Uremic Pericarditis: A Report of 30 Cases and Review of the Literature

Seyed-Ali Sadjadi
Ardavan Mashhadian

Corresponding Author: Seyed-Ali Sadjadi, e-mail: sadjadia@yahoo.com
Conflict of interest: None declared

Case series
Patient: Male, 71 • Male, 69 • Female, 49
Final Diagnosis: Uremic pericarditis
Symptoms: —
Medication: —
Clinical Procedure: Hemodialysis
Specialty: Nephrology

Objective: Rare disease

Background: Uremic pericarditis, common at one time among dialysis patients, has become a rare entity in recent years. Due to its low incidence, its recognition has gained importance among internists, cardiologists, and nephrologists. It can be seen in predialysis patients and in dialysis patients who are on hemodialysis or peritoneal dialysis.

Case Report: We report 3 cases of uremic pericarditis and their presenting manifestations and review 30 cases we have treated. Among these patients, the traditional findings among patients with acute pericarditis such as chest pain, fever, electrocardiographic changes, and leukocytosis are uncommon. Pericardial friction rub has a relatively high incidence but its differentiation by an untrained ear, especially by a non-cardiologist, could be a major problem. Not infrequently, it is complicated by pre-tamponade or tamponade, requiring pericardiocentesis or pericardial surgery.

Conclusions: Uremic pericarditis is a treatable, but not always a preventable, condition. Timely recognition of its presence and its efficient management are essential elements of successful treatment.

MeSH Keywords: Cardiac Tamponade • Pericarditis • Uremia

Full-text PDF: http://www.amjcaserep.com/abstract/index/idArt/893140
Background

Uremic Pericarditis is a major complication of kidney disease and may occur in patients with acute or chronic renal failure, before dialysis or on dialysis treatment. Its incidence was high in the past, was usually considered a terminal event, and was associated with a high mortality rate [1], but in more recent years it is rarely encountered. However, the potential for morbidity and even mortality is high; therefore, it is appropriate to review its pathophysiology, symptomatology, and treatment. This is especially relevant because the most recent generation of internists, cardiologists, and nephrologists rarely encounter a patient with uremic pericarditis and may have difficulty recognizing and managing it in a timely and efficient manner. In this review, we will present 3 scenarios of how the patient may present, review our case series, and discuss the pathophysiology and therapeutics of this entity.

Case Report

Case 1

A 76-year-old African-American man with history of diabetes mellitus, arterial hypertension, chronic kidney disease (CKD) stage 4, congestive heart failure (CHF), coronary artery disease (CAD), and gout was admitted with abdominal pain and was found to have perforated diverticulosis. He underwent hemicolectomy and abdominal wall repair and sustained acute-on-chronic renal failure. His condition rapidly deteriorated, becoming uremic and acidotic and he developed a loud, 3-component pericardial friction rub. He was started on daily hemodialysis treatment and all anticoagulants were discontinued. He tolerated dialysis well and after 5 daily treatments the rub disappeared. Echocardiography did not show pericardial effusion.

Case 2

A 61-year-old African-American man with history of arterial hypertension, obstructive sleep apnea, hyperlipidemia, and CKD stage 4 was becoming increasingly dyspneic and could not walk more than a few blocks. Chest x-ray showed a large cardiac silhouette and bilateral pleural effusion (Figures 1 and 2) and an echocardiogram showed a large to moderate-size pericardial effusion. At this time he was bedridden, with estimated glomerular filtration rate (eGFR) of 15 mL/min, with no pericardial friction rub or neck vein distention. He was started on daily hemodialysis treatment and all anticoagulants were discontinued. He tolerated dialysis well and after 5 daily treatments the rub disappeared. Echocardiography did not show pericardial effusion.

Case 3

A hypertensive 49-year-old African-American woman on chronic hemodialysis for 6 years was frequently hypotensive during dialysis treatments. She was brought to the emergency room because of pain on the left side of her chest, dyspnea, and abdominal pain. Her blood pressure was 96/59, pulse rate 85, with decreased breath sounds in lung bases, no pericardial friction rub, gallop, or murmur and no leg edema. Chest x-ray showed severe cardiomegaly and an echocardiogram showed a large pericardial effusion. Pericardiocentesis produced 1500
Uremic pericarditis, although now uncommon, is a major complication of end-stage renal disease (ESRD). It was first described by Richard Bright in 1836. Its incidence in the ear of patients with end-stage renal disease and 4 patients with acute kidney injury (AKI) died from other medical problems during this work. Over a span of 30 years, we have encountered 30 cases of uremic pericarditis with the following characteristics: 28 males, 2 females, mean age 61.3±10.3 years, 22 White, 8 African-American, 11 with acute renal failure, 1 with a kidney transplant, and 18 with end-stage renal disease (ESRD). One (3.3%) patient had fever, 23 (76%) had a rub, and 10 (33%) had tamponade or pre-tamponade. Creation of a pericardial window was necessary in 1, pericardiectomy in 3, and pericardiocentesis in 6, for an overall incidence of pericardial surgery of 33%. No patient died as a direct consequence of pericarditis, but 2 patients with end-stage renal disease and 4 patients with acute kidney injury (AKI) died from other medical problems during the same admission. In the 16 patients on whom we had detailed information, 8 had a WBC count of >10 000/cmm and in the other 14 the WBC count was in the normal range. Our patients were treated with daily dialysis without anticoagulation and follow-up echocardiogram until pericardial friction rub disappeared. No patient was treated with steroids, indomethacin, or colchicine. Patients needing pericardiectomy or pericardiocentesis tended to be older, with higher peripheral blood cell count and a larger pericardial effusion. Our patient died as a direct consequence of pericarditis, but 2 patients with end-stage renal disease and 4 patients with acute kidney injury (AKI) died from other medical problems during this work. Over a span of 30 years, we have encountered 30 cases of uremic pericarditis with the following characteristics: 28 males, 2 females, mean age 61.3±10.3 years, 22 White, 8 African-American, 11 with acute renal failure, 1 with a kidney transplant, and 18 with end-stage renal disease (ESRD). One (3.3%) patient had fever, 23 (76%) had a rub, and 10 (33%) had tamponade or pre-tamponade. Creation of a pericardial window was necessary in 1, pericardiectomy in 3, and pericardiocentesis in 6, for an overall incidence of pericardial surgery of 33%. No patient died as a direct consequence of pericarditis, but 2 patients with end-stage renal disease and 4 patients with acute kidney injury (AKI) died from other medical problems during the same admission. In the 16 patients on whom we had detailed information, 8 had a WBC count of >10 000/cmm and in the other 14 the WBC count was in the normal range. Our patients were treated with daily dialysis without anticoagulation and follow-up echocardiogram until pericardial friction rub disappeared. No patient was treated with steroids, indomethacin, or colchicine. Patients needing pericardiectomy or pericardiocentesis tended to be older, with higher peripheral blood cell count and a larger pericardial effusion. Our patients’ characteristics are summarized in Table 1.

### Table 1. Characteristic of 30 patients with pericarditis.

| Characteristic                                      | Value           |
|-----------------------------------------------------|-----------------|
| Mean age, years                                     | 61.3±10.3       |
| Male/female                                         | 28/2            |
| White/Black                                         | 22/8            |
| ESRD/AKI                                            | 19/11           |
| Fever                                               | 1/30            |
| Peripheral white blood cell count                   | 11,323±5,881    |
| Pericardial friction rub                            | 24/30           |
| Tamponade/pre-tamponade                             | 10/30           |
| Pericardiectomy/pericardial window/                  |                 |
| pericardiocentesis                                   | 10/30           |

mL of bloody fluid, with 1333 white blood cells, 59% neutrophils, 41 mg/dL glucose, 4.1 gram/dL protein, and LDH 1727 IU/L. All cultures were negative. Her blood pressure and pulse improved after pericardiocentesis.

Over a span of 30 years, we have encountered 30 cases of uremic pericarditis with the following characteristics: 28 males, 2 females, mean age 61.3±10.3 years, 22 White, 8 African-American, 11 with acute renal failure, 1 with a kidney transplant, and 18 with end-stage renal disease (ESRD). One (3.3%) patient had fever, 23 (76%) had a rub, and 10 (33%) had tamponade or pre-tamponade. Creation of a pericardial window was necessary in 1, pericardiectomy in 3, and pericardiocentesis in 6, for an overall incidence of pericardial surgery of 33%. No patient died as a direct consequence of pericarditis, but 2 patients with end-stage renal disease and 4 patients with acute kidney injury (AKI) died from other medical problems during the same admission. In the 16 patients on whom we had detailed information, 8 had a WBC count of >10 000/cmm and in the other 14 the WBC count was in the normal range. Our patients were treated with daily dialysis without anticoagulation and follow-up echocardiogram until pericardial friction rub disappeared. No patient was treated with steroids, indomethacin, or colchicine. Patients needing pericardiectomy or pericardiocentesis tended to be older, with higher peripheral blood cell count and a larger pericardial effusion. Our patients’ characteristics are summarized in Table 1.

# Discussion

Uremic pericarditis, although now uncommon, is a major complication of end-stage renal disease (ESRD). It was first described by Richard Bright in 1836. Its incidence in the early days of dialysis was high – 41% in a study of 83 patients in Peter Brigham Hospital [2] and 12.5% in another study of 125 patients from Denmark [3]. However, more recently, its incidence has decreased to about 5–20% in chronic hemodialysis patients [4,5], perhaps due to more efficient hemodialysis therapy. With earlier dialysis initiation, better dialysis prescription, and more efficient dialyzers, uremic pericarditis has become so uncommon that in a fairly active hemodialysis treatment facility, doing over 13 000 dialysis treatments a year, we usually encounter no more than 1–2 cases of uremic pericarditis a year. The etiology of uremic pericarditis remains unclear. The fact that it improves with intensive dialysis treatment, and its falling incidence in recent decades following the introduction of more precise and efficient dialysis prescription, makes it plausible to think that abnormalities of urea or some other toxin retained because of kidney failure and removed with dialysis is the cause of this syndrome. In the past some thought that, at least in some cases, a viral illness may be the cause of uremic pericarditis [5]. Pathologically, uremic pericarditis is fibrinous in most cases [6], with a rough granular fibrinous surface. Occasionally it is serous and rarely it is hemorrhagic. When there is fluid, it is exudative, with high levels of protein and mononuclear cells.

Acute non-uremic pericarditis presents with chest pain that is usually sudden in onset, felt in the anterior chest wall, is worse on inspiration and in supine position, and may be accompanied by pericardial friction rub, typical ST, and T wave changes, but uremic pericarditis is usually slow in onset and, aside from pericardial friction rub, there may not be any other finding [7]. Pericardial friction rub is usually squeaky and scratchy, and is best heard in the left sternal border while patients is leaning forward, holding breath. It is heard in almost all cases and sometimes it is transient, heard at one time but not at others. The rub typically has 3 components, related to atrial systole, ventricular systole, and rapid ventricular filling during diastole. It is thought to be due to rubbing of the visceral and parietal layers of the pericardium, but sometimes it is heard even when there is a large effusion separating the 2 layers of pericardium, which casts doubt on the purported explanation of rubbing for the presence of the rub. Leukocytosis and fever are very rare. The electrocardiographic changes described in acute non-uremic pericarditis (e.g., diffuse concave ST elevation in most leads, with reciprocal ST depression in leads V1 and AVR in early stages of pericarditis, normalization of ST segment, and diffuse T wave inversion in later stages) are rare in uremic pericarditis [8].

Because most dialysis patients are elderly and diabetic and have a high prevalence of coronary artery disease, acute myocardial infarction, unstable coronary artery disease, expanding or dissecting ascending/thoracic aortic aneurysm, are always possibilities that should be strongly considered in the differential diagnoses. When there is a clear pericardial friction rub, there is very little doubt about pericarditis. However, when no
rub is audible and especially when it is difficult to differentiate a rub from a murmur, diagnosing pericarditis is a challenge. In these cases, respiratory variation of the murmur could help to differentiate a rub from a murmur, with the former remaining unaffected by breathing, while the latter changes with respiration. A chest x-ray may give clues to the presence of cardiomegaly and pericardial effusion, and echocardiography will help with the diagnosis of presence or absence of fluid in the pericardium, especially when pre-tamponade or tamponade is a possibility. Laboratory findings rarely help in differentiating uremic pericarditis from other causes of chest pain, and white blood cell count is rarely elevated.

A major concern with uremic pericarditis is the presence of tamponade, which, if untreated, may be fatal. Tamponade is usually suspected when the patient is tachycardic, hypotensive, and has distended neck veins. In these cases a paradoxical pulse pressure of >10 mmHg, although non-specific, should heighten suspicion for tamponade. Clear evidence for tamponade will come from echocardiography, showing systolic right atrial collapse, with equalization of pressure in all cardiac chambers and swinging septal position [9]. Pulsus paradoxus or “exaggerated respiratory variation”, as some authors would prefer to call it, is an exaggeration of the normally observed drop in blood pressure with inspiration and its rise with expiration. It can also be observed in exacerbations of chronic obstructive lung disease, severe asthma, obstructive sleep apnea, massive pulmonary embolism, profound hemorrhagic shock, and severe hypotension [10]. However, it should kept in mind that certain conditions (e.g., extreme hypotension, acute left ventricular myocardial infarction with effusion, pericardial adhesions, severe aortic regurgitation, and atrial septal defect) may mask the presence of tamponade. Tamponade usually presents with symptoms of right-sided heart failure (e.g., distended neck veins, tender liver, peripheral edema, dropping blood pressure, and tachycardia). Despite heart failure symptoms, there is no elevation of atrial natriuretic peptide and although coronary blood flow is reduced, there is no sign of myocardial ischemia. Occurrence of tamponade depends on how quickly fluid accumulates in the pericardial cavity. Rapid fluid accumulation, even if it is small, can lead to tamponade, while large fluid accumulations occurring over a longer period of time, even as large as 2 liters, may not cause tamponade [11]. Once tamponade develops, urgent treatment is necessary to avoid death [12] or long-term morbidity [13,14].

Intensive dialysis, usually hemodialysis, is necessary for 5–7 days, performed without anticoagulation to prevent pericardial bleeding and tamponade, and with little or no fluid removal to avoid hypotension and cardiovascular collapse. In a study by De Pace et al. [15], admission temperature >102 F, rales, admission blood pressure <100 mmHg, jugular venous distention, peritoneal dialysis, white blood cell count >15000/cmm, and large pericardial effusion on echocardiography were predictors of poor response to intensive dialysis therapy. Oral and intrapericardial administration of corticosteroids [16], indomethacin, and colchicine have been tried for relief of pain of uremic pericarditis, with various degrees of success. Bussemiejer et al. treated 45 patients with intractable uremic pericarditis unresponsive to intensive dialysis therapy with intrapericardial instillation of 100 mg of triamcinolone hexacetonide. All patients responded to treatment immediately and only 1 patient had recurrence of pericarditis [17]. The effect of indomethacin 25 mg 4 times a day was evaluated in a randomized controlled study of 24 patients with ESRD and uremic pericarditis, 11 treated with indomethacin and 13 treated with placebo, for a 3-week period. Indomethacin shortened the duration of fever, but it had no effect on chest pain, pericardial friction rub, or pericardial effusion [18]. In a Cochrane review of published literature on the use of colchicine in pericarditis, Alabed et al. compared the effect of colchicine with indomethacin and corticosteroids and concluded it is effective in recurrent pericarditis, but this was based on a small number of trials [19]. Overall, prognosis of uremic pericarditis is excellent, with a survival rate of 85–90% [20,21].

Occasionally, pericarditis is intractable and in spite of intensive dialysis treatment, patient continues to have a large pericardial effusion that could be associated with cardiovascular compromise. In these cases, pericardial drainage by creation of a pericardial window or total pericardiectomy could be an option [22,23]. This could be done by an open surgical approach or thoracoscopic, limited, or total pericardiectomy [24,25]. Pericardiectomy, however, is a high-risk surgical procedure and therefore should be used only in emergencies in which circulatory integrity is compromised. Successful pericardial decompression is associated with rapid improvement in blood pressure and decrease in tachycardia.

**Conclusions**

Perhaps due to earlier initiation and more efficient dialysis treatment, incidence of uremic pericarditis has decreased significantly in recent decades. It is usually seen in predialysis patients rather than in patients who are undergoing maintenance renal replacement therapy. Efficient treatment of pericarditis requires a high degree of suspicion for the diagnosis and management of this potentially fatal clinical syndrome.
1. Wacker, W, Merrill JP: Uremic pericarditis in acute and chronic renal failure. J AM Med Assoc, 1954; 156(8): 764–65
2. Bailey GL, Hampers CL, Hager EB, Merrill JP: Uremic Pericarditis: Clinical features and management. Circulation, 1968; 38: 582–91
3. Sko PE, Hansen HE, Spencer ES: Uremic Pericarditis. Acta Med Scand, 1969, 186: 421–28
4. Silverberg S, Oreopoulos DG, Wise DJ et al: Pericarditis in patients undergoing long term hemodialysis and peritoneal dialysis. Am J Med, 1977; 63: 874–80
5. Hager EB: Clinical observations on five patients with uremic pericardial tamponade. N Engl J Med, 1965; 273(6): 304–8
6. Roberts WC: Pericardial heart disease: its morphologic features and its causes. Proc (Bayl Univ Med Cent), 2005; 18(1): 38–55
7. Gonulkula SR, Spodik DH: Pericardial disease in renal patients. Semin Nephrol, 2001; 1: 52–58
8. Lange RA, Hillis LD: Acute pericarditis. N Engl J Med, 2004; 351: 2195–202
9. Radhakrishnan A, Granato JE: Electrocardiograms in acute pericarditis. In: Millis RM (ed.), Advances in electrocardiograms – clinical applications, InTech, 2012
10. Hamzaoui O, Monnet X, Teboul JL: Pulsus paradoxus. Euro Respir J, 2013; 42(6): 1696–705
11. Warrant BH, Lynn RR, Allen FH: Echocardiographic observations of ventricular volume changes and swinging septal position in massive pericardial effusion. J Clin Ultrasound, 1975; 3(4): 283–86
12. Spodick DH: Acute cardiac tamponade. N Engl J Med, 2003; 349: 684–90
13. Klyenberg RL, Klyenberg VM, Klyenberg LM, Farahmandian D: Chronic constrictive Pericarditis in association with end stage renal disease. Int J Nephrol, 2011, 2011: 469602
14. Pillay VK, Sarpel SC, Kurtzman NA: Subacute constrictive uremic pericarditis. Survival after pericardiectomy. JAMA, 1976; 235(13): 1351–52
15. De Pace NL, Nestico PF, Schwartz AB et al: Predicting success of intensive dialysis in the treatment of uremic pericarditis. Am J Med, 1984; 76: 38–46
16. Iyoda M, Ajro Y, Sato K et al: A case of refractory uremic pleuropericarditis – successful corticosteroid treatment. Clin Nephrol, 2006, 65: 290–93
17. Busemeier TJ, Davin TD, Simmons RL et al: Treatment of intractable uremic pericardial effusion, avoidance of pericardiectomy with local steroid instillation. JAMA, 1978; 240: 1358–59
18. Spector D, Alfred H, Sleedlecki M, Briefel G: A controlled study of the effect of indomethacin in uremic pericarditis. Kidney Int, 1983; 24(6): 663–69
19. Alabed S, Cabello JB, Irving GI et al: Colchicine for pericarditis Cochrane Database Syst Rev, 2014, 8: CD010652
20. Rutsky EA, Rustand SG: Treatment of uremic pericarditis and pericardial effusion. Am J Kidney Dis, 1987; 10: 2–8
21. Tseng JR, Lee MJ, Yen KC et al: Course and outcome of dialysis pericarditis in diabetic patients treated with maintenance hemodialysis. Kidney Blood Press Res, 2009; 32: 17–23
22. Morin JE, Hollomby D, Gonda A et al: Management of uremic pericarditis: A report of 11 patients with cardiac tamponade and review of the literature. Ann Thorac Surg, 1976; 22(6): 588–92
23. Schlein EM, Bartley TD, Spooner GR, Cade R: A simplified surgical approach to therapy of uremic pericarditis. Ann Thorac Surg, 1970; 10(6): 548–51
24. Gosh SC, Laurieu AI, Ablaaza SG, Grana VP: Clinical experience with subxiphoid pericardial decompression. Int Surg, 1985; 70(1): 5–7
25. Connors JP, Kleiger RE, Shaw RC et al: The indications for pericardiectomy in the uremic pericardial effusion. Surgery, 1976; 80(6): 689–94