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Case report

Haemophilus influenzae peritonitis in a girl on automated peritoneal dialysis: Case report and review of the literature

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ABSTRACT

Haemophilus influenzae is a rare cause of peritonitis in patients on peritoneal dialysis (PD). We report a case of peritonitis due to non-typeable *H. influenzae* in a 5-year-old girl on automated PD. The patient was successfully treated with intraperitoneal cefepime and cefazolin. The isolate was multilocus sequence type 3 and contained the *hmw* and *hia* genes but was *IS1016*-negative. Seven of the eight reported cases were female, indicating that sex-associated factors may be important in *H. influenzae* peritonitis in patients on PD. Determination of the pathogenesis of PD-associated *H. influenzae* peritonitis requires gene analysis and a swab sample from the vaginal introitus.

Introduction

Peritonitis is a major cause of morbidity and mortality for persons on peritoneal dialysis (PD). In such patients, the most common causative organisms of peritonitis are coagulase-negative staphylococci and *Staphylococcus aureus* [1]. The International Pediatric Peritonitis Registry reported that 25% of the peritonitis episodes were caused by Gram-negative organisms [2]. *Haemophilus influenzae* is a rare cause of bacterial peritonitis in children on PD.

Case report

A 5-year-old girl was admitted to our hospital for assessment of abdominal pain and fever up to 39.2 °C. She had a cough from 3 days before admission, but no rhinorrhea, vomiting, diarrhea, or rash.

She was born to a 36-year-old mother by normal spontaneous vaginal delivery after a full-term, uncomplicated pregnancy. However, placental abruption resulted in neonatal asphyxia; Apgar scores were 1 and 1 at 1 and 5 min, respectively. Hypoxic-ischemic encephalopathy and ischemic nephropathy were diagnosed, and automated PD (APD) was started at age 11 days. *H. influenzae* type b (Hib) vaccination was administered in a three-dose primary series with one booster dose by age 2 years.

On physical examination, her abdomen was tense and tender with signs of peritoneal inflammation. The site of peritoneal catheter insertion was slightly reddish, exudate was present. Peritoneal fluid from the catheter was cloudy and had a white blood cell count of 18,710/μL. Blood creatinine level was 3.62 mg/dL, BUN was 55 mg/dL, and C-reactive protein was 11.98 mg/dL. White blood cell count was 11,510/μL, with 83% neutrophils. IgG was 548 mg/dL (23% subclass 2).

H. influenzae was isolated from peritoneal fluid culture and was found to be highly susceptible to all tested antibacterials, including ampicillin and cefepime. A slide agglutination kit (Denka Seiken, Tokyo, Japan) classified the isolates as non-typeable *H. influenzae* (NTHi). The isolate was identified as sequence type (ST) 3 (allele adk-atpG-frdB-fucK-mdh-pgi-recA: 1-1-1-1-1-1-5) by multilocus sequence typing (MLST) (PubMLST, https://pubmlst.org/hinfluenzae/) [3]. The gene sequence *IS1016*, which may be associated with severe infection, was not detected by PCR [4]. The isolate had *hia*—a homologue of the *hsf* gene, which is ubiquitous among Hib strains—and *hmw1* and *2*, adhesin genes that are common in NTHi but absent in encapsulated *H. influenzae* [5].

Blood cultures obtained on the day of admission and a nasal swab sample obtained on day 3 of illness showed no growth. *H. influenzae* was previously isolated from the patient's nasal cavity upon routine screening 6 months before onset; however antimicrobial resistance patterns differed from those identified in peritoneal isolate.

The patient was empirically treated with intraperitoneal cefepime, in accordance with the International Society for Peritoneal Dialysis guidelines/recommendations [1]. The APD catheter was not removed. Her antimicrobial was changed to intraperitoneal cefazolin after *H. influenzae* was identified.

Written informed consent for publication of this case report was obtained from her legal guardian.

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Table 1
Haemophilus influenzae peritonitis in peritoneal dialysis patients.

Case	Age/Sex	PD commenced	PD type	Underlying Diseases	*H. influenzae* typing	Antibiotics		Reference
						Empiric	Definitive	
1	17 yr/F	5 mo before onset	CAPD	Recurrent urinary tract infection	NTHi Ampicillin- susceptible	Ampicillin Gentamicin	Ampicillin Gentamicin	[7]
2	26 yr/F	Not described	CAPD	Not described	Hib Ampicillin- resistant	Vancomycin (IV) Gentamicin (IV)	Cefotaxime (IV) Ciprofloxacin (Oral)	[8]
3	2 yr/F	3 mo before onset	CCPD	Denys-Drash syndrome Wilms' tumor Bilateral nephrectomy	NTHi Biotype II	Cefazolin (IP) Gentamicin (IP)	Cefazolin (IP)	[9]
4	41 yr/F	3 mo before onset	CAPD	Diabetic nephropathy	Hib Ampicillin- susceptible	Cephalothin (IP)	Cephalothin (IP) Gentamicin (IP)	[10]
5	32 yr/F	Not described	CAPD	HIV Hypertensive nephropathy	NTHi BLNAS	Vancomycin (IV) Levofloxacin (IV) Cefazolin (IP)	Ampicillin (IP)	[11]
6	32 yr/F	7 yr before onset	CAPD	Not described	β–lactamase non-producing	Vancomycin (IP) Amikacin (IP)	Cefazolin (IP)	[12]
7	18 yr/M	11 mo before onset	APD	SLE Lupus nephritis	NTHi Biotype II BLNAR ST367	Ceftazidime (IP) Vancomycin (IP)	Ciprofloxacin (Oral)	[13]
8	5 yr/F	5 yr before onset	APD	Ischemic nephropathy Hypoxic-ischemic encephalopathy	NTHi BLNAS ST3	Cefepime (IP)	Cefazolin (IP)	This study

PD, peritoneal dialysis; CAPD, continuous ambulatory peritoneal dialysis; CCPD, continuous cycling peritoneal dialysis; APD, automated peritoneal dialysis; IV, intravenous; IP, intraperitoneal; Hib, *Haemophilus influenzae* type b; NTHi, nontypeable *Haemophilus influenzae*; BLNAS, β–lactamase non-producing ampicillin susceptible strain; BLNAR, β-lactamase non-producing ampicillin resistant strain; ST, sequence type.

Discussion

H. influenzae frequently colonizes the nasopharynx of healthy children [6]. It is a rare causative agent of peritonitis in PD patients; only eight cases (including the present patient) have been reported (Table 1) [7–13]. Two of the eight cases were classified as Hib and six as NTHi. The NTHi isolated from our case was of the ST3 MLST type, which belongs to clonal complex 3. MLST typing was previously reported for only one case (case 7) [13] and yielded a result of ST367, a single locus variant of ST3. However, both ST types have been isolated from various other sources, such as throat swabs, ear discharge, blood, and cerebrospinal fluid (PubMLST), indicating that the clonal complex 3 strains are "common" NTHi types.

A subset of invasive NTHi strains possesses *IS1016* and harbors *hia* but lacks *hmw* [5]. In contrast, non-invasive NTHi strains containing *hmw* genes lack the *hia* gene. Our isolate was *IS1016*-negative but contained both *hmw* and *hia*. It is unclear whether possessing these two genes is associated with peritonitis.

It has been assumed that *H. influenzae* originates in a respiratory source, although the bacterium has been cultured from samples of feces, jejunal fluid, and the genital tract [14]. There is no sex difference in the incidence of peritonitis among patients on PD. However, seven of the eight reported patients in this report are female, indicating that sex-associated factors may important in *H. influenzae* peritonitis in PD patients.

In conclusion, determination of the pathogenesis of PD-associated *H. influenzae* peritonitis requires gene analysis and a swab sample from the vaginal introitus.

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Conflicts of interest

None.

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