

Bulletin de la Dialyse à Domicile

Chylous peritonitis on peritoneal dialysis

(La péritonite chyleuse en dialyse péritonéale)

Hanen Abid^{1,2}, Salma Toumi^{1,2}, Hanen Chaker^{1,2}, Beya Fendri^{1,2}, Ikram Agrebi^{1,2}, Najla Dammak^{1,2}, Fatma Mseddi¹, Khawla Kammoun^{1,2}, Soumaya Yaich^{1,2}, Mohamed Ben Hmida^{1,2}

¹Service de néphrologie, dialyse et transplantation rénale, CHU Hedi Chaker, Sfax, Tunisie

²Laboratoire de pathologie rénale Lr19es11, Faculté de médecine de Sfax, Sfax, Tunisie

Note : ce texte est disponible en Français à la même adresse url : <https://doi.org/10.25796/bdd.v4i3.62623>

Résumé

La péritonite chyleuse (PC) est une complication non infectieuse rare chez les patients en dialyse péritonéale qui prêle souvent à confusion avec les péritonites infectieuses, et peut aussi révéler une néoplasie abdominale dans de rares cas. Ses étiologies sont multiples. Elle peut survenir dans les suites d'une insertion traumatique du cathéter de dialyse péritonéale ou être secondaire à des infections), à une cirrhose du foie, à une pancréatite ou à des causes médicamenteuses surtout les inhibiteurs calciques. L'évolution est en général favorable en traitant ou en éliminant l'agent causal.

Nous rapportons dans ce travail notre expérience de péritonite chyleuse et des étiologies qui y sont associées à travers 3 cas cliniques. Chez 2 patients, la PC était rattachée à la prise d'inhibiteurs calciques et dans 1 cas à la consommation de repas) riches en lipides et favorisée probablement par des séquelles de tuberculose ganglionnaire abdominale.

Mots clés : dialyse péritonéale, péritonite chyleuse, inhibiteur calcique, tuberculose

Summary

Chylous peritonitis is a rare non-infectious complication in patients on peritoneal dialysis that is often confusing with infectious peritonitis but can also be seen in rare cases of abdominal neoplasia. The other causes of occurrence are multiple. Chylous peritonitis can occur following traumatic insertion of the peritoneal dialysis catheter or be secondary to other causes such as infections, liver cirrhosis, pancreatitis or medications, especially calcium channel blockers. The course is generally favorable by treating or eliminating the causative agent. We report in this work our experience with chylous peritonitis and the etiologies associated with it through 3 clinical cases. In 2 patients, CP was associated with the intake of calcium channel blockers and in 1 case with the consumption of meals enriched in lipid, probably favored by the existence of sequelae of abdominal lymph node tuberculosis.

Key words : peritoneal dialysis, chylous peritonitis, calcium channel blocker, tuberculosis

INTRODUCTION

Chyloperitoneum is a rare complication in patients on peritoneal dialysis (PD) characterized by a milky-looking peritoneal effluent with normal cellularity and rich in triglycerides (TG) (1). Chyloperitoneum occurs in presence of alterations affecting the sub-diaphragmatic lymphatic system in the abdominal cavity and has multiple etiologies (1). Most common causes are hepatic cirrhosis, malignant abdominal tumors and infections (tuberculosis). Traumatic or surgical lesions of the lymphatic system, especially during traumatic catheter placement, remain a rare complication, as are drugs, the most implicated of which are calcium channel blockers (CI) (2,3). We describe in this work our experience with chylous peritonitis through 3 observations.

OBSERVATIONS

Case n ° 1:

This was a 60-year-old man with a history of recurrent renal lithiasis, arterial hypertension (hypertension) since 2009 on manidipine and end-stage chronic renal disease (ESRD) secondary to chronic interstitial nephropathy (CIN), on PD since 2011. Her hypertension was well controlled with manidipine (20 mg / d) and furosemide (120 mg / d). The patient presented a first episode of peritonitis on July 12, 2012 with *Pseudomonas* and *Serratia*. He was treated with ceftazidime, amikacin and ciprofloxacin with good improvement. A week later, he presented with a bag of lactescent-appearing drained dialysate (Figure 1).

There was no change in general condition nor fever. The clinical examination of this patient was without abnormalities. Cytobacteriologic examination of the dialysate fluid showed normal cellularity and negative culture. The abdominal ultrasound did not show any suspicious lesions suggestive of neoplasia. Thus, manidipine, suspected as the cause, was replaced by perindopril. The course was marked by the immediate disappearance of the chyloperitoneum (Figure 2) without recurrence during follow-up.



↑ Figure 1. Drained dialysate demonstrating a lactescent aspect



↑ Figure 2. Normal aspect of drained dialysate after cessation of manidipine prescription

Case n° 2:

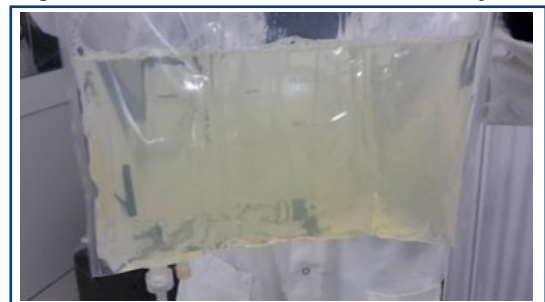
This was a 58-year-old man with hypertension on discontinuation of treatment with a history of abdominal lymph node tuberculosis (TBC) treated with quadruple therapy for 9 months with clinical remission. In addition, the patient had a history of esophageal mycosis, mixed dyslipidemia, and ESRD secondary to primary extra-capillary glomerulonephritis. He underwent a kidney transplant in 1997 from a living donor complicated by chronic allograft nephropathy with transfer to peritoneal dialysis in 2017. His usual treatment included atorvastatin, prednisone, calcium, derivatives of vitamin D, folic acid and iron. He experienced an episode of peritoneal infection with *Staphylococcus aureus* and *Pseudomonas putida* in March 2018 successfully treated with vancomycin, amikacin, ceftazidime and ciprofloxacin for 10 days. In the aftermath of this episode of peritonitis, the patient developed 2 episodes of chyloperitoneum in April and May 2018 at a distance from the antibiotic treatment. His usual treatment did not include calcic inhibitors. On clinical examination, he had lower extremity edema. The remainder of the physical examination was unremarkable. There was no biological inflammatory syndrome. There was no cirrhosis or heart failure. Cytobacteriological examination of the dialysate fluid showed normal cellularity and sterile culture (Figure 3). The human immunodeficiency virus (HIV) and hepatitis C virus (HCV) serologies as well as the Hbs antigen were negative. The test for Koch's bacillus in sputum was negative. An abdominal CT scan performed in April 2018 showed multiple mesenteric and lumbo-aortic lymph node calcifications that looked like a sequel. There were no radiological signs in favor of intra-abdominal neoplasia. A dietary survey revealed a diet enriched in lipids and there was hypertriglyceridemia at 2.3 mmol / l, these episodes of chylous peritonitis were linked to the consumption of large meals probably favored by the existence of sequelae of tuberculosis hampering intra lymphatic drainage abdominal. Chyloperitoneum resolved spontaneously with reduced lipid intake during each episode after an average of 7 days.



↑ figure 3. Lactescent aspect of drainage fluid of case 2

Case n° 3:

This was a 53-year-old man. He had a history of hypertension, mixed dyslipidemia, coronary insufficiency with stenting in 2015, and end-stage chronic renal failure due to glomerular nephropathy. He started peritoneal dialysis in May 2019. PD catheter was placed in May 2019 without incident. His usual treatment included: lercanidipine, moxonidine, a beta blocker, and adjuvant therapy for his CRF. In November 2019, the patient consulted for an accidental rupture of the PD catheter with a coincidental discovery at the same time of a chylous aspect of the effluent dialysate (Figure 4). On clinical examination, the blood pressure was high and he had lower legs edema. The chest X-ray as well as the abdominal ultrasound were without abnormalities. The extension line was



↑ figure 4. Chylous aspect of drained dialysate in case 3

changed and the patient was put on vancomycin and ciprofloxacin for 5 days prophylactically. The cytobacteriologic examination of the effluent dialysate fluid was negative. Biologically there was no biological inflammatory syndrome and the triglyceride (TG) level was 3.18 mmol / l. Faced with the notion of recurrence of the chylous appearance of the effluent dialysate fluid at a distance from the antibiotic treatment, the diagnosis mentioned was that of chylous peritonitis secondary to lercanidipine. The outcome was favorable after stopping lercanidipine. The patient was put on irbesartan, amlodipine and a diuretic. After a 24-month follow-up from stopping lercanidipine, there was no recurrence of chylous peritonitis. Table I summarizes the clinical characteristics of our patients.

↓ Table 1: clinical characteristics of patients

	Age/sex	Time of chylous peritonitis since PD start	Patients' history	Suspected etiology	Evolution
Case 1	60 yrs/ M	17 months	HBP, ESRD, renal stone disease	manidipine	No relapse
Case 2	58 yrs/ M	13 months	HBP, abdominal lymph node tuberculosis, oesophageal mycosis, dyslipidemia, ESRD	lipids enriched meals + abdominal tuberculosis sequelae	No relapse
Case 3	53 yrs/ M	6 months	HBP, dyslipidemia, coronary insufficiency, ESRD	lercanidipine	No relapse

HBP: High Blood Pressure; ESRD: end-stage renal disease

DISCUSSION

Chyloperitoneum is a rare complication in PD. Indeed, PD in our center started in 2001 and, during the period between 2001 and 2020, we only recorded three cases of chyloperitoneum.

The effluent dialysate fluid drained during chyloperitoneum takes on a milky appearance secondary to a large influx of TG associated with obstruction of the abdominal lymphatic vessels. (1) The diagnosis of chyloperitoneum is made on the basis of the milky appearance of the fluid, the normality of the cellularity with a negative culture and the assay of the TG level in the dialysate (4). The increase in the concentration of TG in the dialysate is considered to be an important indicator of chylous ascites but its precise diagnostic value remains poorly determined (5). The diagnosis of chyloperitoneum is retained if the level of TG is > 2.26 mmol / l (200 mg / l) in the dialysate according to some authors, others require a level of TG > 1.24 mmol / l (110 mg / l) (6).

The etiologies of chyloperitoneum are multiple. Cirrhosis is the most common cause (7). Heart failure, retroperitoneal fibrosis, radiation therapy, nephrotic syndrome, pancreatitis, abdominal neoplasia (lymphoma), abdominal trauma, and some autoimmune diseases may also be the cause (7,8). The postoperative causes are dominated by the traumatic placement of the PD catheter which can induce an alteration of the lymphatic duct or one of its collaterals. It remains a rare etiology and can complicate 0.5% of catheter implantations (1.9). The predominant infectious causes are tuberculosis and filariasis, especially in developing countries (7). Tuberculosis has been reported to cause obstruction of lymphatic drainage from the intestine leading to rupture of the lymphatic duct (10).

In addition, certain drugs have been reported to cause chyloperitoneum (11). However, the latter

remains rare (12). Drugs most incriminated are the calcic inhibitors, mainly the dihydropyridinics and more rarely the non-dihydropyridinics (13,14). Some antibiotics, namely cefazoline, cefalotin have also been implicated in the occurrence of chyloperitoneum.

Chyloperitoneum secondary to calcic inhibitors was first described in 1993 by Yoshimoto who reported 5 cases in patients taking manidipine (15). The mechanism underlying the development of chyloperitoneum associated with calcium blockers probably involves impaired lymphatic functions in the removal of TG and increased ultrafiltration through the peritoneal membrane (16). Since manidipine and lercanidipine are highly lipophilic compared to amlodipine (17), they can easily penetrate the lipid bilayer of the cell membrane and act on calcium channels in smooth muscle cells of the intestine and lymphatic vessels (18,19). The peculiarity of our 1st observation is that manidipine had not been recently introduced. Therefore, the hypothesis put forward explaining the timing of this complication is that the concomitant use of ciprofloxacin known to be a CYP 3A4 inhibitor increased the serum bioavailability of manidipine which caused the development of chyloperitoneum. The outcome was favorable with disappearance of the chyloperitoneum upon discontinuation of manidipine.

The ratio of the occurrence of chylous peritonitis in patients taking lercanidipine varies according to the studies from 13 to 57% (20). Some authors have found that patients with chylous peritonitis secondary to lercanidipine have a hyperpermeable-type peritoneal membrane which could lead to the accumulation of lercanidipine in the peritoneal cavity and decrease lymphatic reabsorption (21). In addition, the presence of hypertriglyceridemia seems to favor the occurrence of chyloperitoneum in these patients. This hypertriglyceridemia could interact with the pharmacokinetics of lercanidipine (22). This is the case of our 3rd patient who had hypertriglyceridemia at 3.18 mmol / L.

For the 2nd patient, the damage of the lymph node tuberculosis in the abdominal lymphatic drainage system namely an increase in the size of the nodes or a lymph node fibrosis resulting as a result of tuberculous lymphadenitis, coupled with a meal rich in lipids favored such a complication as well as relapses. Indeed, the risk of developing chyloperitoneum seems to be related to the blood lipid profile (22). The outcome was favorable on a low fat diet.

Usually, treatment is primarily that of the causative agent (23). When these measures are exceeded, it may be useful to use octreotide / somatostatin analogues, surgical ligation, embolization, and transjugular intrahepatic portosystemic shunt in patients with cirrhosis or in post-traumatic chylous peritonitis where appropriate (7,24,25). In addition, optimizing nutrition through a strict medium-fat chain diet with reduced fat intake is helpful (26). The prognosis for chyloperitoneum is good and depends mainly on its etiology (4). Thus, the diagnostic procedure in front of a chylous fluid begins by quickly ruling out a peritoneal infection by carrying out a cytobacteriological examination of the dialysate fluid, then carrying out a complete pancreatic, inflammatory, lipid and infectious assessment, and finally abdominal imaging looking for an abdominal neoplasia. It is through questioning that we will look for traumatic causes, dietary errors or the drug origin which remain diagnoses of elimination.

CONCLUSION

Chyloperitoneum is a rare complication in PD. It could be favored by a diet enriched in lipids.

First of all, a good clinical examination, a study of the effluent dialysate fluid, an analysis of the current treatments as well as the potential interactions must be carried out, and above all, not to miss a neoplasia. A more comprehensive nutritional study could be of support, in particular in subjects at increased risk for PD. On the other hand, calcic-inhibitors, which is certainly a rare cause of chyloperitoneum, but their prescription in patients on PD requires more attention, especially if they are combined with other drugs that interfere with their metabolism.

ROLES OF THE CO-AUTHORS

Ikram Agrebi, and Najla Dammak designed the project; Hanen Abid and Salma Toumi did the writing; Khawla Kammoun, Soumaya Yaich, Mohamed Ben Hmida revised and corrected the text; Hanen Chaker, Beya Fendri and Fatma Mseddi provided data collection

CONFLICT OF INTEREST

The authors declare no conflict of interest for this article.

REFERENCES

1. Cheung CK, Khwaja A. Chylous ascites: an unusual complication of peritoneal dialysis. A case report and literature review. *Perit Dial Int.* 2008;28(3):229-31.
2. Kumar A, Mandavdhare HS, Rana SS, Gupta R, Sharma V. Chylous ascites due to idiopathic chronic pancreatitis managed with endoscopic stenting. *Clin Res Hepatol Gastroenterol.* 2018;42(2):e29-31.
3. Lizaola B, Bonder A, Trivedi HD, Tapper EB, Cardenas A. the diagnostic approach and current management of chylous ascites. *Aliment Pharmacol Ther.* 2017;46(9):816-24.
4. Pomeranz A, Reichenberg Y, Schurr D, Drukker A. Chyloperitoneum: A Rare Complication of Peritoneal Dialysis. *Perit Dial Int J Int Soc Perit Dial.* janv 1984;4(1):35-7.
5. Kim S, Yu YM, Kwon J, Yoo H, Jung SH, Lee E. Calcium Channel Blocker-Associated Chyloperitoneum in Patients Receiving Peritoneal Dialysis: A Systematic Review. *Int J Environ Res Public Health.* 2019;16(8):1333.
6. Campisi C, Bellini C, Eretta C, Zilli A, da Rin E, Davini D, et al. Diagnosis and management of primary chylous ascites. *J Vasc Surg.* 2006;43(6):1244-8.
7. Almakdisi T, Massoud S, Makdisi G. Lymphomas and chylous ascites: review of the literature. *The Oncologist.* 2005;10(8):632-5.
8. Kato A, Kohno S, Ohtake T, Takita T, Hirshida A. Chylous ascites in an adult patient with nephrotic syndrome due to membranous nephropathy. *Nephron.* 2001;89(3):361.
9. Falcon TG, Rodriguez-Carmona A, Fontán MP, Rivera CF, Bouza P, Lozano IR, et al. Complications of permanent catheter implantation for peritoneal dialysis: incidence and risk factors. *Adv Perit Dial.* 1994;10:206-206.
10. Jhittay PS, Wolverson RL, Wilson AO. Acute chylous peritonitis with associated intestinal tuberculosis. *J Pediatr Surg.* janv 1986;21(1):75-6.
11. Yoshimoto K, Saima S, Nakamura Y, Nakayama M, Kubo H, Kawaguchi Y, et al. Dihydropyridine type calcium channel blocker-induced turbid dialysate in patients undergoing peritoneal dialysis. *Clin Nephrol.* 1998;50(2):90-3.
12. Gaied H, Joseph M. Péritonite chyleuse secondaire à Lercanidipine. *Bull Dial À Domic.* 2018;1(1):43-6.
13. Eroglu E, Cirak A, Kocyigit I. Lercanidipine Induced Cloudy Effluent in a Patient with Peritoneal Dialysis. *Jour Ren Med.* 2017;1(2):10.

14. Ram R, Swarnalatha G, Pai BS, Rao CSS, Dakshinamurthy KV. Cloudy peritoneal fluid attributable to non-dihydropyridine calcium channel blocker. *Perit Dial Int.* 2012;32(1):110-1.
15. Yoshimoto K, Saima S, Echizen H, Nakamura Y, Ishizaki T. A drug-induced turbid peritoneal dialysate in five patients treated with continuous ambulatory peritoneal dialysis. *Clin Nephrol.* 1993;40(2):114-7.
16. Cárdenas A, Chopra S. Chylous ascites. *Am J Gastroenterol.* 2002;97(8):1896.
17. McKeage K, Scott LJ. Manidipine. *Drugs.* 2004;64(17):1923-40.
18. Betancourt-Castellanos L, Ponz-Clemente E, Otero-López MS, Blasco-Cabañas C, Marquina-Parra D, García-García M. Turbid acellular peritoneal fluid and the use of calcium antagonists in peritoneal dialysis. *Nefrología.* 2013;33(3):377-80.
19. Hsiao PJ, Lin HW, Sung CC, Wang CW, Chu P, Lin SH. Incidence and clinical course of lercanidipine-associated cloudy effluent in continuous ambulatory peritoneal dialysis. *Clin Nephrol.* 2010;74(3):217-22.
20. Topal C, Sayarlioglu H, Dogan E, Erkoç R, Soyoral Y. Cloudy dialysate due to lercanidipine. *Nephrol Dial Transplant Off Publ Eur Dial Transpl Assoc - Eur Ren Assoc.* oct 2006;21(10):2997-8.
21. Rampino T, Dal Canton A. Peritoneal dialysis and epithelial-to-mesenchymal transition. *N Engl J Med.* 15 mai 2003;348(20):2037-9; author reply 2037-2039.
22. Yang W-S, Huang J-W, Chen H-W, Tsai T-J, Wu K-D. Lercanidipine-induced chyloperitoneum in patients on peritoneal dialysis. *Perit Dial Int.* 1 nov 2008;28(6):632-6.
23. Apikotoa S, Wijesuriya R. Idiopathic acute chylous peritonitis during pregnancy, mimicking perforated acute appendicitis: A case report. *Int J Surg Case Rep.* 2021;81:105790.
24. Bhardwaj R, Vaziri H, Gautam A, Ballesteros E, Karimeddini D, Wu GY. Chylous ascites: a review of pathogenesis, diagnosis and treatment. *J Clin Transl Hepatol.* 2018;6(1):105.
25. Lopez-Gutierrez JC, Tovar JA. Chylothorax and chylous ascites: management and pitfalls. In: *Seminars in pediatric surgery.* Elsevier; 2014. p. 298-302.
26. Browse NL, Wilson NM, Russo F, Al-Hassan H, Allen DR. Aetiology and treatment of chylous ascites. *J Br Surg.* 1992;79(11):1145-50.

received 21/07/18 accepted after revision 21/08/21, published 21/09/15



Open Access This article is licensed under a Creative Commons Attribution 4.0 International

License, which permits use, sharing, adaptation, distribution and reproduction in any medium or format, as long as you give appropriate credit to the original author(s) and the source, provide a link to the Creative Commons license, and indicate if changes were made. The images or other third party material in this article are included in the article's Creative Commons license, unless indicated otherwise in a credit line to the material. If material is not included in the article's Creative Commons license and your intended use is not permitted by statutory regulation or exceeds the permitted use, you will need to obtain permission directly from the copyright holder. To view a copy of this license, visit <http://creativecommons.org/licenses/by/4.0/>.