Original article

Bacteremia due to *Achromobacter xylosoxidans* in neonates: clinical features and outcome

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**A R T I C L E   I N F O**

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**A B S T R A C T**

Objective: We report an outbreak of *Achromobacter xylosoxidans* at a neonatal intensive care unit. We aimed to present clinical, laboratory and treatment data of the patients.

Materials and methods: All consecutive episodes of bacteremia due to *A. xylosoxidans* at our neonatal intensive care unit, beginning with the index case detected at November 2009 until cessation of the outbreak in April 2010, were evaluated retrospectively.

Results: Thirty-four episodes of bacteremia occurred in 22 neonates during a 6-month period. Among the affected, 90% were preterm newborns with gestational age of 32 weeks or less and 60% had birth weight of 1000 g or less. Endotracheal intubation, intravenous catheter use, total parenteral nutrition and prolonged antibiotic therapy were the predisposing conditions. Presenting features were abdominal distention, thrombocytopenia and neutropenia. The mortality rate was 13.6% and the majority of isolates were susceptible to piperacillin-tazobactam, carbapenems and trimethoprim-sulfamethoxazole, and resistant to gentamycin. More than half were breakthrough infections. Despite intensive efforts to control the outbreak by standard methods of hand hygiene, patient screening and isolation, containment could be achieved only after the neonatal intensive care unit was relocated. The investigation was not able to single out the source of the outbreak.

Conclusion: *A. xylosoxidans* has the potential to cause serious infections in premature babies. More studies are needed to determine the importance of different sources of infection in hospital units.

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**Introduction**

*Achromobacter xylosoxidans* is a nonfermentative Gram-negative bacillus which is widely distributed in nature, especially in aquatic environments. 1,2 It was first described by Yabuuchi and Ohyama in 1971 from purulent ear discharge of patients with chronic otitis media. 3 Since it is an opportunistic pathogen it usually affects patients with underlying illnesses and immunosuppression. 4,5 Infections such as bacteremia,
pneumonia, meningitis, urinary tract infections, abscesses, osteomyelitis, corneal ulcers, prosthetic valve endocarditis and peritonitis have been reported.\textsuperscript{1,6–11} Treatment of Acro-
mobacter infections is difficult since the bacterium may be
resistant to several antibiotics.\textsuperscript{2}

Because of limited data and lack of large series of infections
cau sed by Acro mobacter in children, especially in newborns,
we aimed to present an outbreak of A. xylosoxidans bacteremia
that took place at our neonatal intensive care unit (NICU).

Methods

The study was performed in a level III neonatal reference unit
of a tertiary care hospital where a mean of 400 newborns are
admitted annually. All consecutive episodes of bacteremia due
to A. xylosoxidans, beginning with the index case detected in
November 2009 until cessation of the outbreak in April 2010
were evaluated retrospectively. A case of A. xylosoxidans bac-
teremia was defined as one or more blood cultures positive for
A. xylosoxidans when clinical signs of sepsis were present.\textsuperscript{12}
Blood samples were incubated into Bactec 9240 system (Becton
Dickinson, USA) for up to seven days. A sample from
the blood culture bottle with positive bacterial growth was
incubated into 5% sheep blood agar and EMB (eosin methy-
lene blue) agar (Oxoid, England), and incubated at 36.5 °C for
18–20 h. Gram negative bacilli with positive reaction for oxidi-
dase were detected in Gram-stained smears prepared from
colonies. Identification of the microorganisms was done by
API 20 NE system (bioMerieux, France). Susceptibility of the
organisms to antimicrobial agents was performed by using
(Kirby–Bauer) disk-diffusion method on Mueller–Hinton agar,
according to the Clinical Laboratory Standards Institute (CLSI)
Guidelines. Multiple episodes were indicated by the finding
of A. xylosoxidans isolates in blood cultures obtained >four
weeks apart, or >two weeks apart if the blood cultures became
sterile and/or there was evidence of clinical resolution of the
infection.\textsuperscript{4}

Data recorded included sex, gestational age, birth weight,
date of admission, underlying diseases, presence of intravas-
cular catheters, administration of broad-spectrum antibiotics
and total parenteral nutrition, number of positive blood cultures
and sites of other cultures from which A. xylosoxidans was
isolated. Neutropenia was defined as a count less than
1.5 x 10\(^9\)/L.cells/mm\(^3\), thrombocytopenia was defined as a
platelet count of <80 x 10\(^9\)/L.\textsuperscript{33} Infections that occurred more
than 72 h after admission were defined as nosocomial.\textsuperscript{14}
A breakthrough infection was indicated by the isolation of
bacteria from blood cultures obtained while the patient was
receiving systemic antibiotics to which the bacteria was later
confirmed to be susceptible.\textsuperscript{4}

For the investigation of outbreak, bacteriological cultures of
environmental samples were taken including antiseptic
solutions (chlorhexidine digluconate, aqueous and alcoholic),
wash basins, incubator surfaces, liquid soaps, faucets, nebu-
lizers and tap water. Hands of health care workers were
sampled by direct fingerprinting in Petri dishes. Fluids were
filtered through 0.45 μm membranes (Millipore, Bedford, MA,
USA) and cultivated on sheep blood agar (SLB, Turkey), EMB
agar. Swabs were plated on EMB agar and 5% sheep blood agar.

Plates were incubated for 24 h at 36 °C. Environmental cultures
were taken following detection of first four bacteremia cases
in November 2009 and discontinued after April 2010.

Results

Index case

The index case was a 25-week gestational age male (birth
weight 660 g) baby born to a G1P0A0 mother. After birth
he was intubated and transferred to the NICU with a diag-
nosis of respiratory distress syndrome (RDS). He received
ampicillin-sulbactam and gentamycin since congenital pneu-
monia could not be excluded. On the 7th day of life, minimal
enteral feeding was initiated but in the next day abdomi-
nal distension developed and antibiotics were switched to
vancomycin and meropenem with a diagnosis of necrotiz-
ing enterocolitis (NEC). Blood cultures remained sterile and
vancomycin was discontinued after 14 days. On 21st day of
meropenem therapy, he developed apnea, leukopenia and
thrombocytopenia. He was reintubated and meropenem was
switched to sulbactam-cefoperazone and fluconazole pend-
ing culture results. His clinical condition deteriorated and he
developed acidosis, hypotension and bradycardia necessitat-
ing a short duration of adrenaline infusion. Two sets of blood
cultures yielded A. xylosoxidans susceptible to ciprofloxacin,
meropenem and trimethoprim-sulfamethoxazole (TMP-SXM).
Sulbactam-cefoperazone and fluconazole were discontinued and
meropenem plus ciprofloxacin were given. Blood cultures
became sterile after five days. The patient's clinical condition
resolved gradually and he was extubated after seven days. He
was discharged from the NICU when at the age of two months.

Epidemiologic investigation

Following the index case, four additional cases were diag-
nosed within the same week. An outbreak was suspected and
cohorting and contact precautions with gown and glove
use on entry to rooms of patients infected with A. xylosoxi-
dans and enhanced environmental cleaning were instituted.
An investigation for determination of source of infection was
started. Standard infection control practices such as hand
hygiene (hand washing upon unit entry before and after
patient contact and use of alcohol hand sanitizer between
patient contacts), aseptic technique for all invasive proce-
dures, sterile procedures requiring gown, mask, and gloves
and environmental cleaning were overviewed. Education of
healthcare staff was repeated but no flaw was found. Environ-
mental vectors were suspected and bacteriological cultures of
environmental samples were taken but the source could not
be identified. Twelve patients were determined to be infected
during November and December. A second attack affecting 10
patients was observed in March. Patients were transferred to
an other part of the hospital prepared as NICU in April. No
further cases were detected during the following 12 months.

Clinical features and treatment of affected neonates

A total of 22 neonates, 12 (54.5%) male, were diagnosed
with A. xylosoxidans bacteremia. All infecting strains were
considered nosocomially acquired. All patients were preterm and 60% were under 1000 g birth weight. Prematurity and respiratory distress syndrome (RDS) were the most common diagnosis at admission. Most common presenting features of infection were abdominal distention, anemia, thrombocytopenia and leukopenia (Table 1). Three out of 22 patients had cerebrospinal fluid (CSF) abnormalities suggestive of bacterial meningitis and A. xylosoxidans growth was detected in CSF in addition to blood culture. 84% of patients recovered with antibiotic therapy while three patients died due to Achromobacter sepsis. Two patients had multiple growths of A. xylosoxidans. In vitro susceptibility profile of A. xylosoxidans isolates to antimicrobial agents is given in Table 2. Breakthrough infection was observed in 14 patients (63.6%). Patients received 10–21 day course of meropenem alone (9.7%), meropenem in combination with other antibiotics (meropenem plus ciprofloxacin, meropenem plus cefazidime and meropenem plus piperacillin-tazobactam in 50%, 22.7%, and 13.6% of patients, respectively) or ciprofloxacin plus cefazidime (4.5%).

Discussion

**A. xylosoxidans** is an emerging nosocomial pathogen. It represented 12.5% of nonfermenting Gram negative bacilli isolated in Latin America medical centers during SENTRY program 1997–2002. Respiratory tract colonization in cystic fibrosis patients has also been recognized during the last decade. Case reports due to *A. xylosoxidans* infection in Turkey are increasingly reported. Nevertheless, knowledge about neonatal infections caused by *A. xylosoxidans* is relatively scarce. It was reported as a contaminant leading to pseudobacteraemia outbreak at NICU but serious infections such as meningitis and fatal sepsis in premature were also described.

*A. xylosoxidans* bacteremia is almost always a nosocomial infection. Bacteremia due to *A. xylosoxidans* is usually related to intravascular catheters and is frequently polymicrobial in patients with underlying malignancies. Shie et al. evaluated characteristics of *A. xylosoxidans* bacteremia in Taiwan and reported that malignancies, central venous catheter implants and previous major surgery were the most common underlying conditions. Another study in a tertiary care hospital in India identified 20 strains of *A. xylosoxidans* isolated from 15 patients during one year period. Seventeen isolates were from blood, two from CSF and one from pleural fluid; 30% of patients were premature neonates. We identified low birth weight, prematurity, total parenteral nutrition (TPN) and previous broad spectrum antibiotic therapy as the major predisposing conditions for *Achromobacter* bacteremia in our study. 4.5% of patients had undergone surgical interventions. The mean interval from hospital admission to isolation of a positive culture was 21 days. All affected neonates had umbilical catheter insertion and in all bacteremia episodes *A. xylosoxidans* was isolated as the sole pathogen.

Aisenberg et al. reported that *Achromobacter* bacteremia presented with fever (52%), sepsis syndrome (22%) and respiratory complaints (17%). In another report of 40 cases of *A. xylosoxidans* bacteremia, the most common manifestations were fever (82%), chills (37.5%), hypotension (32.5%) and altered consciousness. Dyspnea, abdominal pain, oliguria and diarrhea were also noted. In our study, thrombocytopenia (100%), neutropenia (63.6%), abdominal distension (69%) and anemia (45%) were the most common clinical features. These

### Table 1 – Characteristics of 22 newborns infected with *Achromobacter xylosoxidans*.

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Birth weight, mean ± SD</td>
<td>1197 ± 799 g</td>
</tr>
<tr>
<td>Gestational age, mean (range)</td>
<td>27.8 (23–37) weeks</td>
</tr>
<tr>
<td>Male/female</td>
<td>12/10</td>
</tr>
<tr>
<td>Age (days) at the time of diagnosis, mean (range)</td>
<td>21 (6–45)</td>
</tr>
<tr>
<td>Mortality, no. (%)</td>
<td>3 (13.6)</td>
</tr>
<tr>
<td>Predisposing factors (%)</td>
<td></td>
</tr>
<tr>
<td>Prematurity</td>
<td>100</td>
</tr>
<tr>
<td>Catheter</td>
<td>100</td>
</tr>
<tr>
<td>TPN</td>
<td>100</td>
</tr>
<tr>
<td>Previous broad spectrum antibiotic administration</td>
<td>100</td>
</tr>
<tr>
<td>Diagnosis at admission (%)</td>
<td></td>
</tr>
<tr>
<td>Prematurity</td>
<td>13.6</td>
</tr>
<tr>
<td>Prematurity + respiratory distress syndrome (RDS)</td>
<td>72.7</td>
</tr>
<tr>
<td>Prematurity + RDS + digestive disorders</td>
<td>4.5</td>
</tr>
<tr>
<td>Other (chylolothorax, hydrops fetalis, etc.)</td>
<td>9.1</td>
</tr>
<tr>
<td>Clinical findings at the time of diagnosis (%)</td>
<td></td>
</tr>
<tr>
<td>Fever</td>
<td>4.5</td>
</tr>
<tr>
<td>Abdominal distension</td>
<td>68.2</td>
</tr>
<tr>
<td>Anemia</td>
<td>45</td>
</tr>
<tr>
<td>Neutropenia</td>
<td>63.6</td>
</tr>
<tr>
<td>Thrombocytopenia</td>
<td>100</td>
</tr>
<tr>
<td>Breakthrough infection (%)</td>
<td>63.6</td>
</tr>
</tbody>
</table>

### Table 2 – In vitro susceptibility profile of 34 *Achromobacter xylosoxidans* isolates to antimicrobial agents.

<table>
<thead>
<tr>
<th>Antimicrobial agent</th>
<th>Susceptible (%)</th>
<th>Intermediately susceptible (%)</th>
<th>Resistant (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Trimethoprim-sulfamethoxazole (TMP-SXM)</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Meropenem</td>
<td>100</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Piperacillin-tazobactam</td>
<td>91</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td>82</td>
<td>15</td>
<td>3</td>
</tr>
<tr>
<td>Cefazidime</td>
<td>82</td>
<td>3</td>
<td>15</td>
</tr>
<tr>
<td>Ceferidine</td>
<td>15</td>
<td>9</td>
<td>76</td>
</tr>
<tr>
<td>Gentamycin</td>
<td>0</td>
<td>0</td>
<td>100</td>
</tr>
</tbody>
</table>
findings are common with other Gram negative bacilli and fungi septicemia which makes the diagnosis rather difficult unless proven by culture. Fever was reported less frequently (4.5%) probably because of insufficient immune response of premature neonates. Three deaths were attributable to A. xylosoxidans sepsis with a fatality rate lower than previous reports (15–47.5%).²³,²⁴

There have been many reports of A. xylosoxidans isolation from environmental sources in hospital acquired infections.²³ A. xylosoxidans was detected in deionized water in an intensive care unit and tap water and on the hands of two health care workers in a hemodialysis unit.¹²³ We checked environmental samples and hands of healthcare personnel for colonization but were unable to determine the source. In a similar report from India, Kumar et al. were also unable to determine the source.²⁶ Since there was similarity of antibiotic susceptibility pattern of isolates, probable clonality of the isolates could be predicted but we were unable to perform testing for molecular epidemiology. In addition to enhanced infection control measures and increased awareness of health care staff, decreased patient capacity during the first days following relocation of NICU may have prevented development of additional cases of A. xylosoxidans bacteremia.

A. xylosoxidans has an unusual susceptibility pattern with resistance to aminoglycosides and to the majority of β-lactam antibiotics. Anti-pseudomonal penicillins, TMP-SMZ and carbapenems are the preferred agents in treatment.²⁶²⁷ All of our isolates were sensitive to TMP-SMX and meropenem and the majority were sensitive to piperacillin-tazobactam similar to previous reports. Susceptibility to the fluoroquinolones is variable.²⁸ Gomez et al. and Almuzara et al. have reported that quinolones have poor activity against Achromobacter spp.²³,²⁹ In contrast 82% of our isolates were susceptible to ciprofloxacin. For infections caused by multidrug-resistant A. xylosoxidans, antimicrobial combinations such as piperacillin plus gentamycin, azitromycin plus doxycycline, and azitromycin plus TMP-SMX have been tested with favorable results.²⁴ Since 63% of infections were definite breakthrough infections and the patients were severely ill we used combination therapy in most patients.

Conclusion

A. xylosoxidans has the potential to cause serious infections in hospitalized neonates. Antimicrobial susceptibility profile for each case should be taken into account for determining the therapy. More studies are needed to assess the importance of different sources of contamination in hospital units.

Conflict of interest

The authors declare no conflicts of interest.

REFERENCES


