



# Enfermedades Infecciosas y Microbiología Clínica

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## Scientific letters

### Nosocomial bacteremia due to *Cupriavidus pauculus* in a patient with ulcerative colitis<sup>☆</sup>



#### *Bacteriemia nosocomial por Cupriavidus pauculus en paciente con colitis ulcerosa*

*Cupriavidus* spp. are non-fermenting, environmental Gram-negative bacilli of low virulence, which can cause infections related to intravascular catheters or other devices in immunocompromised patients or patients subject to invasive procedures, with *Cupriavidus pauculus* being the species involved most frequently.

In August 2017, a 27-year-old male, diagnosed in September 2012 with ulcerative colitis, attended the Emergency Department due to presenting with diarrhoea, rectal bleeding, abdominal pain and fever. After being diagnosed with a severe outbreak of ulcerative colitis, he was admitted to the Gastroenterology Department, and immunosuppressive therapy was started. Due to the presence of fever upon admission, it was proceeded to rule out bacterial infection, with the urine culture and blood culture coming back negative. On day 18 of his admission, following another episode of fever, two batches of blood cultures (four vials) were drawn, which were incubated in the Bactec FX<sup>®</sup> system (Becton Dickinson). Following a time-to-positivity of 26 h in the two aerobic vials, growth of Gram-negative, oxidase- and catalase-positive bacilli was observed, subsequently identified, by means of mass spectrometry (MALDI-TOF<sup>®</sup>, Bruker), as *C. pauculus*. The identification was confirmed in the Instituto de Salud Carlos III [Carlos III Health Institute] by means of the amplification and sequencing of a fragment of 1.353 bp of 16S rRNA: a 99.8% similarity was obtained with *C. pauculus* GenBank sequence (AB109753). *C. pauculus* was not identified in other samples from the patient, or in other patients of the Gastroenterology Department in the 30 days prior and subsequent to this isolation. The patient did not have a central venous catheter inserted and had never been admitted to the Intensive Care Unit. Environmental cultures were not performed either and the origin of this infection was not identified.

Antimicrobial susceptibility was performed by broth microdilution using the MicroScan WalkAway<sup>®</sup> system (Siemens Healthcare Diagnostics). The criteria of the European Committee on Antimicrobial Susceptibility Testing (EUCAST), defined for the susceptibility of *Pseudomonas* spp., were applied. It was susceptible to ceftazidime, ciprofloxacin, imipenem, cotrimoxazole and piperacillin-tazobactam and resistant to colistin, meropenem and aminoglycosides. After determining the identification and antibiotic susceptibility, antibiotherapy was started with imipenem, which was later de-escalated to ciprofloxacin.

Given the patient's clinical improvement and with the follow-up blood cultures coming back negative, he was discharged definitively.

*Cupriavidus* spp. are ubiquitous environmental organisms which are found mainly in soil, water and plants.<sup>1</sup> They are motile aerobic, non-spore-forming Gram-negative bacilli, which are catalase- and oxidase-positive, oxidise glucose, use citrate and are urease-positive.<sup>1,2</sup> They grow well in blood agar, where they are not haemolytic, and in MacConkey agar with colourless colonies, as they do not ferment lactose.<sup>1</sup> It was in 2004 when bacteria of the genus *Wautersia* were grouped along with *Cupriavidus necator* and it formed the genus *Cupriavidus*<sup>1</sup>, which currently consists of more than 13 different species.<sup>3</sup> The species which is isolated most frequently in clinical samples is *C. pauculus*. This bacterium, initially known as CDC group IVC-2 and subsequently as *Ralstonia paucula*,<sup>1</sup> has been recognised as an opportunistic pathogen described in various serious infections, fundamentally of nosocomial origin, in immunosuppressed patients, treated by invasive procedures or that require multiple antibiotherapy procedures and that affects both children and adults.<sup>4,5</sup> It has been isolated with greatest frequency in bacteraemia of diverse foci, abscesses, peritonitis, tenosynovitis, respiratory infections<sup>6,7</sup> and septic shock.<sup>3</sup> It has also been isolated in tap water, swimming pools, underground water and bottled water.<sup>1,4</sup>

Although there are no recommended procedures for studying its antimicrobial susceptibility, in our experience the microorganism grew well in commercial microdilution panels. As previously indicated, we applied the EUCAST criteria for *Pseudomonas* spp. for the determination of its antimicrobial susceptibility. These criteria are more restrictive than Clinical and Laboratory Standards Institute (CLSI) criteria for different antibiotics (beta-lactams, colistin, fluoroquinolones, aminoglycosides). However, this is not the case for imipenem and meropenem, which is why this circumstance has to be considered when comparing susceptibility/resistance with other publications. The strain isolated from our patient presented the same susceptibility as that described in various previous publications<sup>2,6,7</sup> and in a recent case of septic shock,<sup>3</sup> in which the EUCAST criteria were also applied.

In summary, we described the first case of bacteraemia due to *C. pauculus* in our setting, an ubiquitous, aerobic Gram-negative bacillus which is usually resistant to meropenem, aminoglycosides and colistin. There is limited clinical experience in the treatment of serious infections caused by this microorganism, but, in view of its isolation in a sterile sample, imipenem could be used as empirical therapy until its antimicrobial susceptibility is known.

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## Skin infection by *Corynebacterium diphtheriae* and *Streptococcus pyogenes*: an unusual association



### *Infección cutánea por Corynebacterium diphtheriae* y *Streptococcus pyogenes*: una asociación inusual

Dear Editor:

*Corynebacterium diphtheriae* is a noncapsulated, club-shaped facultative anaerobic Gram-positive bacilli. Opportunistic or cutaneous co-infection caused by this microorganism, especially non-toxigenic strains, has become important in travellers<sup>1</sup>. The skin lesions are generally ulcerative with a torpid and nonspecific evolution, which usually appear after a bite or minor trauma<sup>2</sup>. These infections have a low incidence<sup>3</sup>, which is why this microorganism is often not considered as the first etiological diagnosis, so in many of the cases can be unnoticed. A study of two cases of infection by *C. diphtheriae* and *Streptococcus pyogenes* was performed. The microorganisms were isolated from swabs of wound exudates and were identified by mass spectrometry (MALDI-TOF MS, Bruker©) and were confirmed with the amplification and sequencing of the 16S rRNA gene. Diphtheria toxin was performed by PCR<sup>4</sup>.

#### Case 1

A 28-year-old man with a recent travel history to Philippines attended for an incised wound on the back of the left foot of 15 days of evolution, with signs of cellulitis. The case was oriented as cellulitis and started intravenous treatment with ceftriaxone 1g for 5 days and linezolid 600mg for 3 days, after that the treatment were change to oral azithromycin for one week. In culture, *S. pyogenes* and *C. diphtheriae* were isolated. Antibiotic susceptibility testing (AST) was performed and both microorganisms were susceptible to penicillin and erythromycin. Diphtheria toxin was negative. The patients evolving favourably and subsequently decided to administer a booster of diphtheria vaccine.

#### Case 2

A 32-year-old man, with a recent travel history to Southeast Asia for 2 months. Attended for a traumatic wound in the heel and erythematous and crusted lesions of 2–3 cm in the right leg. Physical examination reveals a peripheral pustule with inflammation of an inguinal node without signs of cellulitis in the peripheral skin. The case was oriented as skin infection by biting of overinfected

arthropods. Serology was requested for Dengue, Chikungunya and culture. *S. pyogenes* and *C. diphtheriae* were isolated. AST was performed and both microorganisms were susceptible to penicillin and erythromycin. Serologies for Dengue and Chikungunya were negative. Treatment with oral erythromycin 500 mg every six hour for 14 days was started, contact study was carried out and reinforcement of the diphtheria vaccine was administered. Diphtheria toxin was negative; the patient was evaluated for 2 weeks, showing resolution of both traumatic wound and satellite lesions.

Cutaneous infection by *C. diphtheriae* is uncommon, tends to be of torpid evolution and produce nonspecific lesions, so clinical suspicion is low. In recent years this infection has been linked mainly with travellers to endemic areas including Southeast Asia, some countries such as Cambodia, India, Indonesia, Malaysia, New Guinea, Philippines, Thailand, Brazil and others<sup>5,6</sup>. A study in Vancouver reports 37 cases of cutaneous diphtheria for non-toxigenic strains<sup>8</sup> which demonstrates the high distribution of these strains. In Europe, the data was based mainly on patients with a recent travel history<sup>7</sup>, except in some Eastern European countries, which are considered an endemics areas<sup>2</sup>.

Other risk factors for the infection included population with low socioeconomic resources, alcohol abuse, drugs, HIV infection, hepatitis, cirrhosis<sup>8,3</sup>. Identification of Gram positive bacilli colonies may be considered in some cases as non-pathogenic microbiota by the genus of *Corynebacterium*, and presence of *C. diphtheriae* may be misidentified. In these cases we can apply the MALDI-TOF MS, it's an easy technique and effective cost<sup>2</sup>.

Co-infection is a common clinical presentation. *S. pyogenes*, *Staphylococcus aureus*, methicillin-resistant *S. aureus*, *Arcanobacterium haemolyticum* and species of coagulase-negative staphylococci<sup>8</sup> are the more frequently association. In 2016 a third case of cutaneous diphtheria was also reported where colonies of *A. haemolyticum* were also isolated in a 50-year-old patient with a recent travel history to Guinea Bissau and mimicking pyoderma gangrenosum<sup>9</sup>.

Benzylpenicillin and macrolides were considered first line treatment in cases of diphtheria, but in 2015 the first case of *C. diphtheriae* resistant to penicillin was published in a cutaneous infection by a non-toxigenic strain in the United Kingdom<sup>10</sup> However, benzylpenicillin continue to be the first option for treatment in case of diphtheria. In our cases the both strains and both *S. pyogenes* were susceptible to penicillin and erythromycin. In Spain in 2015, the first case of diphtheria was reported since 1986, in a 6-year-old unvaccinated child, who progressed unfavourably and died after one month of medical treatment. However, in relation to cutaneous diphtheria, no previous reports have been found.