



Acute Pericarditis Leading to a Diagnosis of SLE: A Case Series of 3 Patients

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Vishal K. Narang, MD¹ , Jonathan Bowen, MD¹,
Omar Masarweh, MD¹, Shane Burnette, MD¹, Michael Valdez, MD¹,
Leila Moosavi, MD¹, Fowrooz Joolhar, MD, FACC¹,
and Theingi Tiffany Win, MD, FACC¹

Abstract

In systemic lupus erythematosus (SLE), cardiac manifestations are known to be present in up to 50% of patients. However, it is rare for acute pericarditis to be the leading symptom at the time of diagnosis of SLE occurring in up to 1% of patients. We present a case series in which 3 patients with no prior history of SLE presented with acute pericarditis. This was found to be the leading manifestation of their disease, which ultimately led to the diagnosis of SLE. These patients were initially treated with nonsteroidal anti-inflammatory drugs and colchicines; however, steroids and disease-modifying anti-rheumatologic agents were ultimately added to their medical therapy.

Keywords

Systemic lupus erythematosus, pericarditis

Introduction

Determining the etiology of acute pericarditis remains a challenge. It is not apparent at first and is divided into infectious and noninfectious causes. In all, 2% to 24% reported cases of pericarditis attributable to autoimmune etiology such as systemic lupus erythematosus (SLE), with 80% to 90% of cases being labeled as idiopathic or presumed to be viral.¹ Systemic lupus erythematosus commonly affects women of childbearing age, with the most reported symptoms being myalgia, fatigue, and mucocutaneous involvement in the form of rashes and photosensitivity. Cardiac involvement is reported in up to 25% of cases, including myocarditis, endocarditis, and pericarditis.^{2,3} It is rare for acute pericarditis to be the leading manifestation at the time of presentation. The following is a 3-patient case series in which acute pericarditis was the leading manifestation leading to the diagnosis of SLE.

Methods

Ethical and study approval was obtained from the Institutional Board Review at Kern Medical (Study # 21051). Three patients were retrospectively identified with acute pericarditis. Chart review was completed. A literature search was conducted using databases including PubMed, Google Scholar, and ResearchGate. The following search terms were applied:

acute pericarditis, management, diagnosis, SLE, and systemic lupus erythematosus. Patient consent was waived.

Case Presentation I

A young Hispanic man in his early 20s with no medical history presented to the emergency department (ED) with a 2-day history of new onset of shortness of breath with sharp, substernal chest pain worse with inspiration and lying supine, improved with sitting up and leaning forward. In the ED, the patient was febrile, tachycardic, and tachypneic. Physical examination on presentation was significant for pericardial friction rub with bilateral wrist swelling, tender to palpation with restricted range of motion due to pain. No evidence of any rashes or lesions was present. A 12-lead electrocardiogram (ECG) showed sinus tachycardia with diffuse ST elevation and PR depressions (Figure 1). Laboratory workup

¹Kern Medical, Bakersfield, CA, USA

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Corresponding Author:

Theingi Tiffany Win, MD, FACC, Division of Cardiology, Department of Internal Medicine, Kern Medical, 1700 Mount Vernon Avenue, Bakersfield, CA 93306, USA.

Email: theingi.win@kernmedical.com



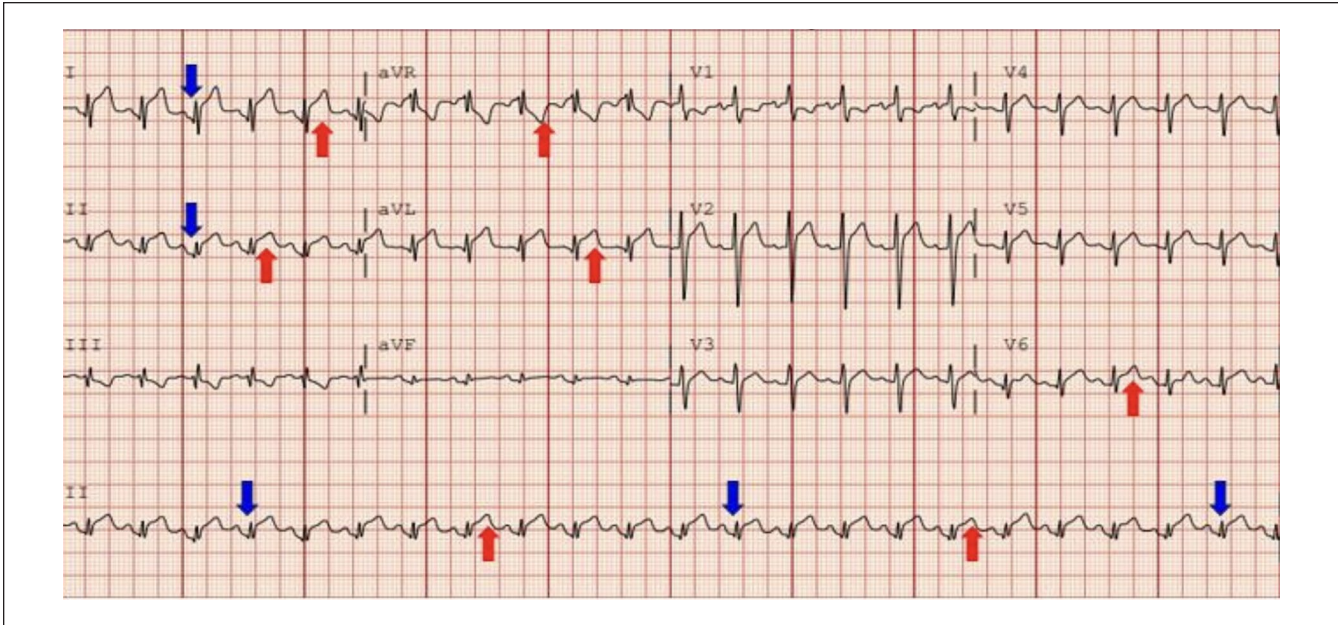


Figure 1. Electrocardiogram on initial presentation demonstrating diffuse ST-segment elevations (red arrows) with PR interval depressions (blue arrows) that are pathognomonic for pericarditis.

showed up-trending neutrophilic leukocytosis and elevated troponin-I to 0.35 ng/mL, with subsequent decrease to 0.21 ng/mL (normal <0.05 ng/mL).

Infectious workup was negative. Chest radiograph showed bilateral pleural effusions, while computed tomography (CT) of the chest was significant for 12 mm pericardial effusion and bilateral mild pleural effusion with bilateral axillary lymphadenopathy (Figure 2). Two-dimensional echocardiography was significant only for the small pericardial effusion with normal left ventricle ejection fraction (Figure 3). Full autoimmune workup with laboratory studies demonstrates an elevated antinuclear antibody (ANA) 1:1280 with positive anti-double-stranded DNA (dsDNA), Smith, and SM/RNP antibody, confirming the diagnosis of SLE.

The patient was subsequently started with colchicine 0.6 mg orally twice a day, indomethacin 25 mg orally thrice a day, and intravenous pantoprazole. Shortly after, the patient's symptoms and vital signs improved. The patient was discharged with colchicine 0.6 mg twice a day for 3 months and indomethacin 25 mg thrice a day for a week. He was followed up with outpatient rheumatology and started on prednisone 20 mg daily. A repeat chest radiograph at 2 months after discharge showed resolution of pleural effusions. Follow-up transthoracic echocardiogram (TTE), demonstrated complete resolution of pericardial effusion.

Case Presentation 2

A young African American woman in her early 40s with hypertension, heart failure with preserved ejection fraction, schizophrenia, and polysubstance abuse presented to the ED



Figure 2. Computed tomographic angiogram of the chest shows 8 mm pericardial effusion (red arrow) with moderate left pleural effusion and small right pleural effusion.

with progressively worsening chest pain and dyspnea for 2 days. Upon evaluation, the patient endorsed sharp, retrosternal chest pain worsened with inspiration. The examination was notable for a heart rate of 140 bpm, hypertension, tachypnea, and temperature of 100.5 °F. The remainder of the physical examination was unremarkable. Acute laboratory workup showed elevated cardiac biomarkers with troponin elevated to 0.14 ng/mL and ECG showing diffuse ST-segment elevations with PR interval depressions (Figure 4). Chest radiograph showed cardiomegaly concerning for a pericardial

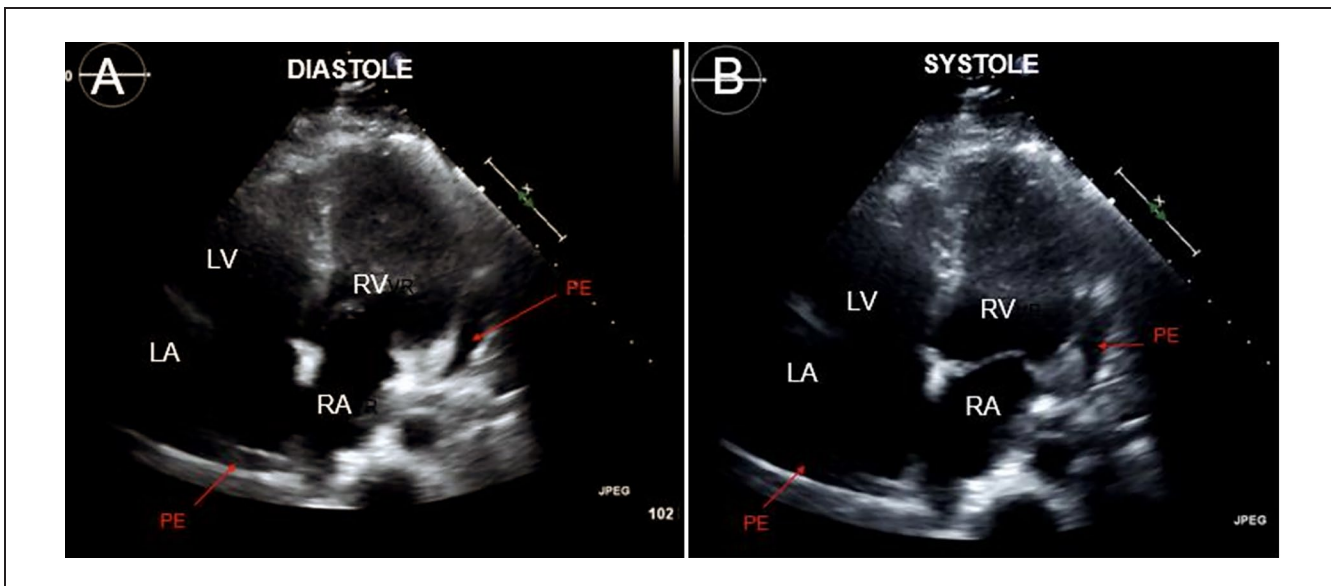


Figure 3. Transthoracic echocardiogram showing a small posterior pericardial effusion and small lateral pericardial effusion present in both (A) diastole and (B) systole without cardiac tamponade. Abbreviations: LV, left ventricle; RV, right ventricle; LA, left atrium; RA, right atrium.

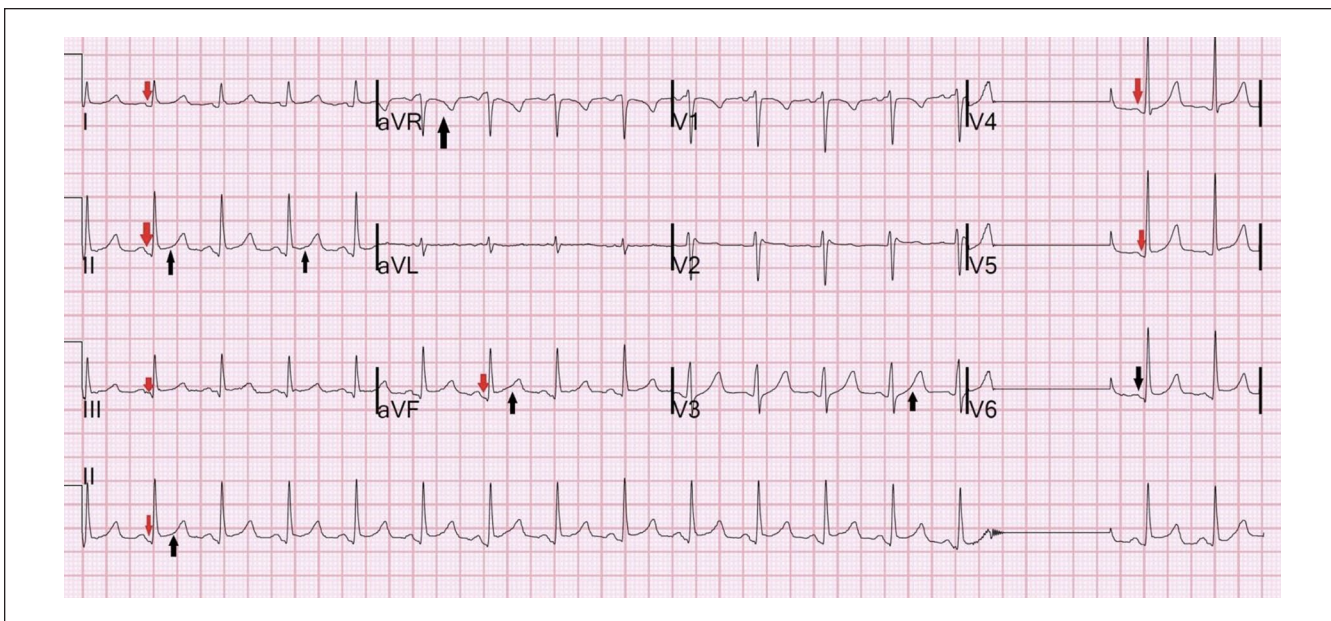


Figure 4. Electrocardiogram on initial presentation demonstrating diffuse ST-segment elevations (black arrows) with PR interval depressions (red arrows) that are pathognomonic for pericarditis.

effusion. Laboratory studies demonstrated a normal white blood cell count, but elevated C-reactive protein (CRP) at 22.70 mg/dL (reference range <0.30 mg/dL) and erythrocyte sedimentation rate (ESR). She was also found to have an elevated procalcitonin at 2.25 ng/mL (reference range <0.50 ng/mL). Infectious workups including blood cultures were negative.

Transthoracic echocardiogram revealed moderate circumferential pericardial effusion without evidence of new wall motion abnormalities (Figure 5). A CT of the chest further characterized the pericardial effusion measuring 16 mm along the left heart border and 19 mm along the right heart border (Figure 6). Indomethacin 50 mg thrice a day, colchicine 0.6 mg orally twice a day, and solumedrol 1 g daily were

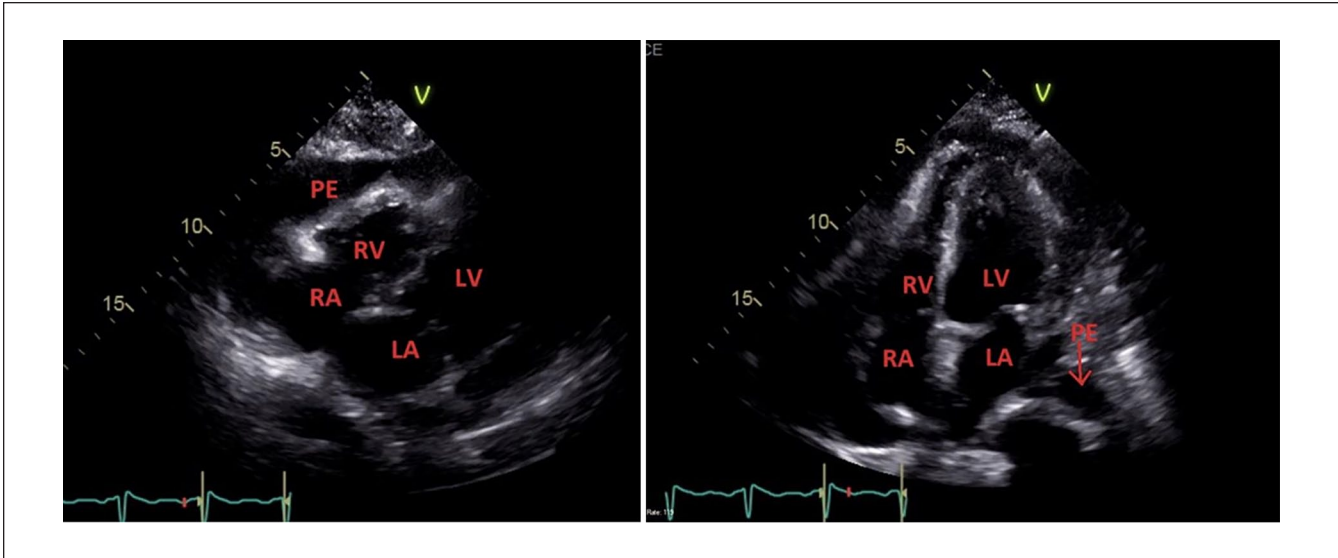


Figure 5. Transthoracic echocardiogram revealed moderate circumferential pericardial effusion. Abbreviations: RV, right ventricle; RA, right atrium; LV, left ventricle; LA, left atrium; PE, pericardial effusion.

subsequently initiated for the treatment of pericarditis. Additional workup revealed microscopic hematuria and proteinuria, which prompted further autoimmune serologic evaluation. Autoimmune workup demonstrated positive serologies of ANA 1:1280 with positive dsDNA, Smith, and SM/RNP antibodies, confirming the diagnosis of SLE. On hospital day 3, the patient began to improve significantly, expressing improved chest pain. She was followed up outpatient where she reported myalgia; however, the physical examination was unremarkable. Laboratory studies were significant for leukopenia; however, TTE demonstrated complete resolution of her pericardial effusion.

Case Presentation 3

An elderly Hispanic woman in her late 70s, with a history of hypertension and heart failure with preserved ejection fraction, was found to have pericardial effusion. The patient stated 2 weeks before admission she began to experience symptoms of generalized weakness. This was accompanied by decreased appetite, weight loss, shortness of breath, cough, and nonradiating chest pain. She previously walked 5 miles without any assistance; however, now she needed help to even use the restroom. The patient denied symptoms of fever, chills, arthralgia, rashes, oral ulcers, photosensitivity, and joint swelling. The family history for autoimmune diseases such as hypothyroidism, hyperthyroidism, lupus, or rheumatoid arthritis was negative. Physical examination was remarkable for mild pitting edema in bilateral lower extremities. Numerous labs were obtained to evaluate for viral versus inflammatory etiology. They were significant for positive ANA with a titer of 1:1280 with a speckled distribution, positive SSA antibody, and low levels of complements C3 and

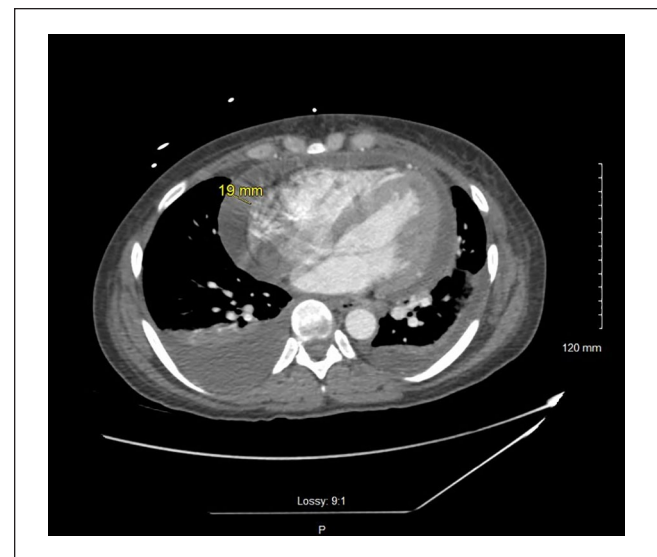


Figure 6. Computed tomography of the chest demonstrating a moderate to large pericardial effusion measuring 16 mm along the left heart border and 19 mm along the right heart border.

C4. The ESR and CRP were unexpectedly negative. An echocardiogram revealed grade I diastolic dysfunction with normal ejection fraction now with a trace of pericardial effusion, new when compared with the study 6 months earlier. The patient was followed up outpatient in rheumatology clinic where she was diagnosed with elderly onset SLE and started on azathioprine. Three months later, she presented to the ED with complaints of chest pain. The patient's symptoms were described as sharp, radiating to the back, worse with lying flat and during inspiration. The ECG was low

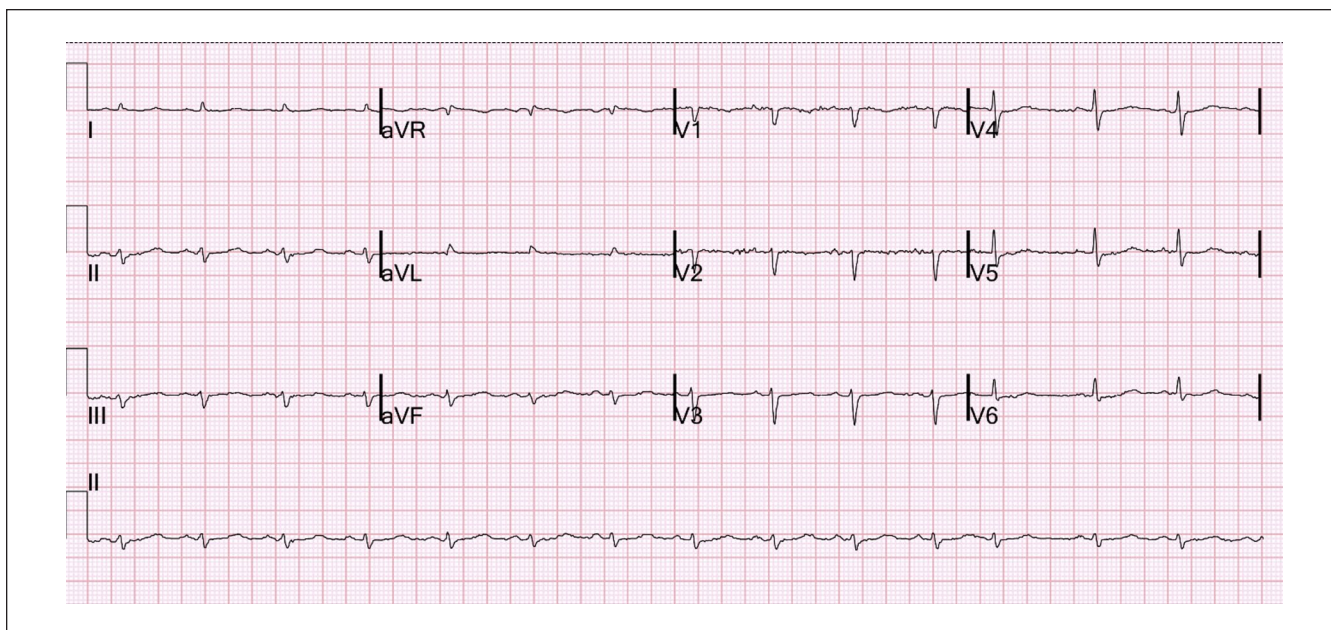


Figure 7. A 12-lead electrocardiogram demonstrating low voltage without signs of PR and ST-segment changes and without electrical alternans.

voltage, normal sinus rhythm, and did not show any signs of ischemia or electric alternans (Figure 7). Chest radiograph would demonstrate an enlarged cardiomeastinal silhouette (Figure 8) with a repeat echocardiogram showing a progressing, moderate-to-large pericardial effusion. She was acutely treated with naproxen 500 mg twice and colchicine 0.6 mg. The following day she had a pericardiocentesis that was unsuccessful. Cardiothoracic surgery was consulted for a pericardial window. About 450 mL of serosanguineous fluid was removed and 2 biopsies of the pericardium were obtained. Biopsies of the pericardium showed collagenous fibrous tissue and mesothelial cells with mild acute and chronic inflammation. Pathology of the pericardial fluid showed predominantly blood with mixed inflammatory cells and negative for malignant cells. The etiology of this pericardial effusion being secondary to SLE was confirmed. The patient was started on prednisone 60 mg daily and azathioprine was continued. She reported marked improvement in her shortness of breath and resolution of her chest pain; however, she was found to have swelling of bilateral shoulder and elbow joints. Laboratory studies were significant for leukopenia and a repeat echocardiogram showed no evidence of pericardial effusion

Discussion

We highlight the presence of acute pericarditis in 3 patients with no history of SLE. Table 1 highlights differences and similarities among our patients. Case 1 presented with chest pain and dyspnea, and was diagnosed with pericarditis. On examination, he was found to have swelling of bilateral wrist

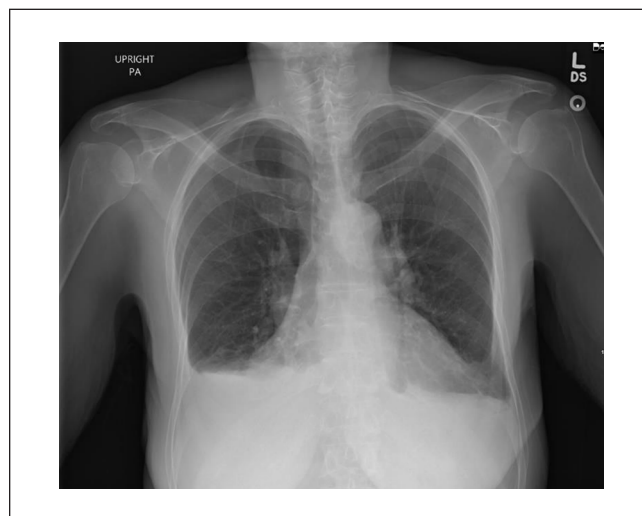


Figure 8. Chest radiography demonstrating enlarged cardiac silhouette.

joints, with no prior symptoms, family history, or diagnosis of SLE existing. Case 2 also presented with acute onset of chest pain, with no history of polyarthralgia, musculoskeletal pain, or diagnosis of SLE before her admission. Finally, our 77-year-old patient presented with insidious onset of generalized weakness and atypical chest pain, with echocardiographic findings demonstrating pericarditis. Cases 2 and 3 exhibited signs of leukopenia, and Case 3 also went on to develop bilateral shoulder and elbow swelling. Studies demonstrate 20% to 50% of patients with SLE will develop

Table 1. Summary of the Investigative Findings.

	Case 1	Case 2	Case 3	Reference range
Manifestations	Myopericarditis	Myopericarditis	Pericarditis	
Troponin-I	0.35 ng/mL	0.16 ng/mL	<=0.05	≤0.05 ng/mL
CK-MB	N/A	9.9 ng/mL	N/A	≤3.6 ng/mL
Echocardiogram	Ejection fraction 60% Normal systolic function Trace of pericardial effusion No wall motion abnormalities	Ejection fraction 55% Normal systolic function Moderate pericardial effusion No wall motion abnormalities	Ejection fraction 65% Normal systolic function Moderate to large pericardial effusion No wall motion abnormalities	
CRP	13.6 mg/dL	22.70 mg/dL	<0.30 mg/dL	≤0.30 mg/dL
ESR	91 mm/h	95 mm/h	1 mm/h	≤20 mm/h
Procalcitonin	0.14 ng/mL	2.25 ng/mL	<0.10 ng/mL	≤0.50 ng/mL
Leukocyte count on presentation	15.2 × 10 ³ /μL	8.6 × 10 ³ /μL	4.8 × 10 ³ /μL	4.5-11.0 × 10 ³ /μL
Infectious workup	Negative	Negative	Negative	
T _{max}	39.5°C	39.6°C	37.4°C	
ANA titer	1:1280	≥ 1:1280	1:1280	≤ 1:40
Anti-dsDNA	Positive	Positive	Indeterminate	
Anti-Smith	Positive	Positive	Negative	
Complement C3	Normal	Normal	Low	
Complement C4	Normal	Normal	Low	
Anti-cardiolipin	N/A	Negative	Negative	
Anti-B2GPI	N/A	N/A	Negative	
Lupus anticoagulant	N/A	Negative	Negative	
Other manifestations	Synovitis	Leukopenia	Synovitis Leukopenia	
Cytology:				
Pericardial fluid	N/A	N/A	Gross: Dark, red, nonclear fluid with piece of red blood clot Microscopy: Predominantly blood with mixed inflammatory cells. Negative for malignant cells Fluid analysis: Red color; bloody clarity, yellow supernatant with clear clarity	
Biopsy:				
Pericardium	N/A	N/A	Biopsy 1: Gross: flat portion of white-gray to pink tissue Microscopy: Collagenized fibrous tissue and mesothelial cells with mild acute and chronic inflammation Biopsy 2: Gross: membranous portion of tan-pink tissue Microscopy: Collagenized fibrous tissue and mesothelial cells with focal minimal acute and chronic inflammation	
EULAR/ACR point total (≥ 10 needed for diagnosis)	20	17	19	

Abbreviations: CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; ANA, antinuclear antibody; dsDNA, double-stranded DNA; EULAR/ACR, European League Against Rheumatism/American College of Rheumatology.

Table 2. Criteria for diagnosis of Pericarditis and Myopericarditis.

Acute pericarditis	Myopericarditis
1. Chest pain	Diagnostic criteria for acute pericarditis are satisfied, plus: 1. Elevated cardiac biomarkers and/or evidence of myocardial inflammatory involvement by an imaging technique 2. No evidence of new wall motion abnormalities or ventricular dysfunction
2. Pericardial rub	
3. Widespread ST-segment elevation or PR depression	
4. New or worsening pericardial effusion	

To make a diagnosis of acute pericarditis, 2 of the 4 criteria must be satisfied.

cardiac manifestations³ However, acute pericarditis as the initial manifestation of SLE is an uncommon finding, occurring in up to 1% of patients.⁴ A meta-analysis compared clinical manifestations of SLE between genders and found women were more commonly found to have the “classic” SLE manifestations of photosensitivity, malar rash, arthritis, and alopecia, whereas men were more commonly found to have renal involvement, serositis, and pleurisies.⁵

The pericardium is electrically silent and divided into parietal and visceral layers, each having a serous component containing mesothelial cells. The fibrous layer of the parietal pericardium consists of epicardial fat and dense collagen fibers. A previous study reported troponin elevation in 32% to 61% of patients with acute pericarditis, compared with a troponin elevation of 34% in patients with myocarditis.^{4,6,7} The term myopericarditis is used when there is the presence of cardiac involvement determined by abnormal cardiac enzymes and imaging demonstrating myocardial involvement, change in baseline cardiac function, or wall motion abnormalities⁸ (Table 2). Our patients experienced a brief rise in troponin levels attributed to acute pericarditis. With the increased recognition of myopericarditis and perimyocarditis, it is important to keep in mind a spectrum of cardiac manifestations that may exist with SLE.

The use of dsDNA and anti-Smith antibodies is highly specific and seen in approximately 70% and 30% of patients, respectively.⁹ A recent study investigated the value of a biomarker panel consisting of traditional markers (eg, ANA and anti-dsDNA). In this multicenter, cross-sectional study, a total of 593 subjects (210 patients with SLE, 178 patients with other rheumatic diseases, and 205 healthy individuals) were enrolled, and it was reported that a positive ANA in combination with anti-dsDNA resulted in a sensitivity of 84.5% and specificity of 90.7% in diagnosing SLE from other rheumatic diseases.¹⁰ In 2019, the European League Against Rheumatism (EULAR) and the American College of Rheumatology (ACR) generated new classification criteria for SLE. In validation of their cohort, they were found to have a sensitivity of 96% (95% confidence interval [CI], 0.95-0.98) and a specificity of 93% (95% CI, 0.91-0.95) when using their scoring system.¹¹ The 2019 EULAR/ACR was found to have a higher specificity than the other classification systems (Figure 9)

A meta-analysis demonstrated that an ANA titer of 1:80 was associated with a sensitivity of 98%.¹² However, in the

presence of a positive ANA titer and acute pericarditis, it is important to consider other differentials. Elevation of ANA is seen in several connective tissue diseases and chronic infections. A previous study demonstrated positive ANA titers have been seen in patients with recurrent pericarditis. When followed outpatient, the most common new diagnosis was primary Sjogren syndrome.¹³ Malignancy should also be considered, as a case report in 1990 demonstrated a man who presented with constitutional symptoms and acute pericarditis and found to have an ANA titer of 1:320 in his pericardial fluid. His serum ANA and antibodies were negative, and complement levels were normal. He was treated with prednisone and discharged with a tapering course. He was quickly readmitted to the hospital and found to have a massive, atypical lymphocytic infiltrate with large irregular nuclei, consistent with cardiac lymphoma.¹⁴ In 2004, another individual was identified to have malignancy after presenting with pericardial effusions and bilateral knee synovitis. The patient underwent pericardiocentesis which revealed elevated ANA 1:5120 in the pericardial fluid with serum ANA titer of 1:1280. He was discharged on steroid therapy but presented 1 month later and was found to have recurrent pericardial effusion. Biopsy at that time showed infiltration of the pericardium with epithelial-type mesothelioma.¹⁵

Nonsteroidal anti-inflammatory drugs (NSAIDs) are the primary choice in the management of pericarditis; however, SLE treatment includes disease-modifying anti-rheumatologic drugs (DMARDs), glucocorticoids, and even immunomodulators as SLE is an organ-threatening condition. Studies report mild pericarditis flares can be treated with methylprednisolone. Another study compared low-dose steroids with high-dose steroids in the treatment of acute pericarditis, which demonstrated reduced hospitalizations in the low-dose group. The high-dose steroids were found to have increased complications.¹ In patients with recurrent pericarditis secondary to SLE, immunomodulators are beneficial.¹⁶ In our case series, we presented multiple patients with acute pericarditis leading to the diagnosis of SLE. These patients recovered after management was tailored to treat the underlying condition

Conclusion

This case series highlights 3 patients with acute pericarditis who were later found to have SLE. In addition, there is a

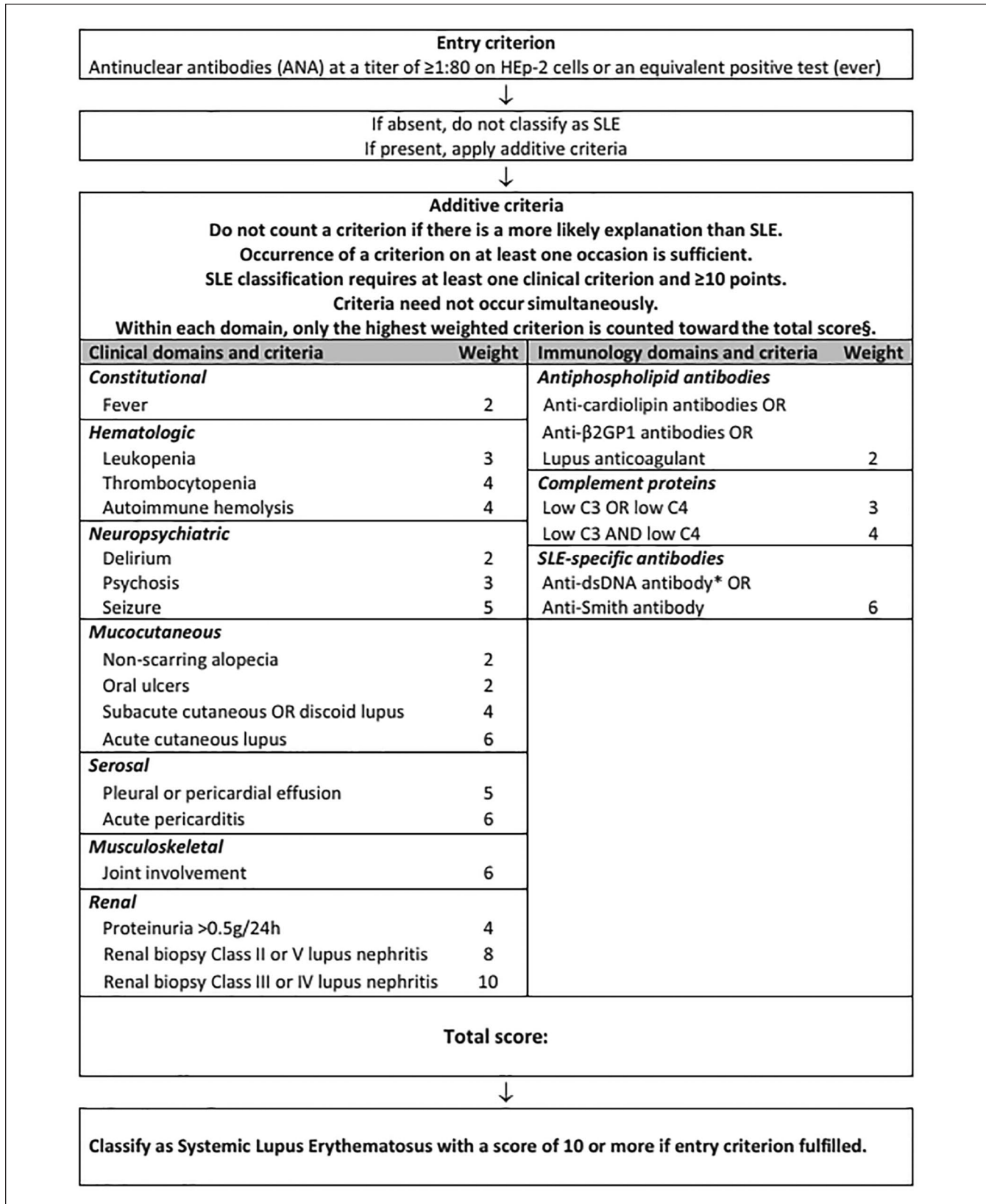


Figure 9. The 2019 EULAR/ACR SLE classification criteria.

Abbreviations: SLE, systemic lupus erythematosus; EULAR/ACR, European League Against Rheumatism/American College of Rheumatology.

difficulty that clinicians face when confronted with a patient with pericarditis that may not fit the prototypical patient picture of SLE. Cardiac manifestations of the disease are commonly reported in SLE patients, however rare on presentation.

Pericarditis is diagnosed in the acute setting and treated with anti-inflammatory agents. However, further investigation is warranted as it is crucial not to exclude an autoimmune etiology, as it is associated with high morbidity and mortality. Typical findings may not be present and require a thorough history and physical with laboratory and diagnostic studies. Despite acute treatment, many patients are dismissed from the primary setting without a thorough workup. The continued workup will provide an adjunctive therapeutic regimen upon confirmation of SLE. Steroids and anti-rheumatologic agents may have to be added to further control the acute condition and chronic progression of the disease. Keeping the autoimmune etiology upon presentation is crucial in the continued management of pericarditis.

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Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Ethics Approval

Ethical approval to report this case was obtained from the Kern Medical Institutional Review Board (Approval ID: 21051).

Informed Consent

Informed consent for patient information to be published in this article was not obtained as patients were unable to be traced.

ORCID iD

Vishal K. Narang  <https://orcid.org/0000-0003-4583-0270>

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