 \times 10^9/\text{l}$, red blood cells $4.41 \times 10^{12}/\text{l}$, hemoglobin 104 g/l, platelets $297 \times 10^9/\text{l}$, lactic acid 2.39 mmol/l (normal value 0.40–2 mmol/l) and blood ammonia 109 $\mu\text{mol/l}$ (normal value 11–32 $\mu\text{mol/l}$). In blood gas analysis, pH was 7.4, HCO_3^- 22 mmol/l and SaO_2 95%. Creatine kinase was 4,012 U/l (normal value 21–232 U/l), C-reactive protein 8.95 mg/l (normal value 0.0–5 mg/l), alanine aminotransferase 435 U/l, aspartate transaminase 1,641 U/l, alkaline phosphatase 92 U/l, total bilirubin 8.1 $\mu\text{mol/l}$ (normal value 1.71–17.1 $\mu\text{mol/l}$) and blood glucose 4.2 mmol/l (normal value 3.9–6.1 mmol/l). Blood and urine cultures were negative. The child was treated empirically with intravenous cefotaxime and glucose.

Three days later, the child collapsed in the ward and blood gas analysis showed metabolic acidosis (pH 7.29, HCO_3^- 12 mmol/l). The child received resuscitative measures. She was diagnosed as having cardiomyopathy that was confirmed by echocardiography. Antifailure treatment was commenced. Creatine kinase was 2,269 U/l. The patient gradually improved and heart failure was under control. By day 34, the overall general condition improved and creatine kinase dropped to 89.9 U/l.

On February 15, 2006 (day 41), she had a fever (40°C) and developed seizure with postictal drowsiness. Meningoencephalitis was suspected. CT was normal. Lumbar puncture was not performed due to the critical state of the patient. Chest examination was normal. Basic biochemical tests were within normal ranges and no evidence of metabolic encephalopathy was found. Laboratory investigations showed the following: white blood cells $7.5 \times 10^9/\text{l}$, hemoglobin 97 g/l, platelets $279 \times 10^9/\text{l}$, lactic acid 3.3 mmol/l, blood ammonia 35 $\mu\text{mol/l}$, creatine kinase 51 U/l, alanine aminotransferase 22 U/l, aspartate transaminase 28 U/l, alkaline phosphatase 111 U/l, total bilirubin 13.2 $\mu\text{mol/l}$, blood glucose 6.5 mmol/l, Na 130.5 mmol/l, K 4.3 mmol/l and C-reactive protein 43.9 mg/l. Blood culture was ordered for possible sepsis episode.

Blood cultures were set up. In brief, on positive signal from the BacT/Alert 3D blood culture cabinet obtained 24 h after incubation, inoculations were made on nutrient agar, blood agar and MacConkey agar plates and incubated at 37°C. The growth was identified as *O. anthropi* by the MicroScan WalkAway 96 SI (Dade Behring) as well as by conventional techniques. The strain had the following characteristics: strictly aerobic Gram-negative bacilli, growth was also obtained under 5% CO_2 conditions, no growth under anaerobic conditions, good growth on usual laboratory media after overnight incubation at 37°C, positive growth at 42°C, no growth at 4–5°C, motile, non-lecithinase producer on serum agar, non-pigment producer, non-lactose fermenting, and catalase, oxidase, urease and nitrate positive but citrate was not utilized in Simmons' citrate medium. No acid was formed from

glucose in peptone water medium. Only glucose was oxidatively broken down in O-F medium. The strain was clearly differentiated from other related species. In fact, more than 30 characteristics were taken into account in the identification process. Importantly, our strain was found sensitive to colistin (10 $\mu\text{g}/\text{disk}$; Hi-Media) and polymyxin B (300 IU/disk; Hi-Media). Therefore, the possibility of *Ochrobactrum intermedium* was ruled out. As the strain produced acid from adonitol and dulcitol, the possibility of other related species like *Achromobacter xylosoxidans* and *Achromobacter* group B was equally ruled out. Being motile both at 37°C and at 20–22°C, it was easily differentiated from *Brucella* spp.

The organism was sensitive to ciprofloxacin, levofloxacin, piperacillin/tazobactam and trimethoprim/sulfamethoxazole and resistant to amikacin, cefotaxime, ceftazidime, ceftriaxone, cefepime, gentamicin, imipenem, piperacillin, tetracycline, ticarcillin/clavulanate and tobramycin. It was also resistant to imipenem by the conventional Kirby-Bauer disk diffusion technique on Muller-Hinton agar with no zone of inhibition around a 10- μg imipenem disk (Hi-Media) using the 0.5 McFarland standard.

The patient was given cefotaxime and acyclovir empirically. On day 42, she became fully conscious but still had a fever. On day 45, her fever resolved completely. The patient made a good recovery with no neurological deficit. On day 54, she was discharged home.

Discussion

O. anthropi is often associated with nosocomial infection in debilitated patients, most commonly catheter-associated bacteremia likely due to its ability to adhere to various synthetic materials such as silicone tubing [5]. A Medline search of the term *Ochrobactrum anthropi* from 1989 to 2006 yielded 145 citations, representing 48 reports of clinical cases of *O. anthropi* infection. Only 9 reports of *O. anthropi* bacteremia in the pediatric population were found; in 7 of them, bacteremia occurred in immunocompromised children with underlying malignancy or severe disease.

In children, *O. anthropi* bacteremia usually presents with fever and nonspecific clinical manifestations [6]. The underlying inborn error of metabolism rendered our patient immunocompromised. The patient manifested primary *O. anthropi* bacteremia with no obvious focus. Of note, throughout her hospital stay, she had had a peripheral venous catheter which was subject to frequent change. It can be speculated that the catheter might have provided a portal of entry to the pathogen or a prior colonization as has been reported with indwelling catheters [3, 5].

Although empirical cefotaxime therapy yielded good clinical response, the *O. anthropi* isolated from her blood was found resistant to β -lactams (such as cefotaxime and

ceftriaxone). It is plausible that the good clinical outcome was not due to cefotaxime therapy but due to low virulence and low pathogenicity of the organism [7]. It has been reported that patients with *O. anthropi* infection that were not given any specific treatment made a rapid recovery [8]. It is therefore possible that the favorable outcome of this infection in our patient could be partly related to the nature of the organism.

The imipenem resistance in this strain is a unique finding as to the best of our knowledge it has never been reported before. According to Bailey and Scott [9], *O. anthropi* is reported to be commonly resistant to all currently available penicillins and cephalosporins but usually susceptible to imipenem. Such a finding was formerly reported by Bizet and Bizet [10] who determined the susceptibility of 13 strains of *O. anthropi* by the agar diffusion method.

In fact, *O. anthropi* is the name given for 3 (A, C and D) of the 6 (A–F) biotypes of *Achromobacter*-like strains from clinical material [11]. Recently, imipenem resistance has been found in *A. xylosoxidans* (a bacterial subspecies to which *O. anthropi* is closely related) isolated from patients hospitalized in the intensive care unit of a Korean tertiary hospital [12]. It is relevant to mention that we not only obtained few imipenem-resistant *Alcaligenes xy-*

losoxidans subspecies *xylosoxidans* (*A. xylosoxidans*) isolates from clinical specimens in our hospital, but we also obtained few isolates of imipenem-resistant *Pseudomonas aeruginosa*. Of note, an imipenem-resistant *A. xylosoxidans* strain was isolated from another patient in the same ward during February 2006 [unpubl. data].

Imipenem has quite often been injudiciously used in treating infections by Gram-negative bacilli globally. It is reasonable to believe that *O. anthropi* has acquired imipenem resistance from either its above racemates or from *P. aeruginosa*. To limit the spread of antimicrobial resistance, we recommend that imipenem should not be used as a first-line drug for treating infections by Gram-negative bacilli. It should be reserved for cases refractory to all antibiotics as is done with vancomycin which is used to treat infections by methicillin-resistant *Staphylococcus aureus* strains.

Conclusion

This study reported *O. anthropi* as a rare nosocomial pathogen that affected a patient who was immunocompromised. *O. anthropi* showed multidrug resistance.

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