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Original article

Pseudomonas putida bacteremia in pediatric patients: A case series study

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ABSTRACT

Introduction: Bacteria of the genus *Pseudomonas* act as opportunistic pathogens. *Pseudomonas putida* has been considered a pathogen of low virulence and susceptible to multiple antibiotics, but in recent years resistant strains have emerged. The objective of this study is to describe the clinical characteristics, evolution and antibiotic resistance of *P. putida* bacteremia documented in pediatric hospitalized patients.
Methods: Retrospective cases series. Pediatric patients admitted to the Prof. Dr. Juan P. Garrahan Hospital of Buenos Aires City, Argentina, with isolation in blood cultures of *P. putida* were included, between August 2015 and August 2020.
Results: Sample consisting of 13 patients. Median age: 81 months (IQR 15–163). Ten of the patients were immunocompromised (77%), 11 (85%) had a central venous catheter, 2 (15%) received transfusions prior to the episode of bacteremia, and 6 (46%) had had an invasive procedure within the previous 30 days. Three patients (23%) presented bacteremia secondary to clinical focus and 10 (77%) had central venous catheter-associated bacteremia. All presented fever, 62% (8) evolved with sepsis and 15% (2) with septic shock. Two patients required admission to the intensive care unit (15%), and in 7 (54%) the central venous catheter was removed. None died. The median days of treatment was 14 (IQR 10–14). Resistance to carbapenems was 30%.
Conclusion: All children had underlying comorbidities, most of them immunocompromised. Catheter-associated infection predominated. The sensitivity to antibiotics was variable. Given the emergence of multi-resistant strains, it is essential to know the local epidemiology.

Bacteriemia por *Pseudomonas putida* en niños: serie de casos

Palabras clave:
Pseudomonas putida
Bacteriemia
Catéter venoso central
Infección nosocomial

RESUMEN

Introducción: Las bacterias del género *Pseudomonas* actúan como patógenos oportunistas. *Pseudomonas putida* se ha considerado un patógeno de baja virulencia y sensible a múltiples antibióticos, pero en los últimos años han emergido cepas resistentes. El objetivo de este estudio es describir las características clínicas, la evolución y la resistencia antibiótica de episodios de bacteriemia por *P. putida* en pacientes pediátricos internados.

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Métodos: Serie de casos retrospectiva. Se incluyeron pacientes pediátricos internados en el Hospital Prof. Dr. Juan P. Garrahan de la Ciudad de Buenos Aires, Argentina, con aislamiento en hemocultivos de *P. putida*, entre agosto de 2015 y agosto de 2020.
Resultados: Muestra formada por 13 pacientes. Mediana de edad: 81 meses (RIC 15–163 meses). Diez pacientes eran inmunodeprimidos (77%), 11 (85%) tenían catéter venoso central, 2 (15%) recibieron transfusiones antes del episodio de bacteriemia y 6 (46%) habían tenido algún procedimiento invasivo en los 30 días previos. Tres pacientes (23%) presentaron bacteriemia secundaria a foco clínico y 10 (77%) bacteriemia asociada a catéter venoso central. Todos presentaron fiebre, el 62% (8) evolucionó con sepsis y el 15% (2) con shock séptico. Dos pacientes requirieron ingreso en la unidad de cuidados intensivos (15%), y en 7 (54%) se retiró el catéter venoso central. Ninguno falleció. La mediana de días de tratamiento fue de 14 (RIC 10–14). La resistencia a carbapenémicos fue del 30%.
Conclusión: Todos los niños tuvieron comorbilidades subyacentes, en su mayoría inmunodepresión. Predominó la infección asociada a catéter. La sensibilidad a los antibióticos fue variable. Ante la emergencia de cepas multirresistentes, es fundamental conocer la epidemiología local.

Introduction

Pseudomonas putida has been documented as the causal agent of several infections in humans. It was previously considered to be a pathogen with low virulence and sensitive to multiple antibiotics[1]. However, in recent years the emergence of carbapenem resistance through the production of metallo-β-lactamases has been described. Fluoroquinolone-resistant isolates have also been reported[2]. There are few publications on bacteraemia due to *P. putida* in paediatrics. A retrospective study of cases of bacteraemia due to *P. putida* identified at the Hospital Nacional de Pediatría Prof. Dr. Juan P. Garrahan, in Buenos Aires, Argentina, and a literature review was conducted with the aim of describing patients' clinical and evolutionary characteristics. The antimicrobial resistance pattern was also evaluated.

Methods

An observational, retrospective study of a case series was conducted. The Hospital Prof. Dr. Juan P. Garrahan is a tertiary care centre with more than 600 hospital beds and five ICUs and is a referral centre for the entire country.

Patients with documentation in *P. putida* blood cultures between August 2015 and August 2020 were identified from the hospital's Microbiology Service register. All patients with identification in *P. putida* blood cultures with clinical relevance in the period studied were included. Patients in whom *P. putida* was identified on a withdrawn catheter tip without bacteraemia (catheter colonisation) or in whom sample contamination was considered were excluded. Clinical and evolutionary data were recorded: age; sex; underlying disease; immunosuppression; carrier of and type of catheter; invasive procedures in the last month; transfusions prior to the bacteraemia episode; clinical presentation; microbiological categorisation in accordance with the *Infectious Diseases Society of America* guidelines according to: primary bacteraemia, catheter-associated bacteraemia, secondary bacteraemia[3]; evolution: requirement for ICU, infection relapse, mortality; empiric and targeted antibiotic treatment, removal of central venous catheter (CVC), days of treatment; microbiological data: antimicrobial sensitivity and coinfection.

Blood samples were inoculated in aerobic (BacT/ALERT® PF Plus, bioMérieux, Argentina) and anaerobic (BacT/ALERT® FN Plus, bioMérieux, Argentina) paediatric bottles and incubated in the BacT/ALERT® 3D (bioMérieux, Argentina) system for a period of 5 and 7 days, respectively. Bacterial identification was performed by mass spectrometry (MALDI-TOF MS) with VITEK® MS (bioMérieux, Argentina). To predict susceptibility, the minimum inhibitory concentrations were determined with the VITEK®2 Compact (bioMérieux, Argentina) automated method and by diffusion using the epsilometric method; cut-off points from the *Clinical and Laboratory Standards Institute* were considered for other non-Enterobacteriaceae[4]. The detection of metallo-β-lactamases was carried out with phenotypic methods by diffusion through imipenem-meropenem-ethylenediaminetetraacetic (EDTA) disk synergy.

Continuous variables are summarised as median and interquartile range (IQR) and categorical variables as frequency and percentage. Stata® 16 was used for the statistical analysis.

The identity of the patients and their families was protected during the review of the medical records and the data. The publication of the work was approved by the hospital's Ethics Committee.

Results

During the study period, 13 patients who met the inclusion criteria were identified. The median age was 81 months (IQR 15–163 months), and 9 of the patients (69%) were male. All of them had underlying disease. The comorbidities were: 7 patients (54%) with oncohaematological disease, 2 patients with intestinal failure secondary to visceral myopathy and short bowel syndrome, respectively (15%), 1 liver transplant patient (8%), another one (8%) with primary immunodeficiency (agranulocytosis), another one with bone marrow aplasia (8%) and finally one patient with complex uropathy (8%). 77% of patients in this series (n = 10) were immunocompromised hosts (Table 1).

11 patients (85%) had a CVC at the time of bacteraemia. The type of CVC was: a semi-implantable catheter in 5 patients, a totally implantable catheter in 4 patients and a short-term catheter in 2 patients. Six (6) patients (46%) had undergone surgery in the 30 days prior to bacteraemia, while 2 patients (15%) had a history of transfusion in the 48 h prior to it. Polymicrobial infection was recorded in 3 patients (Table 1).

Regarding clinical presentation, all the patients had fever at the time of bacteraemia, 8 (62%) evolved with sepsis and 2 (15%) with septic shock. In 10 patients (77%) it was categorised as CVC-associated bacteraemia. Two (2) patients required admission to the ICU for the infection. The CVC was removed from 7 patients (54%). The reasons for removing the CVC were: in 2 patients (15%) due to infection associated with a short-term catheter, in 2 patients (15%) due to septic shock, in 1 patient (8%) as venous access was not required, in another patient (8%) due to the persistence of CVC-associated bacteraemia by *P. putida* and in the last patient (8%) due to polymicrobial infection.

The median length of antibiotic treatment was 14 days (IQR 10–14 days).

Table 1
Demographic characteristics of the 13 patients with isolation of *Pseudomonas putida*.

Variable	n (%)
Median age in months (IQR)	81 (15–163)
Male sex	9 (69)
Immunosuppression	10 (77)
Solid tumour	4 (40)
Acute lymphoblastic leukaemia	2 (20)
Lymphoma	1 (10)
Primary immunodeficiency	1 (10)
Bone marrow aplasia	1 (10)
Liver transplant	1 (10)
Use of CVC	11 (85)
Types of bacteraemia	
CVC-associated	10 (77)
Secondary	3 (23)
Clinical focus	3 (23)
Gastrointestinal	2 (66)
Renal abscess	1 (33)
Sepsis	8 (62)
Septic shock	3 (23)
ICU admission	2 (15)
Median days of treatment (IQR)	14 (10–14)
CVC removal	7 (54)
Coinfection	3 (23)
Klebsiella pneumoniae	1 (33)
Stenotrophomonas maltophilia	1 (33)
Staphylococcus aureus	1 (33)

CVC: central venous catheter; ICU: intensive care unit; IQR: interquartile range.

Table 2
Resistance profiles of the *Pseudomonas putida* isolates.

	Sensitive	Non-sensitive[a]
Imipenem	9	2
Meropenem	9	4[b]
Ceftazidime	11	2
Colistin	7	1
Gentamicin	11	–
Ciprofloxacin	13	–
Piperacillin/tazobactam	11	2
Cefepime	8	2
Amikacin	13	–

[a] Resistant strains and strains with intermediate sensitivity.
[b] The 2 imipenem-resistant strains were also resistant to meropenem.

Empiric treatment was monotherapy in 5 patients (38%) and combined with aminoglycosides in 8 patients (62%).

Carbapenem resistance was documented in 4 isolates of *P. putida*. All 4 were resistant to meropenem, and resistance to imipenem was also documented in 2 of them. In 2strains, the resistance mechanism was the production of metallo-β-lactamases. Resistance to ciprofloxacin and amikacin was not documented in any of the strains.

Definitive treatment was tailored according to documented susceptibility to antimicrobials (Table 2). In carbapenem-resistant isolates, combined treatment was indicated according to the antibiogram (ceftazidime, ciprofloxacin or piperacillin-tazobactam with amikacin). The definitive treatments are summarised in Table 3. There were no infection-related patiet deaths.

Table 3
Definitive antibiotic treatment.

Treatment	n (%)
Monotherapy	
Piperacillin/tazobactam	4 (31)
Combined treatment	
Piperacillin/tazobactam + amikacin	3 (23)
Piperacillin/tazobactam + ciprofloxacin	1 (8)
Ceftazidime + amikacin	2 (15)
Ciprofloxacin + amikacin	1 (8)
Ciprofloxacin + colistin	1 (8)
Meropenem + ciprofloxacin	1 (8)

Discussion

P. putida is an aerobic gram-negative bacillus belonging, together with *Pseudomonas fluorescens* and *Pseudomonas aeruginosa,* to the fluorescent group of the *Pseudomonas* genus. They are environmental microorganisms with a predilection for humid environments. They are reported in outbreaks from contaminated solutions such as distilled water, disinfectants and transfusions, among others[1,5,6]. Unlike *P. aeruginosa,* which is associated with enteritis, sepsis and serious skin and soft tissue infections in patients with comorbidities, *P. putida* generally presents as bacteraemia associated with endovascular devices.

Since the first reports of bacteraemia due to *P. putida*, this opportunistic pathogen has played a major role, causing infections in hospitalised patients, with underlying diseases, mainly immunosuppressed, post-surgical and CVC carriers, similar to the patients in this series[5,7–9].

In a literature review published in 2011, Yoshino et al. described 28 adult patients with bacteraemia due to *P. putida*. Of 21 cases in which the site of infection was identified, 12 were CVC-associated bacteraemia. In the aforementioned review, coinciding with the characteristics of the patients in our series, immunocompromised patients predominated[8]. More recently, Tan et al. reported 44 infections with identification of *P. putida* in different samples (blood, urine, sputum). Immunocompromised patients and patients with endovascular devices also predominated. Only 4 patients in that series were paediatric[9].

As in other catheter-associated infections, the recommended treatment is antibiotic therapy with or without removal of the prosthetic material or catheter[3]. In the published series, both patients with bacteraemia due to *P. putida* in which the CVC was removed and cases in which antibiotic treatment was performed without its removal and with a good response were reported[7,10]. In our series, the indication to remove the CVC was individualised, taking each patient's clinical and microbiological aspects into account and the catheter was maintained in half of the patients without any complications.

In recent years, multiresistant strains of *P. putida*have been reported[11,12]. The resistance mechanisms described for the *Pseudomonas* genus are: hyperproduction of efflux pumps, reduced expression of porins in its outer membrane, chromosomal mutations in topoisomerase genes and acquisition of resistance-transmitting plasmids, among others. In most cases, carbapenem resistance is due to the VIM and IMP enzymes[13]. Identification of KPC-2 and resistance to all antimicrobial agents except polymyxin B in a child with bacteraemia has also been reported[14]. *P. putida* could act as a reservoir and dispersal vector for these resistance mechanisms, representing a serious public health problem[15]. Depending on each strain's resistance mechanisms, different profiles of antibiotic sensitivity are observed. The hyperproduction of efflux pumps can be associated with selective resistance to carbapenems, without other β-lactam antibiotics such as ceftazidime or piperacillin-tazobactam being affected. In the series presented, the search for resistance mechanisms using molecular methods was not performed systematically[16].

However, the different resistance profiles to different β-lactams in this series could be explained by resistance mediated by efflux pumps and impermeability.

In our experience, patient evolution was favourable with antibiotic treatment, with or without the removal of the central venous catheter (CVC). Infection relapse was documented in a single patient, who evolved favourably following removal of the CVC.

The exact mortality rate is unknown. Adults have a good prognosis[9].

Although the series presented is the largest in the paediatric population available to date, the work's main weak point is the lack of data on antimicrobial sensitivity and resistance mechanisms in some of the *P. putida* isolates, which is related to the research's retrospective nature.

Conclusions

In this series of children with bacteraemia due to *P. putida*, all the patients had underlying comorbidities, and catheter-associated infection predominated. The CVC was maintained in half of the patients. There were no infection-related patiet deaths. In our series, the sensitivity to antibiotics was variable. The emergence of multiresistant strains makes it difficult to standardise an empiric treatment, hence it is essential to understand each institution's epidemiology.

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Conflicts of interest

The authors declare that they have no conflicts of interest.

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