Management Of “Difficult To Treat Peritonitis”
A Case Report And Brief Outline Of Management

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Abstract:
Peritonitis is one of the major complications of ambulatory peritoneal dialysis in India. With improvement of technique, increasing experience of physicians and caregivers and gradual improvement in living conditions of Indians, peritonitis rates have come down over the years. However many physicians who are involved in caring peritoneal dialysis patients are often faced with difficult management decisions related to management of refractory peritonitis. Often the CAPD catheter is left for too long leading to multiple complications and mortality. We report a case of refractory peritonitis with catastrophic abdominal complication. We also briefly discuss the basic outline of management of “difficult to treat peritonitis.

Key Words: Peritonitis, mesenteric ischemia, catheter removal, treatment

Introduction:
Peritonitis is one of the major complications of ambulatory peritoneal dialysis in India. With improvement of technique, increasing experience of physicians and caregivers and gradual improvement in living conditions of Indians, peritonitis rates have come down over the years. However many physicians who are involved in caring peritoneal dialysis patients are often faced with difficult management decisions related to management of relapsing/refractory peritonitis. Often the CAPD catheter is left for too long leading to multiple complications and mortality. We report a case of “difficult to treat” peritonitis with catastrophic abdominal complication. We also briefly discuss the basic outline of management of such patients.

Case Report:
A 62 year old lady, a known case of diabetes mellitus, hypertension and dyslipidemia was admitted in our hospital with abdominal pain, vomiting and loose stools of seven days duration.

She was detected to have chronic kidney disease six years back and was initiated on hemodialysis. She was subsequently offered peritoneal dialysis (PD) as a treatment modality of her end stage renal disease. She agreed to the medical decision and for the last six years she has been on continuous ambulatory peritoneal dialysis (CAPD), which has been largely uneventful. She had a culture negative peritonitis two years back which was managed with intraperitoneal (IP) cephalosporin and aminoglycoside. She had similar symptoms about four weeks back which was diagnosed as peritonitis (raised peritoneal fluid cell count) and was treated with IP cephalosporin, aminoglycoside and vancomycin. Her cultures were negative this time also. She showed gradual improvement and her antibiotics were stopped after 14 days of therapy. After a week her transfer set was changed and peritoneal fluid was sent for analysis. The fluid showed 83 cells/ml with 56% lymphocytes. Her fluid culture grew no organism. The transfer set tip grew enterococcus. At this point of time she was asymptomatic. However after 48 hours of her transfer set change she started having abdominal pain, vomiting and diarrhea. She was restarted on intravenous antibiotics (Meropenem and Amikacin). As she did not show any improvement she was transferred to Mumbai and she was subsequently admitted in our hospital.

On admission her vitals were stable and she was afebrile.

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There was no elevated venous pressure or edema feet. She had marked abdominal guarding without any rigidity and sluggish bowel sounds. The exit site was clean, without any erythema or purulent discharge and there was no tenderness over the tunnel tract. Her rest of the systemic examination did not reveal any abnormality.

Her initial complete blood count showed normal hemoglobin (12.9 gm/dl), leukocytosis (TLC 17500) with neutrophilic predominance (84% neutrophils) and normal platelet count. Her renal profile showed hyponatremia (Na 126 mmol/l), hypokalemia (K 3.62 mmol/l), renal failure (Creatinine-6.17 mg/dl) and hypocalcemia (Calcium-6.1 mg/dl). Her liver functions revealed the presence of hypoalbuminemia (Albumin 1.9 g/dl) and raised alkaline phosphatase (ALP 152 U/l). Rest of the liver functions were normal. Her stool examination was negative for occult blood no organism were grown. Her serum and lipase levels were normal. Peritoneal fluid was sent for analysis. The cell count came as 3233 cells/mm³ with 85% neutrophilic predominance. The culture did not grow any pathogenic bacteria or fungus. AFB were not seen on ZN stain and mycobacterial culture was asked for.

A relapse of CAPD-associated peritonitis was diagnosed, and she was continued started on intravenous Meropenem and Vancomycin. The issue of removing the peritoneal catheter was discussed with the patient family and a surgical consult was asked for. She was kept nil by mouth and managed with intravenous fluids. A Ryles tube (RT) was inserted. Her peritoneal signs did not improve after initiating antibiotic therapy in the next 24 hours. A repeat peritoneal fluid cell count was 8090 cell/mm³ with 88% neutrophilic predominance.

Her CT scan revealed moderate ascites with omental stranding immediately adjacent to abdominal wall with few enlarged lymph nodes and minimal bilateral pleural effusion. (Fig. 1). Her CRP was 11.9 mg/dl and serum procalcitonin was 1.69 ng/ml. With the consent of the family the CAPD catheter was removed. As she showed hemodynamic deterioration during the day a quick surgical procedure was performed. The peritoneal lavage was sent for cultures and an omental biopsy was taken. A complete inspection of the abdomen to look for any gut pathology (as the initial transfer set culture grew enterococcus) had to be abandoned. The CAPD catheter tip and peritoneal fluid had no growth on culture. Her omental biopsy was not contributory. She had a negative Clostridium difficile toxin assay which was sent as she has received prolonged course of antibiotics.

Her post-operative course was satisfactory with decreased abdominal pain and peritoneal signs. She started to take orally. She was regularly hemodialysed through a jugular approach. However on fourth postoperative day she had severe abdominal pain, vomiting and loose stools. Her RT aspirate increased to 400 cc. Her hemogram showed increased leukocytosis (TLC 26300 cells/mm³ with leftward shift). On the advise of the infectious disease consultant her antibiotics were changed to Tigecycline, Metronidazole and Daptomycin. A repeat CT scan was done. It revealed dilated duodenum and jejunum with thin and fuzzy appearing wall of a segment of jejunal loop with air in relation to its wall. The peritoneal fat in relation to it appeared mostly heterogenous and inflammed. The cecum, ascending colon and right half of transverse colon appeared edematous with thickened adjacent peritoneal fat suggestive of colitis. Also noted was a intraperitoneal hematoma to the right rectus muscle in the hypogastrium region. (Fig 2)
An exploratory laparotomy was done and it revealed extensive infarction of the gut extending from jejunum to transverse colon. (Fig3) No vascular occlusive lesion was found and no resection was attempted in view of poor outcome. She was started on heparin and reexplored after 48 hours. The laparotomy revealed worsening of the bowel infarction. The patient's condition rapidly deteriorated over the next 48 hours and she expired two weeks after her initial admission to our facility.

Discussion:
Peritonitis is a serious complication of peritoneal dialysis (PD) and probably most commonly caused by technique failure. (1) Peritonitis does contribute to the death of approximately 16% of patients on PD. (2) Peritonitis treatment goals include rapidly resolving inflammation by eradicating the causative organism(s) and preserving the function of the peritoneal membrane. In certain instances these goals are difficult to achieve and in such situations, the treating team often has to address multiple issues which include:

1. The type of peritonitis based on clinical presentation and the organism responsible for the infection.

2. The microbiological diagnosis and appropriateness of therapy

3. The presence of other organisms if peritonitis is unresponsive to standard antibacterial therapy.

4. Removal of catheter/rest to the abdomen.

5. Exclusion of intraabdominal pathology as a cause of peritonitis—especially sterile peritonitis or peritonitis secondary to enterococci and multiple gram negative organisms.

The clinical presentation of peritonitis and its type is often determined based on ISPD guidelines.

The ISPD Guidelines(3) give the following definitions:

- Refractory peritonitis results when there is failure of the effluent to clear after 5 days of appropriate antibiotics.

- Relapsing peritonitis can be defined by an episode that occurs within 4 weeks of completion of a therapy of a prior episode with the same organism or 1 sterile episode.

- Recurrent peritonitis refers to an episode that occurs within 4 weeks of completion of therapy of a prior episode but with a different organism.

- Repeat peritonitis occurs more than 4 weeks after completion of therapy of a prior episode with the same organism.
Our patient was classified as a relapsing peritonitis as she developed peritonitis within fourteen days of antibiotic therapy.

Diagnosis of peritonitis should be obtained as quickly as possible. A tunnel infection should be excluded which often presents with erythema, edema, or tenderness over the subcutaneous pathway but is often clinically occult. (4) A tunnel infection usually occurs in the presence of an exit-site infection but rarely occurs alone.

It is very important to obtain a microbiological diagnosis as soon as possible. The gram stain should be used to define the presence of bacteria and yeast and permit initiation of therapy and also help decide about timely removal of catheter; however, the gram stain alone should not be used for empiric therapy guidance. A rapid bacteriological diagnosis (cultures) should be obtained so as to offer appropriate antibiotic therapy. In many instances culture yield is often poor especially if proper techniques for culture are not followed. Our patient had a culture negative peritonitis at the first instance and was treated with empiric antibiotics.

When considering empiric antibiotic treatment, it is important for the selection to encompass gram negative and gram-positive organisms concurrently. Gram-positive antibiotic options include vancomycin or cephalosporins. Gram-negative coverage may be obtained through the use of aminoglycosides or third-generation cephalosporins. The preferred administration of antibiotics is intraperitoneal; intermittent and continuous dosing is equally effective. It is well known that the preferred method of dosing antibiotics in peritonitis is intraperitoneal (IP). IP dosing is favored over intravenous (IV) dosing because the local levels that can be achieved are higher with IP. Additionally, IP route is advantageous because the patient can perform it at home after adequate training. It also avoids venipuncture necessary for IV access. Optional dosing regimens of IP antibiotics include once daily (intermittent) or per each exchange (continuous). The antibiotic must dwell for a minimum of 6 hours to ensure adequate absorption. Our patient had intraperitoneal administration of antibiotics for 14 days during her last episode of peritonitis and had successful resolution of symptoms. In general, patients are to be treated with effective antibiotics for 14 days and a total of 21 days for episodes caused by Staphylococcus, Enterococcus or Pseudomonas species. (5)

If symptoms recur within 14 days, consideration should be given to the presence of fungal or mycobacterial peritonitis. A serious complication that can occur subsequent to an episode of bacterial peritonitis treated with antibiotics is fungal peritonitis. Approximately 25% of fungal peritonitis episodes result in death. The catheter should be removed as soon as possible to decrease risk of death. Flucytosine and amphotericin B can be used empirically for infections caused by Candida species, while echinocandins such as caspofungin, anidulafungin, and micafungin, are recommended for Aspergillus. The prevention of fungal peritonitis may be achieved by the use of antifungal prophylaxis during antibiotic treatment, as it is commonly associated with antibiotic use.

Tuberculous (TB) peritonitis is a rare complication of PD, although in some studies, the prevalence of this infection has been as high as 3%, particularly in populations with a high prevalence of TB. (6) Smears of the peritoneal effluent often fail to reveal acid-fast bacilli, thus diagnosis must rely on TB cultures which usually take 6 weeks. In order to make an earlier diagnosis in patients not responding to therapy, invasive procedures such as exploratory laparotomy or laparoscopy with biopsy of the peritoneum or omentum should be considered. Detection of mycobacterial DNA amplified by polymerase chain reaction techniques from peritoneal effluent hold the greatest promise for rapid detection of tuberculosis. However the overall usefulness of these rapid tests need to be ascertained in our subset of patients. A diagnosis of tuberculous peritonitis was considered and an omental biopsy was taken during the removal of the catheter.

If enterococci are cultured, ampicillin and an aminoglycoside should be used in the recommended doses. Our patient grew enterococcus from the transfer set which was changed after the treatment of peritonitis. She had received vancomycin in her last episode of peritonitis, hence a vancomycin resistant
enterococcus causing her current infection was also considered. An abdominal pathology responsible for her peritonitis was also considered and a CT abdomen was obtained immediately.

If no clinical response is noted after 96 hours of therapy for relapsing peritonitis, catheter removal is indicated. In our patient, catheter removal was recommended within 24 hours of her hospital admission as she had remarkable abdominal symptoms and her peritoneal fluid cell counts were quite high. There was a strong suspicion of an intra-abdominal abscess in our patient. Catheter removal in difficult to treat peritonitis should always be an early option. The focus should always be on saving the peritoneum rather than the catheter. The indications of catheter removal are given in Table 1.

Table 1: Indications of catheter removal (3)

| Indications for Catheter Removal for Peritoneal Dialysis –Related Infections |
|---|---|
| 1 | Refractory peritonitis |
| 2 | Relapsing peritonitis |
| 3 | Refractory exit-site and tunnel infection |
| 4 | Fungal peritonitis |
| 5 | Catheter removal may also be considered for |
| 6 | Repeat peritonitis |
| 7 | Mycobacterial peritonitis |
| 8 | Multiple enteric organisms |

Catheter replacement as a single procedure can also be done in relapsing peritonitis if the effluent can be cleared. However, catheter replacement is not advised in fungal and refractory peritonitis. (7) Some studies suggest that temporary withdrawal of peritoneal dialysis without removing the catheter (peritoneal rest) is effective in eradicating recurrent peritonitis due to Staphylococcus aureus and Enterococcus, and in resistant peritonitis due to Klebsiella. There are several reasons that may explain why discontinuation of CAPD is effective in peritonitis. Intestinal perforation, pancreatitis and hepatobiliary pathologies should be considered in the differential diagnosis of CAPD peritonitis. (10) Visceral infarction like splenic infarction can also present as culture negative peritonitis in CAPD patients. (11) Our case was distinctive in a sense that the presence of mesenteric ischemia was the underlying cause which was responsible for her peritonitis.

In summary, peritonitis is a major problem in patients undergoing peritoneal dialysis in India. Often physicians involved in caring PD patients face many challenges especially in patients whose infection is difficult to treat. Isolation of the culprit organism is often difficult, diagnosis of life threatening fungal infections are often delayed and tuberculous peritonitis is always a possibility. (12) There is also a lingering dilemma of timing of removal of the peritoneal catheter in these patients. In some instances, despite best efforts, the patient does not respond to treatment as the etiology of the peritonitis turns out to be remotely related to the PD.

References:


