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.

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 (alleles *adk-atpG-frdB-fucK-pgi-recA: 1-1-1-1-1-1*) by multilocus sequence typing (MLST) (PubMed, https://pubmlst.org/hinfluenza/) [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

| Case | Age/Sex | PD commenced | PD type | Underlying Diseases | H. influenzae typing | Antibiotics |
|------|---------|--------------|---------|---------------------|---------------------|-------------|
| 1    | 17 yr/F | 5 mo before onset | CAPD    | Not described        | NTHi Biotype II     | Cefazolin (IP) Gentamicin (IP) |
| 2    | 26 yr/F | Not described   | CAPD    | Not described        | NTHi Biotype II     | Cefazolin (IP) Gentamicin (IP) |
| 3    | 41 yr/F | Not described   | CAPD    | Not described        | NTHi Biotype II     | Cefazolin (IP) Gentamicin (IP) |
| 4    | 52 yr/F | 7 yr before onset | APD     | Not described        | NTHi Biotype II     | Cefazolin (IP) Gentamicin (IP) |
| 5    | 18 yr/M | 5 yr before onset | APD     | Not described        | NTHi Biotype II     | Cefazolin (IP) Gentamicin (IP) |
| 6    | 32 yr/F | 6 mo before onset | CAPD    | Not described        | NTHi Biotype II     | Cefazolin (IP) Gentamicin (IP) |
| 7    | 18 yr/M | 7 yr before onset | APD     | Not described        | NTHi Biotype II     | Cefazolin (IP) Gentamicin (IP) |
| 8    | 5 yr/F  | 5 yr before onset | APD     | Not described        | NTHi Biotype II     | Cefazolin (IP) Gentamicin (IP) |

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, 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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References

[1] Warnady BA, Bakkaloglu S, Newland J, Cantwell M, Verrina E, Neu A, et al. Consensus guidelines for the prevention and treatment of catheter-related infections and peritonitis in pediatric patients receiving peritoneal dialysis: 2012 update. Perit Dial Int 2012;32(Suppl 2):S32–S6.

[2] Chadha V, Schaefer FS, Warnady BA. Dialysis-associated peritonitis in children. Pediatr Nephrol 2010;25:425–40.

[3] Meats E, Feil EJ, Stringer S, Cody AJ, Goldstein R, Kroll JS, et al. Characterization of encapsulated and noncapsulated Haemophilus influenzae and determination of phylogenetic relationships by multilocus sequence typing. J Clin Microbiol 2003;41:1623–36.

[4] Ohkusu K, Nash KA, Inderlied CB. Molecular characterisation of Haemophilus influenzae type a and untypeable strains isolated simultaneously from cerebrospinal fluid and blood: novel use of quantitative real-time PCR based on the cap copy number to determine virulence. Clin Microbiol Infect 2005;11:637–43.

[5] Satola SW, Napier B, Farley MM. Association of IS1016 with the hia adhesin gene and biotypes V and I in invasive nontypeable Haemophilus influenzae. Infect Immun 2008;76:5221–7.

[6] Otsuka T, Chang B, Shirai T, Iwaya A, Wada A, Yamanaka N, et al. Individual risk factors associated with nasopharyngeal colonization with Streptococcus pneumoniae and Haemophilus influenzae: a Japanese birth cohort study. Pediatr Infect Dis J 2013;32:709–14.

[7] Ferrari R, Dasgupta MK. A case of CAPD peritonitis due to Haemophilus influenzae. Perit Dial Int 1993;13:323–4.

[8] Maxwell PH, Abbott J, Koffman GG, Dave J. Haemophilus influenzae as a rare cause of CAPD peritonitis. J Infect 1993;26:340–1.

[9] Neuhaus TJ, Iselin H, Nadal D. Haemophilus influenzae: a cause of peritonitis in peritoneal dialysis. Nephrol Dial Transplant 1996;11:199–200.
[10] Chew CG, Clarkson AR, Faull RJ. Relapsing CAPD peritonitis with rapid peritoneal sclerosis due to Haemophilus influenzae. Nephrol Dial Transplant 1997;12:821–2.
[11] Ghosh M, Eras J. Haemophilus influenzae CAPD peritonitis in an HIV-infected patient. J Infect 2007;54:e119–20.
[12] Unal A, Perçin DE, Sipahioglu MH, Kavuncuoglu F, Tokgoz B, Oymak O, et al. A rare cause of peritoneal dialysis-related peritonitis: Haemophilus influenzae. Mikrobiyol Bull 2009;43:477–80. (Turkish).
[13] Kadihbowski M, Wolskowicz T, Miklaszewka M, Klepacka J, Hryniewicz W. Automated peritoneal dialysis-associated peritonitis due to Haemophilus influenzae showing the BINAR phenotype. Int J Infect Dis 2009;13:e470–2.
[14] Musher DM, Nichol AC, Rueda AM. Nontypeable Haemophilus influenzae as a cause of spontaneous bacterial peritonitis. J Clin Microbiol 2006;44:2304–6.