JIDC | THE JOURNAL OF INFECTION IN DEVELOPING COUNTRIES

Case Report

Extensively drug-resistant *Pseudomonas putida* bacteremia that was resolved spontaneously

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Abstract

Pseudomonas putida (P. putida) is a rare pathogen that causes various infections in newborns, neutropenic and cancer patients, or in patients with risk factors leading to immunosuppresion. Antibiotic resistance in *P. putida* is seen in growing numbers. Although it is less virulent compared to *Pseudomonas aeruginosa*, mortal infections are reported.

Here, a *P. putida* case after an invasive procedure in a patient with gastrointestinal malignancy is reported. Although, it caused an antibiotic resistant bacteremia, it resolved spontaneously without any treatment.

P. Putida might have lower virulence and a different antibiotic susceptibility when compared to *Pseudomonas aeruginosa* in different cases. More clinical information is needed for further evaluation.

Key words: *Pseudomonas putida*; extensive drug-resistance; low virulence.

J Infect Dev Ctries 2019; 13(6):577-580. doi:10.3855/jidc.11213

(Received 09 January 2019 – Accepted 08 April 2019)

Introduction

Pseudomonas putida, is a non-fermenting Gram-negative bacillus from Pseudomonadaceae family. It is fluorescent, has variable metabolic features and exists in soil [1]. It usually presents as skin and soft tissue infection, pneumonia, urinary infection or bacteremia in immunocompromised or traumatized patients. It can colonize on moist and inanimate hospital surfaces and cause nosocomial infection. Also, bloodstream infections associated with contaminated intravenous fluids, intensive care units, specialized wards or war wounds have been reported [2-5]. It shows altered pathogenicity, which might result as a fatal infection. [6,7].

P. putida is usually susceptible to antipseudomonal carbapenem treatment. Here, a case report presenting with fever after a distal esophageal stent replacement for malignancy, that was diagnosed with *P. putida* bacteremia and found to be multidrug resistant including carbapenem and resolved spontaneously is presented.

Case Presentation

A 59- year-old male patient presented to our hospital with belly pain and dark stool. He had been diagnosed with distal esophageal adenocancer in an outpatient clinic 18 months ago and he received only chemotherapy as the cancer was inoperable. He had not been admitted to hospital before or given any other medications than chemotherapy. He lost 10% of his body weight due to malnutrition and has had poor oral intake for the past week.

His body mass index was 20 kg/m2 and he had decreased skin turgor and muscular tonus. His pathological laboratory results were: Hb; 8 gr/Lt (N: 13.5-18.1), Hct; 24% (N:40-53.7), Total protein; 6.2 gr/Lt (N:6.6-8.3), Albumin; 2.1 gr/Lt (N:3.5-5.2), Procalcitonin; 0.76 ng/mL (N 0-0.5) and hsCRP 159 mg/L (N 0-5).

Supportive treatment was given for his acute upper gastrointestinal bleeding. Upper gastrointestinal tract gastroscopy was performed. Esophagus was completely obstructed in distal region by tumoral lesion. The tumor was passed by guide and passage to stomach was succeeded with replacement of a 120*20 cm partially coated antireflux esophageal stent. Passage clearance was observed following an oral intake in 24 hours.

The patient developed fever (38.3 °C) 48 hours after stent replacement. 2 blood cultures (from 2 different arms with a half-an-hour break) were taken and *P. putida* growth was detected in the cultures on the 5th day. Meantime, as the patient's fever did not last and

general condition was good, he was followed with supportive treatment untill blood culture results were obtained.

Blood samples which were collected with aseptic technique were injected to BACTEC medium bottles and incubated under normalatmospheric conditions, at 35°C in automatic BACTEC blood culture machine (Becton Dickinson, Franklin Lakes, USA). The media were monitored for 7 days and the bottle showing positive was Gram-stained. It was subbed onto 5% sheep blood agar (Salubris, Istanbul, Turkey) and EMB (Eosin methylene blue) agar (RTA, Kocaeli, Turkey) and then was incubated at 37°C for 24 hours. Disc diffusion test was used for susceptibility of microorganisms isolated. Gram-bacilli negative and high concentration of leukocytes were seen in gram-staining. In the culture *P. putida* was grown.

EUCAST protocol [8] was used for antibiotic susceptibility testing. The species displayed resistance to carbapenem, ciprofloxacin, ceftazidime and colistin and intermediate-susceptibility to amikasin (Table 1-Culture antibiogram). According to these results, the pathogen was accepted as XDR (extensively drug resistant= non-susceptibility to at least one agent in all but two or fewer antimicrobial categories) [9]. The patient refused the treatment and left hospital although the possible outcomes were declared clearly. After 20 days, he presented to emergency room with recurrent upper gastrointestinal bleeding. He stated that he had subfebrile fever for 2 days after his discharge from hospital, the fever reduced spontaneously and he showed no further symptoms of infection.

Discussion

P. putida is a bacterium that is rarely isolated in infections. It exists in soil and is not a part of normal human bacterial flora [10,11]. It is a non-lactose fermenting, oxidase-positive Gram-negative bacilli and a member of the fluorescent group of pseudomonas. It produces pyoverdin, a yellow–green pigment that fluoresces under UV light [12]. It can cause pandemics as nosocomial infection after invasive procedures in hospitals [13-15]. It is isolated in sputum, skin lesions and urine. Presence of a solid tumor or a hematological malignancy increases tendency to develop infection caused by *P. putida* [16].

Yang *et al* showed that 55 % of *P. putida* infection was nosocomial and its incidence was higher among patients who underwent invasive procedures like placement of intravascular devices, urinary catheterization and intubation [13].

Yoshino *et al* isolated five *P. putida* bacteremia in a 4-year-period and declared that four of them had medical devices as the primary infection site. The percentage of *P. putida* isolation was 0.22% in their hospital [6]. On the other hand, Anaissie *et al* identified *P. putida* on 3 of 15 cancer patients' cultures and they were all catheter-related and one of them resolved spontaneously after catheter removal [17].

P. putida is a bacterium that can promote formation of a biofilm [18]. In medical device-related infections, microorganisms adhere to materials and biofilm development is accelerated. This feature is an important part of its pathogenicity [19]. *P. putida* can colonize in the normal oropharyngeal flora and also in the intestine to cause cholecystitis [20,21]. Our case is also probably a medical device-related infection as bacteremia developed after a stent implantation to esophagus.

Prognosis of *P. putida* bacteremia is usually good and the treatment should be planned according to antimicrobial susceptibility as it is in other infections. Removal of infected medical implants and debridement of the wound if present are also important. After removal of the source, the blood culture result should be repeated with clinical stable time.

In previous reports, clinical isolates of *P. putida* showed high susceptibility to various antibiotic regimens. Fass *et al.* declared 100% susceptibility to

Table 1. Antibiotic resistance patterns of isolated bacteria.

Antibiotic name	Zone diameter	Result
Piperacillin zone diameter	6mm	Resistant
Piperacillin/tazobactam	10mm	Resistant
Ceftazidime	12mm	Resistant
Cefepime	10mm	Resistant
Imipenem	10mm	Resistant
Meropenem	6mm (MIC = 32) Gradient E-Test	Resistant
Amikacin	16 mm	Intermediate-susceptible
Gentamicin	13mm	Resistant
Ciprofloxacin	6mm	Resistant
Colistin	10 mm	Resistant

ciprofloxacin and tobramycin and 87% susceptibility to imipenem and piperacillin / tazobactam [22]. But still carbapenem resistant *P. putida* infections in sputum, blood and urine cultures were reported [23,24]. Kim *et al*. reported that 4 of their 18 *P. putida* isolates were resistant to imipenem (22%) and 5 (28%) were resistant to meropenem [25]. Our isolate showed resistance to imipenem, meropenem, ceftazidime and colistin and intermediate-susceptibility to amikacin.

Several mechanisms are suggested for carbapenem resistance; derepression of chromosomal AmpC cephalosporinase; production of plasmid or integron-mediated beta-lactamases from different molecular classes (carbenicillinases and extended-spectrum beta-lactamases belonging to class A, class D oxacillinases and class B carbapenem-hydrolysing enzymes); diminished outer membrane permeability, overexpression of active efflux systems with wide substrate profiles [26-29]. In our country, most common carbapenem resistance mechanisms in *P. aeruginosa* infection are the ones mediated by metallo-β-lactamase (MBL) and OXA-23 carbapenemase enzymes but also *oprD* downregulation and *mexB, mexY,* and *mexD* overexpression were demonstrated. [30-34].

Generally, *P. putida* is considered less virulent and clinically less important than *Pseudomonas aeruginosa*. [35]. In his mini review, Yoshino *et al*. declared that in his *P. putida* -case-series, *P. putida* recovery rate was 93 % [6]. Kim *et al.* declared their recovery rate as 40%. The difference could be due to severity of their cases as they had pneumonia which worsened the prognosis [25]. Yank *et al.* [13] reported that in one of their two cases in which the patient died, inappropriate antibiotic therapy for co-pathogens could have been a contributing factor. Our case had only presented fever and although the infection was resistant to carbapenem, it resolved spontaneously which could be interpreted as the pathogen had low virulence.

Although we did not have the chance to use them, there are novel treatment options for serious infections that are difficult to treat. Ceftazidime-avibactam and ceftolozane-tazobactam are promising agents for such complicated infections [36,37].

In conclusion; *P. putida* produces an infection with higher prevalence in patients with co-morbidities and medical device implants. It might have lower virulence and a different antibiotic susceptibility profile when compared to *P. aeruginosa* in different occasions. Thus, more clinical information is needed to understand its nature and possible outcomes.

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Conflict of interests: No conflict of interests is declared.