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Case Report

Achromobacter Xylosoxidans Bloodstream Infection in Elderly Patient with Hepatocellular Carcinoma: Case Report and Review of Literature

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ABSTRACT

Achromobacter xylosoxidans is a nonfermentative Gram-negative organism, known to cause opportunistic infection in humans. We report a case of septicemia in a 76-year-old male patient with underlying hepatocellular carcinoma due to *A. xylosoxidans*, which showed a different antimicrobial susceptibility pattern from what is usually reported. From aerobic blood culture of the patient, *A. xylosoxidans* was isolated which was found to be sensitive to amoxicillin-clavulanic acid, piperacillin-tazobactam, ceftazidime, cefoperazone-sulbactam, meropenem, minocycline, tigecycline, and trimethoprim/sulfamethoxazole. The patient recovered with amoxicillin-clavulanic acid treatment, which was given empirically to the patient. The present case highlights the possible role of amoxicillin-clavulanic acid for treatment of bloodstream infection with *A. xylosoxidans*.

Key words: *Achromobacter xylosoxidans,* amoxicillin-clavulanic acid, blood stream infection

INTRODUCTION

Members of genus *Achromobacter* (formerly *Alcaligenes*) are nonfermentative Gram-negative bacilli usually found in the aquatic environment. It is considered an opportunistic pathogen, known to cause infections such as bacteremia, pneumonia, meningitis, urinary tract infection, abscesses, osteomyelitis, corneal ulcers, prosthetic valve endocarditis, and peritonitis.[1]

Bloodstream infection with *Achromobacter* has been reported among patients with malignancy, IgM immunodeficiency, post valve replacement patients, and in neonates.[2-5] Literature search has shown case fatality rates varying from 3% for primary or catheter-associated bacteremia to 80% for neonatal infection.[3]

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Previous studies have shown that *Achromobacter* strains are frequently resistant to aminoglycosides, ampicillin, first and second generation cephalosporins, chloramphenicol, fluoroquinolones, tetracycline and rifampin, and are usually susceptible to antipseudomonal third generation cephalosporins, carbapenem and cotrimoxazole.[2,3]

We are reporting a case of *Achromobacter xylosoxidans* as a causative agent of septicemia, which showed a different susceptibility pattern from what is usually reported. The case report reinforces the need to identify this organism, especially among febrile patients with malignancy.

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CASE REPORT

A 76-year-male presented with complaints of fever, lump in the right upper abdomen, and weight loss for duration of 2 months. His examination revealed findings of firm nodular hepatomegaly. Computed tomography showed evidence of hepatocellular carcinoma with deposits in the lesser sac. He was started on chemotherapy with cisplatin, leucovorin, etoposide, and 5 fluorouracil. His chemotherapy was upgraded to oxaliplatin and gemcitabine.

After 3 weeks of starting the upgraded chemotherapy, he developed high-grade fever without chills and rigors that lasted for next 2 days. He presented to the outpatient unit on the 3rd day of fever where aseptically his blood sample was collected, and he was started empirically on amoxicillin-clavulanic acid 625 mg twice daily. The blood sample was processed as per standard microbiological procedure. Positive signal was detected after 48 h of incubation in Bac T/Alert 3D (BioMérieux, Durham, North Carolina/USA). The broth was subcultured on Mac Conkey agar and blood agar. After overnight incubation at 37°C MacConkey agar showed small nonlactose fermenting colonies and blood agar showed 1–2 mm, round, moist, grey, smooth, entire edge, nonhemolytic colonies. Gram-stained smear showed Gram-negative bacilli, which were oxidase and catalase positive. The growth was subjected to identification by automated VITEK®2 Compact (C) system version: 06.01 (BioMérieux, North Carolina/USA) using GNID 21 341 and antibiotic susceptibility was done using AST-N 280 and AST-N 281 cards. The organism was identified as *A. xylosoxidans*. Antibiotic sensitivity was expressed as sensitive, intermediate, and resistant according to CLSI M 100 S 24 (2014).[6]

The isolated organism was sensitive to amoxicillin-clavulanic acid, piperacillin-tazobactam, ceftazidime, cefoperazone-sulbactam, meropenem, minocycline, tigecycline, and trimethoprim/sulfamethoxazole. However, it was intermediately sensitive to imipenem, ciprofloxacin, and levofloxacin and resistant to ampicillin, cefuroxime, ceftriaxone, nalidixic acid, aztreonam, amikacin, and gentamicin. On the follow-up visit after 9 days of starting the treatment, the patient informed us that he was afebrile after 2 days of treatment. Repeat blood culture was sterile. Patient had responded to the treatment with amoxicillin-clavulanate.

DISCUSSION AND REVIEW OF LITERATURE

Achromobacter initially characterized by Holmes, was later studied and isolated by Yabuuchi and Ohyama in 1971 from seven patients with chronic otitis media.[7] There are 2 subspecies of *A. xylosoxidans* namely *Denitrificans* and *Xylosoxidans* according to a recent reclassification.[2]

Achromobacter species are oxidase, catalase, and nitrate positive. They are ornithine and lysine negative.[2]

Gómez-Cerezo *et al*. in his study found neutropenia and age more than 65 years to be a predisposing factor for bacteremia with *A. xylosoxidans*.[8] In our case, the predisposing factors present were the age of the patient and underlying malignancy.

Achromobacter infection is often associated with multiple episodes. Multiple episodes is indicated by the finding of *A. xylosoxidans* isolated in blood culture samples obtained more than 4 weeks apart, or more than 2 weeks apart if blood culture became sterile or there was evidence of clinical resolution of the infection; hence regular follow-up of the patients is required. In our case, the patient was found to be afebrile after 2 weeks of completion of treatment and also after 4 weeks of completion of treatment.

Table 1 briefly outlines studies with *Achromobacter* isolates from blood across various parts of the world.

The antibiotic regimen for this organism has not been described. Turel *et al*., and Aisenberg *et al*., in their respective studies showed that combination of carbapenem with ciprofloxacin, ceftazidime or piperacillin-tazobactam to be an effective treatment for bloodstream infection in neonates and cancer patients.[1,4] Trimethoprim-sulfamethoxazole was found to be treatment option according to studies done by Legrand and Anaissie, Shie *et al*. Duggan *et al*., and Padmaja *et al*.[5,9-11] Gómez-Cerezo *et al*., had shown that antibiotic therapy with antipseudomonal penicillin or carbapenems would be an effective treatment for *Achromobacter* species.[8] Till date, the maximum number of blood culture isolates (92) have been reported by Kaur *et al*.[12] They have reported 88% of the isolates to be resistant to cefuroxime and 70% of the isolates to be resistant to aminoglycosides, first and second generation cephalosporins. They have also done a comparative analysis of various typing methods on all 92 isolates. The antibiogram typing in their study had a discriminatory power of 96.9% compared to 98.9% of pulse field gel electrophoresis. They found that whole cell protein profiling with a discriminatory power of 94% was a faster,

Table 1: Various studies showing bloodstream infection caused by *Achromobacter* species

Reference	Species isolated	Underlying medical condition	Number of isolates	Year and place of isolation	Treatment given and response to treatment
Aisenberg *et al.*[4]	*A. xylosoxidans*	Cancer	47	1989-2003 Texas	Meropenem with piperacillin-tazobactam; 7 patients expired, rest recovered
	A. denitrificans		2		
Legrand and Anaissie[9]	*A. xylosoxidans*	Cancer, pneumonia	26	1992 Houston	Trimethoprim-sulfamethoxazole, antipseudomonal penicillin, ceftazidime, cefoperazone, imipenem; all patients recovered
Duggan *et al.*[10]	*A. xylosoxidans*	Cancer, renal failure	4	1996 Michigan	1. Trimethoprim-sulfamethoxazole with tobramycin-patient expired
					2. and 3. Ticarcillin-clavulanic acid-patients recovered
					4. Ciprofloxacin and ceftazidime-patient recovered
Weitkamp *et al.*[3]	*A. xylosoxidans*	IgM syndrome	1	2000 Tennessee	Amikacin, imipenem, tobramycin; recurrent episodes of bacteremia on follow-up
Gómez-Cerezo *et al.*[8]	*A. xylosoxidans*	Cancer	54	2003 Spain	Antipseudomonal penicillins and carbapenem; 8 patients expired, rest recovered
Shie *et al.*[11]	*A. xylosoxidans*	Cancer, intravascular catheters, neutropenia	40	2005 Taiwan	Piperacillin, imipenem, ceftazidime, and trimethoprim-sulfamethoxazole; 19 patients expired, rest recovered
Al-Jasser and Al-Anazi[7]	*A. xylosoxidans*	Cancer	1	2007 Saudi Arabia	Colistin - patient expired
Kaur *et al.*[12]	*A. xylosoxidans*	-	92	2009 India	Comparison of different typing methods in clinical isolates is done
Padmaja *et al.*[5]	*A. xylosoxidans* subsp. denitrificans	Post valve replacement	1	2013 India	Meropenem with trimethoprim-sulfamethoxazole; patient recovered
Krause *et al.*[13]	*A. piechaudii*	Immunocompetent individual	1	2012 USA	Levofloxacin and patient recovered
Turel *et al.*[1]	*A. xylosoxidans*	Neonates	22	2013 Turkey	Meropenem in combination with ciprofloxacin/ceftazidime/ piperacillin tazobactam
					3 patients expired, rest recovered
Peterson *et al.*[2]	*A. xylosoxidans*	Neonate	1	2014 India	Meropenem; patient expired
Otta *et al.*[14]	*A. xylosoxidans*	Hypertensive, alcoholic, acute pancreatitis	1	2014 India	Amikacin with piperacillin-tazobactam; patient recovered

A. xylosoxidans: *Achromobacter xylosoxidans*, *A. denitrificans*: *Achromobacter denitrificans*, *A. piechaudii*: *Achromobacter piechaudii*

easier, and technically less demanding typing method. In our case, the patient recovered with amoxicillin-clavulanic acid treatment, which was given empirically to the patient and on doing antibiotic susceptibility testing it was found that the strain was susceptible to it.

Our patient was diagnosed to have *A. xylosoxidans* and had responded to treatment with amoxicillin-clavulanic acid. Similar findings of *Achromobacter* sensitivity to amoxicillin-clavulanate have been reported by Ng *et al.*[15] More light on this aspect may generate enough evidence to show that amoxicillin-clavulanic acid is a proper drug for curing *Achromobacter* septicemia, which is definitely a safer and well-tolerated drug.

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Conflicts of interest

There are no conflicts of interest.

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