Pantoea agglomerans Bloodstream Infection in Preterm Neonates

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Key Words

Pantoea agglomerans • Bloodstream infection • Preterm neonates

Abstract

Objective: To report an uncommon incidence of sporadic bloodstream infection (BSI) caused by *Pantoea agglomerans* in preterm neonates. **Case Presentation and Intervention:** Five cases of nosocomial BSI with *P. agglomerans* in preterm neonates (weight $\leq 1,500$ g; age 8–17 days; gestational age 26–30 weeks) are presented. All cases were late onset neonatal sepsis (>7 days of age). Lethargy, skin mottling and bradycardia were often present. Although there was no evidence of pneumonia, desaturation was a common feature. Thrombocytopenia developed in 4 patients, metabolic acidosis in 2 and jaundice in 2. No bleeding tendency or disseminating intravascular coagulation was recorded. Organisms cultured from blood were identified by the Vitek-2 system (bioMérieux, France) and the findings confirmed by testing the isolate on the API 20E system. All isolates shared in vitro susceptibility to gentamicin, amikacin, ciprofloxacin, piperacillin/tazobactam and meropenem. One patient was treated with a cefotaxime/amikacin combination, 2 with meropenem and the remaining 2 with tazocin. All patients responded well to antibiotic treatment and survived. **Conclu-**

sion: *P. agglomerans* is an unusual pathogen in the etiology of neonatal sepsis. Despite significant clinical deterioration, early detection and proper antibiotic therapy carry a favorable outcome.

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Introduction

The species of the genus *Pantoea*, i.e. *P. agglomerans*, *P. ananatis*, *P. citrea*, *P. dispersa*, *P. punctata*, *P. stewartii* and *P. terrea*, are usually isolated from soil, fruit, and vegetables. Only a limited number of clinical cases with bacteria belonging to this genus have been described. Among the species of this genus, only *P. agglomerans*, formerly known as *Enterobacter agglomerans*, is most commonly isolated in hospitals [1]. *P. agglomerans* has traditionally been reported in septic arthritis after thorn injury [2]. It has also been reported in spondylodiscitis [3], tibial osteitis [4], and among other organisms in polymicrobial peritonitis [5]. A recent report, which described the clinical picture of an almost fatal infection caused by *Pantoea* spp., was observed during an outbreak caused by contaminated parenteral nutritional fluids in a Malaysian neonatal intensive care unit in 2006 [6]. To the best of our knowledge, such incidents in neonates have not been re-

ported previously in Kuwait. Due to the paucity of literature related to this organism in neonates, this study reports 5 cases of bloodstream infection (BSI) with *P. agglomerans*.

Case Report

All 5 cases reported here were from the neonatal intensive care units (NICU1 and NICU2) of Farwaniya and Maternity Hospitals in Kuwait, but were not connected to each other in time.

Case 1

A 1,500-gram preterm baby, delivered vaginally as a second twin, developed respiratory distress shortly after birth and was managed using nasal continuous positive air pressure (CPAP). Intravenous (i.v.) ampicillin and gentamicin were started empirically after collection of an initial blood sample for culture. I.v. fluids were initiated and the baby was given nothing orally for the first day. He was weaned gradually from CPAP and kept in an oxygen hood. Initial cultures proved negative after 5 days and antibiotic therapy was stopped. The baby then developed jaundice and was treated with phototherapy. At the age of 10 days, he became desaturated and lethargic with skin mottling. Sepsis workup was done. I.v. cefotaxime and amikacin were instituted. Blood gas analysis showed metabolic acidosis and the baby was mechanically ventilated for 1 day. Cerebrospinal fluid and urine cultures showed no growth. However, two blood culture bottles showed the growth of *P. agglomerans*. The baby showed good response to a 10-day course of antibiotic treatment and was discharged in good general condition. During the episode, the baby did not develop pneumonia or necrotizing enterocolitis.

Case 2

A preterm baby, admitted directly due to respiratory distress, was intubated and mechanically ventilated. At the age of 7 days, he became well, was extubated and connected to nasal CPAP. However, on day 12, he became lethargic with bradycardia, skin mottling and frequent attacks of desaturation and required reventilation. The baby was kept nil per os. Intravenous meropenem was given for 2 weeks. Blood culture was positive for *P. agglomerans*. The baby responded well to treatment. There was no evidence of pulmonary infiltrate on chest radiograph.

Case 3

This preterm baby was delivered by lower segment cesarean section and transferred immediately to the neonatal intensive care unit for ventilatory support. Empiric treatment with ampicillin and amikacin was started. Echocardiogram revealed a small atrial septal defect. The patient developed uncomplicated pre-necrotizing enterocolitis during her first week of life. On day 15, she was accidentally extubated and then connected to nasal CPAP. On day 17, she became inactive, with abdominal distension, temperature instability and had repeated attacks of apnea. A full sepsis workup was done. Blood culture grew *P. agglomerans* in less than 24 h. The baby was connected to mechanical ventilation and given meropenem i.v. Treatment continued for 2 weeks. The patient showed clinical improvement and was transferred to the special care baby unit.

Case 4

A preterm neonate was delivered by spontaneous vaginal delivery after 26 weeks of pregnancy. The mother had premature rupture of membranes shortly before delivery. The baby developed severe respiratory distress, so he was intubated and mechanically ventilated. Initial blood cultures were negative but on day 8, the baby became pale, lethargic with evident skin mottling, desaturation and bradycardia. Full sepsis workup was initiated and the patient was treated with piperacillin/tazobactam (Tazocin). Blood culture showed the growth of *P. agglomerans*. Tazocin was continued for 10 days. Following antibiotic therapy, the baby became stable and was in good general condition.

Case 5

A septic episode was suspected at the age of 11 days in a baby with clinical features similar to case 4. The baby was successfully treated with tazocin for 10 days.

Discussion

Generally, *Pantoea* infection is uncommon in humans. There are few reports of systemic infection with this organism in preterm neonates. Surveillance between January 2005 and December 2006 in neonatal intensive care units of the two governmental teaching hospitals in Kuwait reported 5 sporadic episodes of nosocomial BSI due to *P. agglomerans*. During that period, 2 of 42,101 and 8 of 13,264 blood culture bottles were positive for the organism in the 2 hospitals, respectively. That is, 1 of 644 patients admitted to NICU1 and 4 of 1,021 patients admitted to NICU2 were infected. The *Pantoea* isolates were not previously isolated from neonates in the preceding years.

Neonatal BSIs are commonly caused by coagulase-negative staphylococci, multi-resistant *Klebsiella* spp. and *Candida* spp. in central-line-associated infections, and by *Pseudomonas* spp., multi-resistant *Klebsiella* spp. and others in non-central-line-associated infections. The high mortality associated with BSI makes it very important to rapidly diagnose and treat these infections.

In all cases, 2 pediatric blood culture bottles grew the organism upon incubation in the BacTec System (Becton Dickinson, Sparks, Md., USA) within 24 h. The organism was a Gram-negative, motile bacillus belonging to the family of Enterobacteriaceae. All strains produced a yellow pigment on blood agar. With biochemical testing, it was found to be oxidase- and urease-negative and did not produce H₂S on triple sugar iron agar. It also showed a negative reaction with arginine dihydrolase, ornithine decarboxylase and lysine decarboxylase. Microbial identification was done using the Vitek-2 system (bioMérieux, Marcy l'Etoile, France). In the isolate from case 1,

Table 1. Summary of clinical features

	Case 1	Case 2	Case 3	Case 4	Case 5
Location	NICU1	NICU2	NICU2	NICU2	NICU2
Gestational age, weeks	30	29	28	26	27
Delivery	NVD, breech extraction	NVD	Emergency LSCS	NVD, PROM	NVD
Gender/birth weight, g	M/1,500	M/1,030	F/815	M/855	F/1,020
Apgar scores at 1 and 5 min	7, 9	6, 8	6, 8	6, 8	7, 9
Clinical condition	HMD	HMD II	HMD II, pre-NEC	HMD III, PDA	HMD, PDA
Timing of sepsis after admission, age in days	11	12	17	8	11
Intravascular catheterization	Peripheral	Left femoral long line	Left femoral long line	Right cephalic long line	UAC/UVC
Total ventilator days	1	17	19	17	15
Ventilator days during sepsis	1	9	8	10	5
Skin mottling	Yes	Yes	Yes	Yes	Yes
Lethargy	Yes	Yes	Yes	Yes	Yes
Bradycardia	Yes	Yes	Yes	Yes	Yes
Apnea/desaturation	No	Yes	Yes	No	Yes
Pneumonia/pulmonary hemorrhage	No	No	No	No	No
Jaundice	Yes	No	No	No	Yes
Metabolic acidosis	Yes	No	No	Yes	No
Hemoglobin, g/l	119	113	139	144	152
Platelet count, $\times 10^9/l$	167	63	59.5	31.5	11
White cell count, $\times 10^9/l$	9.4	12	8.75	26.4	9.56
CRP, mg/l	3.48	24	48	12	96
Treatment, duration	Cefotaxime/ amikacin (10 days)	Meropenem (14 days)	Meropenem (14 days)	Piperacillin/ tazobactam (10 days)	Piperacillin/ tazobactam (10 days)
Outcome	Survived	Survived	Survived	Survived	Survived

NVD = Normal vaginal delivery; LSCS = lower segment cesarean section; PROM = premature rupture of membranes; HMD = hyaline membrane disease; NEC = necrotizing enterocolitis; PDA = patent ductus arteriosus; UAC = umbilical artery catheter; UVC = umbilical vein catheter. NICU1 refers to the neonatal intensive care unit at Farwaniya Hospital and NICU2 to the neonatal intensive care unit at the Maternity Hospital.

the following tests contradicted a typical biopattern: negative reactions to L-lysine arylamidase, phosphatase and D-raffinose. However, retesting of the isolate by API 20E confirmed the identity. The full API profile identified 81.7% of this isolate and more than 90% in the others as *P. agglomerans*.

Antibiotic susceptibility was performed on Vitek-2 using the AST-N020 card. All isolates showed in vitro susceptibility to amikacin, gentamicin, piperacillin/tazobactam and meropenem. However, variable susceptibility to other antibiotics was noticed: isolate 1 was fully sensitive, and isolate 4 was resistant to all cephalosporins. The two isolates (No. 4 and 5) that showed resistance to cephalosporins did not give a positive result with the ESBL E-test with clavulanate.

In a recent study at a children's hospital [7], the antimicrobial susceptibilities of 53 pediatric cases with *P. agglomerans* infections, cultured from normally sterile sites, were determined over a 6-year period. All isolates were uniformly susceptible to amikacin, gentamicin, meropenem and trimethoprim-sulfamethoxazole. In ad-

dition, 92.5% of the isolates were susceptible to broad-spectrum cephalosporins and semisynthetic penicillins, 62.3% to extended-spectrum cephalosporins, and 47.2% to ampicillin.

In previous reports, *Pantoea* infections among pre-term neonates, primarily sepsis, were basically related to hospital outbreaks by this organism and traced to contamination of total parenteral nutrition (TPN) fluids [6–9]. It is most likely that in these reports heavy bacterial contamination of TPN fluids or virulent bacterial strains were responsible for the rapid development of shock, poor response to antibiotics and death.

However, the clinical profile of sporadic neonatal BSI due to *P. agglomerans* has not been reported elsewhere. Bergman et al. [10] reported that in an 11-year study, 2% of all patients in a level III neonatal intensive care unit were colonized with *P. agglomerans* and only 3 newborns developed late-onset septicemia and died.

Interestingly, and in contrast to the previously reported fatal outcome of this infection [6, 8], all patients in the present study survived. We believe that the favorable out-

come of our patients was partly due to early diagnosis and the adequacy of the antibiotics, and probably because the infection was caused by relatively less virulent strains.

Our cases were late onset sepsis (≥ 7 days of age) in neonates weighing $\leq 1,500$ g. Lethargy, skin mottling and bradycardia were often present. There was neither a special predilection for the lungs nor evidence of pneumonia; however, desaturation was a common feature. Thrombocytopenia developed in 4 patients, metabolic acidosis in 2 and jaundice in 2. No bleeding tendency or disseminated intravascular coagulation was recorded. None of the patients had leukopenia (table 1). In case 1, C-reactive protein was not elevated, most probably because it was measured early in the course of illness. It was not repeated as the patient showed a rapid response to treatment.

On a single occasion, we conducted an extensive epidemiologic investigation but could not identify a potential source. Investigating the source of infection was not attempted in the other cases. The mode of nosocomial acquisition of the organisms was not clear. However, it is known that the use of broad-spectrum antibiotics increases the risk of colonization with Enterobacteriaceae

and gastrointestinal colonization could possibly be a reservoir for the organism [10]. Case 3 had pre-necrotizing enterocolitis with increased intestinal permeability that could favor passage of the bacteria to the blood. A recent study in a community setting revealed that *P. agglomerans* was isolated from the hands and environment of individuals in households where it might serve as a potential pathogen for either community- or hospital-acquired infections [11]. In analogy, the hands of healthcare workers might offer transient carriage for the organism though, in our case, such speculation was not confirmed.

Conclusion

P. agglomerans is an unusual pathogen in the etiology of neonatal sepsis. Despite significant clinical deterioration, early detection and appropriate antibiotic therapy carry a favorable outcome. The first-line choice of antibiotic could be piperacillin/tazobactam with amikacin, which later could be changed to meropenem, if necessary.

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