Asymptomatic Peritoneal Leukocytosis After Exteriorization of Buried Peritoneal Dialysis Catheters: A Case Series

Peritonitis is a major complication of peritoneal dialysis (PD), the leading cause of technique failure, and an important contributor to mortality. A diagnosis of PD peritonitis requires that 2 of the 3 following criteria are present, abdominal pain, elevated peritoneal leukocyte count, and positive effluent culture. Sterile peritonitis, where the effluent culture is negative, accounts for approximately 20% of the first episode of peritonitis in PD patients (1). It often reflects bacterial infection in which the culture may be negative, because of either recent use of antibiotics or suboptimal microbiology methodology. A number of non-infectious causes have also been identified as possible etiologies of sterile peritonitis (2). For example, allergic reaction to the tubing or to certain intraperitoneal antibiotics may present as sterile eosinophilic peritonitis, while use of icodextrin may, rarely, precipitate a monocytic-predominant sterile peritonitis (2).

The use of the Moncrief-Popovich technique, which involves burying the free end of the PD catheter under the skin and leaving it embedded for 4 – 6 weeks before exteriorization, has been extensively used at our institutions. Our published reports of over 400 buried PD catheters have shown that this technique is associated with low rates of surgical, mechanical, and infectious complications (3). Over the years, we have noted from time to time asymptomatic peritoneal leukocytosis with negative effluent cultures immediately after exteriorization of a buried catheter. Herein we report all cases of this entity encountered in 2 centers since 2007.

METHODS

At our centers, we diagnose and treat peritonitis according to the International Society for Peritoneal dialysis (ISPD) guidelines (4). Patients with chronic kidney disease who are followed by the Progressive Renal Insufficiency (PRI) clinic and anticipated to require dialysis within 6 – 12 months and opt for PD are chosen for insertion of buried double cuff, swan neck, coiled peritoneal catheter dialysis catheters. At the Ottawa

Hospital, when the patient is ready to start PD, the catheter is exteriorized by the home dialysis nephrologist at the bedside through a small incision using local anesthetic and under sterile technique. The transfer set is then attached and the patient begins PD training the same day (3). At the Toronto General, the catheter is usually exteriorized a few days to a week prior to training. If cloudy effluent persists after 2 or more flushes then an effluent cell count and culture are sent.

Peritonitis is tracked prospectively using the multicenter Baxter Peritonitis Organism Exit sites Tunnel infections (POET) system (Baxter Healthcare, Deerfield, IL, USA). At the Ottawa Hospital, NEPHROCARE (Fresenius Medical Care, Bad Homburg, Germany) and OASIS (Telus Health, Longueuil, QC, Canada) are also used as electronic medical records. The system records of all patients who came to the home dialysis unit for exteriorization of an embedded PD catheter between January 2007 and December 2012 were reviewed for peritoneal cell counts sent in the first week post-initiation of PD. In addition, the home dialysis unit at the Toronto General Hospital started placing buried catheters in 2010 and records were similarly reviewed.

RESULTS

At the Ottawa Hospital, a total of 290 patients had exteriorization of a buried catheter between January 2007 and December 2012, and at the Toronto General Hospital 31 buried catheters have been placed, and 16 exteriorized since 2010. The total number of patients included is 306. Of these patients, 5 (1.6%) were noted to have had elevated peritoneal effluent white blood cell (WBC) counts immediately after starting PD training, within hours of exteriorization. In none of these 5 cases were the peritoneal effluent cultures positive and none of the patients had abdominal pain, fever, or physical findings of peritoneal irritation. At the Toronto General Hospital, 1 patient developed sterile peritoneal leukocytosis 1 month after exteriorization and during the first week of outpatient continuous ambulatory PD (CAPD). This patient had very mild abdominal symptoms, out of keeping with a peritoneal fluid cell count that eventually exceeded $30,000 \times 10^6/L$ with persistently negative effluent cultures.

The characteristics of the patients with sterile peritonitis are shown in Table 1. There was significant variability in the time embedded prior to exteriorization, from 38 days to approximately 5 years. There was also a broad range of effluent WBC counts from 435 to $7,200 \times 10^6/L$, and there was no clear pattern of neutrophil or monocytic cell predominance with most having 35 – 65% neutrophils. All but 1 patient had detectable red blood cells (RBCs) in the effluent, and in 2 cases the counts were $>1,000 \times 10^6/L$.

With respect to treatment, 4 of the 6 patients (1, 4, 5, and 6) had empiric treatment for infectious peritonitis, but in only 2 cases (patients 5 and 6) was a full course of treatment given. In the other cases, treatment was discontinued after a negative culture was returned. Patient 5 received a 2-week course of intraperitoneal cefazolin as a cautionary measure,

TABLE 1
Summary of All Patients with Post-Exteriorization Culture-Negative Asymptomatic Peritoneal Leukocytosis

	Age	Sex	Cause of ESRD	Time elapsed*	Effluent RBC $\times 10^6/L$	Effluent WBC $\times 10^6/L$	N %	L %	M %	E %	Time to clear	Time to first symptomatic peritonitis/organism/outcome
Case 1	55	F	Diabetes	60 days	2,450	1,417	58	10	32	0	2 days	1 year. <i>Acinetobacter</i> peritonitis leading to technique failure
Case 2	66	M	Diabetes	≈ 1 year	4,500	7,200	4	84	10	2	24 hours	2 years. Relapsing CNSA peritonitis that was successfully treated.
Case 3	50	M	Diabetes	38 days	131	538	60	5	23	12	4 days	None. Patient opted to switch to hemodialysis for social reasons after training.
Case 4	53	M	IN	≈ 5 years	23	537	63	3	22	12	2 days	4 years. Culture-negative peritonitis which was successfully treated.
Case 5	28	F	IgA	92 days	33	435	37	4	59	0	2 days	None. Patient switched to hemodialysis after 2 months because of catheter malfunction
Case 6	76	F	Diabetes	67 days	N/R	2,950	89	0	11	0	9 days	None. Patient continues on PD.

ESRD = end-stage renal disease; RBC = red blood cells; WBC = white blood cells; N = neutrophils; L = lymphocytes; M = monocytes; E = eosinophils; F = female; M = male; CNSA = coagulase-negative *Staphylococcus aureus*; IN = interstitial nephritis; IgA = immunoglobulin A; N/R = not recorded; PD = peritoneal dialysis.

* Between PD catheter insertion and exteriorization.

as he had required a guidewire manipulation of his catheter prior to it becoming functional. Patient 6 was left empty of PD for 3 days with the antibiotics given intravenously during that time, then completed a 2-week course of intraperitoneal antibiotics. None of the patients had a relapse or early recurrence of cloudy effluent and the time to first infectious peritonitis varied between 1 and 4 years.

DISCUSSION

The phenomenon of asymptomatic peritoneal leukocytosis post-exteriorization of buried PD catheters has not previously been reported. While it is not uncommon to note cloudy effluent during break-in of a standard PD catheter, the effluent in these cases is usually acellular and the effluent opacity is related to fibrin. In none of our cases were classic criteria for PD peritonitis met as all patients were essentially asymptomatic and the cultures were negative. None of our patients had icodextrin exposure or recent surgery or air installation and thus these episodes are otherwise completely unexplained.

Animal models of PD suggest the possibility of a foreign body reaction to a PD catheter which is maximal at 4 weeks and subsequently subsides (5). It has also been shown in animal models that the presence of a silicone catheter increases the inflammatory response of the peritoneal membrane to sterile solutions and these changes are more prominent than those seen in animals receiving daily intraperitoneal

injections of dialysis solutions without a catheter (6,7). We postulate that, in humans, there may be some inter-individual variability in susceptibility to a foreign body response to a dormant PD catheter and that this accounts for the fact that only 2% of those with a buried catheter will develop peritoneal leukocytosis.

We feel it is quite unlikely that the leukocytosis was due to culture-negative infectious peritonitis given the absence of pain and the fact that buried PD catheters heal in a sterile environment and do not develop biofilm prior to exteriorization (8). In addition, only 2 of the 6 patients received a proper course of antimicrobial therapy, and none of the patients had a relapse or early repeat peritonitis which would be expected for an undertreated infectious peritonitis. The absent or low eosinophil counts suggest that these episodes are not a variant of an eosinophilic peritonitis.

We do note some variability in the cases presented. While 4 of the 6 had a predominance of neutrophils, 2 had a predominance of monocytic cells, arguing that the pathophysiology of the peritoneal inflammation may not be the same in all individuals. In addition, the number of RBCs in the effluent was significantly elevated in 2 cases. It has, however, been noted previously that PD patients with symptomatic sterile peritonitis tend to have a higher RBC:WBC ratio than culture-positive patients (9). In addition, 5 of 6 patients presented with cloudy effluent in the first day of PD training, while 1 patient did not have cloudy effluent noted during training but only after commencing independent outpatient PD.

In conclusion, we report 6 patients with asymptomatic peritoneal leukocytosis and sterile effluent post-exteriorization of buried PD catheters. The pathophysiology of this phenomenon is not clear. We recommend that persistent cloudy effluent post-exteriorization of a buried PD catheter be empirically treated for PD peritonitis, but if patients are asymptomatic and cultures return negative, then our data suggest that antibiotics may safely be stopped.

DISCLOSURES

The authors have no conflicts of interest to declare. There was no external financial support for this study.

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REFERENCES

1. Port FK, Held PJ, Nolph KD, Turenne MN, Wolfe RA. Risk of peritonitis and technique failure by CAPD connection technique: a national study. *Kidney Int* 1992; 42:967–74.
2. de Freitas DG, Gokal R. Sterile peritonitis in the peritoneal dialysis patient. *Perit Dial Int* 2005; 25:146–51.
3. McCormick BB, Brown PA, Knoll G, Yelle JD, Page D, Biyani M, *et al.* Use of the embedded peritoneal dialysis catheter: experience and results from a North American center. *Kidney Int Suppl* 2006; 103:S38–43.
4. Li PK, Szeto CC, Piraino B, Bernardini J, Figueiredo AE, Gupta A, *et al.* Peritoneal dialysis-related infections recommendations: 2010 update. *Perit Dial Int* 2010; 30:393–423.
5. Flessner MF, Li X, Potter R, He Z. Foreign-body response to sterile catheters is variable over 20 weeks. *Adv Perit Dial* 2010; 26:101–4.
6. Flessner MF, Credit K, Henderson K, Vanpelt HM, Potter R, He Z, *et al.* Peritoneal changes after exposure to sterile solutions by catheter. *J Am Soc Nephrol* 2007; 18:2294–302.
7. Flessner MF, Credit K, Richardson K, Potter R, Li X, He Z, *et al.* Peritoneal inflammation after twenty-week exposure to dialysis solution: effect of solution versus catheter-foreign body reaction. *Perit Dial Int* 2010; 30:284–93.
8. Moncrief JW, Popovich RP, Dasgupta M, Costerton JW, Simmons E, Moncrief B. Reduction in peritonitis incidence in continuous ambulatory peritoneal dialysis with a new catheter and implantation technique. *Perit Dial Int* 1993; 13(Suppl 2):S329–31.
9. Penders J, Fiers T, Dhondt AM, Claeys G, Delanghe JR. Automated flow cytometry analysis of peritoneal dialysis fluid. *Nephrol Dial Transplant* 2004; 19:463–8.

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