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Brief report

Mycobacterium phlei peritonitis: a rare complication of chronic peritoneal dialysis

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Abstract. We report the first case of chronic ambulatory peritoneal dialysis-associated peritonitis caused by *Mycobacterium phlei*. This organism was isolated from the peritoneal fluid of a patient who presented with recurrent episodes of "culture-negative" peritonitis. The therapeutic regimen was based on previous experience with other rapidly growing atypical mycobacteria, and included removal of the Tenckhoff catheter, institution of hemodialysis, and anti-mycobacterial therapy with amikacin, cefoxitin, and doxycycline. This successfully eradicated the organism, and permitted subsequent cadaveric renal transplantation with routine immunosuppression.

Key words: Continuous ambulatory peritoneal dialysis – Atypical mycobacteria – Peritonitis – Amikacin – *Mycobacterium phlei*

Introduction

Peritonitis remains the most important complication of chronic ambulatory peritoneal dialysis (CAPD), with an average incidence of 1.3 episodes per patient per year [1]. These infections are usually caused by Gram-positive (60%–70%), Gram-negative (20%–30%) or fungal (3%–5%) species. In many cases [ranging from 3% to as many as 30% of CAPD peritonitis, as defined by peritoneal fluid white blood cell (WBC) count $>$ 100 cells/μl], the above organisms are not isolated [1]. Increased awareness and improved diagnostic procedures have revealed that such cases may be caused by a number of rare pathogens, including a variety of atypical mycobacteria. We report a case of CAPD peritonitis due to *Mycobacterium phlei,* which is generally considered to be a non-pathogenic environmental organism. Successful therapy, including removal of the Tenckhoff catheter, hemodialysis, and anti-mycobacterial therapy (amikacin, cefoxitin, and doxycycline) allowed for subsequent cadaveric renal transplantation with routine immunosuppression.

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Case report

A 17-year-old male on CAPD was admitted for evaluation of abdominal pain. Three years previously, CAPD had been instituted via a Tenckhoff catheter for end-stage renal disease secondary to biopsy-proven focal and segmental glomerulosclerosis. He had been well until 3 weeks prior to admission, when he developed abdominal pain, fever, and cloudy dialysate. Peritoneal fluid WBC count was elevated at 760 cells/μl, but Gram stain and routine cultures revealed no organisms. Vancomycin was given as empiric therapy (intravenously, since he had a history of non-compliance with intraperitoneal antibiotics), with resolution of symptoms. Abdominal pain returned 4 days prior to admission, with elevated peritoneal fluid WBC count. Once again, Gram stain and cultures were negative for bacteria. Despite intraperitoneal cefuroxime, the pain persisted, and was accompanied by fever and vomiting, prompting his hospitalization.

On admission, he had moderate discomfort and a low-grade fever. His abdomen was not distended but diffusely tender, with guarding, rebound tenderness, and hypoactive bowel sounds. The Tenckhoff exit site and tract were benign. The blood urea nitrogen and serum creatinine were at the baseline values of 60 mg/dl and 15.0 mg/dl, respectively. Peripheral WBC count was 9,000 cells/μl, with a normal differential. The dialysate was cloudy, with 733 WBC/μl (75% neutrophils, 10% lymphocytes, 12% monocytes, 3% eosinophils), but no organisms were seen by Gram stain. Intravenous vancomycin and a regimen of rapid exchanges were instituted. Over the ensuing 3 days, the abdominal pain and rebound tenderness persisted. Daily dialysate cultures remained negative for bacteria and fungi. Abdominal radiographs, ultrasound, and computed tomographic scan revealed a fecolith in the right iliac fossa. Surgical exploration revealed purulent peritoneal fluid and a chronically inflammed appendix. Both the appendix and peritoneal fluid were negative for routine bacterial and fungal cultures, but the fluid was positive for acid-fast bacilli by smear. Subsequent serial dialysate examinations were all positive for acid-fast bacilli. Chest X-ray, cultures of blood, urine, and sputum, and human immunodeficiency virus testing were negative. A preliminary report of the initial isolate was a rapidly growing atypical mycobacterium, type IV, which includes *M. fortuitum* and *M. chelonae*.

The Tenckhoff catheter was surgically removed and a permacath placed for hemodialysis. He was started on intravenous amikacin (5 mg/kg daily, with supplemental 1 mg/kg post dialysis) and cefoxitin (1 g daily with an additional 1 g post dialysis). Within 3 days, the fever subsided and all his symptoms resolved. The organism from several of his peritoneal fluid cultures was consistently identified as *M. phlei*,

Table 1. Atypical mycobacteria associated with chronic ambulatory peritoneal dialysis-associated peritonitis

Runyon group	Features[b]	Species	Cases[a]
I	Slow-growing photochromogen	*M. kansasii*	1
II	Slow-growing scotochromogen	*M. gordonae*	1
		M. xenopi	1
III	Slow-growing non-chromogen	*M. avium*	1
		M. gastri	1
IV	Rapidly growing non-chromogen	*M. fortuitum*	7
		M. chelonae	19
		M. phlei	1

[a] All cases cited in reference 6, except the *Mycobacterium kansasii* infection in reference 9 and the *M. phlei* case reported here

[b] Photochromogen isolates are buff colored in the dark but turn yellow upon exposure to light; scotochromogens are yellow even in the dark

sensitive to amikacin, cefoxitin, rifampin, and doxycycline, and resistant to isoniazid and ethambutol. The cultures of his appendix and Tenckhoff catheter were negative for mycobacteria. Amikacin dosage was adjusted to a trough level of 25 μg/μl, which was achieved at a dose of 4 mg/kg three times a week given post dialysis, and was discontinued after 2 months. In addition, intravenous cefoxitin was given for 1 month, and then replaced with oral doxycycline for the next 6 months. The patient was maintained on hemodialysis for 2 years, during which time his clinical course was benign. He then successfully underwent a cadaveric renal transplant, and has now been stable for 4 years on cyclosporine, azathioprine, and prednisone. He has had no symptoms or signs of recurrent mycobacterial infection.

Discussion

Atypical mycobacteria are emerging as important pathogens in "culture-negative" CAPD-associated peritonitis [2, 3]. These environmental mycobacteria are ubiquitous in soil and water, and most likely infect the peritoneum through contamination of the dialysis catheter or fluid. They are classified into four Runyon groups based on growth and pigmentation characteristics (Table 1). The group IV organisms account for most of the mycobacterial cases of CAPD-associated peritonitis. They grow rapidly (5–7 days) on non-selective media, and appear fragmented and beaded by Gram stain, resembling diphtheroids or other contaminants. Since routine dialysate cultures are discarded in 3–4 days, these organisms may escape detection. Within this group, *M. fortuitum* and *M. chelonae* are established pathogens, whereas *M. phlei* has been traditionally viewed as a non-pathogenic environmental organism [4, 5]. Our case represents the third report of human disease and the first instance of CAPD-associated peritonitis caused by *M. phlei* [6, 7]. Based on our experience and a literature review, we propose that in "culture-negative" CAPD-associated peritonitis unresponsive to empiric antibiotic therapy, routine cultures should be held for at least 7 days, and additional peritoneal fluid samples obtained for acid-fast bacilli and mycobacterial cultures.

For the clinician, the importance of the Runyon classification revolves around drug susceptibility. Unlike the slower-growing organisms, the group IV mycobacteria are resistant to traditional anti-tuberculosis agents, i.e., isoniazid, rifampin, ethambutol, streptomycin and pyrazinamide [4]. Instead, routine susceptibility testing should include amikacin, cefoxitin, doxycycline, sulfamethoxazole, and ciprofloxacin. Furthermore, it is recommended that: (1) amikacin dosage should be adjusted to provide serum levels of about 25 μg/μl, (2) additional intravenous anti-microbials (e.g., cefoxitin) should be administered for 2–4 weeks, and (3) surgical excision of abscesses and foreign bodies (e.g., Tenckhoff catheter) is essential for recovery [4].

These cases highlight a growing area of concern in CAPD-associated peritonitis. Changes in infusion and drainage equipment, and adjustment of the dialysate composition to minimize host immune suppression, have reduced the incidence of bacterial peritonitis over the past decade [8, 9]. Nonetheless, peritonitis remains the most common complication of CAPD and the most common reason for changing to hemodialysis [1, 8]. We are faced with an increasing number of reports of atypical mycobacteria in what may have previously been diagnosed as aseptic peritonitis [2, 3]. Interestingly, in contrast to the group III *M. avium-intracellulare* complex which infects the immunocompromised host, the three known human cases of *M. phlei* infection and most of the other mycobacterial peritonitis cases have been in immunocompetent patients [6, 7]. Better understanding of environmental mycobacterial infections is needed so that strategies to avoid peritoneal contamination can be implemented. Perhaps dialysate composition can be adjusted to be non-permissive for mycobacterial growth, or possibly immune function of peritoneal macrophages can be boosted [9, 10]. For the time being, it is reassuring to know that anti-mycobacterial regimens such as the one presented in this case report appear to successfully and completely eradicate *M. phlei*, to the point where kidney transplantation and routine immunosuppression posed no danger to our patient.

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