

Teaching Point
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White tide

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Introduction

Infectious problems, such as exit-site infection and peritonitis, are common complications of peritoneal dialysis (PD). Peritonitis is usually bacterial and either caused by gram-positive organisms as a sequel to handling errors or by gram-negative bacteria as a result of underlying gastrointestinal pathology. Several antibiotic guidelines have been formulated. We present a case of PD peritonitis that provided an interesting challenge after cultures grew a rare organism. We discuss the case with an emphasis on rare organisms and the factors associated with these infections.

Case

A 35-year-old female patient on peritoneal dialysis (PD) presented with abdominal pain and turbid dialysis fluid in August 2004 after several previous episodes of PD peritonitis.

She had been diagnosed with medullary cystic disease on the basis of a renal biopsy and reached end-stage renal disease in February 1998 when CAPD was initiated. An inguinal hernia was repaired in September 2000, and an umbilical hernia was repaired in 2001. She had two episodes of peritonitis due to coagulase-negative staphylococci in 2002 and another two episodes, again due to staphylococci, in April and December 2003. All of these episodes were believed to be due to handling errors, and the patient underwent re-training. She presented, again, with peritonitis in April 2004, and cultures grew coagulase-negative staphylococci. A new catheter was inserted in April 2004. In spite of the new catheter, she presented again in May 2004

with another episode of gram-positive PD peritonitis. Plans were made to switch the patient to haemodialysis while she sustained yet another episode of PD peritonitis in August 2004, with turbid peritoneal fluid and a PD fluid leukocyte count of 246/ μ l. She was admitted and treated with intra-peritoneal vancomycin and oral ciprofloxacin as per unit protocol at the time. Cultures grew coagulase-negative staphylococci and another organism that was initially identified as yeast. The patient continued to be clinically well with clear PD fluid. Oral fluconazole and flucytosine were administered, and the PD catheter was removed; the patient was switched to haemodialysis. The cultures were finally identified as *Prototheca spec*, a rare achlorophyllous infectious algae.

Discussion

PD peritonitis is defined as the presence of at least two out of the following three criteria: (1) fever, abdominal pain or tenderness, (2) presence of $>100/\mu$ l white blood cells per millilitre of dialysate fluid and (3) identification of organisms in the dialysate. Most cases of PD peritonitis are straightforward and either gram positive due to handling error or gram negative due to intra-abdominal pathology. Some cases remain culture negative and a variety of non-infectious causes need to be considered as well [1].

PD peritonitis can also be due to uncommon organisms (Table 1) [2]. Among the gram-positive cocci, *Streptococcus* is an uncommon pathogen in PD peritonitis and associated with severe disease [2]. *Streptococcus pneumoniae* is sometimes seen with the presence of an intrauterine device (IUD) [2]. Gram-positive rods are rarely isolated from PD fluid, usually after the patient had some form of contact with soil [2]. *Neisseria gonorrhoeae* is a gram-negative coccus that is associated with gonorrhoea and passage of the organism through the fallopian tube into the PD fluid. Contact with animals seems to be a particular risk factor for acquisition of gram-negative rods from the genus *Pasteurella*. *P. multocida* has been reported in conjunction with dog and cat exposure [3]. PD peritonitis due to

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Table 1. Rare micro-organisms as a cause of PD peritonitis [2]

Category	Organism	Associated factors/remarks	References
Gram-positive cocci	Group A, B, C streptococci	Severe disease	[2]
	<i>Streptococcus pneumoniae</i>	Presence of an IUD	[2]
Gram-positive rods	<i>Bacillus cereus</i>	Spores ubiquitously present	[2]
	<i>Listeria monocytogenes</i>	Dairy products, raw milk cheese	[2]
	<i>Nocardia asteroides</i>	Soil origin	[2]
	<i>Actinomadura madurae</i>	Soil origin	[2]
	<i>Nocardia asteroides</i>	Soil	[2]
	<i>Lactobacillus spp.</i>	Enteric translocation, previous vancomycin treatment	[2]
	<i>Oerskovia spp.</i>	Soil	[2]
Gram-negative cocci	<i>Neisseria gonorrhoeae</i>	Genital gonorrhoe and passage of the organism through the fallopian tube	[2]
	<i>Branhamella catarrhalis</i>	Colonizes the upper respiratory tract	[2]
Gram-negative rods, fastidious	<i>Pasteurella multocida</i>	Contamination from cat or dog	[3]
	<i>Pasteurella pneumotropica</i>	Pet hamster origin	[4]
	<i>Campylobacter spp.</i>	Diarrhoea	[2]
Gram-negative rods, nonfermenters	<i>Alcaligenes spp.</i>	Contaminated water	[2]
	<i>Bordetella bronchiseptica</i>	Dog origin	[2]
	<i>Pseudomonas spp.</i> (<i>P. putida</i> , <i>P. fluorescens</i> , <i>P. mesophilica</i> , <i>P. paucimobilis</i> , <i>P. stutzeri</i>)	Contaminated water (e.g. bath used to pre-heat dialysis bags); severe infection, concomitant HIV infection as a risk factor	[2]
Anaerobes	<i>Acinetobacter spp.</i>	Colonized skin or contaminated water	[2]
Fungal	<i>Clostridium perfringens</i>	Enteric translocation	[5]
	<i>Aspergillus spp.</i>	Prolonged treatment for bacterial peritonitis as a risk factor; hospitalization and HIV infection are further risk factors. Severe disease with abscesses, adhesions and sclerosing peritonitis. Catheter removal often required. Mortality even despite treatment	[7]
	<i>Fusarium spp.</i>		[7]
	<i>Hormonema dematioides</i>		[7]
	<i>Mucor spp.</i>		[7]
	<i>Paecilomyces spp.</i>		[7]
	<i>Rhodorula spp.</i>		[7]
	<i>Torulopsis glabrata</i>		[7]
	<i>Trichosporon spp.</i>		[7]
	<i>Trichoderma spp.</i>		[7]
Mycobacteria	<i>M. tuberculosis</i> , atypical spp.	Slow growth in culture	[6]
Algae	<i>Prototheca wickerhamii</i>	Water, infected animals	[12,13,15]
Viral	<i>Herpes virus</i>		[2]
	<i>Cytomegalovirus</i>		[16]

P. pneumotropica has been reported after contamination of the PD tubing by a pet hamster [4]. PD peritonitis due to *Pseudomonas* often requires removal of the PD catheter. Other *Pseudomonas* species, such as *P. putida*, are uncommon [2]. Rare gram-negatives include *Alcaligenes* and *Flavimonas*, which are associated with exposure to contaminated water. Gram-negative rods (Vibrionaceae) have been reported in PD peritonitis in conjunction with houseplant spray and scuba diving [2]. Mixed gram-negatives in culture usually signal a serious intra-abdominal problem, and urgent imaging is warranted with a low threshold for further investigations, surgical exploration and removal of the PD catheter. Finally, PD peritonitis due to anaerobes is extremely rare [5].

Mycobacteria have also been reported to cause PD peritonitis. The diagnosis can be delayed due to the slow growth rate of some mycobacterial species, and these organisms can be overlooked unless adequate culture media are used [6]. Fungal peritonitis is overwhelmingly due to *Candida* species. Unusual species of fungi in PD peritonitis are listed in Table 1. The management of fungal peritonitis is beyond

the scope of our little teaching point and reviewed elsewhere [7]. Suffice to say that a variety of anti-fungal agents are used but that removal of the PD catheter is often required. Finally, viral PD peritonitis is very rare and cytomegalovirus has been described in anecdotal reports.

Algae or algae-like organisms are rarely isolated in PD peritonitis. The genus *Prototheca* denotes achlorophyllic algae [8] that reproduce asexually. Five species have been recognized, *P. stagnora*, *P. ulmea*, *P. blaschkeae*, *P. zopfii* and *P. wickerhamii*. The last three have been implicated in human infections. *Prototheca* species are found in soil, marine water and sewage. Protothecosis in animals is well documented [8] and affects cows, cats, dogs, deer, salmon, carp and flying foxes [8]. Mastitis is common in cows whereas clinical syndromes in dogs include skin disease, colitis and eye involvement. Bovine mastitis usually leads to udder atresia, and canine systemic protothecosis is often fatal.

Clinical syndromes in humans include cutaneous disease, wound infection and, rarely, systemic disease. Bursitis has also been described, as has been intestinal disease.



Fig. 1. *Prototheca* in culture. The figure shows *Prototheca zopfii* (isolated from another patient) on Sabouraud-dextrose agar after 72 h at 37°C.

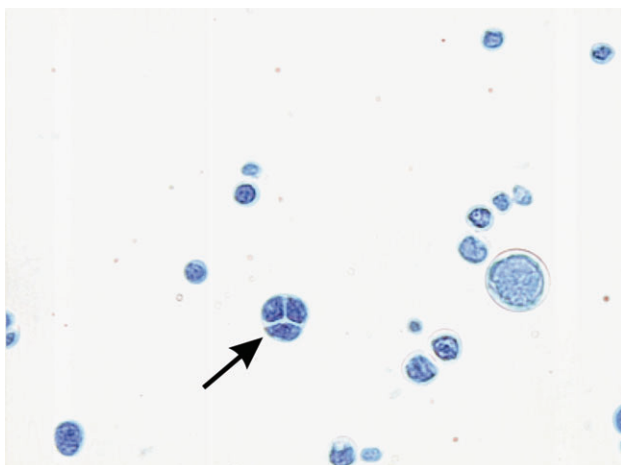


Fig. 2. *Prototheca zopfii* (isolated from another patient) stained with Lactophenole-cotton-blue. The arrow denotes a sporangiospore, a characteristic feature of asexual reproduction in these organisms, within a mature cell (sporangium).

Systemic protothecosis is exceedingly rare [9]. Mohabeer and colleagues described a 75-year-old patient with myasthenia gravis who developed algaemia due to *Prototheca wickerhamii* from a skin lesion on his hand [10]. The clinical spectrum of human protothecosis is reviewed in great detail elsewhere [11].

The diagnosis of protothecosis rests on cultures of these rare organisms on a mycological culture medium. Macroscopically, the cultures can be mistaken for *Candida* although their microscopic features have been described as unique and characteristic [9] (Figures 1 and 2). The cell membrane of these organisms is glucosamine deficient;

they stain with periodic acid-Schiff (PAS) and Gomori-methenamine silver (GMS). The diagnostic features of *Prototheca* species in culture are discussed elsewhere [8]. Therapeutic recommendations are difficult, given that the number of human cases is so small. *Prototheca* species are believed to be sensitive to amphotericin B and the azoles whereas flucytosin is believed to be ineffective [8]. Gentiana violet, polymixin B and a variety of other preparations have been advocated for topical treatment. Others have emphasized that removal of infected tissue is very effective in localized disease [9].

To our knowledge, we describe the fifth patient with PD peritonitis due to *Prototheca* in the literature. O'Connor and colleagues in 1986 reported a 41-year-old woman on CAPD who required removal of her PD catheter after peritonitis with *Prototheca wickerhamii* that was unresponsive to amphotericin B. [12]. In this case, another attempt to place a Tenckhoff catheter 3 months after the episode proved unsuccessful due to dense intra-peritoneal adhesions. Gibb and co-workers saw another PD patient with *Prototheca wickerhamii* peritonitis and removed the PD catheter [13]. Sands *et al.* described the case of a 72-year-old PD patient with peritonitis due to *Prototheca wickerhamii* who needed PD catheter removal and was subsequently treated with intravenous amphotericin and oral doxycycline [14]. This patient died of post-operative complications, and dense adhesions were found at autopsy. Finally, Pérez Melón reported on a 36-year-old PD patient with *Prototheca* peritonitis who also needed removal of the catheter [15]. Most cases of human protothecosis are believed to originate from contact with dirty water [9]. When asked, our patient could only attribute the infection to the fact that water pipes and sanitation in her home were in need of modernization. She had no pets, and she could not recall any other exposure to water or sewage.

It is difficult to draw any conclusions from these reports as to the treatment of *Prototheca* peritonitis in PD patients. A variety of anti-microbial agents, such as amphotericin [14], the azoles and doxycyclin [14], have been described to be effective in human and animal protothecosis while contact with a reference laboratory and resistance testing are mandatory. However, in algal PD peritonitis, removal of the catheter was required in the majority of patients. In this regard, algal peritonitis appears to have a clinical course not unlike fungal PD peritonitis. Previous reports also report a high incidence of intra-peritoneal adhesions after algal peritonitis, thus precluding further attempts at PD.

Infectious problems are common in PD. The case presented here took an unexpected turn when the microbiologist observed a smooth, creamy-white organism that eventually proved to be *Prototheca wickerhamii*. Algae sometimes make the headlines after an algal bloom in coastal waters, and the term 'red tide' has been used. In truth, this phenomenon is not associated with tidal movement. Some red tides are associated with the production of toxins and wildlife mortality. To us, this case provided a first encounter with 'white tide' and algae in the peritoneal cavity as well as an opportunity to review the differential diagnosis of PD peritonitis due to uncommon organisms.

Teaching points

- (i) PD peritonitis is usually gram positive due to handling error or gram negative due to intra-abdominal disease. However, a broad variety of rare organisms are sometimes isolated as well.
- (ii) These rare organisms may be uncommon bacteria, mycobacteria, fungi, algae or viruses.
- (iii) Many of these organisms are acquired through contact with animals, soil or water. This underpins the importance of teaching good hand hygiene during PD training.
- (iv) Algae are a rare cause of PD peritonitis. The clinical characteristics of algal PD peritonitis seem to resemble those of fungal disease.
- (v) A variety of antimicrobial agents may be effective, but removal of the PD catheter is often required.

Conflict of interest statement. None declared.

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