Peritonitis Due to *Neisseria mucosa* in an Adolescent Receiving Peritoneal Dialysis

A. K. Shetty, S. K. Nagaraj, W. B. Lorentz, M. Bitzan

Abstract

Neisseria mucosa is part of the normal nasopharyngeal flora and rarely pathogenic in humans. Reports of serious infections associated with this pathogen are very unusual. A 17-year-old boy with end-stage renal disease due to IgA nephropathy presented with acute, spontaneous, symptomatic peritoneal dialysis-associated peritonitis without reported break in sterility or PD catheter exit site infection. β-lactamase-negative *N. mucosa* was isolated from the dialysate effluent. Intraperitoneal antibiotic treatment with cephalothin/gentamicin for 5 days and subsequent ceftriaxone led to complete resolution of the infection. This case demonstrates that "non-pathogenic" *Neisseria* species can cause clinically severe peritonitis with high intraperitoneal neutrophil counts, elevated C-reactive protein levels in the peritoneal effluent (in the presented case, 27,600/µl and 3.6 mg/l, respectively) and impaired peritoneal membrane transport function. To our knowledge, this is the first case of *N. mucosa* peritonitis complicating chronic peritoneal dialysis in an adolescent patient.

Infection 2005; 33: 390–392
DOI 10.1007/s15010-005-5074-4

Introduction

Neisseria mucosa is a gram-negative diplococcus, commonly found in the commensal flora of the human nasopharynx and considered nonpathogenic [1, 2]. However, it may occasionally cause serious invasive disease, including endocarditis, meningitis, septic arthritis, ocular and urinary tract infection [1–4]. Peritonitis associated with *N. mucosa* is extremely rare: we have identified only two case reports of adults who developed peritonitis associated with this organism while receiving continuous ambulatory peritoneal dialysis (CAPD) [5, 6].

Case Report

The patient was a 17-year-old boy with end-stage renal failure secondary to IgA nephropathy, diagnosed 2 years before this admission when he commenced dialysis in the form of cycler-assisted peritoneal dialysis (APD). He had no prior history of unusual or frequent infections. He now presented to the Nephrology Clinic at the Brenner Children's Hospital because of abdominal pain, nausea, and vomiting during the past 8 h. He also reported intermittent loose dark stools without visible blood since 2 weeks. Physical examination revealed that he was afebrile, normotensive and in no respiratory distress. He had no signs of upper respiratory tract infection or cervical lymphadenopathy. There was diffuse abdominal tenderness. Abdominal peritoneal dialysis (PD) catheter exit site and tunnel were without exudate or signs of inflammation or trauma. The remainder of the examination was unremarkable. The dialysate effluent was cloudy.

The peripheral white blood cell (WBC) count was 20.3×10^9/l with predominantly neutrophil (12.0×10^9/l) and band forms (5.3×10^9/l). Hemoglobin was 104 g/l, platelets 187×10^9/l. Serum sodium was 136 (all mmol/l), potassium 4.2, chloride 88, total CO_2 18, calcium 2.58 (10.3 mg/dl), glucose 4.7 (84 mg/dl), total protein 69 g/l, albumin 40 g/l, and creatinine 1,320 µmol/l (15 mg/dl). Serum transaminases were normal. C-reactive protein (CRP) was significantly elevated (Table 1). The effluent dialysate showed Na^+ 137 (mmol/l), K^+ 4.6, Ca^{2+} 1.65 (6.6 mg/dl), total CO_2 14. Albumin and total protein were 3 and 5 g/l, respectively, CRP 2.6 mg/l and amylase 3 U/l. Microscopic analysis revealed 28,500 leukocytes/µl (97% neutrophils), fibrin clots and gram-negative cocci. The dialysate fluid was cultured according to standard recommendations and yielded growth of *Neisseria* within 1 day. The isolate was identified as *N. mucosa* on the basis of mucoid, non-pigmented colonies growing on plain chocolate agar at 22 °C and on nutrient agar at 35 °C, and Gram staining (gram-negative diplococci). The organism was oxidase and catalase negative and nitrate-positive. It was differentiated from other *Neisseria* species by its ability to produce acid from glucose, sucrose, and maltose

A. K. Shetty, S. K. Nagaraj , W. B. Lorentz, M. Bitzan
Dept. of Pediatrics, Wake Forest University Health Sciences, and Brenner Children's Hospital, Winston-Salem, North Carolina, USA
M. Bitzan *(corresponding author)*
Montreal Children's Hospital, Division of Nephrology, 2300, rue Tupper, Montreal, Quebec, Canada H3H 1P3; Phone: (+1/514) 412-4461, Fax: -4359, e-mail: martin.bitzan@muhc.mcgill.ca

Received: May 10, 2005 • Revision accepted: August 9, 2005

This paper is dedicated to the founders of the Walter Marget Foundation, D. Adam and F. Daschner, in gratitude for their support of the training in infectious diseases.

but not from lactose (BBC Minetek, Cockeysville, MD). It was β-lactamase negative (minimal inhibitory concentrations [MIC, mg/l] penicillin 0.5, cephalothin 2, ceftriaxone < 0.25, gentamicin 0.5, gatifloxacin < 0.25, clindamycin > 2). Blood culture was negative. Nasal, throat, and stool culture were not obtained.

Empiric antibiotic treatment was initiated with cefazolin (500 mg/l) and gentamicin (8 mg/l) intraperitoneally (IP) as "loading" dose and 125 mg/l and 4 mg/l, respectively, for maintenance APD. Heparin was added to the dialysate at a concentration of 500 units/l during the acute treatment. Increased blood pressure on the 2nd day post admission was attributed to volume overload secondary to impaired peritoneal transport. Diffuse abdominal and dialysate drain pain improved within 48 h of antibiotic treatment. The patient remained afebrile, diarrhea and nausea resolved. He was discharged home after 6 days. Based on a previous case report [6], antibiotic treatment was changed on the day of discharge without repeat culture to IP ceftriaxone (125 mg/l dialysate) for 2 weeks. When the patient was reexamined a month later, he was asymptomatic, and lab results were at baseline (Table 1). A peritoneal equilibration test at this time revealed no apparent loss of peritoneal membrane function.

Discussion

Neisseria mucosa, originally described as *Diplococcus mucosus* by *von Lingelsheim* [7] in 1906, is a saprophytic organism that frequently colonizes the nasopharynx and rarely causes human infections [1, 3–6]. *Neisseria* species other than *Neisseria meningitidis* and *Neisseria gonorrhoeae*, such as *Neisseria sicca*, *Neisseria subflava*, *Neisseria lactamica*, *Neisseria cinerea*, and *N. mucosa*, are unusual pathogens in humans [1, 2].

Peritonitis is a serious problem in patients treated with PD [8]. Most peritonitides are due to constituents of skin or nasal flora, such as coagulase-negative S*taphylococci*, *Staphylococcus aureus* and *Corynebacterium* species, followed by gram-negative bacteria including *Enterobacteriaceae* and *Pseudomonas* and *Stenotrophomonas* species [8]. PD peritonitis associated with *N. mucosa* is very rare and has not been reported in the pediatric age-group [5, 6]. Similarly, only few cases due to other "non-pathogenic" *Neisseria* species have been published [9–12]. The first reported case of *N. mucosa* peritonitis was a 30-year-old woman with end-stage renal disease (ESRD) secondary to focal segmental glomerulosclerosis and failed transplants, who developed peritonitis 3 days after a self-limiting sore throat. Peritoneal effluent (25,600 WBC/μl) grew *N. mucosa* after 48 h (β-lactamase negative), and she recovered uneventfully after an unspecified course of IP vancomycin and ceftazidime treatment [5]. The second report describes a 61-year-old patient with diabetes mellitus and ESRD, who had a history of ureteral transitional cell carcinoma with peritoneal invasion. She presented with persistent ultrafiltration failure and subsequently cloudy dialysate (> 2,600 neutrophils/μl, Gram stain negative), which grew *N. mucosa* after prolonged incubation (antimicrobial sensitivities were not reported). Clearing of the cloudy dialysate and improvement of ultrafiltration were only noted after changing the antibiotic treatment from IP cefazolin/tobramycin to IP ceftriaxone [6].

Despite technical advances and emphasis on patient training, peritoneal infections continue to be the major cause of acute and chronic complications of this dialysis modality [8]. Intrusion of microorganisms into the peritoneal cavity of PD patients occurs via (1) exogenous (intraluminal) contamination due to a break in sterile procedures, thereby contaminating the catheter lumen and the dialysate; (2) pericatheter migration (extraluminal), thereby traversing the subcutaneous and intramuscular cuffs and forming a biofilm on the surface of the indwelling silicone rubber catheter; (3) the endogenous route, due to trans-

Table 1
***Neisseria mucosa* peritonitis: systemic inflammatory response.**

Day of onset	Cell count Total white blood cells (Neutrophils) (per mm³)		C-reactive protein (mg/l)		Protein/albumin (g/l)	
	Blood	Effluent dialysate	Plasma[a]	Effluent	Serum	Effluent
–7	9,700	-	-	-	70/42	-
1	20,300 (17,300) (bands 31%)	28,500 (27,645)	182.2	2.6	69/40	5/3
2	-	2,805 (1,907)	-	3.6	65/38	4/2
3	12,200 (8,500) (bands 8%)	260 (130)	174.5	2.0	60/34	2/1
32	-	1	< 0.5	< 0.5	-/38	-

[a] Ref value (plasma) 0–10 mg/l (detection limit 0.5 mg/l); - (not done)

mucosal migration of intestinal bacteria; and (4) the hematogenous route, due to bacteremia. We were unable to ascertain the mechanism by which *N. mucosa* gained access to our patient's peritoneal cavity, although contamination (self-inoculation) by upper respiratory tract commensals is likely, possibly via the exogenous (intraluminal) route. The presence of loose stools prior to peritonitis onset is intriguing, but there is no precedent to implicate *N. mucosa* in support of the transmucosal migration hypothesis.

The pathogenesis of infections by "non-pathogenic" *Neisseria* spp. including *N. mucosa* is poorly understood. They lack common virulence factors, such as pili, opacity-associated protein and the H8 antigen, which are expressed by meningococci and gonococci. It is of note, however, that the *N. mucosa* strain in our patient was able to induce an impressive inflammatory response resulting in the influx of large numbers of neutrophils and in an estimated 300-fold induction of serum CRP, which was also detected in the dialysate (Table 1). Replacement of the catheter was not necessary in the present or previous reports, suggesting that these strains may not form therapy-resistant biofilms on the catheter material [8, 13].

Due to a paucity of published cases, no specific guidelines or data are available for the treatment of *N. mucosa* peritonitis. *Neisseria* spp. are generally susceptible to penicillin or ampicillin [1]. However, *N. mucosa* isolates vary in their penicillin sensitivity, and MICs range from 0.125 to 4.0 mg/l [3]. In addition, penicillin-resistant β-lactamase producing *N. mucosa* strains with MICs for penicillin greater than 4 mg/l have been reported [2]. Clinical resistance and treatment failure to amoxicillin have been documented in gravidic urinary tract infection with *N. mucosa* [4]. Thus, it is important to determine whether the organism produces β-lactamase as a guide to appropriate antibiotic treatment. Changing the antibiotic therapy to ceftriaxone in our case, which was motivated by a previous report [6], may have been overcautious, given that clinical symptoms and dialysate cell count had already improved (Table 1).

In conclusion, *N. mucosa* is a rare cause of peritonitis in patients undergoing PD; it should be considered as a possible etiologic agent when encountering patients with peritonitis associated with gram-negative organisms.

References

1. Murphy T: *Moraxella (Branhamella) catarrhalis* and other gram-negative cocci. In: Mandell GL, Bennett JE, Dolin R (eds): Mandell, Douglas, and Bennett's principles and practice of infectious diseases, 5th edn vol. 2. Churchill Livingstone, Philadelphia 2000, pp 2259–2266.
2. Herbert DA, Ruskin J: Are the "nonpathogenic" Neisseria pathogenic? Am J Clin Pathol 1981; 75: 739–743.
3. Ingram RJH, Cornere B, Ellis-Pegler RB: Endocarditis due to *Neisseria mucosa*: two case reports and review. Clin Infect Dis 1992; 15: 321–324.
4. Hanau-Bercot B, Rottman M, Raskine L, Jacob D, Barnaud G, Gabarre A, Sanson Le Pors MJ: Clinical resistance to amoxicillin of a gravidic urinary tract infection caused by *Neisseria mucosa*. J Infect 2001; 43: 160–161.
5. Macia M, Vega N, Elcuaz R, Aterido T, Palop L: *Neisseria mucosa* peritonitis in CAPD: another case of the "nonpathogenic" Neisseriae infection. Perit Dial Int 1993; 13: 72–73.
6. Lee WC, Yang WC, Chen TW, Huang CH, Lin CC: Unusual presentation of *Neisseria mucosa* peritonitis with persistent ultrafiltration failure and clear effluent. Perit Dial Int 1993; 23: 198–199.
7. von Lingelsheim W: Die bakteriologischen Arbeiten der Kgl. hygienischen Station zu Beuthen O.-Schl. während der Genickstarreepidemie in Oberschlesien im Winter 1904/05. Klinisches Jahrbuch 1906; 15: 373–489.
8. Troidle L, Gorban-Brennan N, Kliger A, Finkelstein FO: Continuous ambulatory peritoneal dialysis-associated peritonitis: a review and current concepts. Semin Dial 2003; 16: 428–437.
9. Neu AM, Case B, Lederman HM, Fivush BA: *Neisseria sicca* peritonitis in a patient maintained on chronic peritoneal dialysis. Pediatr Nephrol 1994; 8: 601–602.
10. George MJ, DeBin JA, Preston KE, Chiu C, Haqqie SS: Recurrent bacterial peritonitis caused by *Neisseria cinerea* in a chronic ambulatory peritoneal dialysis (CAPD) patient. Diagn Microbiol Infect Dis 1996; 26: 91–93.
11. Vermeij CG, van Dam DW, Oosterkamp HM, Verburgh CA: *Neisseria subflava* biovar perflava peritonitis in a continuous cyclic peritoneal dialysis patient. Nephrol Dial Transplant 1999; 14: 1608.
12. Konner P, Watschinger B, Apfalter P, Horl WH, Vychytil A: A case of continuous ambulatory peritoneal dialysis peritonitis with an uncommon organism and an atypical clinical course. Am J Kidney Dis 2001; 37: E10.
13. Sepandj F, Ceri H, Gibb A, Read R, Olson M: Minimum inhibitory concentration (MIC) versus minimum biofilm eliminating concentration (MBEC) in evaluation of antibiotic sensitivity of gram-negative bacilli causing peritonitis. Perit Dial Int 2004; 24: 65–67.