

Chest Pain in the Dialysis Patient

Roxana Narat, MD; Bernard M. Karnath, MD—Guest Authors
Gregory W. Rouan, MD—Column Editor

ABSTRACT

Acute pericarditis is common in patients with end-stage renal disease. In these patients, the condition has been classified as uremic- and dialysis-associated pericarditis. Diagnosis of pericarditis usually is based on a new pericardial friction rub with or without evidence of an effusion on transthoracic echocardiogram (TTE). A patient may present with changes on electrocardiogram and chest radiograph. Of note, the S-T segment elevations classically seen in acute pericarditis are rare in uremic pericarditis patients. These diagnostic study results, along with clinical status, guide patient management. Treatment consists of intensive hemodialysis, surgery, and pericardiocentesis. Patients should be followed up with serial TTEs.

The patient was a 23-year-old African American woman with a past medical history of renal dysgenesis status after 3 failed renal transplants, who presented with a 2-day history of chest pain. She was receiving inadequate dialysis secondary to noncompliance. Ten hours after her last dialysis session, she had begun to experience sharp chest pain associated with nausea. The chest pain originated from the epigastric region, radiating to the right side of her chest and neck and down her right arm. The pain worsened on inspiration and movement and improved only with morphine. Physical examination was significant for tachycardia, a pericardial friction rub, and tenderness to palpation of the epigastric region without guarding or rigidity. White blood cell count was 19 900/mm³. Blood urea nitrogen (BUN) and creatinine levels were 30 and 8.69, respectively. Chest x-ray showed a normal heart size. Electrocardiogram (ECG) results showed diffuse acute S-T segment elevations with PR-segment depression suggestive of acute pericarditis (Figure 1). Computed tomography scan of the thorax revealed a moderate to large pericardial effusion. Bedside

transthoracic echocardiogram (TTE) confirmed the presence of a moderate-sized pericardial effusion, along with evidence of mild compression of the right-sided chambers. The patient subsequently received 4 hours of dialysis daily for a week with repeat TTEs demonstrating a gradual decrease in size of the pericardial effusion. During her admission the patient did not experience a recurrence.

DISCUSSION

Pericardial disease remains a significant source of morbidity and mortality in patients with end-stage renal disease (ESRD). Pericardial involvement frequently manifests as pericarditis with possible complications including pericardial effusion, cardiac tamponade, recurrent pericarditis, and chronic constrictive pericarditis.^{1,2} In patients with ESRD, pericarditis has classically been subdivided into 2 forms: uremic- and dialysis-associated pericarditis. Uremic pericarditis occurs in patients before or within 8 weeks of the initiation of maintenance dialysis.¹ Dialysis-associated pericarditis presents in patients who have been on dialysis more than 8 weeks.¹

ETIOLOGY

The precise etiology of pericardial disease in patients with ESRD remains elusive. It is thought that uremic pericarditis is caused by retention of toxic metabolites.^{1,3} This is strongly supported by the observation that initiation of dialysis usually results in complete resolution. However, no specific metabolite has been isolated as the biochemical cause. It is debatable whether dialysis-associated pericarditis is caused by the same factors as is uremic pericarditis. The key difference between the 2 is that uremic pericarditis is reversible with dialysis in $\geq 76\%$ of cases, whereas dialysis-associated pericarditis is less responsive to dialysis, resolving in $< 66\%$ of cases.^{1,3,4} Proposed causes for dialysis-associated pericarditis include inadequate dialysis as a result of missed sessions or vascular access problems, relative underdialysis as a result of a hypercatabolic state, and fluid overload.^{1,5,6}

It also is essential to remember other causes of pericarditis in patients with ESRD. Factors that may trigger pericarditis include infection (viral, bacterial, or fungal), an underlying autoimmune or inflammatory disease (eg, systemic lupus erythematosus or Wegener's granulomatosis), trauma, an adverse drug reaction (eg, hydralazine, procainamide, α -methyl dopa, minoxidil), and acute myocardial infarction (MI).^{1,3,4}

Dr Narat will begin a PGY-1 internship at the University of Texas Southwestern Medical Center, Dallas, Texas; Dr Karnath is Associate Professor of Internal Medicine, The University of Texas Medical Branch, Galveston, Texas.

Dr Rouan is Richard W. and Sue Vilter Professor of Clinical Medicine and Associate Chairman of Education, Department of Internal Medicine, School of Medicine, University of Cincinnati, Cincinnati, Ohio.

Figure 1. Electrocardiogram Showing Diffuse S-T Segment Elevations and PR-Segment Depression in a Patient With End-Stage Renal Disease and Acute Pericarditis



CLINICAL PRESENTATION AND DIAGNOSIS

SIGNS AND SYMPTOMS

The classic presentation of acute pericarditis, regardless of its origin, is a patient with chest pain that is sharp, pleuritic in nature, sudden in onset, and retrosternal or left-sided in location. Pain often is exacerbated by lying down and is relieved by sitting up or leaning forward. The pain may radiate to the neck, arms, or left shoulder, making it difficult to differentiate from MI. Nonspecific symptoms include malaise, fever, chills, dyspnea, and cough. A concurrent pericardial effusion may manifest itself as the latter 2 symptoms.

The most specific sign of acute pericarditis is a pericardial friction rub, although it is intermittently present and often varies in intensity. It is characterized as a high-pitched scratchy sound, heard best in end expiration and along the left sternal border with the patient leaning forward. Classically, a triple cadence is described, which coincides with atrial systole, ventricular systole, and rapid ventricular filling during early diastole.² It is heard throughout the respiratory cycle and should not be confused with a pleural rub, which varies with respirations.²

The clinical presentation of uremic and dialysis-associated pericarditis is quite similar to pericarditis resulting from other causes, although there are differences. Patients with ESRD are less likely to experience chest pain from acute pericarditis¹ and many patients on dialysis have no accompanying signs or symptoms suggestive of acute pericarditis.⁵ Without a concurrent infection, fever is variable, though it occurs more commonly in dialysis-associated pericarditis than in uremic pericarditis.⁴ Uremic pericarditis produces the classic pericardial rub, but it is louder than in pericarditis because of other etiologies, it is commonly palpable, and it often persists even after the biochemical abnormalities have been corrected.⁴

Cardiac tamponade is a serious complication of pericarditis, leading to hemodynamic compromise and even to death. Clinical signs and symptoms suggestive of a significant effusion include tachycardia, hypotension, pulsus paradoxus, jugular venous distension, muffled heart sounds, dyspnea, orthopnea, and postural dizziness.^{1,2}

LABORATORY AND DIAGNOSTIC FINDINGS

In general, laboratory testing for acute pericarditis is fairly nonspecific and provides little guidance in determining etiology. An elevated white blood cell count, erythrocyte sedimentation rate, and serum C-reactive protein are commonly present in acute pericarditis of any etiology.² Patients with uremic pericarditis almost always have a BUN greater than 60 mg/dL⁴ and leukocytosis often is mild in dialysis-associated pericarditis.¹ The clinical presentation should direct decisions for further laboratory studies, such as rheumatoid factor, cardiac enzymes, or antinuclear antibodies.

Typically, chest radiographs of patients with ESRD show cardiomegaly and an abnormal cardiac silhouette.¹ However, cardiomegaly on chest radiography is nonspecific and may represent left-ventricular hypertrophy or a pericardial effusion.

The classic electrocardiographic findings in a patient with acute pericarditis consist of diffuse upright, concave (saddle-shaped) S-T segment elevation and PR-segment depression. Additionally, electrocardiographic abnormalities may be noted to evolve through 4 stages (Table).⁴ Stage I, consisting of S-T segment elevation and upright T-waves, may last several hours or a few days, eventually leading to normalization of these changes in stage II. In stage III, there is an evolution to widespread T-wave inversions; these may resolve within a few days, but are frequently present for weeks or months. Stage IV is characterized by normalization of T-wave changes.⁷

Table. Classic 4-Stage Electrocardiogram Changes Seen in Acute Pericarditis

Stage	S-T segment	T-wave	PR-segment
I	Elevated	Upright	Depressed or isoelectric
II*	Isoelectric	Upright	Isoelectric or depressed
III†	Isoelectric	Low to flat to inverted	Isoelectric or depressed
IV	Isoelectric	Inverted	Isoelectric or depressed
V	Isoelectric	Upright	Isoelectric

*Early.

†Late.

Adapted with permission from Gunukula SR, Spodick DH.⁴

Although ECG changes are not essential to a diagnosis of acute pericarditis, they are helpful in differentiating between acute pericarditis and myocardial ischemia. It is important to remember that in acute pericarditis, T-wave inversions do not occur until there is resolution of S-T segment elevation. Thus, if T-wave abnormalities occur before the S-T segment has normalized, the patient likely has myocardial ischemia rather than acute pericarditis.^{8,9}

Although most patients with ESRD and pericarditis have an abnormal ECG, only a minority show the classic ECG changes. Such characteristic changes are rare particularly in those with uremic pericarditis.^{1,3,4} In contrast, more than 80% of non-ESRD patients with acute pericarditis will have the classic stage I ECG findings. This discrepancy arises from the fact that S-T segment elevations reflect subepicardial myocarditis.⁴ In uninfected uremic pericarditis, inflammatory cells do not penetrate the myocardium and therefore do not produce the characteristic S-T segment elevations.⁴ Thus, when the typical ECG changes are seen in a uremic patient, an alternative cause for pericarditis, such as infection, should be investigated.⁴

A TTE is useful for detecting a pericardial effusion in patients with ESRD who have suspected pericarditis. However, an effusion in this population does not confirm the presence of pericarditis and may actually represent fluid overload or an underlying disease state.¹ The TTE also is essential for evaluating patients for cardiac tamponade.

TREATMENT

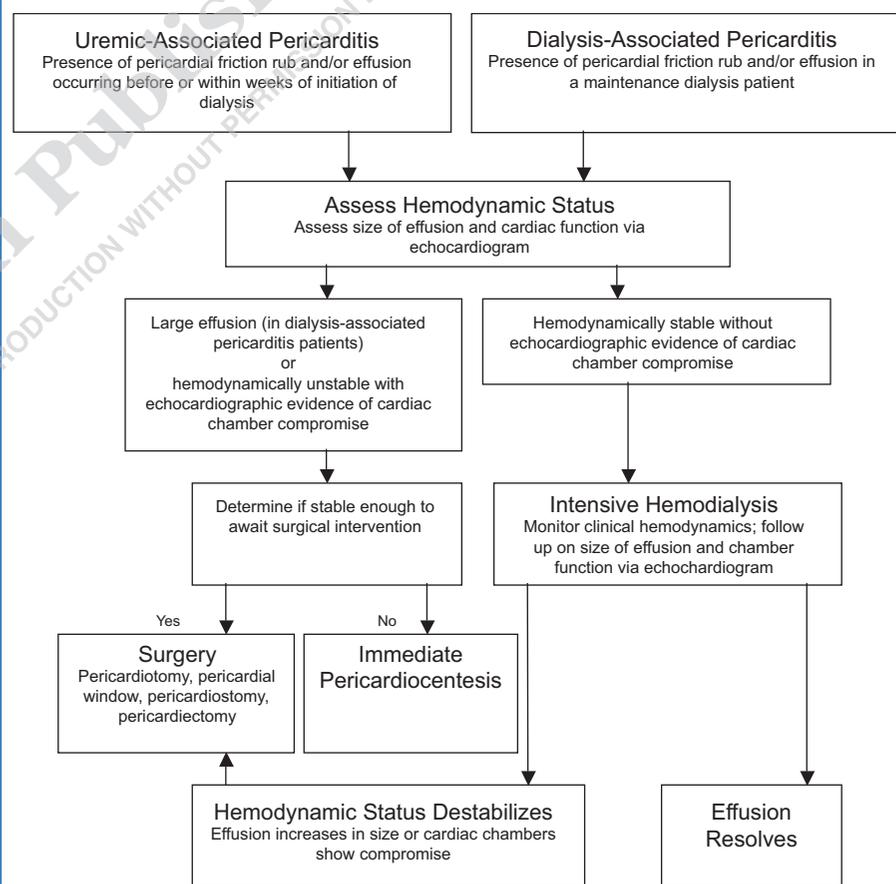
When determining the course of treatment for uremic pericarditis and dialysis-associated pericarditis, the first step is to assess the hemodynamic stability and size of the pericardial effusion with echocardiogram. This will direct management toward either dialysis in stable patients or more invasive procedures, as outlined in Figure 2, in unstable patients.

In the hemodynamically stable patient with a small to moderate effusion, uremic pericarditis responds impressively well to intensive hemodialysis and peritoneal dialysis.^{1,5,10} Intensive hemodialysis is defined as daily hemodialysis for a period of 10 to 14 days, over which time the pericardial effusion should resolve.¹ Because intrapericardial hem-

orrhage is a possible complication, heparin should be avoided during hemodialysis. If this is not possible, peritoneal dialysis may be a reasonable alternative, although results vary.³ Patients should be monitored with TTE every 3 to 5 days.¹

Patients with hemodynamic instability or evidence of a cardiac tamponade should undergo prompt surgical intervention. The surgical procedure used usually is dependent on the clinical and hemodynamic status, comorbidities, and experience of the surgeon, though a pericardial window is often favored because of its safety and efficacy. It has led to excellent results among ESRD patients with refractory or hemodynamically significant pericardial effusion.¹ Complications of this procedure include arrhythmias, pleural effusion, and minor surgically related complications.¹⁵ Pericardiocentesis carries a significant morbidity and mortality, so it probably should be reserved for patients who are at immediate risk for death and cannot await a surgical drainage procedure. Recurrence of significant pericar-

Figure 2. Algorithm for the Management of a Patient With Uremic-Associated and Dialysis-Associated Pericarditis and a Concurrent Pericardial Effusion*



*Data from Wood JE, Mahnensmith RL.⁵

dial effusion or hemodynamic compromise has been shown to occur in up to 70% of reported cases. Complications from pericardiocentesis include myocardial laceration, coronary artery laceration, and hemorrhagic tamponade.^{1,3}

Dialysis-associated pericarditis is much more refractory to intensive hemodialysis than is uremic pericarditis. Thus, follow-up with serial TTEs to monitor for enlargement or cardiac chamber compression is even more important, and prompt surgical intervention is recommended if the effusion is large, persists despite treatment, or results in hemodynamic compromise (Figure 2).⁵

Both uremic- and dialysis-associated pericarditis should be monitored frequently via clinical status, physical examination, and TTE. Chest pain should be managed with analgesics (eg, hydrocodone, oxycodone).¹ Although nonsteroidal anti-inflammatory drugs (NSAIDs) commonly are used to treat chest pain in acute pericarditis, they do not affect the course of pericarditis in patients with ESRD.^{1,3} Oral steroids also have had limited success in treating ESRD patients with pericarditis.^{1,11} Therefore, NSAIDs and steroids are no longer recommended for patients with uremic- and dialysis-associated pericarditis.¹

CONCLUSION

A distinction should be made between uremic- and dialysis-associated pericarditis, primarily because of patient management decisions. Dialysis-associated pericarditis is significantly more refractory to intensive hemodialysis than is uremic pericarditis. Follow-up TTEs and clinical reassessment of the patient are essential in both cases to determine the presence of a pericardial effusion. However, a more aggressive approach should be taken

when there is evidence of a large pericardial effusion in a patient with dialysis-associated pericarditis. This should prompt surgical intervention, in contrast to a more conservative approach initially used in uremic pericarditis. Recognizing these differences can lead to avoidance of complications and more favorable outcomes in patients with ESRD.

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