Pleuroperitoneal communication-associated pleuritis as an uncommon cause of fever of unknown origin in a child on peritoneal dialysis: a case report

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Pleuroperitoneal communication (PPC) is a rare mechanical complication of peritoneal dialysis (PD), which causes dialysate to move from the peritoneal cavity to the pleural cavity, resulting in pleural effusion. Typically, PPC is discovered through pleural effusion in patients on PD who are not in volume overload status. A unique characteristic of the pleural effusion caused by PPC is that it is not resolved by increasing ultrafiltration by dialysis. In this report, we present a 7-year-old girl with PD after birth with the history of various infectious PD-related complications, presenting with fever ongoing for 6 months. PPC-associated pleuritis was suspected as the cause of fever, which eventually developed after long-term PD and induced complicated pleural effusion, lung inflammation, and prolonged fever for 6 months.

Keywords: Case reports; Child; Fever; Peritoneal dialysis; Pleural effusion

Introduction

Children with end-stage kidney disease (ESKD) should receive kidney replacement therapy through hemodialysis or peritoneal dialysis (PD). Given the lack of comparative studies of PD and hemodialysis outcomes in children with ESKD, the choice primarily depends on patient and family preference or the availability of nearby medical centers [1]. However, PD holds various advantages over hemodialysis, such as fewer dietary restrictions, including fluid intake, allowing treatment to be performed at home without needing vascular access. Therefore, PD is the most common dialysis treatment modality for pediatric patients with ESKD [2,3].

Complications associated with PD typically range from infectious (peritonitis, exit site or tunnel infection) to non-infectious problems (hernia, hydrothorax, hemoperitoneum, nutritional or metabolic issues) [4,5]. Hydrothorax (pleural effusion) in patients on chronic PD can be caused by various etiologies such as heart failure, uremic pleuritis, or volume load due to decreased dialysis efficiency, tuberculosis, neoplasm, and parapneumonic effusion. Pleuroperitoneal communication (PPC; fistula or leak), is a rare and potentially life-threatening complication of chronic PD that causes pleural effusion. Usually, PPC is discovered through pleural effusion in patients on PD who are not in volume overload status, which persists despite increasing dialysis efficiency using high osmolar dialysate or increasing dialysis frequency and instill-dialysate volume.

In adults with PD, the estimated incidence of PPC is 0.64% to 5.10%. However, the incidence in children is unclear, with reports ranging from 0.9% from 3.0%, given the lack of pediat-
A 7-year-old girl with ESKD on PD was admitted due to fever, malaise, and poor oral intake on December 31, 2021. An intermittent fever (37.8–38.5 °C) persisted for 2 weeks despite oral antibiotic treatment (cefditoren 3 mg/kg/day) in the outpatient clinic. She was born at gestational age 33 weeks 6 days, weighing 4,120 g. She was admitted to the neonatal intensive care unit owing to a prenatally identified large sacrococcygeal immature teratoma (size 17×14×7 cm) and multiple anomalies, including rectal atresia and fixed equinus of both feet. Excisional operation of the teratoma was performed on the eighth day after birth. She developed ESKD due to teratoma-induced renal vessel compression and ischemic events with cardiac arrest during the operation, which was treated with continuous kidney replacement therapy for 3 months, followed by chronic continuous PD. She was discharged at 5 months at 3.9 kg body weight with a PD modality consisting of eight dialysis cycles with 60 mL of 2.5% dextrose dialysate at 2.5-hour intervals. As she grew up, she adapted to an automated continuous-cyclic PD schedule: 350 mL of 1.5% dextrose dialysate exchanges for six cycles at 2-hour intervals from 8 PM to 8 AM, followed by 300 mL of 7.5% glucose dialysate retention for 12 hours. She had suffered from several infectious PD complications, including peritonitis, exit site infections, and wound dehiscence and underwent three rounds of PD catheter change operations and two rounds of laparoscopic exploration and peritoneal adhesiolysis operations. The most recent case of peritonitis due to *klebsiella aerogenes* occurred 2 months before admission. On admission, she had symptoms including fever, chill, general weakness, weight loss of 1 kg over 1 month, intermittent cough, and rhinorrhea. She had no signs of respiratory distress, such as tachypnea, dyspnea, and cyanosis. Her height was 93.3 cm (<3rd percentile), and her weight was 11.6 kg (<3rd percentile). Her vital signs were as follows: systolic/diastolic blood pressure 68/38 mmHg, heart rate 123/min, respiratory rate 20/min, body temperature 37.8 °C, and oxygen saturation 95% in room air. On physical examination, she appeared chronically ill. Lung sounds were clear without wheezing or crackles. Bowel sounds were normal, with a soft abdomen without focal abdominal tenderness. The vesicostomy and ileostomy (due to rectal atresia) sites were clear. Pitting edema was not observed. Initial laboratory evaluation was as follows: white blood cell counts 26,600/μL (neutrophils 82.7%, lymphocytes 8.5%, monocytes 6.1%), hemoglobin 9.2 g/dL, platelets 365,000/μL, blood urea nitrogen 50 mg/dL, creatinine 8.23 mg/dL, B-type natriuretic peptide 2 pg/mL (normal range: <36 pg/mL), and C-reactive protein (CRP) 7.44 mg/dL (normal range: 0–0.6 mg/dL). PD fluid analysis was clear with a differential count of nucleated cells 82/μL consisting of 41% neutrophils and 15% lymphocytes. Chest radiography and computed tomography (CT) revealed multifocal peribronchial infiltration with subpleural consolidation in both lower lungs and suggestive complicated bilateral pleural effusion with diffuse enhancing pleural thickening (Fig. 1). Multiple reactive lymph node hyperplasias were also observed in the mediastinum, subcarinal, interlobar, and axillae. Left ureteral residual contrast dye from voiding cystourethrography, performed 80 days before admission, was observed on X-rays. Abdominopelvic CT results were as follows: PD catheter insertion with its tip in the pelvic cavity, moderate ascites with mild peritoneal thickening in the upper abdomen, bilateral hydronephroureterosis, a severe parenchymal atrophic change in both kidneys, residual contrast material in the left pelvicalyceal system, and irregular lobulated margin bladder. Considering her pneumonic features, we initially treated her with ampicillin–sulbactam (50 mg/kg/day ampicillin, 30 mg/kg/day sulbactam). However, we amended to piperacillin–tazobactam (100 mg/kg/day piperacillin, 25 mg/kg/day tazobactam) on the seventh hospital day to cover *K. aerogenes*, which was the cause of peritonitis 2 months before. Nevertheless, her CRP increased to 117 mg/dL with persistent mild fever (<38.0 °C). We subsequently switched to vancomycin (10 mg/kg/day) and meropenem (20 mg/kg/day) combination therapy on hospital day 13, and initial and repeated culture studies, including blood, PD fluid, sputum, and stool, were all negative. Tests for severe acute respiratory syndrome coronavirus 2, other respiratory viruses, tuberculosis interferon-gamma, and mycoplasma antibodies were also negative. We had performed a cystoscopy to remove contrast media of the left pelvicalyceal system injected during the voiding cystourethrography study for the transplantation work up 4 months before, considering the possibility of contrast-induced inflammation; however, the patient’s fever elevated to 40.2 °C and CRP to 13.3 mg/dL after the procedure. The culture result of the drained contrast was...
negative. We also performed whole body positron emission tomography–CT (18F-fludeoxyglucose) (Fig. 2). Despite observing mild hypermetabolic uptake in both lungs and pleural effusion, ascites, and lymph nodes in the right lower paratracheal, subcarinal, pulmonary hilar, and left inguinal areas, we concluded that the possibility of malignancy was low. Although we requested that a radiologist and a thoracic surgeon drain the pleural effusion to identify any undiscovered organisms or malignancies that might have caused prolonged inflammation, they could not aspirate or drain the effusion as the absolute amount of fluid was too small. We discontinued vancomycin first to rule out drug fever after 4 weeks of treatment. The intermittent fever occurred up to 38.3 °C but then dropped, and CRP decreased to 5.63 mg/dL. Nine days later, intravenous meropenem treatment was converted to intraperitoneal imipenem administration to cover potentially undetected pleural or peritoneal K. aerogenes infection. The fever disappeared, CRP further decreased to 4.61 mg/dL, and the patient was discharged after 52 days of admission (Fig. 3A). She was re-admitted a week later due to re-aggravated fever and CRP of 40.2 °C and 9.61 mg/dL, respectively. Intraperitoneal imipenem treatment was changed to intravenous meropenem. A total of 12 times PD fluid bacteria/fungus/acid-fast bacilli culture tests performed for 3 months were all negative, and white blood cell counts of PD fluid analyses were normal (Table 1). We discontinued antibiotics 9 days after readmission, as we could not identify any infection focus and had to differentiate drug fever. We performed a follow-up CT of the chest and abdomen, indicating findings similar to previous studies. We evaluated the fever of unknown origin (FUO), including immunologic workups, brain magnetic resonance images, and bone marrow biopsy, and the results were nonspecific. We diagnosed her with systemic juvenile idiopathic arthritis as we could not find any other cause (Table 2).
Fig. 3. The clinical courses, laboratory findings, and treatment of a 7-year-old girl on PD with prolonged fever. (A) First admission (Dec 31, 2021–Feb 20, 2022). (B) Second admission (Feb 28, 2022–Mar 22, 2022). (C) Third admission (May 1, 2022–Jun 25, 2022). CRP, C-reactive protein; BT, body temperature; CT, computed tomography; APCT, abdominal and pelvic CT; EGD, esophagogastroduodenoscopy; PET-CT, positron emission tomography-CT; SAM, ampicillin-sulbactam; TZP, piperacillin-tazobactam; VAN, vancomycin; MEM, meropenem; IP IPM, intraperitoneal imipenem; HD, hospital day; FUO, fever of unknown origin; Ig, immunoglobulin; ANA, antinuclear antibody; C3, complement component 3; C4, complement component 4; CH50, complement component CH50; MRI, magnetic resonance imaging; PO, per oral; PD, peritoneal dialysis; AZA, azathioprine. a) Bladder augmentation and left nephroureterectomy operation for preparing the future kidney transplantation (May 2, 2022).
started naproxen on hospital day 15, and subsequently added prednisolone (2 mg/kg/day) on day 18. The fever disappeared, and CRP dropped to 2.02 mg/dL. She was discharged after 22 days of admission (Fig. 3B), and azathioprine (1–2 mg/kg/day) was added at the outpatient clinic with CRP ranging from 2.16 to 4.44 mg/dL. She was admitted for bladder augmentation before
kidney transplantation on May 1, 2022. We discontinued immuno-
osuppressants, added stress-dose hydrocortisone, and started prophylactic antibiotics (piperacillin-tazobactam) before surgery. Bladder augmentation and left nephroureterectomy operation were electively performed on hospital day 4. After open abdominal surgery, we stopped her PD and started hemodialysis. CRP elevated to 34.9 mg/dL 2 days after surgery with a mild fever (<38.0 °C). We, therefore, switched from piperaci-
lin-tazobactam to vancomycin and meropenem. CRP slowly decreased without fever while the patient was on hemodialysis for 2 weeks instead of PD. CRP was normalized to 0.42 mg/dL for the first time within 6 months after initial fever onset. A small amount of pleural effusion was still observed on chest X-rays. Three weeks after surgery, after restarting PD, a mild fever de-
veloped (37.9 °C), and CRP elevated to 4.93 mg/dL. We planned to perform peritoneal scintigraphy to identify the presence of a PPC, but the test was not available for children at our center. We requested a thoracic surgeon to explore the diaphragm to find a fistula or foramen; however, he refused the procedure because pleural thickening had already progressed, and diaphragm detach-
tment was expected to be very difficult. We ceased PD and restarted hemodialysis, which normalized body temperature, and CRP dropped to 0.78 mg/dL. After resuming PD to confirm if PD and the PPC were the cause of the fever and elevation of in-
flammary markers, body temperature rose and CRP in-
creased. We finally decided to stop PD to switch to hemodialysis. The PD catheter was removed, the right subclavian perm cath-
eter was inserted on June 17, 2022, and hemodialysis was sta-
bilized and maintained at a 3 times/week schedule (Fig. 3C). Since she started hemodialysis, her fever has not re-
curred, and pleural effusion, pneumonia, and inflammation markers have slowly improved. The FUO that persisted for 6 months, despite treatment with broad-spectrum antibiotics and immunsuppressants, was finally resolved. The bilateral pleural effusion also gradually improved after discontinuing PD (Fig. 1C). Currently, she attends outpatient clinics and adapts well to hemodialysis, which is scheduled 3 times a week, while awaiting kidney transplantation.

**Discussion**

Herein we report the case of a 7-year-old female child on PD with complicated pleural effusion and pleuroperitoneal inflam-
mation due to PPC, who developed a prolonged fever. PPC is a mechanical complication of PD [4]. Although the pathophys-
ology of PPC is unknown, the negative thoracic pressure with increased intra-abdominal pressure caused by dialysate instil-
lation is considered to open small defects in the diaphragm and promote migration of dialysate into the pleural space [6].

Several predisposing factors for PPC include congenital factors with a predominance of right-sided effusions such as diaphragmatic muscular hypotonia, congenital diaphragmatic defects, WT1 mutation syndromes, lymphatic drainage disor-
ders, polycystic kidney disease [5,7,8], and acquired factors such as previous episodes of peritonitis and long-term dialysis with high osmolar dialysate [6,9]. Our patient was on PD for 7 years, during which she had several bouts of peritonitis, contributing to make small defects of diaphragm. We did not perform genet-
ic tests for WT1 mutation in this patient.

In this case, we reached a delayed diagnosis of PPC-associat-
ed pleuritis after 6 months of fever. Despite conducting various workups to identify the cause of the FUO, no specific causes could explain the fever except complicated pleural effusion, pneumatic consolidation, and pleuroperitoneal thickening. She had no symptoms of dyspnea, respiratory difficulties, or signs of volume overload such as edema and weight gain. To our knowledge, no other case of PPC manifesting as fever has been reported.

Diagnosis of PPC is complicated because there are no stan-
dardized methods. Many patients with PPC are asymptomatic, but classic symptoms include hypertension, edema, dyspnea, pleuritic chest pain, increased demands of O₂, and inadequate ultrafiltration despite increasing dialysate fluid volume or os-
molarity (high dextrose dialysate fluid) [9,10]. Thoracentesis for pleural fluid analysis can identify the characteristics of the pleural fluid to determine whether its composition is close to that of the dialysate fluid, including low lactate dehydrogenase and protein levels and glucose levels higher than the plasma glucose level by 50 mg/dL (sweet hydrothorax) [11]. However, thoracentesis is an invasive test that cannot be performed if the fluid amount is too small to drain. Failure to perform thorac-
centesis contributed to the delay in diagnosis. In our case, thoracentesis and draining of the pleural fluid for fluid analyses and various cultures were planned but canceled as it was con-
sidered dangerous due to the small amount and stickiness of the fluid, causing a delay in diagnosis. CT peritoneography is a common and noninvasive diagnostic tool for cases of large PPC; however, its low sensitivity prevents it from detecting smaller defects [12], and contrast may cause nephrotoxicity [13]. Among the current diagnostic methods, peritoneal scintigraphy is the
safest and most accurate method, with 40% to 50% sensitivity [9,12]. Confirming the presence of radioactive nuclear medicine (technetium 99m) in the thoracic cavity over time is possible after injecting the dialysis solution with the medicine into the peritoneal cavity [9]. However, the test has limited utility in locating the site of a fistula [5,7]. We could not perform peritoneal scintigraphy because the test was unavailable for children at our center, complicating our ability to diagnose PPC.

In this case, we had to stop PD and change to permanent hemodialysis to treat PPC-associated pleuritis. After starting hemodialysis, the inflammation markers decreased, the fever subsided, the pleural effusion improved, and she recovered from the fever, which led to three hospitalizations and discharges over 6 months. Additionally, due to its difficulty, we did not perform a thoracoscopic examination to evaluate the PPC-associated pleuritis. There is no guideline for treating PPC, so the choice of treatment depends on the severity of the patient’s symptoms [10]. Treatment options include decreasing the intraperitoneal pressure by stopping the PD temporarily for 6 weeks to 3 months, avoiding daytime dwell, or reducing dialysate fluid volume with continuous pleural fluid drainage [14], which is successful in approximately 50% of PD patients [10,12,14]. Other methods also include changing to hemodialysis permanently [5] or performing chemical pleurodesis using autologous blood, tcalc, tetracycline, or bleomycin [3]. Video-assisted thoracoscopic pleurodesis or direct repair can also be considered [15]. The rate of resuming PD without recurrence of PPC after surgical repair is 90% for both adults and children; however, surgical treatment is not performed universally as it is complicated and difficult to identify the site of the fistula, especially in children [15].

Early suspicion and a systematic approach to PPC are essential to minimize misdiagnosis or diagnosis delay, especially in patients on chronic PD who present with refractory or recurrent pleural effusions that do not respond to conventional therapy [13]. Diagnosing and treating PPC in children promptly is challenging, given the lack of cases. However, the sum of patients can lead to the implementation of guidelines for diagnostic tools and novel treatments. Fever is a rare manifestation of PPC-associated pleuritis, but this case highlights that PPC-induced complicated pleural effusion and inflammation could cause prolonged fever when no other factor is identified.

**Ethical statements**

This report was approved by the Institutional Review Board of Asan Medical Center (IRB number S2023-0609-0001), and the informed consents were waived due to the nature of the retrospective study.

**Conflicts of interest**

Joo Hoon Lee is an editorial board member of the journal but was not involved in the peer reviewer selection, evaluation, or decision process of this article. No other potential conflict of interest relevant to this article was reported.

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**References**


