

Pseudomonas aeruginosa as a Potential Cause of Antibiotic-Associated Diarrhea

Although *Pseudomonas aeruginosa* is not generally considered as a cause of antibiotic-associated diarrhea, several cases of diarrhea caused by *P. aeruginosa* have been reported. We experienced seven cases of nosocomial diarrhea presumably caused by *P. aeruginosa*, which was the predominant organism isolated from stool cultures. *Clostridium difficile* toxin was also positive in one patient. No other potential or recognized enteropathogens were identified from stools. All patients had underlying diseases and had been receiving antibiotics before the diarrheal onset. All of the seven *P. aeruginosa* isolates were resistant to previously given antibiotics. Diarrhea stopped three days after withdrawal of probable offending antibiotics without specific treatment in two patients. The other five patients having continuous diarrhea despite withdrawal of probable offending antibiotics, were successfully treated with antipseudomonal agents. The median duration of diarrhea after the initiation of treatment was 6.3 days. These data suggest that *P. aeruginosa* can be a potential cause of antibiotic-associated diarrhea. Further investigations are warranted to evaluate the possible etiologic role of *P. aeruginosa* in antibiotic-associated diarrhea.

Key Words : *Pseudomonas aeruginosa*; Diarrhea; Colitis

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Received : 22 March 2001
Accepted : 27 August 2001

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*Part of this data was presented at the ASM conference on *Pseudomonas* '99 in Hawaii (September 1-5, 1999). Abstract No. 117

INTRODUCTION

Antibiotic-associated diarrhea or colitis (AAD or AAC) can be caused by nearly all kinds of antibiotics. While *Clostridium difficile* is the most frequently identified cause of AAC, *Clostridium perfringens*, *Staphylococcus aureus*, drug-resistant *Salmonella* species, and *Candida* species were reported to cause AAC (1). Although *Pseudomonas aeruginosa* is not generally considered as a cause of AAC, several cases of diarrhea probably caused by *P. aeruginosa* have been reported (2-4). We experienced seven cases of nosocomial diarrhea presumably caused by *P. aeruginosa*.

PATIENTS AND METHODS

To investigate the clinical relevance of *Pseudomonas*-induced diarrhea, microbiologic reports of stool cultures were reviewed at a university hospital (Samsung Medical Center, Seoul, Korea) from January 1997 to June 1999. Stool cultures were done on blood agar plates and MacConkey agar plates. To

detect etiologic organisms of diarrhea, direct microscopy of stool, stool cultures for *Salmonella* and *Shigella*, and tests for *C. difficile* toxin (Vidas[®], bioMerieux, MO, U.S.A.) were done at the same time. The sensitivity and specificity of Vidas for *C. difficile* toxin are higher than 90%. Detection of enteric virus was not done. Our clinical microbiology isolated *P. aeruginosa*, *S. aureus*, or *Candida* spp. from stool if they were the only predominant organisms. *P. aeruginosa* was identified by automated MicroScan[®] system and Vitek[®] system. *P. aeruginosa* was the only predominant organism isolated from stool cultures in seven patients. Medical records of these patients were reviewed retrospectively. We defined any diarrhea as nosocomial if the onset was 48 hr or later after admission.

RESULTS

All of the seven patients had nosocomial diarrhea when *P. aeruginosa* was isolated from their stool cultures. Among seven patients, four were males and three were females. The

median age of patients was 58 (41-71) yr. All patients had various underlying diseases: acute myelogenous leukemia, myelofibrosis, rectal cancer, sepsis, hemorrhagic fever with renal syndrome, subarachnoid hemorrhage, and rheumatoid arthritis. The median duration of hospitalization before the onset of nosocomial diarrhea was 19 (4-148) days (Table 1). All patients had been receiving antibiotics and median duration of antibiotics before diarrheal onset was 6 (3-21) days. No patients had concomitant infections caused by *Pseudomonas* other than diarrhea.

All isolates of *P. aeruginosa* from stool cultures were not susceptible to previously given antibiotics (Table 2). No other potential or recognized enteropathogens were identified from stools except one patient whose stool was also positive for *C. difficile* toxin at the same time. Sigmoidoscopy, which was done in four patients, revealed nonspecific colitis with edematous, hyperemic mucosa, erosion, and several hemorrhagic spots.

Diarrhea stopped three days after withdrawal of probable offending antibiotics without specific treatment in two patients. The other five patients with continuous diarrhea

despite withdrawal of probable offending antibiotics, were treated with antipseudomonal agents (Table 1). The median duration of diarrhea after the initiation of treatment was 6.3 (1-9) days. Antipseudomonal agents were given 2-4 more days after resolution of diarrhea. One patient with positive *C. difficile* toxin was treated with metronidazole and amikacin. No patient died of AAC.

DISCUSSION

P. aeruginosa is one of the most important nosocomial pathogens. Even though *P. aeruginosa* is not generally considered as a cause of AAC, there are evidences that *Pseudomonas* can cause the infections of gastrointestinal tracts with diarrhea in infants. *Pseudomonas* septicemia in infants was manifested as necrotizing bowel lesions with a history of diarrhea (5). There have been some reports on community-acquired *Pseudomonas* infection of the gastrointestinal tract causing diarrhea in infants (6, 7).

Seven patients in the present report developed diarrhea

Table 1. Characteristics of the patients

Patients	Sex/Age (yr)	Underlying diseases and infectious diseases	Probable offending antibiotics (duration: days)	<i>C.difficile</i> Toxin assay*	Antibiotics for AAD
1	M/62	Acute myelogenous leukemia, CRBSI	Imipenem (21), Vancomycin (21)	-	Ciprofloxacin
2	F/71	Sepsis	Ceftriaxone (4), Imipenem (7)	+	Amikacin, metronidazole
3	M/48	HFRS, possible sepsis	Ceftriaxone (5)	ND	-
4	M/67	Rectal cancer, perioperative prophylactic antibiotics	Cefotetan (6)	-	-
5	F/41	Subarachnoid hemorrhage, pneumonia	Ceftizoxime (19)	-	Ceftazidime, tobramycin
6	M/59	RA, possible sepsis	Cefotetan (3)	-	Ciprofloxacin
7	F/52	MF, BMT, neutropenic fever	Imipenem (5)	-	Ciprofloxacin

*done at the same time with stool cultures.

Abbreviations: CRBSI: Catheter-related blood stream infection caused by *Staphylococcus aureus*, HFRS: Hemorrhagic fever with renal syndrome, RA: Rheumatoid arthritis, MF: Myelofibrosis, BMT: Bone marrow transplantation, ND: not done.

Table 2. Antibiograms of *Pseudomonas aeruginosa* isolated from stool cultures of the patients

Patients	Sex/ Age (yr)	Probable offending antibiotics	Resistance pattern																	
			Amikacin	Aztreonam	Cefazolin	Cefotaxime	Cefoxitin	Ceftazidime	Ceftizoxime	Ceftriaxone	Cefturoxime	Cefalothin	Ciprofloxacin	Getamycin	Imipenem	Piperacillin	Tobramycin	SXT	TICCV	
1	M/62	Imipenem	S	S	R	I	R	S	R	R	R	R	S	I	R	S	S	R	R	
2	F/71	Ceftriaxone	S	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R	R
3	M/48	Ceftriaxone	S	R	R	R	R	R	R	R	R	R	S	S	I	R	S	R	R	
4	M/67	Cefotetan	S	S	R	I	R	S	R	S	R	R	S	S	S	S	S	R	S	
5	F/41	Ceftizoxime	S	S	R	I	R	S	I	R	R	R	S	S	S	S	S	R	S	
6	M/59	Cefotetan	S	S	R	I	R	S	I	S	R	R	S	S	S	S	S	R	S	
7	F/52	Imipenem	S	I	R	I	R	S	R	R	R	R	S	S	R	S	S	R	S	

SXT: trimethoprim/sulfamethoxazole, TICCV: ticarcillin/clavulanic acid, S: susceptible, I: intermediate, R: resistant.

after the administration of antibiotics and in five patients thereof, diarrhea persisted without improvement 3-5 days after cessation of offending antibiotics. Diarrheas in these five patients were successfully controlled by antipseudomonal agents. This time sequence of treatment and resolution of diarrhea raised the probability of *P. aeruginosa* as the cause of diarrhea. Porco and Visconte reported a patient with *P. aeruginosa*-induced enteritis whose symptoms rapidly resolved with oral ciprofloxacin therapy (4). *P. aeruginosa* was suggested to cause diarrhea in a report of 23 patients with diarrhea that developed after use of antibiotics (3).

The pathogenetic mechanism by which antibiotics cause AAC is a disturbance of the composition and function of the normal intestinal flora, followed by an overgrowth of pathogenic microorganisms. Drug-resistant *P. aeruginosa* could be selected by antibiotics. Antibiotic susceptibility patterns of *P. aeruginosa* strains in these cases support the good relationship between antibiotic pressure and selection of resistant organism (8, 9). Cellular adhesion and cytotoxic activity of *P. aeruginosa* could be a putative mechanism of enterotoxigenicity and *Pseudomonas*-induced enterocolitis (3), although no enterotoxin was documented from *P. aeruginosa* isolates in a patient with AAC (2).

For the treatment of *Pseudomonas*-induced AAC, oral ciprofloxacin therapy was recommended (4). Other antipseudomonal agents, such as ceftazidime, aztreonam, and aminoglycosides, seem to be effective based on our experience.

Our data have several limitations because it is a retrospective study: there are no stool culture data at the time of admission to assure the nosocomial acquisition of *P. aeruginosa*; no follow-up cultures of stool to demonstrate the eradication of *P. aeruginosa* after treatment and no bacteriologic study on the isolated *P. aeruginosa* is available because the strains were not saved. However, our data and several other reports suggest

that *P. aeruginosa* could be a potential cause of AAC on the basis of the clinical courses. Further investigations are warranted to evaluate the possible etiologic role of *P. aeruginosa* in antibiotic-associated diarrhea.

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