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Characteristics of *Plesiomonas shigelloides* infection in Taiwan

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From January 1999 through December 2000, a total of 111 cases of *Plesiomonas shigelloides* infections were diagnosed in a medical center of northern Taiwan. The patients ranged in age from 22 days to 72 years. One third (39/111, 35%) of the positive cultures were found in young children (<2 years old). There was no significant difference in the incidence between males (56/111, 50%) and females (55/111, 50%). The peak seasons for the disease were summer (45/111, 41%) and autumn (42/111, 38%). The major clinical presentations in children were diarrhea (66/69, 96%) and fever (38/69, 55%), whereas diarrhea (41/42, 98%) and abdominal pain (30/42, 71%) were the most common presentations in adults. Most adults with *P. shigelloides* infection visited the emergency room (38/42, 90%) and received empirical antimicrobials (37/42, 88%), whereas children were more likely to be treated as outpatients (53/69, 77%) and inpatients (27/69, 39%). One third (23/69, 33%) of pediatric patients had mixed enteric infection, and 74% (17/23) of them were younger than 2 years. *Salmonella* species (17/24, 71%), especially group B *Salmonella* (12/17, 71%), were the most common mixed enteric pathogen. The disease is usually mild and self-limited. Symptomatic management is adequate and antimicrobial therapy is seldom required.

Key words: Gastroenteritis, mixed enteric infection, *Plesiomonas shigelloides*

Plesiomonas shigelloides is a gram-negative rod-shaped bacterium, which can be isolated from water, fish, and fecal samples of cats, dogs, and humans, and, on rare occasions, human samples of extraintestinal origin [1,2]. It has been reported to cause mild, self-limited infectious diarrheal disease in previously healthy adults and children [3-5]. Asymptomatic colonization is very rare [6,7].

P. shigelloides infection is prevalent worldwide [8, 9]; however, it had rarely been noted in Taiwan until 1990 when an oxidase test for this organism was suggested to be included as a routine examination of stool specimens in microbiological laboratories [10]. This retrospective study investigated the clinical, epidemiological, and laboratory findings of Taiwan patients whose fecal isolates revealed *P. shigelloides*.

Materials and Methods

Patients

During the period from January 1999 through December 2000, all patients in the Department of Bacteriology at the Mackay Memorial Hospital in northern Taiwan whose stool culture showed positive results for *P. shigelloides* were included in this study. Clinical data of these patients were reviewed from medical records.

Epidemiological information collected included (1) epidemiological associations, such as the age at the time of *P. shigelloides* cultured, sex, the month in which positive stool cultures were collected, history of travel to a tropical/or subtropical area within 2 weeks before the onset of illness, consumption of seafood within 5 days before the onset of illness, and underlying diseases or conditions; (2) clinical data including the presence of diarrhea, bloody and/or mucoid stool, vomiting, abdominal pain, and fever (oral temperature ≥38°C); the availability of an emergency room and access to antibiotics; admission to the hospital (inpatients) and/or treatment in the outpatient department (outpatients), duration of hospitalization; changes in white blood cell count (≥12,000, <4000, or band form ≥10%), and duration of symptoms before examination (≥2 weeks, chronic diarrhea); (3) presence or absence of concomitant infections with enteric pathogens other than *P. shigelloides*; and (4) results of antimicrobial susceptibility tests.

Patients were categorized into different age groups; children were divided into groups with 2-year intervals of age and adults with 7-year intervals.

Bacterial isolates

All stool specimens were cultured on *Salmonella-Shigella* agar, MacConkey agar, Hektoen enteric agar,

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and *Campylobacter* agar (BBL, Microbiology System, Cockeysville, MD, US). A culture was considered positive for *Plesiomonas* if the triple-sugar-iron agar showed alkaline/acid and no gas; the lysine-iron agar showed alkaline/alkaline; the motility-indole-ornithine agar was positive; and the urea and citrate tests were negative. If on top of these findings, positive results of an oxidase and an arginine test and negative results of a deoxyribonuclease test were found, *P. shigelloides* was identified.

Antimicrobial susceptibility testing

Standard disc diffusion methods were used to test *Plesiomonas* isolates for susceptibility to the following antimicrobial agents: ampicillin, trimethoprim/sulfamethoxazole, chloramphenicol, tobramycin, gentamicin, amoxicillin/clavulanate, cephalothin, cefoxitin, cefmetazole, cefuroxime, and cefotiam (BBL, Microbiology System).

Statistical analysis

Differences in categorical data between groups were analyzed using chi-square test. A p value of less than 0.05 was considered statistically significant.

Results

Between January 1999 and December 2000, a total of 1622 positive stool specimens were cultured at the Department of Bacteriology of the Mackay Memorial Hospital. Pathogenic isolates included 119 (7.3%) *Plesiomonas* species, 123 (7.6%) *Campylobacter* species, 167 (10.3%) *Salmonella* species group D, 173 (10.7%) *Aeromonas* species, 188 (11.6%) *Salmonella* species group C, and 690 (42.5%) *Salmonella* species group B.

Epidemiological associations

We were able to retrieve patient medical records for 116 of the 119 *Plesiomonas* isolates and excluded 3 of these patients who were foreign travelers to Taiwan, resulting in a total of 111 (113 isolates) patient records. The mean age of all 111 patients was 18 years (range, 22 days-72 years). There were 69 (62%) children and 42 (38%) adults. Infections were seen among all age groups. One third (39/111, 35%) of the positive cultures were found in younger children (<2 years old) and the incidence declined dramatically after that age (Fig. 1). In adult patients, the infection occurred sporadically in all age groups. The overall male to female ratio was 1:1 (56:55), but in children under 2 years old, boys slightly outnumbered girls by a ratio of 1.4:1 (23:16).

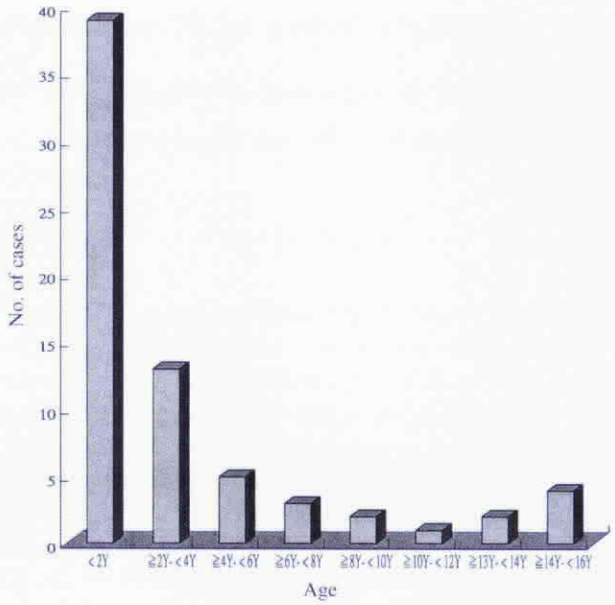

Fig. 1. Distribution of enteric *P. shigelloides* infection in children (<16 years old). Most (39/69, 57%) cases occurred in young children (<2 years old).

Plesiomonas-associated diarrhea was seen throughout the year, but the peak seasons for the disease were summer (May to July; 45/111, 41%) and autumn (August to October; 42/111, 38%). Only 7 (6%) of all 111 patients had traveled to a tropical/or subtropical area within 2 weeks before the onset of illness. Only 6 (5%) of 111 patients believed that their illness was associated with consumption of seafood within 5 days before the onset of illness (Table 1). There were no evident underlying diseases or conditions related to *P. shigelloides* infections in either pediatric or adult patients.

Table 1. Number of children and adults with enteric *P. shigelloides* infection who had risk factors of tropical or subtropical travel and seafood consumption

Age group	No. of cases (%)	No. of cases (%) associated with	
		Tropical/subtropical travel	Seafood consumption
<2 years old	39 (35)	0	1 (3)
≥2 to <16 years old	30 (27)	4 (13)	3 (10)
≥16 years old	42 (38)	3 (7)	3 (7)
Total	111 (100)	7 (6)	6 (5)

Table 2. Clinical manifestations between children and adults with enteric *P. shigelloides* infection

Symptom/sign	Children n = 69 (%)	Adults n = 42 (%)	*p*
Fever ≥38°C	38 (55)	19 (45)	0.32
Diarrhea	66 (96)	41 (98)	1.00
Bloody or mucoid stool	30 (43)	20 (48)	0.67
Vomiting	25 (36)	21 (50)	0.15
Abdominal pain	20 (29)	30 (71)	<0.001
WBC ≥12 000, <4 000, or band ≥10%	14 (20)	23 (55)	<0.001
Chronic diarrhea >2 weeks	16 (23)	5 (12)	0.14

Abbreviation: WBC = white blood cell count

Clinical characteristics

Diarrhea was the predominant manifestation of infection in both pediatric (66/69, 96%) and adult (41/42, 98%) patients. The next most common symptom was fever (38/69, 55%) in children and abdominal pain (30/42, 71%) in adults. Chronic diarrhea was seen in 23% (16/69) of children, compared with 12% (5/42) of adults (p=0.14). Change in white blood cell count was significantly more frequent in adults (23/42, 55%) than in children (14/69, 20%) (p<0.001) (Table 2). A more invasive dysenteric form of disease resembling colitis was found on abdominal sonography or sigmoidoscope examination in 9 patients (5 children and 4 adult).

More children than adults were treated as outpatients (53/69, 77% vs 14/42, 33%; p<0.001) and inpatients (14/42, 33% vs 6/42, 14%; p=0.005), whereas adult patients visited emergency rooms more frequently than children (38/42, 90% vs 42/69, 61%; p=0.001), and received empirical antimicrobials more often (37/42, 88% vs 20/69, 29%; p<0.001) (Table 3). The mean duration of hospitalization was 5.4 days in children compared with 15.8 days in adults, due to the more severe underlying diseases or conditions found in adults.

The outcome of the *P. shigelloides* infections was usually favorable, and only one adult patient died of severe underlying disease of end stage breast cancer.

Mixed enteric infection

Mixed enteric infection was found in 24 (22%) of 111 patients (25 isolates). Mixed *Salmonella* species was isolated in 17 (71%) of these patients, *Aeromonas* species in 4 (17%), and positive fecal rotavirus antigen in 4 (17%) children younger than 2 years. One boy aged 1 year 9 months had 2 isolates of *P. shigelloides* identified on different hospital days, one mixed with *Salmonella* species group B and another with *Aeromonas* species. One third (23/69, 33%) of pediatric patients had mixed enteric infection and most (17/23, 74%) of them were younger than 2 years old. *Salmonella* species was the most frequent pathogen in cases of mixed enteric infection with *P. shigelloides* (17/24, 71%), with group B comprising 71% (12/17) of these cases (Table 4).

Antimicrobial susceptibility test

P. shigelloides isolates were susceptible to most of the antibiotics tested (susceptible rate, ≥72%) except ampicillin (susceptible rate, 13%). Results of antimicrobial susceptibility testing are shown in Table 5.

Discussion

Plesiomonas, from the Greek word "*plesio*" which means "neighbor," was so named because the organism is closely related to *Aeromonas*. It is in fact more closely related to *Proteus*, though it is currently classified under the family *Vibrionaceae* [2]. One hundred and seven serotypes exist, several of which cross-react with *Shigella* typing antisera, hence the name *Shigelloides* [4]. *P. shigelloides* is the only species in the genus. The organism was originally isolated in 1947 and given the

Table 3. Number of children and adults with *P. shigelloides* infections who visited an emergency room or an outpatient department, were admitted to the hospital, or received antibiotic therapy

	Children n = 69 (%)	Adults n = 42 (%)	*p*
Visited an ER	42 (61)	38 (90)	0.001
Visited an OPD	53 (77)	14 (33)	<0.001
Hospitalized	27 (39)	6 (14)	0.005
Antibiotics treatment	20 (29)	37 (88)	<0.001

Abbreviations: ER = emergency room; OPD = outpatient department

Table 4. Isolates in cases of mixed enteric infection in children and adults

Pathogen	Children n = 69 (%)	Adults n = 42 (%)
Salmonella group B	12 (17)	0
Salmonella group C	2 (3)	0
Salmonella group D	1 (1)	0
Salmonella unidentified group	2 (3)	0
Aeromonas species	3 (4)	1 (2)
Rotavirus	4 (6)	0
Total	23[a] (33)	1 (2)

[a]One boy aged 1 year 9 months had mixed infection with *Salmonella* group B and *Aeromonas* species in separate culture results.

name C27.

P. shigelloides remains a known but infrequent cause of gastroenteritis in humans, despite its wide distribution in the natural world [11]. In this study, the isolation rate of *P. shigelloides* was 7.3% (119/1622). At least 3 major clinical presentations of *Plesiomonas* gastroenteritis are documented, including a secretory (watery) type of diarrhea, a more invasive dysenteric form resembling colitis, and a subacute or chronic disease lasting between 14 days and 2 to 3 months [7].

The diagnosis of *P. shigelloides* infection may be missed if stool culture is not done for patients with fever and diarrhea. Fever of unknown origin may be the initial presentation of the disease. Two patients in this series, a 9-month-old boy and a 20-year-old woman, were admitted due to fever of unknown origin. Seizure in a 25-month-old boy in this series who had a history of febrile convulsion could have been induced by fever caused by enteric *P. shigelloides* infection.

P. shigelloides infection generally arises after travel to tropical regions or ingestion of uncooked seafood; this unusual food-borne pathogen may also have a role in travelers' diarrhea [8,12,13]. However, this study showed only 6% (7/111) and 5% (6/111) incidence of these 2 risk factors (Table 1); this low incidence may be partly due to an inadequate data collection on seafood consumption and travel history.

The temperature range of growth for *Plesiomonas* is between 8°C and as high as 44°C; optimal growth occurs between 37°C and 38°C [7,13]. This suggests that *Plesiomonas*-associated diarrhea may be expected to occur more often in summer and autumn months, as supported by data in this study (89/111, 79%).

The existence of a relationship between salmonellosis and subsequent *P. shigelloides* infections remains speculative. An outbreak of *P. shigelloides* infections occurred in New York in June 1996, in which 30 persons experienced diarrheal illness after a party. Their illness was attributed to the consumption of water contaminated by *P. shigelloides* mixed with *Salmonella* serotype Hartford [14]. Mixed infection with *Aeromonas sobria* was reported to have caused mortality in a 19-year-old woman by unrelenting diarrhea [15]. In this study, pediatric patients had a higher incidence (12/69, 33%) of mixed enteric infection than adults (1/42, 2%), and the most common pathogens were *Salmonella* species and *Aeromonas* species (Table 4). One 15-year-old girl experienced septic shock (blood pressure, 73/37 mm Hg; white blood cell count, 4900 with 14% band forms) caused by mixed infection with *Salmonella* group C.

Plesiomonas isolates can be easily misidentified as other members of the family *Enterobacteriaceae*; therefore the importance of introducing the oxidase test at the preliminary stage of identification is stressed [1, 7,8,10]. Bile peptone broth enrichment for 24 h was observed to be 6 times more effective than direct plating alone on *Salmonella-Shigella* agar [1,2,16]. Five restriction endonucleases of *Plesiomonas* strains were described as tools for molecular typing in an outbreak [17].

Table 5. Results of antimicrobial susceptibility test for enteric *P. shigelloides* isolates by disk diffusion method

Antimicrobial agent	No. of isolates tested	No. of isolates (%)		
		Susceptible	Intermediate resistant	Resistant
Ampicillin	111	14 (13)	11 (10)	86 (77)
Trimethoprim/sulfamethoxazole	112	81 (72)	1 (1)	30 (27)
Tobramycin	110	91 (83)	7 (6)	12 (11)
Chloramphenicol	112	92 (82)	0	20 (18)
Gentamicin	113	102 (90)	5 (4)	6 (5)
Amoxicillin/clavulanate	107	101 (94)	0	6 (6)
Cefoxitin	112	106 (95)	2 (2)	4 (3)
Cephalothin	113	110 (97)	0	3 (3)
Cefmetazole	111	108 (97)	0	3 (3)
Cefotiam	111	111 (100)	0	0
Cefuroxime	113	113 (100)	0	0

In an experiment involving healthy adult volunteers, *P. shigelloides* strains isolated from patients with diarrhea did not induce diarrhea when fed to the volunteers [6,8,11]. Most strains of *P. shigelloides* secrete a β-hemolysin, which may be the major virulence factor associated with gastrointestinal infection [2,18,19]. It has been suggested that the bacterium is more pathogenic to children than to adults [20]. In this study, children with *P. shigelloides* tended to have a more protracted course as outpatients (53/69, 77%) than adults (14/42, 33%, $p<0.001$) (Table3).

P. shigelloides may occasionally cause systemic infection in both immunocompromised and non-compromised patients. Such extraintestinal infections include septicemia, meningitis, cellulitis, septic arthritis, osteomyelitis, endophthalmitis, spontaneous bacterial peritonitis, and acute cholecystitis [21-25]. No such case was found in this series.

Plesiomonas-associated diarrhea in normal hosts is usually mild and self-limited. Patients always respond to symptomatic treatment (eg, antidiarrhea and antiflatulence agents, digestants), and antimicrobial therapy is rarely needed [2,20]. In a study of Thai children with *Plesiomonas*-associated diarrhea, antibiotics did not shorten the duration of fever or diarrhea [26]. In this series, the high incidence of antibiotics use in adult patients (37/42, 88%) may be associated with the use of empirical antibiotics when they visited the emergency room (38/42, 90%) under the impression of infectious diarrhea (Table 3).

Extraintestinal infection with *P. shigelloides* is usually more severe and requires antimicrobial treatment. *P. shigelloides* isolated from immuno-suppressed patients with diarrhea should be regarded as pathogenic in the absence of other enteric pathogens, and the patients should be treated aggressively with antibiotics. Antimicrobial therapy should also be considered in case of mixed enteric infection.

In this study, *P. shigelloides* isolates were susceptible to most of the antibiotics tested (susceptible rate, ≥72%) except ampicillin (susceptible rate, 13%) (Table 5). Most strains are capable of producing β-lactamase [1, 2]. The oral agents commonly used to treat infectious diarrhea (eg, trimethoprim/sulfamethoxazole, quinolones, cephalosporins, chloramphenicol) may be useful if treatment is deemed necessary [27,28].

In conclusion, it is important not to mistake *P. shigelloides* for *Shigella* species. One third of the cases (39/111, 35%) in this study were found in young children (<2 years old). If diarrhea with fever or abdominal pain is present, a stool culture should be collected and sent to a microbiology laboratory for oxidase test. Mixed infection with *Salmonella* species, *Aeromonas* species, or rotavirus is a typical feature of the illness, especially in pediatric patients. Enteric *P. shigelloides* infection is usually mild and self-limited. Symptomatic management is adequate and antimicrobial therapy is rarely required.

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