CLINICAL MEETING SUMMARIES ON 18TH JANUARY 2018

A small leak will sink a great ship

Drs Steven TSENG and LY NG
Department of Medicine & Geriatrics
Kwong Wah Hospital

Case 1

A 68 years old Chinese retired male hairdresser with an 8 pack years smoking history. He has significant medical history of hyperlipidemia, hypertension, gout, pulmonary tuberculosis completed treatment over 20 years ago, and diabetes mellitus since 1990 complicated by retinopathy and nephropathy. His diabetic nephropathy deteriorated gradually and complicated by end stage renal failure in 2017. He was offered renal biopsy for confirmation of the underlying cause, but refused as diabetic nephropathy is the likely culprit. After renal assessment, he opted for continuous ambulatory peritoneal dialysis (CAPD).

Tenchkhoff catheter(TKC) was inserted on 22/6/2017, and intermittent peritoneal dialysis(IPD) started since 29/6/2017. He had 4 sessions of IPD that was well tolerated, and proceeded with CAPD training since 22/7/2017. He was then admitted on 25/7/2017 during CAPD training session when turbid peritoneal fluid was noted. Upon admission, he complained of of breathlessness and his oxygen saturation was marginal. Chest x-ray (CXR) shows a new onset right sided pleural effusion. Peritoneal dialysis was terminated, and a diagnostic pleural aspirate yielded a transudative effusion (Total protein 1.4g/L, LDH 36 IU/L) with high pleural fluid:serum glucose gradient (27.9 : 9.2 mmol/L). A diagnosis of hydrothorax secondary to peritoneal dialysis was made.

Further IPD was attempted but poor ultrafiltration achieved and CXR shows worsening right sided effusion despite small volume of dialysate used. Thus, peritoneal dialysis was terminated. He had satisfactory urine output on oral diuretics, clinically not in fluid overload, and blood results did not reveal significant metabolic acidosis or hyperkalemia, and no urgency for dialysis was necessary at that juncture.

His condition was reviewed after 4 weeks of resting his abdomen from peritoneal dialysis. IPD was repeated on 31/8/2017 as CXR shows complete resolution of right sided effusion. However, ultrafiltration remains poor despite increasing tonicity and an abdominal X-ray confirms correct positioning of TKC. Repeated CXR with clinical correlation shows recurrence of right hydrothorax after resuming peritoneal dialysis.

Collaborated discussion between renal team, respiratory team and patient

regarding management plan included the following

1. *Repeat interruption of peritoneal dialysis* and retry 4 weeks later, but declined by patient as previous resting still resulted in recurrence of hydrothorax
2. Other means of *renal replacement therapy*, but limited availability for hemodialysis at local center and even less for pre-emptive renal transplantation
3. Referral to *cardiothoracic surgeons* for further management, declined by patient due to general anesthetic risk and lack of in-house cardiothoracic support
4. *Conventional chest drain insertion and chemical pleurodesis*, decided against as success rate from literature review not appealing, and may preclude further intervention due to adhesions
5. *Medical Pleuroscopy*, despite limited literature, may identify diaphragmatic defect, and talc poudrage may offer better success rate than conventional pleurodesis.

After thorough consideration, patient opted for medical pleuroscopy which was performed on 29/9/2017. Prior to pleuroscopy, 10ml 1% Methylene blue was diluted into 2litres of peritoneal dialysate fluid and instilled into peritoneum through TKC. During pleuroscopy, approximately 1 liter of greenish pleural fluid was drained (Image 1).

Image 1. Pleural fluid stained green after instillation of methylene blue stained PD fluid to peritoneum

Inspection of right hemi-diaphragm did not reveal any pleural mass or large diaphragmatic defect, and no active leakage of greenish fluid was noted during procedure. A tiny suspicious diaphragmatic pore was located over dome of hemi-diaphragm with a droplet of fluid adjacent to it (Image 2&3).

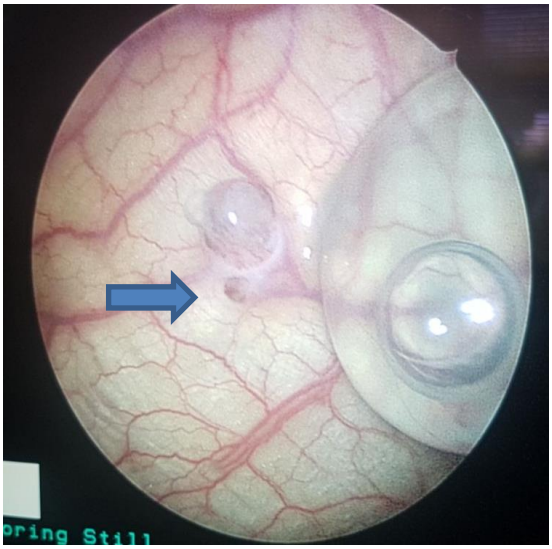

Image 2 A suspicious pore over dome of hemi-diaphragm with a droplet of fluid adjacent to it

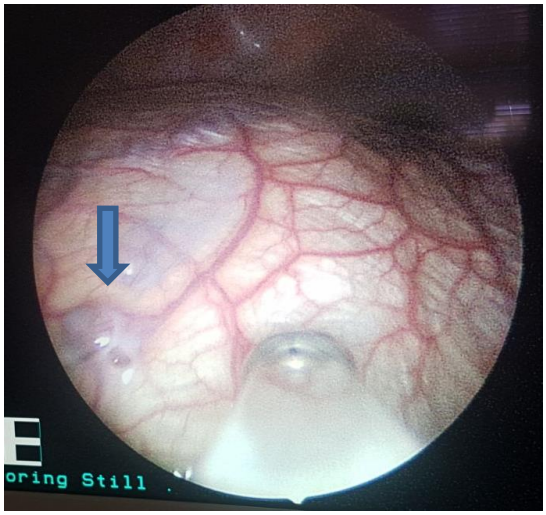

Image 3 Suspicious pore with adjacent droplet removed

Talc poudrage with 4g talc performed with adequate distribution particularly over the above suspicious area confirmed by thoracoscopic visualization. Post-procedure chest drain was removed few days later, and abdomen was rested for over 4 weeks.

Upon follow up, CXR was clear and IPD was restarted on 10/11/2017 with gradually increased volume and no recurrence of pleural effusion noted on serial CXR. CAPD was then restarted on 30/11/2017 with good ultrafiltration. Unfortunately, he presented on 9/12/17 with dyspnea and poor ultrafiltration. CXR on admission shows recurrence of pleural effusion. Diagnostic aspirate yielded a transudative effusion with a high fluid:serum glucose gradient (24.9:13.4 mmol/L).

After another thorough discussion, long term hemodialysis was offered and accepted by patient. Serial follow up CXR shows no recurrence of R pleural effusion.

Case 2

A 53 years old Vietnamese male freelance construction site worker, with a 15 pack year smoking history. He has a background history of hypertension, hyperlipidemia, and diabetes mellitus, complicated by renal impairment since 2010 and eventual resulted in end-stage renal failure in 2013. During initial renal assessment, he refused renal biopsy and renal replacement therapy as he preferred conservative management.

However, he was admitted in early Feb 2014 with fluid overload. CXR shows right sided effusion, and diagnostic pleural aspirate yielded a transudative effusion (Total protein 3.7g/L, LDH 40IU/L). He was treated with diuretics and responded clinically to treatment, serial CXR shows reduced right effusion. Nonetheless, in view of progression of symptoms, patient opted for continuous ambulatory peritoneal dialysis(CAPD).

Tenchkhoff catheter(TKC) insertion was arranged on 20/3/2017, pre-procedure CXR shows small amount of right pleural effusion and diuretics was again given as patient was in fluid overload state, with

repeated CXR showing reduced right effusion. Intermittent peritoneal dialysis(IPD) done on 24-25/4/2014, with an acceptable negative ultrafiltration. However, CXR shows a persistent right sided effusion, and repeat diagnostic aspirate was offered but refused by patient initially, but subsequently agreed and done on 27/3/2014, 2 days after last cycle of peritoneal dialysis. Analysis of pleural fluid reveals a transudative effusion (Total protein 2.3g/L, LDH 26IU/L) and Fluid:Serum Glucose gradient (10.5 : 15.5 mmol/L) not suggestive of peritoneal leak at that juncture likely due to the delay of pleural aspirate 2 days after last cycle of peritoneal dialysis. He requested early discharge when symptoms improved. He was readmitted on 31/3/2014 for further IPD, and pre-IPD CXR shows resolved pleural effusion. After few cycles of IPD, positive ultrafiltration was noted and CXR shows accumulation of pleural fluid. Trial of interruption of IPD was done which revealed resolved effusion, and recurred when IPD resumed.

Joint discussion between renal team, respiratory team and patient was similar to case 1, and medical pleuroscopy was performed on 12/5/2014. No obvious diaphragmatic defect detected during procedure, and talc poudrage insufflated for chemical pleurodesis.

Peritoneal dialysis was withheld for over 4 weeks, and retrial of IPD on 9/6/2014 was smooth, followed by CAPD in late 6/2014 which was well tolerated and serial CXR shows clear lung field. He was able to continue with CAPD smoothly until 5/2017, with no recurrence of pleural effusion all along. Unfortunately, he expired abruptly in mid-2017 with an out-of-hospital cardiac arrest.

Discussion

Introduction

The above two cases underline an uncommon but well recognized complication of continues ambulatory peritoneal dialysis(CAPD). First described in 1967, hydrothorax related to CAPD is due to migration of fluid from the peritoneal cavity into the pleural space via pleuroperitoneal communication, thus also known as "Porous Diaphragm Syndrome".[1] Diagnosis is usually made clinically, with a high index of suspicion, particularly with temporal relationship to initiation of peritoneal dialysis, combined with a pleural analysis occasionally supplemented by radiological imaging.

Epidemiology

Hydrothorax related to continuous ambulatory peritoneal dialysis has a reported incidence ranging from 1.6-6%, generally presenting within 30days of initiating peritoneal dialysis.[2,3] It is usually right sided, with a female predominance of 61%.[4] Dyspnea is the most common presenting symptom. Pleuritic pain and incomplete recovery of fluid from peritoneal catheter with impaired CAPD performance are less common. Up to 25% of patients may be asymptomatic.[5]

Pathogenesis

Hydrothorax related to CAPD is proposed to be the result of a disruption of a congenital diaphragmatic defect, as suggested by autopsy and operative observation of diaphragmatic fluid-filled blebs overlying a tendinous diaphragm discontinuities caused by collagen fiber loss. Tsunezuka et al. performed a VATS

resection of pleuroperitoneal communication. Histologically, the resected diaphragm was lacking in common tissue, tendons, skeletal muscle tissues and was displaced by fibrous connective tissue, which suggested it was a congenital diaphragmatic defect. Negative pressure in the pleural cavity and positive pressure in the peritoneal cavity promote the transfer of dialysate from the abdomen to the chest.[6] The theory of congenital diaphragmatic defect explains the preponderance of right-sided hydrothorax because left-sided defects as such are covered by the heart and pericardium, thereby protecting against the leak.

Acquired diaphragmatic defect was suggested by Gagnon et al. An autopsy of a patient with right hydrothorax showed marked diaphragmatic involvement of systemic amyloidosis resulting in the pleuroperitoneal communication in a patient with history of adjuvant chemotherapy for ovarian cancer.[7]

Regardless of the nature of the defect, coughing and straining could be contributing factors to pleural defects. The intra-abdominal pressure reaches 120–150 cm H2O when coughing or straining, compared to 0.5–2.2 cm H2O under normal circumstances, whereas the pressure in patients with peritoneal fluid is between 2–10 cm H2O.[8]

Prognostic indicators

Female gender, polycystic kidney disease, and early leak defined as hydrothorax within 30 days of catheter insertion, are all associated with a less favorable success rate of long-term peritoneal dialysis.[9]

Diagnosis

Pleural fluid analysis

Pleural fluid analysis typically reveals a transudative effusion. However, a simultaneously obtained peritoneal and pleural fluid usually only show concordance in protein content (consistently<4 g/l). While fluid glucose and lactate dehydrogenase levels were not comparable, ratio of pleural fluid to serum glucose is dynamic, and varies depending on the type of fluid instilled, the volume and the contact time.[10] As in case 2 above, the pleural fluid glucose level was much lower than expected as it was aspirated 2 days after last cycle of dialysis.

Chow et al. evaluated seven consecutive cases of hydrothorax secondary to pleuroperitoneal communication, and the absolute values of pleural fluid glucose level was higher than control cases (243±29 vs 149±21 mg/dL, P=0.017), but no cutoff level could reliably distinguish the two groups. Therefore, the pleural fluid-to-serum glucose concentration gradient of greater than 2.77 mmol/L (50 mg/dl) was proposed as the cut-off to diagnose the pleuroperitoneal communication.[11]

Momentin N et al. evaluated 45 cases from literature and suggested that glucose concentration gradient >2mg/dL or a pleural fluid-to-serum(PF/S) glucose ratio >1 have a sensitivity of 100%.[5]

Imaging

Radiological investigations can be utilized to demonstrate pleuroperitoneal communication if diagnostic uncertainties remain after pleural fluid analysis. CT Peritoneography, the intraperitoneal infusion of contrast material through the catheter with subsequent computed tomography, has a reported sensitivity of approximately 33%.[12]

Alternatively, the intraperitoneal infusion

of a radioisotope (technetium-tagged macroaggregated albumin) followed by peritoneal scintigraphy, has a reported sensitivity of approximately 40-50%. [13,14]

Thoracoscopy

Diaphragmatic defects can occasionally be directly visualized during thoracoscopy. Additional maneuvers may be attempted to encourage this illustration. Instillation of colored dialysis fluid into peritoneal cavity, either 5 ml 1% methylene blue or 10 ml of indocyanine green,[15] was demonstrated in Case 1 above. Another "check-air-leak" method, by continuous carbon dioxide inflation via peritoneal catheter while observing for continuous air bubbles if a defect exists.[16]

Treatment

Currently, there are no guidelines or standard of care for hydrothorax in patients on peritoneal dialysis(PD). There are a few case series reported but no comparative controlled trials comparing different treatment strategies available.

Interruption of peritoneal dialysis

Considered as first line of treatment, peritoneal dialysis should first be withheld to permit spontaneous resolution of hydrothorax and diaphragmatic connection. Peritoneal dialysate is hypothesized to act as a sclerosant and allows a spontaneous seal of the pleuroperitoneal communications in some patients. In a systemic review of case series by Chow et al., resuming long-term CAPD was successful after temporary discontinuation of PD in 24 of the 45 patients (53%).[9]

In general, interruption of CAPD for a period of 2 weeks to 4 months is considered as first line treatment. During this period, patients may require conversion to temporary hemodialysis. Therapeutic thoracocentesis is only indicated for acute or persistent symptoms, and PD should be reintroduced gradually with low-volume exchanges

Conventional Pleurodesis

Chemical pleurodesis is generally the next step if conservative treatment failed. Sclerosing agents including talc, tetracycline, doxycycline, and autologous blood may be used, although no randomized study data support one agent over another. Following chemical pleurodesis, patients should wait at least 10 days before recommencing PD to allow time for sufficient scar formation over defect. The likelihood of successfully resuming PD following chemical pleurodesis is ~ 50%. [9]

Surgical Intervention

Surgical thoracotomy enables identification of diaphragmatic defects, allowing repair with or without reinforcement with patches and pleurodesis in the form of pleurectomy or mechanical abrasion. All cases undergoing open thoracotomy as reported in literature were able to resume CAPD.[5,9]

In 1996, Di Biseglie et al. reported the usefulness of Video-assisted thoracoscopic surgery (VATS) in obliteration of pleuroperitoneal fistula in CAPD.[17] Since then, the advantages of VATS over conventional thoracotomy have been increasingly recognized. Surgical pleurectomy, mechanical abrasion and pleurodesis, chemical pleurodesis, and diaphragmatic patching/closure of the diaphragmatic defects can also be performed by VATS.[18] Systematic review of published literature by Chow et al. resuming long-term CAPD was successful

after VATS pleurodesis in 15 of the 17 patients (88%)[9]

Medical Pleuroscopy

Literature on application of medical pleuroscopy in hydrothorax complicating peritoneal dialysis is extremely limited, and its role in managing these case is yet to be determined. In selected cases, it may be a suitable alternative to surgery. From our limited experience, pleuroscopy with talc insufflation may allow continuation of peritoneal dialysis without complications, particularly if no major defect identified during procedure.

Summary

Hydrothorax complicating peritoneal dialysis is an uncommon but well recognized complication of continuous ambulatory peritoneal dialysis. Diagnosis is from clinical suspicion with temporal relation to initiation of peritoneal dialysis, as well as pleural fluid demonstrating a transudative effusion with an elevated fluid to serum glucose gradient. Initial treatment should be interruption of peritoneal dialysis. Conventional pleurodesis offers a similar success rate as resting the abdomen, and surgical intervention may achieve a near 100% success rate of continuing with peritoneal dialysis. For those who fail conservative management but are not a surgical candidate, conversion to other means of renal replacement therapy may be necessary. The role of medical pleuroscopy is yet to be determined in this disease entity, although it may be viable option of management in selected cases.

Reference:

1. Edward SR, Unger AM: Acute hydrothorax-a new complication of peritoneal dialysis. *JAMA*199:853-855,1967

2. Nomoto Y Et al. Acute hydrothorax in continuous ambulatory peritoneal dialysis-a collaborative study of 161 centers. *Am J Nephrol* 1989;9:363-7

3. Van Dijk CM et al. Patient characteristics associated with defects of the peritoneal cavity boundary. *Perit. Dial Int* 2005;25:367-73

4. Szeto CC, Chow KM. Pathogenesis and management of hydrothorax complicating peritoneal dialysis. *Curr Opin Pulm Med* 2004;10:315-19

5. Momentin N Et al. Low pleural fluid-to-serum glucose gradient indicates pleuroperitoneal communication in peritoneal dialysis patients: presentation of two cases and a review of the literature. Nephrol Dial Transplant 2012, v27:1212-1219

6. Tsunezuka Y Et al. Video-assisted thoracoscopic treatment for pleuroperitoneal communication in peritoneal dialysis. *Eur J Cardiothorac Surg* 2001,20:205-207

7. Gagnon RF et al. Systemic amyloidosis involving the diaphragm and acute massive hydrothorax during peritoneal dialysis. *Clin Nephrol* 2002,57:474-479

8. Tian Xu et al. Peritoneal-Pleural Leaks Demonstrated by CT Peritoneography . Case Rep Nephrol Dial 2015; 5:135-139

9. Chow KM et al. Management options for Hydrothorax Complicating Peritoneal Dialysis. Seminars in Dialysis 2003. v16:5 p389-394

10. Tang S Et al. Video-assisted thoracoscopic talc pleurodesis in effective for maintenance of peritoneal dialysis in acute hydrothorax complicating peritoneal dialysis. Nephrol Dial Transplant. 2003, 18: 804-808.

11. Chow KM et al. Hydrothorax complicating peritoneal dialysis: diagnostic

value of glucose concentration in pleural fluid aspirate. *Perit Dial Int* 2002,22:525-528

12. T. W. Kang et al. Pleuroperitoneal communication of peritoneal dialysis demonstrated by multi-detector-row CT peritoneography. *Abdominal Imaging 2009:* v34; 6:780– 782.

13. H. Tokmak et al. The role of peritoneal scintigraphy in the detection of continuous ambulatory peritoneal dialysis complications. *Renal Failure 2006:* v28, no. 8:709–713.

14. K. Nishiyama et al. SPECT/CT to diagnose pleuroperitoneal communication-associated hydrothorax in peritoneal dialysis. *Kidney International 2015: v87:866*

15. H. Kumagai et al. Simple surgical treatment for pleuroperitoneal communication without interruption of continuous ambulatory peritoneal dialysis. Gen Thorac Cardiovasc Surg 2007 v55:508–511

16. Hsu-Ting Yen Et al. Video-assisted thoracoscopic surgery for hydrothorax in peritoneal dialysis patients – check air-leakage method. *European Journal of Cardio-thoracic Surgery 2005;28: 648-649*

17. De Bisceglie M Et al. Video-thoracoscopic obliteration of pleuroperitoneal fistula in continuous ambulatory peritoneal dialysis. *Ann Thorac Surg* 1996; 62:1509-10

18. Yaxley J Et al. Peritoneal Dialysis Complicated by Pleuroperitoneal Communication and Hydrothorax. Ochsner Journal 2017. 17:124–127