An Unusual Neurological Complication in a CAPD Patient

Editor:

Neurological complications in dialysis patients include multi-infarct dementia, chronic subdural hematoma, hydrocephalus, and intracranial hemorrhage (1). Here we report an unusual neurological complication, subdural hygroma, of rapid onset in a patient on continuous ambulatory peritoneal dialysis (CAPD).

A 68-year-old female vegetarian patient with diabetic end-stage renal disease and hypertension, who was on CAPD for the previous 30 months using 2 L Dianeal [Baxter (India) PVT; IMT Manesar, Gurgaon, Haryana, India] 3 or 4 exchanges/day, was admitted to hospital for treatment of protocolitis. On the third day, she developed a stroke while asleep; her Glasgow coma scale was 9/15, with difficulty in speech. Computed tomography (CT) scan of the brain showed a right corona radiata and caudate nucleus infarct, with no midline shift. Her neurological status, including speech, improved with treatment. She was able to ambulate after a week and was discharged home on subcutaneous insulin along with aspirin and clopidogrel.

The patient was readmitted a month later with generalized edema and fluid overload; she weighed 68 kg. Blood pressure was 130/90 mmHg. She had normal neurological status. Her parameters revealed hemoglobin 7.8 g/dL, white blood cell count 10 100/mm^3, platelets 451 ×10^3/µL, red blood cell count 2.6 × 10^6/mm^3, random blood sugar 309 mg/dL, BUN 24 mg/dL, serum creatinine 6.9 mg/dL, Na⁺ 128 mmol/L, K⁺ 3.6 mmol/L, HCO₃ 29 mmol/L, total protein 5.2 g/dL, and albumin 1.7 g/dL.

Dialysis was done four times per day with hypertonic exchanges, and an infusion of human albumin 20% 100 mL was given for the hypoalbuminemia. Strict salt and water restriction was enforced. The edema began to subside rapidly and her weight came down to 59.2 kg at the end of the third day. She became drowsy and gradually lost her consciousness again by the fourth day. Her blood sugar was 156 mg/dL and Na⁺ was 143 mmol/L.

A repeat CT scan of the brain showed a large bifrontal parietal subdural hygroma in addition to the previous CT scan findings (-5HU) (Figure 1). The hypertonic dialysis exchanges were stopped and the patient was given isotonic exchanges along with oral hydration. She improved and was discharged home ambulant. She was reviewed after 3 weeks and continues on aspirin and clopidogrel, and is doing well.

Subdural hygroma is a collection of cerebrospinal fluid in the subdural space, occurring following trauma or rapid decompression of the ventricular system after shunting. Excessive dehydration may also result in passive development of subdural hygroma (2). Small subdural hygromas get reabsorbed on their own. Rehydration and expansion of the brain can result in resolution of subdural hygromas. Since the majority of patients with a subdural hygroma do not show a mass effect, surgery is rarely required (3).

In our patient, the temporal onset of symptoms, signs, and CT findings suggest dehydration as a possible cause for the development of subdural hygroma. The improvement of the patient with hydration over a period of 1 week supports this hypothesis.

This case report highlights the fact that patients with pre-existing neurological damage may develop symptomatic subdural hygroma following rapid removal of extracellular fluid.

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Figure 1 — Arrow showing subdural hygroma
A 52-year-old male with end-stage renal disease (ESRD) secondary to focal segmental glomerulosclerosis presented initially with wetness at the exit site and without pathology at the exit site, tunnel, or catheter. Five days later, he presented with cloudy peritoneal fluid without abdominal pain. Gram stain of the peritoneal fluid did not reveal any organism. White blood cell count was 177/mm³, with 85% polymorphonuclear cells and 15% mononuclear cells. Peritoneal fluid culture was negative for organisms. He was initially treated with both daily intraperitoneal (IP) cefazolin 1 g and ceftazidime 1 g, then with only cefazolin once the organism was identified and sensitivity confirmed (1). Several days after completing a 14-day antibiotic regimen and achieving clear peritoneal fluid, his Tenckhoff catheter was removed eight days after his initial presentation with cloudy peritoneal fluid. Peritoneal fluid culture grew Staphylococcus auricularis. He was then again treated with daily IP cefazolin 1 g and ceftazidime 1 g for another 14 days. Thirty-eight days after his initial presentation with cloudy peritoneal fluid, his Tenckhoff catheter was removed due to persistent peritonitis. He was transitioned to intermittent hemodialysis, where he continued to receive antibiotic therapy for an additional week to assure complete eradication of S. auricularis. One month later, a new Tenckhoff catheter was placed; peritoneal dialysis (PD) was reinstituted 3.5 weeks later without additional complication.

This is the first reported case of S. auricularis peritonitis in a patient with ESRD receiving PD. Staphylococcus auricularis is coagulase negative and novobiocin susceptible. Most infections due to coagulase-negative staphylococci are nosocomial. Approximately 80% to 90% of the coagulase-negative strains isolated from human specimens produce an inducible β-lactamase. Moreover, 60% to 80% of nosocomial coagulase-negative staphylococci are methicillin resistant.

This patient with S. auricularis peritonitis presented with cloudy PD effluent and no other symptom. Risk factors for the development of PD-associated peritonitis include diabetes mellitus, age less than 20 years or greater than 60 years, and the black race, particularly when the patient lived with their families; gender was not a factor (2). However, in studies from single centers, the reported frequency of peritonitis did not differ between diabetic and nondiabetic patients on continuous ambulatory PD (3). Our patient did not have any of the traditional risk factors. A break in the catheter integrity has always been associated with gram-positive organisms, which was true in this case.

Our patient had several risk factors for developing peritonitis. Patients with ESRD are immunocompromised hosts. The presence of an indwelling foreign body, namely the PD catheter, provides a conduit for organisms to enter the peritoneum (4). Organisms migrate along the lumen (intraluminal) during a touch contamination at the time of an exchange, or along the outer surface of the catheter (periluminal) during progression of a catheter-tunnel infection. Leakage of peritoneal fluid in our patient suggested a communication along the periluminal space between the sterile internal peritoneal environment and the external unsterile environment, which is known to harbor organisms classified as “normal skin flora” as well as pathogens. Staphylococcus auricularis is part of the normal skin flora of the ears. It is not clear how this organism entered the peritoneum and resulted in peritonitis. Both touch contamination and periluminal migration were possible in this case. In both situations, S. aureus or S. epidermidis rather than S. auricularis would have been the leading cause for peritonitis.

In summary, this case report illustrates an atypical skin flora, S. auricularis, causing peritonitis. Coagulase-negative staphylococci are found naturally on the skin and mucous membranes of humans, and thus are often found in clinical specimens. Persistent peritonitis despite appropriate antibiotic therapy resulted in removal of the peritoneal catheter.

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The patient was a 22-year-old female with chronic interstitial nephritis diagnosed by renal biopsy in September 1999. Beginning February 2000, the patient was put on CAPD, with an uneventful course except for an episode of peritonitis in March 2000. On 15 February 2003, she suffered from exit-site infection. Culture of the discharge grew Staphylococcus aureus; she was treated with oral cefazolin. On 24 February (day 1), she presented with fever, turbid dialysate fluid, and abdominal pain. Dialysate leukocyte count was 7200/mm³, with 93% polymorphonuclear cells; her serum C-reactive protein level was 1.0 mg/dL (normal <0.5 mg/dL). Gram stain was negative. Fever and abdominal pain subsided after empiric antibiotic therapy with cefazolin 250 mg in each peritoneal dialysis bag. She was discharged on day 3 with continuous administration of intraperitoneal antibiotics at home. The initial response to antibiotics was excellent and dialysate leukocyte count was 57/mm³ on day 4. Unfortunately, fever and abdominal pain developed again on day 6, when her dialysate leukocyte count was 23,400/mm³, with 99% polymorphonuclear cells. Blood culture taken on day 1 grew K. oxytoca on day 6, and dialysate culture taken on day 1 grew K. oxytoca and Citrobacter freundii on day 6; both were sensitive to cefazolin. Abdominal computed tomography scan did not reveal significant intra-abdominal lesion. Unfortunately, symptoms persisted despite 4 days of antibiotic treatment; hence, the CAPD catheter was removed on day 10 and she was transferred to hemodialysis.

On the same day, dialysate culture grew Pseudomonas aeruginosa and antibiotics were shifted to ciprofloxacin according to the sensitivity test. After a complete course of antibiotic therapy for 21 days, the patient was discharged in stable condition.

As far as we know, only a few cases of spontaneous peritonitis due to K. oxytoca have been reported in patients with cardiac ascites (1) and hepatic cirrhosis (2). Due to the extensive use of antibiotics, mutant strains of K. oxytoca resistant to ceftazidime or aztreonam, derived from hyperproduction of chromosomal β-lactamases (K1 type) or acquisition of extended-spectrum β-lactamases (ESBLs), have developed. Carbapenems or ciprofloxacin should be regarded as the treatment of choice for infections due to either K1 hyperproducers or ESBL producers (3). In Asia, the biliary tract is the most common site of K. oxytoca infection. In Western countries, the urinary and respiratory tracts are the most common sites of infection. The incidence of polymicrobial bacteremia is high in patients with K. oxytoca bacteremia. Kim et al. (3) reported that polymicrobial bacteremia was diagnosed in up to 40% of these patients. Holley et al. (4) found that three times as many patients with polymicrobial peritonitis transferred to hemodialysis compared with patients with single-organism peritonitis (18% vs 7%). Kim and Korbet (5) found that 24% of patients transferred to hemodialysis because of polymicrobial peritonitis, and 70% of patients with polymicrobial peritonitis will be transferred to hemodialysis.

Prompt and adequate surgical intervention as well as appropriate antibiotic therapy might contribute to lower mortality in patients with K. oxytoca bacteremia. Therefore, surgical intervention, if indicated, should always be considered to reduce the mortality rate and to improve the prognosis.
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The Icodextrin Black Line Sign to Confirm a Pleural Leak in a Patient on Peritoneal Dialysis

Editor:

We report the application of the black line sign previously described with icodextrin (1) in the context of a pleural leak secondary to peritoneal dialysis (PD).

A 50-year-old lady with end-stage renal failure secondary to mesangiocapillary glomerulonephritis has been treated with PD for the past 10 years. She had two renal transplants, in 1981 and 1985. She also has a history of juvenile rheumatoid arthritis and myocardial infarction. Her automated PD prescription consisted of seven 1.5-L exchanges of 1.36% Dianeal at night, one of 1.5 L Extraneal, and one of 1.5 L 2.27% Dianeal during the day (all by Baxter Healthcare, Norfolk, UK).

She presented to us with a history of fever, dyspnea, rigors, and upper epigastric pain. On examination, she had a low-grade temperature of 37.5°C and dullness to percussion on the right base of the lung. Chest x ray showed a raised right hemidiaphragm with possible pleural effusion. Her automated PD prescription consisted of seven 1.5-L exchanges of 1.36% Dianeal at night, one of 1.5 L Extraneal, and one of 1.5 L 2.27% Dianeal during the day (all by Baxter Healthcare, Norfolk, UK).

She presented to us with a history of fever, dyspnea, rigors, and upper epigastric pain. On examination, she had a low-grade temperature of 37.5°C and dullness to percussion on the right base of the lung. Chest x ray showed a raised right hemidiaphragm with possible pleural effusion. Blood tests revealed a neutrophil leukocytosis and an elevated C-reactive protein 63 mg/L. Thoracocentesis was performed and showed the following results: protein 5 g/L, glucose 4.2 mmol/L, LDH 6 U/L. Since this patient had an icodextrin exchange in situ, we requested our laboratory to add povidone iodine to the pleural aspirate. This gave the characteristic blue-black color (Figure 1). The patient responded well to antibiotic treatment for her chest infection and her pleural leak resolved with smaller volumes on automated PD and dry days.

The characteristic icodextrin black line sign has been described before (1). It occurs secondary to a reaction between iodine and starches. Icodextrin is a glucose polymer and bears major similarities to starch. Usually pleural leaks are diagnosed on the basis of pleural fluid characteristics that include low protein and LDH and high glucose. In patients on icodextrin, an additional simple test could be employed as described above.

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Early Morning Blues — a Complication of Icodextrin

Editor:

Icodextrin and newer non-glucose-based solutions are considered more physiological solutions compared to traditional glucose-based dialysate (1,2). Preliminary
animal studies suggest long-term use may help preserve membrane function and now their use is advocated in patients with ultrafiltration failure. In this paper, we report an unusual complication associated with icodextrin.

The patient, a 77-year-old man, reported a 3-day history of black early morning dialysate. He was extremely concerned that there was some internal pathology, despite feeling well with no pain, fever, or abdominal tenderness.

He had commenced peritoneal dialysis (PD) in April 1998 secondary to diabetic nephropathy. Since commencing dialysis, he has had few complications other than 1 episode of Escherichia coli peritonitis in the summer of 1999. His medical history was pertinent only for vascular disease (affecting the cardiac, carotid, and peripheral vascular trees), neuropathy, and retinopathy. He has been a life-long smoker, having smoked for 65 years.

Until December 2002, he had been maintained on continuous ambulatory PD using traditional glucose solutions; however, because of ultrafiltration problems, an icodextrin exchange was introduced for the long overnight dwell. The patient experienced no problems with his dialysis, in particular with his overnight dwell, until April 2003, when he noted a black discharge into his dialysis tubing shortly after rising. He denied any pain, fever, or other symptoms. A full clinical examination was unremarkable. Routine laboratory tests done at the time of presentation were unremarkable. The dialysate was negative for blood and white blood cells.

We hypothesized that a trace of iodine from the tubing connector was leaking around the catheter and coming in contact with the icodextrin, causing this blue–black discoloration. The patient was reassured that this was not of concern. To prevent further concern, he underwent a tube change and the problem resolved. A simple laboratory simulation was performed to see if we could reproduce the black discoloration (Figure 1).

Even though peritoneal ultrafiltration capacity and small solute transport characteristics remain stable in many patients treated with PD, the quality of the peritoneal membrane may deteriorate progressively as a result of chronic hypertonic glucose exposure with PD duration. Membrane failure is associated with impaired ultrafiltration, a clinical symptom increasingly treated with dialysis using an icodextrin-containing dialysate (3,4).

Icodextrin is an alternative osmotic agent based on a polymer of glucose. It acts as a high molecular weight osmotic agent, with an average molecular weight of 16 800 Da (5,6). Icodextrin is not metabolized in the peritoneal cavity and its absorption is mainly by uptake into the lymphatic system. Thus, it is a valuable osmotic agent in the treatment of PD patients with defective ultrafiltration (3,4,6).

Unlike other commonly reported side effects[e.g., allergic skin lesions and noninfective peritonitis (7,8)], the complication reported here, called the “black line effect,” is harmless (9). The black line or blue/black color seen in the dialysis tubing results from interaction of starch with iodine (10). Starch molecules contain both amylase and amylopectin. Both of these components complex with iodine. The complex of amylase with iodine results in a pure blue color, while the complex with amylopectin results in a blue–violet color. Amylopectin takes up less iodine than does amylase. As a result of a variable amylase-to-amylopectin ratio, patients can present with various shades of blue color in the tubing. The state of starch also determines the uptake of iodine: native and raw starch adsorbs less iodine, whereas cooked and shaken starch adsorbs progressively larger amounts (10). As an in vitro diagnostic test, adding iodine to icodextrin causes a similar black color (see Figure 1).

The icodextrin black line effect is rarely seen; however, when it presents it causes undue alarm. We suggest that patients be informed during their training that, with icodextrin solution, they may see a black reaction in the tubing and that this is a normal consequence of iodine complexing with icodextrin solution.

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No Beneficial Effect of Icodextrin on Blood Glucose Control

Editor:

The development of icodextrin for peritoneal dialysis (PD) has been described as one of the major improvements in the field of PD, as its use has greatly changed prescription options, results, and technique survival (1). The efficacy and safety of icodextrin have been well established, in both continuous ambulatory PD (CAPD) and automated PD, by large, randomized, controlled, multicenter clinical trials (2–4). These studies demonstrated that the mean carbohydrate absorption with icodextrin PD solution (29 ± 5 g) was lower compared to 3.86% glucose (62 ± 5 g) at 8 hours (2,5). Intraperitoneal metabolism of icodextrin is negligible and little if any glucose is released into the peritoneal cavity. After absorption into the systemic circulation, icodextrin polymer is metabolized by plasma amylase to smaller oligosaccharides such as maltose, maltotriose, and maltotetraose. Due to the absence of circulating maltase, further metabolism of these oligosaccharides to glucose occurs intracellularly (5). Therefore, the glucose load arising from the use of icodextrin is “functionally invisible” to both the peritoneal cavity and systemic circulation and thus, icodextrin functions as a “non-glucose” osmotic agent (6). These factors were expected to have a beneficial effect on the glycemic status of diabetic PD patients. The use of non-glucose-based PD solutions, such as icodextrin and amino acids, was associated with improved diabetic control in a study that used a continuous glucose monitoring system (CGMS) to assess overall 24-hour glycemic control in 8 insulin-treated diabetic CAPD patients (7). In that study, mean 24-hour interstitial fluid glucose, measured by CGMS, and mean HbA1c were 7.82 ± 0.06 mmol/L and 7.5% ± 0.4% respectively. In a study of 17 PD patients who were started on icodextrin for refractory and symptomatic fluid overload, Johnson et al. reported an improvement in the mean HbA1c level of 12 diabetics over a 3-month period, from 8.9% ± 0.7% to 7.9% ± 0.7%, leading to a reduction in insulin dose in 7 of them (8). However, Gradden et al., while examining the incidence of hyponatremia and the impact of icodextrin on hyponatremia, found that, in 18 diabetics with suboptimal diabetic control, in the pre-icodextrin period (mean HbA1c 8.13% ± 1.82%), there was no change in diabetic control over the 12-month observation period after icodextrin use (9).

We investigated changes in the glycemic status (HbA1c levels) and subsequent modifications in the treatment of 8 diabetic PD patients who were on icodextrin exchanges for more than 3 months and up to 12 months. There were 5 females and 3 males. Their mean age was 66.1 ± 17.8 years. Two of the 8 patients had type I diabetes and the other 6 had type II diabetes. Of the 8 patients, 5 were on insulin; 1 patient was on oral hypoglycemic agents, and 2 patients were not receiving any medications to control their blood sugar. Only 1 patient was receiving insulin intraperitoneally, the rest through subcutaneous route. Six of them were on automated PD and the rest on CAPD. Mean duration of PD before starting icodextrin was 27.49 ± 32.15 months. These patients were on icodextrin for an average period of 14.3 ± 7.2 months (range 5–27 months). All these patients were either high (2 patients) or high-average (6) membrane transporters. We recorded HbA1c values for 3 months before and at 3-month intervals for up to 12 months after introducing icodextrin. Mean values at each time point are shown in Table 1. Mean HbA1c at the time of introduction of icodextrin was 7.7% ± 1.5%. The mean HbA1c level between the periods before and after icodextrin use showed a slight increase that was not statistically significant (Table 1). The mean HbA1c values of all 5 patients who were followed sequentially for 12 months were also not significantly altered (Table 2). Of the 5 patients receiving insulin, 2 had improved glycemic control requiring a reduction in insulin dose, 1 maintained stable glycemic control without modification in insulin dose, and the other 2 patients required higher
insulin doses to control hyperglycemia. The patient on oral hypoglycemic agents had these drugs decreased after icodextrin. The 2 patients who maintained stable glyemic status without medications continued to do so even after icodextrin use.

In conclusion, contrary to the findings of Johnson et al. (8) and in agreement with the study of Gradden et al. (9), we found no significant alteration in the mean HbA1c level of diabetic PD patients who were on icodextrin for 3 to 12 months. Longer follow-up might be the reason for the differences.

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