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Clinical and microbiological characteristics of *Pantoea agglomerans* infection in children

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ABSTRACT

Pantoea agglomerans is an environmental Gram-negative bacterium that rarely is responsible for the infections in humans but it is often a causative factor of a number of occupational diseases. This study evaluated the clinical and microbiological characteristics and pathogenicity of *P. agglomerans* in children.

We retrospectively reviewed microbiological test results for all children (1 month old to 18 years old) who were admitted to our pediatric hospital between January 2000 to June 2015 and had positive clinical specimen cultures for *P. agglomerans*. Isolates were identified using conventional tests and the BBL Crystal E/NF ID or MALDI-TOF MS systems. Antibiotic susceptibilities were evaluated using the Kirby-Bauer disc diffusion method.

We identified fifteen positive cultures from 14 patients with confirmed infections. The positive specimens included pus, urine, tracheal aspirate, blood, and central venous line samples that yielded *P. agglomerans*. The median patient age was 8.8 years (range: 1.5 months to 16.5 years), and all patients had underlying comorbidities. Five patients had medical devices, and two devices were removed. The most common *P. agglomerans* infections involved wound infections (35.7%), pneumonia (21.4%), and urinary tract infections (21.4%). Three patients had concomitant infections (*Enterococcus faecium, Pseudomonas aeruginosa,* and *Aspergillus fumigatus*). Five patients had anemia. Three patients (21.4%) died, and all three had carbapenem-resistant *P. agglomerans* that was detected after the first week of hospitalization; two cases involved pneumonia, which was ineffectively treated.

P. agglomerans infections may be life-threatening, especially in young patients with pneumonia. Hospital-acquired *P. agglomerans* may have different pathogenicity and clinical features, compared to community-acquired *P. agglomerans*, although further studies are needed to understand the drug-resistance patterns in this bacterium.

Introduction

Pantoea agglomerans is a yellow-pigmented, rod-shaped Gram-negative aerop bacillus that belongs to the *Enterobacteriaceae* family, and has previously been known as *Enterobacter agglomerans* or *Erwinia herbicola* [1,2]. It was reclassified into a new genus in 1989 [3]. *P. agglomerans* is an environmental and agricultural organism that is frequently isolated from plants, soil, water, and food [1]. This organism is an opportunistic pathogen, and infection usually requires an immunocompromised host [4]. Nevertheless, despite human infections being uncommon, they may be associated with trauma that was caused by penetration with vegetative material during performing of agricultural occupations, gardening or children playing, and also with secondary bacteremia, or nosocomial infections that are related to medical equipments such as intravenous catheters or contaminated intravenous fluids [5–7]. Furthermore *P. agglomerans* is often a causative factor of a number of occupational diseases, caused by the effects of protein allergens and endotoxin produced by this pathogen, with the allergic and/or immunotoxic background [8,9].

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P. agglomerans has been identified as a possible cause of vertebrate animal diseases but compared to humans, there are only few reports for *P. agglomerans* infections in this group. Apart from vertebrate animals, *P. agglomerans* has been isolated from some arthropods and *P. agglomerans* may be also pathogenic for plants [7].

In recent years, the beneficial traits of *P. agglomerans* have been mentioned such as its a set of antibiotics production and the role of the immunepotentiator from *P. agglomerans* 1 (IP-PA1) in the prevention and treatment of for the animals and human diseases or food preservation in contrast to the proven pathologic role of *P. agglomerans* [8].

In the present study, we evaluated the clinical and microbiological characteristics (including carbapenem resistance) of *P. agglomerans* infections among children who were treated at our hospital over the past 15 years due to limited data in childhood.

Patients and methods

Hospital setting

The Hacettepe University İhsan Doğramacı Pediatric Hospital is a 270-bed, tertiary-care, pediatric referral hospital in Turkey. This hospital treats approximately 215,000 outpatients and 11,000 inpatients each year. In the present study, we retrospectively identified all children (1 month old to 18 years old) who were admitted to our hospital between January 2000 and June 2015 and had clinical specimens that provided positive culture results for *P. agglomerans*. This study's retrospective design was approved by the institutional review board of the Hacettepe University Faculty of Medicine.

Specimen collection

Microbiological data were retrieved from the microbiology laboratory's electronic records, and the patients' clinical and microbiological data were considered together. Specimens that yielded *P. agglomerans* were collected from venous blood, urinary collection bags (in cases of urinary tract infections with $\geq$100,000 colony-forming units), incision sites, abscess drainage, and tracheal aspirate. However, six isolates were excluded because of contamination and seven isolates were excluded because of insufficient clinical data. Thus, 15 isolates from 14 patients were included in this study (Fig. 1)

Bacterial identification and antimicrobial susceptibility testing

The blood, catheter, tracheal aspirate, and pus specimens were inoculated onto 5% sheep blood agar and chocolate agar, and urine specimens were inoculated onto 5% sheep blood agar and MacConkey agar. All cultures were incubated at 37 °C for 24–48 h in a 5% CO_2 atmosphere. Gram-negative bacteria from the cultures were identified using conventional tests and the BBL Crystal E/NF ID system (Becton Dickinson Microbiology Systems, Cockeysville, Maryland, USA) or a matrix-assisted laser desorption ionization-time of flight mass spectrometry system (BioMerieux, France). Antibiotic susceptibilities were tested using the Kirby-Bauer disc diffusion method, according to the Clinical and Laboratory Standards Institute guidelines [10,11].

Statistical analysis

All data were analyzed using SPSS software (version 20.0 (SPSS, Inc., Armonk, NY, USA)). Descriptive statistics were used to summarize the baseline patient characteristics. Median values and interquartile ranges (IQR) were calculated for continuous variables and frequency distributions were calculated for categorical variables.

Results

We identified 36 *P. agglomerans* isolates. However, 13 isolates were excluded because of contamination or insufficient clinical data (Fig. 1), and 8 isolates of newnborn patients were excluded. Only 15 isolates from the 14 patients with clinically documented were included. The median age was 8.8 years, (range: 1.5 months to 16.5 years) who were treated during 2000–2015. One patient had two isolates. The male-to-female ratio was 1.8:1, and the patients' demographics, clinical characteristics, and comorbidities are summarized in Table 1. The specimens with detectable *P. agglomerans* included pus (6 specimens, 42.8%), urine (3 specimens, 21.4%), tracheal aspirate (3 specimens, 21.4%), and blood (3 specimens, 21.4%). The most common clinical diagnoses for patients with significant culture growth were wound infections (35.7%), pneumonia (21.4%), and urinary tract infections (21.4%) (Table 1). Three cultures exhibited concomitant pathogens: One pus specimen with *Enterococcus faecium*, one tracheal aspirate with *Pseudomonas aeruginosa*, and one pus specimen with *Aspergillus fumigatus*.

Most patients required hospitalization (85.7%), although 2 patients were treated as outpatients. The median length of hospitalization was 22.5 days (range: 5–292 days; IQR: 7.2–49.5 days), and the median length of hospitalization after the positive culture result was 11 days (range: 0–126 days, IQR: 7.0–30.2 days). Five patients had medical devices (three central venous catheters, one renal double J stent, one dialyzing catheter, and one cardiac pacemaker), although one central venous catheter and the renal double J stent were removed because of growing *P. agglomerans* in the central venous catheter and nephrolithiasis. Patient 12 had both a central venous catheter and a cardiac pacemaker. Two patients (14%) required mechanic ventilation on the date of their positive culture results, and both patients died. Among the 14 patients, 11 patients (78.5%) had medical records with documented laboratory findings of new-onset *P. agglomerans* infection. There was no evidence of colonization prior to onset of infection.

The median values for white blood cell counts, hemoglobin levels, and thrombocyte counts were 8900/μL (range: 4300–30,300/μL), 10.7 g/dL (range: 8.1–15.3 g/dL), and 361,000/μL (range: 55,000–652,000/μL), respectively. Five patients had anemia, and one of these patients had systemic lupus erythematosus, hemolytic uremic syndrome, thrombocytopenia (55,000/μL), and lymphopenia (300/μL). Only two patients had leukocytosis. Ten patients recovered (71.4%), and their treatment was selected based on the susceptibility testing results (Tables 2 and 3).

Three patients exhibited carbapenem-resistant *P. agglomerans* (21.4%), and all three patients died (Table 4). The first patient had cystic fibrosis, was hospitalized because of pneumonia, and required mechanical ventilation during the follow-up. The patient received ciprofloxacin, meropenem, liposomal amphotericin B, vancomycin, ornidazole, and piperacillin with tazobactam. *P. agglomerans* with concomitant *Pseudomonas aeruginosa* was isolated from tracheal aspirate. Although the *Pseudomonas aeruginosa* was susceptible to ciprofloxacin and piperacillin, the *P. agglomerans* was resistant to carbapenems, ciprofloxacin, and piperacillin. The second patient was a 6-month-old hypotonic infant who was born prematurely and was hospitalized for pneumonia, bradycardia, and to diagnose the etiology of the hypotonicity. Carbapenem-resistant *P. agglomerans* was detected on day 12 of the hospitalization, and *Acinetobacter baumannii* was detected on day 36 in a culture of tracheal aspirate. The antimicrobial treatments during the hospitalization were ceftriaxone, meropenem, fluconazole, teicoplanin, vancomycin, and amikacin. That patient ultimately died on day 48

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