Pericardial Effusion Due to Tuberculosis in a Peritoneal Dialysis Patient: A Case Study

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KEYWORDS

Pericardial effusion, CKD stage 5, CAPD, Tuberculosis

ABSTRACT

Pericardial effusion in CAPD patients is a rare complication, often caused by viral infections, tuberculosis, autoimmune diseases, chronic kidney disease, and malignancy. In Indonesia, a tuberculosis-endemic country, pericardial effusion due to tuberculosis should be considered. It can be aggravated by uremic conditions and can be life-threatening if cardiac tamponade occurs. A 31-year-old man with CKD stage 5 on CAPD and massive pericardial effusion due to tuberculosis was diagnosed. The clinical outcome showed improvement with pericardiocentesis, intensive hemodialysis, and anti-tuberculosis therapy with dose adjustment. The patient's pericardial effusion was due to a delayed hypersensitivity response to tuberculoprotein mycobacterium tuberculosis. Treatment with pericardiocentesis, dose adjustment for antituberculosis treatment, and reducing uremic conditions can prevent tamponade and recurrent pericardial effusion.

Introduction

The pericardium is the membrane encasing the heart, comprising visceral and parietal layers. Under typical conditions, the pericardial cavity holds 15 to 50 cc of ultrafiltered plasma. Pericardial effusion is characterized by an abnormal buildup of fluid in the pericardial cavity that surpasses 50 mL [(1)]. Pericardial effusion impacts approximately 19–35% of individuals with end-stage renal disease (ESRD). Chronic massive pericardial effusion is uncommon, with an incidence of 2-3.5% among all pericardial effusions. The prevalence of cardiac tamponade in the United States is 2 cases per 10,000 individuals [(2)].

The etiologies of pericardial effusion include infections (viral, bacterial, particularly mycobacterium tuberculosis), neoplasms, connective tissue disorders, pericardial injury syndromes, metabolic conditions (e.g., hypothyroidism), myocardial pericardial diseases (pericarditis, myocarditis, and heart failure), uremia, and idiopathic pericardial effusion [(3)]. The first issue for the doctor is to determine the etiological diagnosis of the pericardial effusion. Pericardial effusion can often be linked to a recognized underlying condition, such as acute myocardial infarction, cardiac surgery,

end-stage renal disease, or extensive metastatic neoplasm. However, epidemiological factors are significant; in developed nations, acute idiopathic pericarditis and idiopathic pericardial effusion are the predominant causes, whereas in developing countries, tuberculous pericarditis is the primary cause of pericardial effusion [(4)].

The incidence of end-stage renal illness is rising globally. Consequently, related problems such as uremic pericarditis and pericardial effusion are also on the rise. Despite the reduction in uremic pericarditis incidence to less than 5%, asymptomatic pericardial effusion may remain undetected until it becomes sufficiently severe to impact the patient's hemodynamics [(5)]. This case involves a peritoneal dialysis patient who experienced significant pericardial effusion due to TB and uremic circumstances.

Case

A 31-year-old man came with a chief complaint of shortness of breath; the patient complained that the shortness felt since the last 3 months was getting worse; the patient complained of shortness once in the last 3 days. The patient sleeps using two pillows and gets worse when sleeping on his side and half sitting. Low-grade fever is felt to be lost and arises for the last 3 months. The patient complained of coughing sometimes, coughing up phlegm for the past week, and white sputum. There is no complaint of coughing up blood in the patient. The patient felt weak a few days before admission and had decreased appetite a few days before admission.

History of past diseases: history of HT (+) 5 years ago, rarely took medicine, history of CKD (+) since 5 years ago, with Continuous Ambulatory Peritoneal Dialysis (CAPD) since 5 years ago, said that until now the access is smooth, no seepage, no abdominal pain, no diarrhea, and no nausea. Patients routinely take CAPD fluids without control facing the doctor; the last 1 month of UF from CAPD averaged 100 cc/day DOE +, orthopneu +. History of Diabetes (-), History of Stroke (-), History of medication taken: Amlodipine. The patient is currently taking Amlodipine 1 x 10 mg, Clonidine 1 x 0.15 mg, $CaCO_2$ 2 x 1, and folate acid 2 x 1 tablets. Lung infection, hepatitis B, hepatitis C, and HIV are unknown.

On physical examination, the patient was fully conscious (GCS E4V5M6) and vital signs were obtained; Blood pressure 160/70 mmHg, pulse 110 x/minute regular, respiratory rate 28 x/minute regular, SpO_2 98% nasal cannula 3 lpm, axial temperature 36.2°C. Body mass index: kg/m² (BW: 63 kg, body height: 169 cm). Appearance is anemic, JVP is elevated, and inspection of the thorax wall appears symmetrical. On palpation, the icus cordis was not palpable. Percussion of the heart borders was difficult to evaluate. On auscultation, heart sounds were obtained away from single heart sounds, with no murmurs or gallops. Auscultation of the lungs obtained decreased breath sounds, no rales, or wheezing. Inspection of the abdomen: there is no distension, no mass palpable, supple, no epigastric tenderness, no hepatosplenomegaly, and the condition of the CAPD exit site is good; there is no sign of infection or discharge. Extremities were warm, dry, and pale with no edema.

Laboratory examination results showed Hb 8.6 g/dL, RBC 2.86 × 109 /L, HCT 27.4%, MCV 95.8 fL, MCH 30.1 pg, MCHC 31.4 g/dL, WBC 8.63 /µL (Eos% 0.6, Bas% 0.5, Neu% 82.7%, Lim% 8.2, Mon% 8.0), PLT 309 × 103/µL, BUN 39.1 mg/dL, serum creatinine 15.3 mg/dL, eGFR 4 ml/min/1.73 m², sodium 137 mmol/L, potassium 3.4 mmol/L, chloride 97 mmol/L; SGOT 27 U/L, SGPT 16 U/L, serum albumin 3.72 mg/dL. Thoracic X-ray examination: The bilateral pleural effusion is difficult to evaluate. ECG obtained low QRS voltage.

Echocardiography showed massive pericardial effusion was found at anterior 3.8 cm, posterior 3.0 cm, and inferior 3.3 cm. Basal: 2.4 cm. The left lateral is 49 cm.

The right lateral measures 6.0 cm. The apical region measures 4.5 cm. 12. There are signs of RA/RV collapse (RAITI 45%, Mitral Respirophashic 32%, Tricuspid Respirophasic 48%). Hemodynamic Parameters PCWP: 7.95 mmHg SVR: 1041 dynes.sec/cm5 mPAP: 27.7 mmHg PVR: 253.4 dynes.sec/cm5 LVC0: 6.17 L/min LVCI: 3.43 L/min/m² LVOT VTI: 18.6 cm IVC expiration: 2.3 cm IVC inspiration: 1.7 cm Est RAP: 15 mmHg BP: 115/75 mmHg HR 108 bpm Support: none Conclusion: Massive pericardial effusion, LV concentric remodeling.

The working diagnosis for the patient is pericardial effusion with impending tamponade, pleural effusion, ESRD on CAPD (BUN 39.1, SK 15.3), and micrositer hypochromic anemia (Hb 8.6).

On the first day of treatment, the diagnosis of massive pericardial effusion with impending tamponade, severe uncontrolled hypertension, and end-stage renal disease (on CAPD), the patient was planned for hemodialysis with vascular access, but the patient refused, so CAPD was continued. The therapy given was an infusion of normal saline 250 cc/24 hours drinking max 1000 ml/day, pump nicardipine 0.5 mic/kg bw/min titration every 15-30 minutes, Adalat Oros 1x30 mg, performed pericardiocentesis installed pigtail out serohemorrhagic fluid: 500 cc, taping at 00.00 am: 120 cc, taping at 06.00: 100 cc total taping 720/12 hours taping pericard effusion every 6 hours. On the second day, pericardial fluid analysis results were obtained: pH 8, WBC 3.874, RBC 0.613, MN 94.7%, PMN 5.3%, GLU 84.5, cell count (pericard) 3,892, protein 4.97, LDH 609 U/L, ADA 64.5 U/L. Pleural pigtail insertion, pleural fluid analysis, planning: TCM sputum Mtb, TCM pericard fluid Mtb, OAT therapy: Rifampicin tablets 600 mg every 24 hours, Isoniazid tablets 300 mg every 24 hours, Etambutol 1000 mg three times/week, and Pyrazinamide 1250 mg three times/week, pleural fluid evacuation if clinically aggravated. On the third day, fluid balances: input 600 cc/24 hr, output 2200/24 hr, balances -1600 cc/24 hr, taping at 17.00: 500 cc, 5 am: 500 cc total taping 1720 cc/38 hours. Pleural fluid analysis results obtained pH 8, WBC 0.129, RBC 0.014, PMN 13.9%, MN 86.1%, Glu 153, Prot 2.27, LDH 204.62, pleural evacuation 800 cc. On the fourth day, fluid balances: input 400 cc/24 hours, output 2135/24 hours balances -1735 cc/24 hours. Taping at 17.00: 560 cc, at 05.00: 525 cc total taping 2805 cc/60 hours, pleural drain 1000 cc/24 hours, ultrafiltration CAPD 50 cc.

The patient's condition improved from day 5 to day 9. Average pericardial fluid tapping is 300-400 cc/24 hours, average pleural fluid tapping is 500-750 cc/24 hours, and average CAPD ultrafiltration is 50-100 cc/24 hours. The patient's condition is still shortness of breath. On day 10, the patient was planned for regular hemodialysis 3 times a week with the consideration that CAPD was not effective. First hemodialysis: 2.5 hours, QB 125-150 QD, 500 dialysate bicarbonate, heparin, minimum UF 2000 ml. On day 12, hemodialysis 3 hours QB 125-150 QD 500 dialysate bicarbonate heparin minimum UF 2000 ml. Pericardial fluid taping (100 cc/24 hours) and pleural fluid taping (150 cc/24 hours).

On day 14, hemodialysis 5 hours, QB 125–150, QD 500 dialysate bicarbonate heparin, minimal UF 2000 mL. Pericardial fluid taping: 40 cc/24 hours; pleural fluid taping: 50 cc/24 hours. On day 16, hemodialysis 5 hours QB 125-150 QD. The minimum amount of dialysate, bicarbonate, and heparin required is UF 2000 ml. Pericardial fluid taping 4 cc/24 hours pleural fluid taping 4 cc/24 hours. On Day 17, we removed the pericardial and pleural pigtails and observed complaints of tightness and bleeding. On day 17, the patient was discharged and underwent regular outpatient HD.

Discussion

The patient is in stage 5 CKD, on CAPD for 5 years, with a history of hypertension. Symptoms include shortness of breath and difficulty breathing during activity and lying down. CAPD access, no leakage or abdominal pain. Vital signs show blood pressure at 160/70 mmHg, pulse 110 bpm, respiratory rate 28 x/min, elevated JVP, and non-palpable ictus cordis. Lung auscultation reveals decreased breath sounds, distant heart sounds, and low QRS voltage on ECG. Lab results: Hb 8.6 g/dL, BUN 39.1 mg/dL, serum creatinine 15.3 mg/dL, serum albumin 3.72 g/dL. X-ray shows bilateral pleural effusions and double contours, while echocardiography reveals a massive pericardial effusion with RA/RV collapse. The patient was diagnosed with massive pericardial effusion with impending tamponade and underwent pericardiocentesis with pigtail insertion.

The clinical manifestations of pericardial effusion encompass dyspnea upon exertion, a sensation of chest fullness, orthopnea, and chest pain in the presence of pericarditis. In tamponade, Beck's triad (hypotension, elevated jugular venous pressure, and muffled heart sounds) accompanied by tachycardia and pulsus paradoxus is characteristic. The preliminary assessment includes medical history, clinical examination, electrocardiogram, blood analyses, chest radiography, and echocardiography. A chest X-ray may reveal an enlarged heart silhouette in mild effusions above 300 ml. The sensitivity of ECG is diminished, frequently exhibiting reduced QRS voltage. Pericardial effusion is categorized by severity: mild (<100 ml), moderate (100-500 ml), and severe (>500 ml) as determined by echocardiography [1,2].

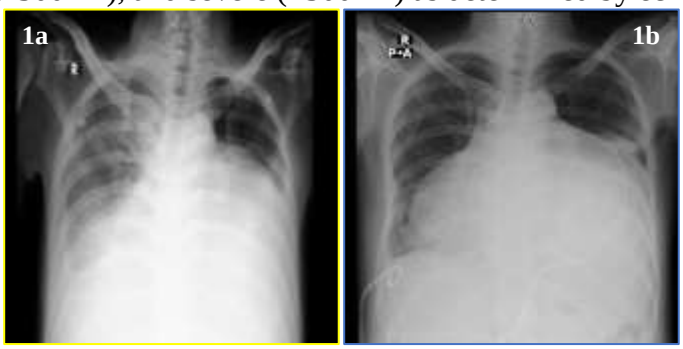

Fig. 1 Chest x-rays that show: (a) The chest X-ray shows a normal appearance of the right lung; (b) the chest X-ray reveals an installed pigtail in the thoracic cavity the chest X-ray shows a normal appearance of the right lung.

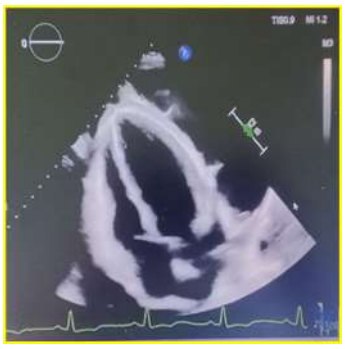

Fig. 2 Massive pericardial effusion RA/RV collapse

In this patient, after the pericardial fluid analysis examination, the results of the pericardial fluid analysis of serohemorrhagic fluid pH 8, WBC 3.874, RBC 0.613, MN

94.7%, PMN 5.3%, GLU 84.5, cell count (pericard) 3,892, protein 4.97, LDH 609U/L, ADA 64.5U/L

Fig. 3 An electrocardiogram (ECG) recording that displays the heart rhythm with some abnormalities in the rhythm, which may indicate a disturbance in the conduction system of the heart.

Fig. 4 A Syringe containing blood collected for pericardial effusion testing.

The primary problem for clinicians is determining the etiology of pericardial effusion. It is frequently associated with illnesses such as myocardial infarction, cardiac surgery, renal disease, or metastatic cancer. Epidemiology is essential, as idiopathic pericarditis and idiopathic pericardial effusion are prevalent in affluent nations, but tuberculous pericarditis is a predominant cause in certain developing areas [(4)]. Pathological pericardial effusions can contain transudative, exudative, hemorrhagic, sanguineous, or chylous (milky) fluid. Transudative effusions result from reactive processes like uremia or inflammation, while exudative effusions are typically due to malignancy, infection (pyopericardium), or trauma-related hemopericardium. Hemorrhagic effusions are commonly caused by tumors, tuberculosis, heart rupture, or trauma. Light's criteria, with 98% sensitivity and 72% specificity, classify an effusion as exudative if at least one of the following is met: fluid protein/serum protein ratio > 0.5, fluid LDH/serum LDH ratio > 0.6, or fluid LDH activity > 200 U/L, or 2/3 of the upper limit of serum LDH [(2)]. Effusion biomarkers to detect Mycobacterium tuberculosis (M.Tb)-induced inflammation, such as adenosine deaminase (ADA), are helpful biomarkers for the diagnosis of TB effusion [(6)]. Measurement of ADA in effusion is a rapid and accurate method for diagnosing tuberculous pericardial effusion, with a reported diagnostic efficiency of 83% to 100%, sensitivity of 89% to 100%, and specificity of 74% to 100% [(7)].

Table 1. Laboratory examination of pericardial fluid [2].

Analysis	Test	Etiology
Blood chemistry	Specific gravity >1,015, protein level >3 g/dL, fluid protein/serum ratio >0.5, LDH >200 mg/dL, fluid/serum ratio >0.6, glucose, blood cell counts	Exudates
Cytology	Cytology (higher volumes of fluid, centrifugation, and rapid analysis improve diagnostic yield)	Cancer
Biomarkers	Tumor Markers (i.e. CEA >5 ng/mL or CYFRA 21-1 >100 ng/mL) Adenosine deaminase >40 U/L, IFN-gamma	Cancer
Polymerase chain reaction	Polymerase chain reaction (PCR) for specific infection agents (e.g. TB)	TB
Microbiology	Acid-fast bacilli painting, mycobacterium culture, aerobic, and anaerobic culture	TB, Other bacteria aerobic, and anaerobic cultures

The link between TB and CKD has been recognized for over 40 years, though how they interact remains unclear. People with CKD have a higher risk of developing active TB after infection with Mycobacterium tuberculosis. Immune deficiency in uremic conditions increases the risk of TB by 6.9 to 52.5 times compared to the general population [8,9]. This is due to systemic inflammation and immune dysfunction caused by uremic toxins. Demographic, socio-economic factors, and comorbidities also raise the risk of TB infection in CKD patients [10,11].

Dysfunction of the immune response in CKD occurs through several mechanisms, including oxidative stress and systemic inflammation, decreased phagocytic activity of granulocytes and monocytes/macrophages, impaired antigen presentation capacity by dendritic cells, decreased production of B cells and natural killer (NK) cells, increased apoptosis of T cells, and impaired cellular-based immune system dominated by CD8 cells [9,12,13]. Vitamin D deficiency and malnutrition also lead to suboptimal activation of monocytes and macrophages. These changes in the immune system begin to occur as early as stage 3 CKD and will worsen as advanced toxic metabolites accumulate. The higher the stage of CKD, the higher the risk of developing TB [14,15].

The management in this patient was pericardiocentesis, administration of anti-tuberculosis drugs with dose adjustment, and intensive hemodialysis because CAPD was not effective (ultrafiltration during treatment 100-200 cc/24 hours). The first-line OAT regimen was given in the form of discharges, namely, rifampicin tablets 600 mg every 24 hours, isoniazid tablets 300 mg every 24 hours, etambutol tablets 1000 mg 3x/week, and pyrazinamide tablets 1250 mg 3x/week.

The 2015 ESC Guidelines on Pericardial Disease propose a straightforward diagnostic criteria for patients with pericardial effusion, which determines therapy based on the evaluation of etiology, clinical presentation, and imaging findings, resulting in a cumulative score. A score of 6 or higher necessitates immediate pericardiocentesis, whereas a score below 6 allows for a wait of 12 to 48 hours for patient transfer to a specialist referral center. The catheter must be retained as long as the drainage volume exceeds 25 mL per day (Table 2) [1,2].

Table 2. The 2015 ESC Guidelines on Pericardial Disease recommends

		Score
Etiology	Malignant disease	2
	Tuberculosis	2
	Recent radiotherapy	1
	Recent infection	1
	Recurrent pericardial effusion, previous pericardiocentesis	1
	Chronic terminal renal failure	1
	Immunodeficiency or immunosuppression	1
	Hyper- or hypothyroidism	-1
	Systemic autoimmune disease	-1
Clinical Presentation	Orthopnea without rales on lung auscultation	3
	Rapid worsening of symptoms	2
	Pulsus paradoxus > 10 mmHg	2
	Oliguria	1
	Progressive tachycardia without an alternative apparent reason	1
	Dyspnea/tachypnea	1
	Pericardial friction rub	0.5
	Pericardial chest pain	0.5
	Hypotension (Systolic BP < 95 mmHg)	0.5
Imaging	Slow evolution of the disease	-1
	Circumferential pericardial effusion (> 2 cm in diastole)	3
	Left atrial collapse	2
	Inferior vena cava > 2.5 cm, < 50% inspiratory collapse	1.5
	Right ventricular collapse	1.5
	Mitral or tricuspid respiratory flow variations	1
	Swinging heart	1
	Right atrial collapse > 1/3 of cardiac cycle	1
	Cardiomegaly on chest X-ray	1
	Moderate pericardial effusion (1–2 cm in diastole)	1
	Microvoltage in ECG	1
	Electrical alternans on ECG	0.5
	Small pericardial effusion (< 1 cm) in diastole, no trauma	-1

From Ristić AD, et al. Eur Heart J. 2014;35(34):2279-84, with permission of Oxford University Press [(15)].

The pathogenesis of tuberculous pericardial effusion is the presence of tubercle proteins that cause a cell-mediated hypersensitivity response with predominant cytokine release of T-helper cells (subtype 1), resulting in an inflammatory exudative effusion. The morbidity associated with tuberculous pericarditis is due to the immune response to acid-resistant bacilli penetrating the pericardium [(16)].

According to the World Health Organization (WHO), OAT administration in TB pericarditis is the same as other OAT administration, namely category I, according to the Indonesian pulmonary physician association (PDPI), OAT administration in TB pericarditis for 9-12 months. In certain conditions (hepatic impairment, renal impairment), fixed-dose pill combination preparations cannot be used. Components R and H are metabolized by the liver and excreted through the biliary system. Meanwhile, components Z and E will be metabolized and excreted through the kidneys so that in patients with stage 3-5 CKD, dose adjustment is required according to the glomerular filtration rate.

Table 3. Adjustment of OAT dose in patients with renal impairment [17].

Drug name and normal dosage	Dose adjustment based on creatinine clearance			Dose adjustment based on *renal replacement therapy*		Note
	30-60 ml/min	10-29 ml/min	<10 ml/min	Intermittent hemodialysis	Peritoneal dialysis	
Rifampicin (10 mg/kgBW/day)	No need for dose adjustment	No need for dose adjustment	No need for dose adjustment	No need for dose adjustment	No need for dose adjustment	Safe for people with kidney problems
Isoniazid (5 mg/kgBW/day)	No need for dose adjustment	No need for dose adjustment	No need for dose adjustment	No need for dose adjustment	No need for dose adjustment	Pyridoxine 1x25 mg is recommended.
Pyrazinamide (30-40 mg/kgBW/day)	No need for dose adjustment	30-40 mg/kgBW administered every 48 hours	30-40 mg/kgBW administered 3 times per week	30-40 mg/kgBW administered 3 times per week after hemodialysis	No need for dose adjustment	Excreted mainly via the hepatic route. Monitor for hepatotoxicity and serum uric acid levels.
Ethambutol (15 mg/kgBW/day)	15 mg/kgBW administered every 24 hours	15 mg/kgBW administered every 48 hours	15 mg/kgBW administered every 48 hours	15 mg/kgBW administered 3 times per week after hemodialysis	15 mg/kgBW administered every 48 hours	Should be avoided unless absolutely necessary. Excreted mainly through the kidneys. Periodic eye examinations are required.
Streptomycin 15 mg/kgBW administered at time-dependent intervals that (15 mg/kgBW/day) needed until the drug cannot be detected in plasma						

The pathogenesis of pericarditis and pericardial effusion in chronic kidney disease is likely due to the accumulation of uremic toxins that cause inflammation in the pericardium, in addition to chronic fluid overload conditions and hypoalbuminemia, which are also very instrumental factors [18]. Initial management of patients with pericardial effusion in CKD patients is to immediately start dialysis and dialysis intensification in patients who are already on dialysis [19].

The prognosis for patients with pericarditis/pericardial effusion is good if diagnosed early and treated promptly. In addition to cardiac tamponade, the complication that is feared is the occurrence of constrictive pericarditis [19].

Conclusion

A patient with stage 5 CKD with CAPD complaining of shortness of breath for 3 months was diagnosed with massive pericardial effusion due to tuberculosis confirmed by pericardial fluid analysis examination of high LDH and high ADA and ineffective CAPD. This patient underwent pericardiocentesis, intensive hemodialysis, and administration of antituberculosis drugs. The first-line anti-tuberculosis drug regimen was administered with a dosage adjustment of Rifampicin 600 mg tablets/24 hours, Isoniazid 300 mg tablets/24 hours, Ethambutol 1000 mg tablets 3x/week, and Pyrazinamide 1250 mg 3x/week. Clinical monitoring, pericardial fluid production, and side effects of anti-tuberculosis drugs were performed in this patient to see the success of therapy.

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