Candida Pericarditis and Tamponade in a Patient With Systemic Lupus Erythematosus

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- *Candida* pericarditis and tamponade developed in a patient with sterile purulent pericarditis secondary to systemic lupus erythematosus. Therapy with amphotericin B and properly timed surgical intervention led to a clinical and microbiological cure. This article emphasizes the importance of differentiating an infected pericardial effusion from the sterile pericarditis of systemic lupus erythematosus and provides suggested guidelines for the management of that complication.

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Although pericarditis is a common manifestation of systemic lupus erythematosus (SLE), the occurrence of cardiac tamponade is a rare event. Moreover, a review of the literature indicates that only four cases of infective pericarditis complicating SLE during life have been reported. We recently had the opportunity to treat a patient with SLE in whom a large pericardial effusion rapidly evolved to tamponade. Following surgical drainage, tamponade resolved and proved to be due to a superimposed infection with *Candida albicans*. Therapy with amphotericin B and pericardectomy led to survival. This case underscores the importance of identifying infectious complications in patients with SLE who have active disease and would otherwise be treated with immunosuppressive agents. The differentiation of infected from sterile pericarditis in SLE and a combined medical-surgical approach to its management are addressed herein.

**REPORT OF A CASE**

A 17-year-old girl presented with a facial rash, polyarthralgias, a low antinuclear antibody titer (1:80), and hypocomplementemia (C3, 0.6 g/L [58 mg/dL] [normal, 0.8 to 1.5 g/L (83 to 177 mg/dL)]; C4, 0.1 g/L [8 mg/dL] [normal, 0.2 to 0.5 g/L (15 to 45 mg/dL)]). She was treated successfully with nonsteroidal anti-inflammatory agents.

At the age of 18 years, she underwent a normal spontaneous vaginal delivery and developed thrombophlebitis and knee synovitis during the postpartum period. There was no evidence of a circulating anticoagulant. She was treated with anticoagulation, without sequelae.

She then remained well until two weeks before admission at the age of 20 years, when she developed an upper respiratory tract infection characterized by a low-grade fever and pharyngitis. One week later (March 1, 1986), she was admitted to a local hospital with a temperature of 39.4°C, dyspnea, a nonproductive cough, and a pulmonary infiltrate seen on a chest roentgenogram. Urinalysis revealed pyuria, and a urine culture was positive for *Escherichia coli*, with a count of more than 100,000/mL. Therapy with cefazolin sodium was begun. An antineutrophil antibody was present, at a titer of 1:640. Over the next few days, the patient became progressively more catabolic and developed atrial fibrillation. Chest roentgenography revealed cardiomegaly; echocardiography demonstrated a pericardial effusion.

On March 9, 1986, pericardiocentesis was performed, and 70 mL of serosanguineous fluid was obtained. A percutaneous pericardial drain was placed, with removal of an additional 670 mL. The pericardial drain was then withdrawn, and digoxin therapy was begun. The leukocyte count was 10,000 leukocytes/mL (with 95% polymorphonuclear leukocytes); the erythrocyte count was 55.7 x 10^10/L (55,700/mm^3); and the culture was negative. The patient then developed hemolytic anemia with a positive Coombs' test and was transferred to the University Hospital, State University of New York at Stony Brook.

On admission, the patient's pulse rate was 100 beats per minute and the blood pressure was 140/80 mm Hg, with a systolic ejection murmur heard along the lower left sternal border with an S_2 gallop, and the liver was palpable 8 cm below the right costal margin with a span of 15 cm in the right midclavicular line. Laboratory values were as follows: leukocyte count, 7.5 x 10^9/L (7500/mm^3) (with 0.49 [49%] polymorphonuclear leukocytes, 0.38 [38%] nonsegmented, and 0.13 [13%] lymphocytes); hemoglobin, 7.6 g/dL (7.6 g/dL normal, 11–13 g/dL [normal]); platelet count, 130 x 10^9/L (130,000/mm^3); prothrombin time, 10.4 s; activated partial thromboplastin time, 26 s; partial thromboplastin time, 42.4 s; antithrombin III, 60% (normal, 75–90%); C3, 0.1 g/L (11 mg/dL); C4, 0.04 g/L (4 mg/dL); and erythrocyte sedimentation rate, 100 mm/h. Anti-Ro, anti-La, anti-RNP, and anti-Sm were negative. Chest roentgenography revealed bilateral pleural effusions, no infiltrate, and cardiomegaly. Thoracentesis disclosed an exudative sterile fluid. Empiric therapy with cefotaxime sodium (2 g/6 h, given intravenously) and methylprednisolone sodium succinate (100 mg/d, given intravenously) was initiated.

Three days later (March 12, 1986), recurrent pericardial effusion and tamponade were present, as indicated by echocardiography and measurements with a Swan-Ganz catheter. Percutaneous pericardiocentesis was again performed, and 260 mL of serosanguineous fluid was removed. The leukocyte count was 16.4 x 10^9/L (16,425/mm^3) (9.80 [90%] polymorphonuclear leukocytes, 0.09 [9%] lymphocytes, 0.02 [2%] monocytes, 0.01 [1%] neutrophilic bands, and 0.005 [0.5%] eosinophils); the platelet count was 34.4 x 10^9/L (34,425/mm^3), and the culture was negative. Recurrent fever (38.9°C to 39.4°C) developed on March 16, and therapy with nafcillin sodium was begun for a suspected *Staphylococcus aureus* infection at the site of the Swan-Ganz line.

On March 21, a third pericardiocentesis was performed, because of persistent spiking fevers, recurrent tamponade, and multiple negative blood cultures obtained on March 10, 15, 16, and 20. The...
leukocyte count was 12.6 × 10^9/L (12,600/mm^3) (0.97 [97%] polymorphonuclear leukocytes, 0.03 [3%] monocytes); the erythrocyte count was 1.3 × 10^12/L (1270/mm^3). *Candida albicans* was grown from the cultures of the catheter site from March 16, the pericardial fluid from March 21, and two of the five sets of blood cultures from March 22. Therapy with amphotericin B was initiated at a dosage of 35 mg/d (0.6 mg/kg/d).

On April 2, 1986, pericardial fluid reaccumulated and subxiphoid drainage tubes were surgically inserted. Approximately 1000 mL of purulent fluid was removed (leukocyte count, 42.3 × 10^9/L [42300/mm^3]) [0.90 (90%) polymorphonuclear leukocytes, 0.10 (10%) monocytes], erythrocyte count, 2.2 × 10^12/L (2200/mm^3)], and a pericardial biopsy specimen was obtained. There was histological evidence of an organizing fibrinous pericarditis. There was no evidence of vasculitis, a periodic acid–Schiff stain was positive for hyphal elements, and a culture of the pericardial fluid was positive for *C. albicans*. Fever persisted. Echocardiography indicated loculation of pericardial fluid, and equalization of diastolic pressures was demonstrated by Swan-Ganz measurements.

Because of the possibility of pericardial constriction, an extended anterior pericardiotomy was performed through a left-sided thoracotomy on April 18. The pericardium was noted to be thickened, and the plane between the visceral and parietal pericardium was obliterated, with the exception of an occasional area of loculated fluid. Histologically, acute and chronic pericarditis were demonstrated. A methenamine silver stain showed degenerating hyphal forms (Figure), and the pericardial fluid was sterile.

A full course of amphotericin B was completed, and the patient remained hemodynamically stable thereafter. Tapering doses of methylprednisolone were given, and no further serositis developed.

**COMMENT**

Pericarditis is a common manifestation of SLE, being demonstrated in 21% to 46% of patients by means of echocardiography. However, cardiac tamponade is rare and in a recent review was noted in only 11 of 1332 cases of lupus pericarditis (0.8%). The pericardial fluid is generally sterile and resembles the pleural fluid described in patients with SLE characterized by low complement levels and an occasional LE cell. A depressed pericardial fluid pH has also been noted. Resolution is usually achieved with non-steroidal anti-inflammatory agents or, in more severe instances, with corticosteroids. Infective pericarditis is an unusual and life-threatening complication of the pericardial effusion typically seen in SLE.

The patient described herein continued to be febrile and reaccumulated pericardial fluid despite treatment with high doses of methylprednisolone sodium succinate (100 mg/d). Severe hypocomplementemia, elevated DNA binding, and other serologic abnormalities supported a diagnosis of active SLE. Sequential *C. albicans*–positive cultures from a catheter site, blood, and pericardial fluid suggested hematogenous seeding of an aseptic purulent pericarditis due to SLE. It is likely that this patient’s active disease and previous therapy with multiple antibiotics and high-dose corticosteroids predisposed her to fungal colonization and subsequent fungemia. To our knowledge, this is the first reported case of fungal pericarditis in SLE and the second patient reported to have survived *Candida* pericarditis. All of the previous reported cases of infective pericarditis in SLE were due to *S. aureus* and *Mycobacterium tuberculosis*.

The spectrum of purulent pericarditis is changing. Specifically, as reflected by our patient, there has been an increasing number of opportunistic fungal infections. To our knowledge, there were no reports of fungal pericarditis prior to 1957, and there have been only ten reported cases of pericarditis due to *Candida* species. Only one of these ten patients survived.

In the past, it has been recommended that pericardio¬centesis not be performed once a diagnosis of SLE is established. This recommendation is based on reports of myocardial and coronary artery lacerations in patients with SLE subjected to pericardial aspirations. Clearly, however, the presence of cardiac tamponade and/or the need to distinguish superinfection justify the risk of this procedure.

As noted, the outcome for *Candida* pericarditis has been poor. Our experience with the patient described herein, and

### Reported Cases of Purulent Pericarditis in Systemic Lupus Erythematosus

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*Method of drainage not specified.*

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the experience of others, suggests that a combined medical-surgical approach is best. The finding of an initial positive pericardial fluid culture followed by a negative culture and the later demonstration of degenerating hyphae in pericardial tissue indicate that the infection was cured microbiologically. Adequate amphotericin B levels are obtained in the pericardial fluid during therapy for fungal pericarditis.2,8,9

Although sterility can be achieved within the inflamed pericardium, medical therapy alone is probably insufficient. As indicated by the findings at thoracotomy and by the presence of loculated fluid on the echocardiograms, an effusive-constrictive process had rapidly developed in our patient. Such a condition will frequently lead to constriction without surgical intervention.22 This rapid evolution of infectious pericarditis to a subacute effusive-constrictive stage within weeks is in contrast with the natural history of constriction seen (rarely) with SLE alone or (most commonly) with rheumatoid arthritis, wherein the duration of disease prior to constriction can be as long as 20 years.23 Furthermore, the therapy of choice for constrictive pericarditis in rheumatoid arthritis is also surgical, since corticosteroids or remittive agents do not appear to alter its development or progression.24

In our patient, we decided to use a left-sided thoracotomy in performing the pericardiectomy because of our fear that a midline sternotomy might further disseminate the organism in the form of a Candida osteomyelitis. Our approach avoids that potential hazard and provides an outcome equal to that of a midline sternotomy.25

CONCLUSION

Previously reported experience and our experience favor an aggressive approach to the treatment of purulent pericarditis in SLE. We propose that the presence of a rapidly enlarging pericardial effusion, with or without evidence of tamponade, requires pericardiocentesis to identify or exclude the presence of an infective pericarditis. Once that diagnosis is established, therapy with antibiotics and subxyphoid surgical drainage is initially useful but may not be definitive. Patients should then be followed up closely (at weekly intervals) with echocardiographic assessment. Evidence of pericardial thickening and loculation suggest a progressive effusive-constrictive pattern. Such a pattern must be confirmed by hemodynamic measurements and indicates the need for early pericardiectomy.

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References