

Alcaligenes Xylooxidans Infections in Children

Five Cases in Different Sites

AUTHORS: Sanz Santaefemia FJ See correspondence
Ramos Amador JT¹ jramos.hugf@salud.madrid.org
Muley Alonso R² rmuley.hdoc@salud.madrid.org
Bodas Pinedo A⁴ abodas.hcsc@salud.madrid.org
Hinojosa Mena-Bernal J³ jhinojosa.hdoc@salud.madrid.org
García Talavera ME⁵ garciatalaverame@gmail.com

Department of Pediatrics. Hospital Niño Jesús. Madrid. 1. Immunodeficiency Unit.
2. Pediatric Nephrology. 3. Pediatric Neurosurgery. Department of Pediatrics.
Hospital 12 Octubre. Madrid. 4. Department of Pediatrics. Hospital Clinico Madrid.
5. Family Physician. Centro Salud Felipe II, Móstoles.

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Correspondence and reprint requests:

Fco José Sanz Santaefemia, MD

Pediatría

Hospital Niño Jesús

Avenida de Menéndez Pelayo 65

28009 Madrid, Spain

☎ 34-91-5035900. Ext 410

E-mail: sanzssantaefemiafj@gmail.com

ABSTRACT

Alcaligenes xylosoxidans, formerly known as *Achromobacter xylosoxidans* is a non-fermenting gram-negative rod, that is increasingly been identified as a pathogen in the last decade. Nowadays the name commonly accepted for correct taxonomy is *Achromobacter xylosoxidans*¹. It has been isolated from several aqueous environmental sources, some of which have been associated with nosocomial outbreaks of infections². Infections caused by *Alcaligenes xylosoxidans* have been documented in patients with a variety of indwelling devices, but it has been shown as a causing disease bacteria in other cases without risk factors (previous surgery or catheter carrier). It could be also encountered in all kind of organs and body systems, so this microorganism is acquiring major importance in recent years.

Keywords: children, *Alcaligenes*, infection

INTRODUCTION

Alcaligenes xylosoxidans has been encountered in central venous catheters³, shunts⁴ and peritoneal dialysis catheters⁵. It has been reported mostly in patients with predisposing conditions, including diabetes mellitus, chronic pulmonary obstructive disease or alcoholism⁶⁻⁸ and immunodeficiency states, such as HIV-infection⁹⁻¹⁰. *Alcaligenes xylosoxidans* has been described as the etiologic agent of a wide variety of infections, including bacteremia¹¹⁻¹³ pneumonia¹⁰, meningitis¹⁴, urinary tract infections^{2,6}, keratitis¹⁵, osteomyelitis¹⁶ and rarely peritonitis^{5,17}. It appears to be more severe in the elderly⁸ and the newborn¹⁸⁻¹⁹. There are very few cases reported in the pediatric age group. We herein describe 7 infections caused by *Alcaligenes xylosoxidans* isolated from 5 children in three hospitals in Madrid, Spain.

PATIENTS AND METHODS

The 7 strains of *Alcaligenes xylosoxidans* were isolated from 5 children admitted to three large teaching spanish hospitals in Madrid from April 1996 to August 2004. All cases of *Alcaligenes xylosoxidans* infections were not associated with each other by time or space. One child had 3 recurrent episodes of catheter associated bacteremia. The other 4 strains were isolated from 4 each patient: one from peritoneal fluid in a child undergoing continuous ambulatory peritoneal dialysis, one from the cerebrospinal fluid (CSF) in a child with a ventriculoperitoneal shunt in place, one from a wound infection, and one from subacute otitis respectively.

The biochemical identifications were performed by a semiautomated method (Pasco, Difco. Detroit) in two hospitals and Vitek 2 Compact. Biomerieux. Marcy L'étoile in the other one) Antibiotic susceptibility testing was carried out by the microtiter broth dilution method (See Table 2). The following antibiotics were tested: Amikacin, Ampicillin, Aztreonam, Cefazolin, Cefotaxime, Ceftazidime, Cefuroxime, Chloramphenicol, Ciprofloxacin, Fosfomicine, Gentamycin, Nalidixic Acid, Nitrofurantoin, Ofloxacin, Piperaciline, Ticarcilin, Cotrimoxazol, Tobramycin, Amoxicillin-Clavulanate, Cefepime, Imipenem, Meropenem and Piperaciline-Tazobactam.

There was no identification for the microorganism by other different methods than culture with biochemical test, because of no availability for molecular biology exams as polymerase chain reaction among others. So, only the growth in adequate culture was considered positive for each case.

RESULTS

A summary of the patient characteristics is shown in Table 1.

Case 1. A 4-year-old black male with sickle-cell disease presented with a 48 hours history of fever, myalgia and respiratory symptoms. He had a subcutaneous port-a-cath placed 8 months earlier. Physical examination revealed hepatomegaly, with liver edge felt 4 cm below the right costal margin and tonsillar exudates. Laboratory evaluation showed a hemoglobin level of 8.4 gr/dl and a leucocyte count of 30700/mm³ (62.4% neutrophils, 21.2% lymphocytes, 15.5% monocytes). Bilirrubine 1.7 mg/dl and LDH

446 IU/L. Empiric treatment with cefotaxime was begun. On the second day of admission the hemoglobin level dropped to 6.6 gr/dl, needing a red blood cell transfusion. A throat culture grew mixed flora and culture of a transcatheter blood sample yielded *Alcaligenes spp.* susceptible to cefotaxime. The child remained afebrile throughout his hospitalization. He did well and was discharged 8 days after admission. Eighteen days after the patient was readmitted with febrile syndrome, enlargement of the liver and spleen with extension of the edge 4 cm below the right costal margin and 3 cm below the left costal margin, respectively. The peripheral white blood cell count was 24100/mm³ (59.5% neutrophils, 21.7% lymphocytes, 8% monocytes). Bilirrubine 2.6 mg/dl and LDH 439 IU/L. Therapy with cefotaxime was given during four days but the fever continued. Blood samples were cultured and reported to be *Alcaligenes spp.* by day 4 of hospitalization. Susceptibility testing showed that the organism was resistant to aminoglycosides, ampicillin and ceftazidime, and susceptible to imipenem. Therapy was changed to imipenem infused through the catheter. The patient defervesced after introduction of imipenem. Control blood culture yielded no growth. The catheter was not removed. The patient was discharged six days after. One month later he was admitted again with fever. Blood cultures were positive for *Alcaligenes spp.* A catheter withdrawal was done and therapy with imipenem on the basis on susceptibility testing was given. There was complete clinical recovery in 10 days. After one year of follow-up there was no evidence of relapse of *Alcaligenes* infection.

Case 2. A 2-month-old black female with congenital hydrocephalus and a ventriculoperitoneal shunt in place, underwent reducer cranioplasty, receiving treatment with vancomycin, ceftazidime and gentamicin. 20 days later an ultrasound showed a dilated cerebral ventricle requiring a ventricular tap. 6 days after a ventriculoscopy with prophylactic cefazolin was performed. 7 days thereafter a cerebral scan showed ventriculitis with thick hyperdense edging around the ventricular cavities, needing ventriculostomy, externalization of the catheter and removal of the shunt. She completed treatment with vancomycin, ceftazidime and gentamicin. In cultures of CSF, catheter and the surgical wound *Alcaligenes xylosoxidans* grew resistant to aminoglycosides, quinolones, cephalosporins except ceftazidime, susceptible to ampicillin, carbapenems and intermediate to trimethoprim/sulfamethoxazole. She continued treatment with ceftazidime and meropenem for ten days more until a sterile culture of the CSF was obtained.

Case 3. A 5-year-old white male with terminal renal failure secondary to nephronophthisis on maintenance dialysis for the last eight months presented in a routine clinical visit with skin lesions surrounding the insertion of the peritoneal catheter. Several samples for peritoneal fluid specimens were collected for culture. His past medical history was remarkable for congenital hepatic fibrosis and mopia magna. Forty-eight hours later he was admitted with abdominal crump. Physical examination revealed tense skin and periumbilical erithema. He was apyretic. The peritoneal fluid yielded 6250 leucocytes/mm³ (76% mononuclears). The patient was initially treated with intravenous gentamicin and ciprofloxacin and intraperitoneal ceftazidime. 72 hours after admission a blood culture was negative but cultures of the peritoneal fluid and exudation of the skin lesions were positive for *Alcaligenes xylooxidans* resistant to aminoglycosides and cephalosporins except for ceftazidime, susceptible to trimethoprim/sulfamethoxazole and quinolones. Oral trimethoprim/sulfamethoxazole and fluconazole were added. The dialysis catheter was removed because of persisting abdominal pain. A new peritoneal fluid yielded 1180 leucocytes/mm³ (70% polymorphonuclears). The patient underwent hemofiltration with clinical improvement and posterior negative cultures. One month later he had a new peritoneal dialysis catheter placed. He underwent renal transplantation eleven months later with an uneventful outcome.

Case 4. A 13-year-old white male with an unremarkable medical history was admitted for surgery eleven days after a traffic accident with a type III open fracture of the proximal left tibia and fibula with amputation of the anterior tibial artery and external sciatic nerve palsy. Despite antibiotic therapy with metronidazole and tobramycin for seven days, physical examination revealed tenderness in the left leg and a temperature of 38.5°C. The white cell count was 23360/mm³ (85% neutrophils). Culture of the scar and adjacent tissue yielded growth of *Alcaligenes xylooxidans*. There was no evidence of bone infection. The organism was resistant to aminoglycosides, cephalosporins, aztreonam and ciprofloxacin and was sensible to carbapenem and ceftazidime. Blood culture was negative. He received treatment for seven days with imipenem (500mg/ 6 hours intravenous). Seven days after surgery a generalized multiform rash appeared with hiperpirexia. Antimicrobial therapy was switched to intravenous vancomycin for ten days. The patient remained well taking no antibiotics with no evidence of relapse of

the infection. Subsequent sequential radiographs did not demonstrate progressive bone destruction or sequestrum formation.

Case 5. A 3-year-old white male with no underlying condition was visited at the emergency pediatric department due to mild hyperpyrexia and subacute otorrhea during seven days despite of use of antibiotic therapy (amoxicillin-clavulanate per mouth). A swab culture from right ear discharge was collected and it showed growth of *Alcaligenes xylosoxidans* susceptible to cefotaxime and trimethoprim/sulfamethoxazole, intermediate for fluorquinolones and resistant to aminoglycosides and ampicillin. For ten days the child was given oral cefuroxime-axetil and topical ciprofloxacin-flucinolone during five days previous to know culture results with good evolution. In a new appointment fourteen days after first visit complete clinical recovery was confirmed, so no new antibiotic was ordered. In two weeks he was seen again at the office checking normal right middle ear and he was referred to primary care paediatrician for follow-up.

DISCUSSION

Alcaligenes xylosoxidans, subspecies *xylosoxidans*, has been formerly known by a variety of names such as CDC group Vd, *Alcaligenes fecalis*, *Alcaligenes dentrificans* and *Achromobacter xylosoxidans*. It is a gram negative motile, aerobic, oxidase-positive and non-lactose fermenting rod, that grows well in McConkey agar medium²⁰. The differentiation from other oxidase-positive gram-negative rods may be difficult⁷. Special tests are required to distinguished it from *Pseudomonas spp*, *Ochrobactrum spp* or *Agrobacterium spp*. This differentiation can be accurately done by the semiautomated systems now available. This easier identification systems may have contributed to the increasing reports of *Alcaligenes xylosoxidans* in recent years. Its natural habitat has not been clearly defined. In the community this microorganism has been recovered from water sources²¹. Epidemiologic data suggest that water is the natural reservoir of *Alcaligenes xylosoxidans*

The recognition and identification of this pathogen is important because it may be involved in nosocomial outbreaks and result in important morbidity and mortality. Among the 41 patients with *Alcaligenes xylosoxidans* bacteremia reviewed by Ramos¹¹ et al, the overall mortality was 39%, higher than the mortality associated with other *Alcaligenes xylosoxidans* infections without bacteremia²². Most patients in whom

infections caused by *Alcaligenes xylosoxidans* have been reported had underlying conditions. *Alcaligenes xylosoxidans* has been well described in cancer patients¹³, and occasionally in other immunodeficiency states, usually as case reports, resulting in a wide variety of illnesses including pneumonia¹⁰, meningitis^{14,23}, urinary tract infections⁶, keratitis¹⁵, osteomyelitis²⁴ and peritonitis^{5,25}.

Catheter-associated bacteremia has been described in a few children with cancer¹³ and with AIDS^{3,9}. Catheter-associated bacteremia was diagnosed in our patient on the basis of positive blood cultures obtained from the central venous line, although no quantitation of the colonies of the organism was done. The recurrent episodes of bacteremia and cure after the third episode with catheter removal clearly suggest that the catheter was the source of the bacteremia. Our limited experience is in agreement with most reported cases of catheter related bacteremia, in which line withdrawal was required to cure the infection. Similarly, the patients with peritonitis secondary to continuous ambulatory peritoneal dialysis required removal of the peritoneal catheter¹⁷. The few such cases reported in adults and in one children²⁵ with peritonitis due to *Alcaligenes xylosoxidans* were not cured until the catheter was not withdrawn. It is not clear whether the portal of entry of *Alcaligenes xylosoxidans* is the peritoneal catheter or the peritoneal fluid. Moffet et al have suggested that this second possibility is most likely⁵.

Although arthritis and osteomyelitis have been reported in children secondary to open fractures of the tibia²⁴, there was no evidence of bone involvement in case 4. The outcome was good and sequential radiographs did not show any sign consistent with osteomyelitis. At presentation, the diagnosis of osteomyelitis can be difficult because initial radiographs may not show any sign of infection and isotopic bone scans may show increased uptake consistent with either bone infection or healing fracture. In cases of open fractures and wounds secondary to plantar punctures through sneakers¹⁶ osteomyelitis may occur and *Alcaligenes xylosoxidans* should be considered as a possible etiologic agent, similar to other much more common organisms as *Pseudomonas spp.*

Alcaligenes xylosoxidans infections has rarely been reported in the pediatric age group. Apart from the neonatal period, very few cases of *Alcaligenes xylosoxidans* have

been reported in children. Most cases in children described in the neonatal period occurred in preterm or low birth weight infants. Nosocomial transmission is the usual mode of acquisition of *Alcaligenes xylosoxidans* in the nursery, although a case of well documented perinatal transmission has been described²⁶. Meningitis is a frequent manifestation of neonatal infections¹⁷, resulting frequently in ventriculitis and a high mortality. Doxiadis et al found an overall mortality of 60% in their series of 33 neonatal infections¹⁸. The high mortality seems mainly related to the immune immaturity and related pathology of the newborn. Most cases of ventriculitis have been described in patients with associated meningitis, although there are some reports of ventriculitis⁴ resulting from shunt infections, in which the mortality appears to be lower as illustrated in case 2.

Alcaligenes xylosoxidans is resistant to most antiseptics, what needs to be taken into account since nosocomial neonatal infection have been described transmitted by antiseptic solutions²⁷. In addition, the pattern of susceptibilities of *Alcaligenes xylosoxidans* to antibiotics is different to most gram-negative rods. In vitro susceptibility shows good activity for imipenem, ceftazidime, moderate activity for the fluorquinolones and poor activity for ceftriaxone, cefotaxime and the aminoglycosides. Usually trimethoprim/sulfamethoxazole has excellent activity against *Alcaligenes xylosoxidans*, although several strains have been reported to be resistant²⁸. The optimal treatment for infections caused by *Alcaligenes xylosoxidans* is not known. It has been suggested that a combination of antibiotics might be superior to a single antimicrobial agent, based on some data showing that sometimes the antibiotics with good activity may not be bactericidal¹². However the need for combination therapy has not been established, nor the best combination regimen to be used. In addition, it is important to keep in mind the difficulties observed to eradicate this organism from indwelling devices, and therefore there is frequently a need for withdrawal of foreign material associated with antibiotic therapy due to *Alcaligenes xylosoxidans* infections. In most cases of catheter-associated bacteremia, the catheter needed to be withdrawn, and at least in one case, catheter removal was the only measure required¹³. Due to the scarce reported experience on *Alcaligenes xylosoxidans* infection, it is not possible to draw conclusions about the best treatment options, and therapy must be individualized based mainly on the underlying disease and the site of infection.

In non-immunocompromised children *Alcaligenes xylosoxidans* can be isolated in throat or stools²⁹ not being responsible of illness. Occasionally *Alcaligenes xylosoxidans* has been encountered in purulent ear discharge as first description by Yabuuchi and Ohyama and in case 5³⁰

In conclusion, *Alcaligenes xylosoxidans* is a relatively new bacteria that may be pathogenic, mostly in immunocompromised hosts, in whom it may cause severe infections and a high mortality. In recent years the incidence of infections due to *Alcaligenes xylosoxidans* seems to have increased along with the placement of indwelling clinical devices and as the proportion of immunocompromised patients also increases. The differentiation of *Alcaligenes xylosoxidans* from other non-fermentative gram-negative rods can be difficult. Clinicians and microbiologists should consider *Alcaligenes xylosoxidans* as a potential pathogen and try to identify it in cases of growth of oxidase-positive gram-negative rod infections. An accurate identification is necessary since the response to conventional antibiotics can be inadequate.

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