CARDIAC TAMPONADE AND PERICARDIAL DISORDERS IN CONNECTIVE TISSUE DISEASES: CASE REPORT AND LITERATURE REVIEW

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Pericardial disorders occurring in connective tissue diseases are not uncommon and may present as acute or chronic pericarditis with or without an effusion. In many instances, a diagnosis of pericardial involvement is not found until autopsy. Echocardiography and other currently employed radiographic techniques have enhanced the ability to make a diagnosis. Approximate frequencies of common connective tissue disorders with pericardial involvement include scleroderma (59%), systemic lupus erythematosus (44%), mixed connective tissue disease (30%), rheumatoid arthritis (24%), and polymyositis/dermatomyositis (11%). Cardiac tamponade or constriction is rare. This article describes a patient with clinical features consistent with mixed connective tissue disease that presented with a pericardial effusion and cardiac tamponade. In addition, a review of pericardial involvement in connective tissue diseases and the occurrence of cardiac tamponade or constriction is included. (*J Natl Med Assoc.* 1994;86:149-153.)

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Pericardial disorders in connective tissue diseases such as systemic lupus erythematosus (SLE) may present as acute or constrictive pericarditis with or without effusions.[1] Symptoms may be insidious or may present suddenly and progress rapidly to acute life-threatening occurrences. Etiologically, pericardial disorders may be classified as infectious pericarditis, idiopathic pericarditis (at times, probably due to undiagnosed viral disease), and pericardial involvement related to hypersensitivity or autoimmunity.[2]

Pericardial disorders are not unusual in connective tissue diseases. However, cardiac tamponade is rare. This report describes a case of cardiac tamponade in an individual with clinical features consistent with mixed connective tissue disease and no previous history of rheumatologic or cardiac disease. A review of pericardial disorders in other connective tissue diseases also is presented.

CASE REPORT

A 26-year-old black male was in good health until 2 weeks before admission when he presented to the emergency room complaining of chest pain related to breathing, sore throat, and greenish-yellow sputum. Physical examination was positive for pharyngitis. Chest radiograph revealed a small pleural effusion at the left lower base. Throat, blood, and sputum cultures were negative. He was treated with a 10-day course of oral ampicillin, 500 mg three times daily. Three days later, he returned with complaints of a swollen, tender right elbow

and a 2-day history of fever and chills. Physical examination revealed: blood pressure 110/70 mm Hg, pulse 108 beats/min, respiratory rate 22 breaths/min, and a temperature of 38.3°C. Breath sounds were decreased in the region of the left lower lobe with dullness to percussion and E to A changes. A resting tachycardia was present without murmurs, gallops, or rubs. The right elbow was tender, swollen, and warm to touch. He was admitted for further evaluation.

Admission laboratory studies showed a white blood cell count (WBC) of 11.1 K/mm^3 with a differential of 72% polymorphonuclear cells, 11% bands, 5% lymphocytes, 11% mononuclear cells, 1% eosinophil, and 1% basophil; a red blood cell count (RBC) of 5.07 million/mm^3 with normal indices, and a normal chemistry profile except for an albumin of 3.1 g/dL (normal 3.5-5.0) and lactate dehydrogenase 301 IU/L (normal 100-225). A urinalysis revealed 4+ albumin, 3-5 WBCs per high-power field, 0-2 RBCs per high-power field, and a few bacteria. A urine culture was negative. A 24-hour urine test revealed a creatinine clearance of 83 mL/min (normal 85-125) and a total protein of 9.3 g/24 hours (normal 25-150 mg/24 hrs).

Fifteen milliliters of purulent fluid was aspirated from the elbow. An analysis of the fluid demonstrated a WBC of 38 K/mm^3 with 98% polymorphonuclear cells and 2% mononuclear cells; 6 K/mm^3 RBCs; a total protein of 5.1 g/dL (normal 1-3); and glucose of 86 mg/dL (normal 70-110). Gram stains, bacterial cultures, acid-fast bacteria, fungal smears and cultures, and countercurrent immunoelectrophoresis all were negative. Thoracentesis of the left lower lobe revealed a WBC of 41.5 K/mm^3 with 99% polymorphonuclear cells and 1% mononuclear cells (normal WBC $<$1000 K/mm^3 and $<$25% polymorphonuclear); total protein of 4.5 g/dL; glucose 52 mg/dL; pH of 7.14; and lactate dehydrogenase of 714 IU/L. Gram stains, fungal and acid-fast bacterial smears, countercurrent immunoelectrophoresis, and cultures all were negative. Suspecting an empyema, a chest tube was placed into the left hemithorax. The patient was treated with a 7-day course of intravenous cefamandole and gentamicin until cultures were confirmed to be negative.

On the fourth hospital day, a pericardial rub was noted, and a moderate posterior pericardial effusion was demonstrated by a two-dimensional echocardiogram. The patient was noted to have a right-sided pleural effusion, and a thoracentesis revealed a WBC of 3.6 K/mm^3 with 83% polymorphonuclear cells and 17% mononuclear cells, RBC of 60 K/mm^3, total protein of 4.6 g/dL, glucose of 92 mg/dL, lactate dehydrogenase 1240 IU/L, and pH of 7.31. Cultures remained negative.

Three days later a repeat echo showed an increased amount of pericardial fluid but no sign of tamponade. The next morning he became tachypneic and hypotensive (90/60 mm Hg). His radial pulse was noted to be 50-60 beats/min. A pulsus paradoxus of 12 mm Hg was noted using a sphygmomanometer. An electrocardiogram demonstrated low voltage and diffuse ST segment evaluation. He was transferred to the intensive care unit where an attempted pericardiocentesis was unsuccessful. His condition continued to deteriorate, and a pericardiostomy was performed and yielded approximately 600 mL of serosanguinous fluid. A Jackson Pratt drain was placed within the pericardial space. A gram stain of the pericardial fluid showed few WBCs but was negative for organisms. Routine bacterial, acid-fast bacterial, and fungal cultures were negative. A biopsy of the pericardium showed fibrinous pericarditis with neutrophilic and lymphocytic infiltrates throughout but no granulomas. On June 11, 1984, the patient experienced a brief episode of second and third degree heart block, which required no specific therapy. He remained asymptomatic from further episodes of heart block and was transferred out of the intensive care unit.

An antinuclear antibody screen by standard indirect immunofluorescence[3] demonstrated a speckled pattern with a titer of 1:40 000. An extractable nuclear antigen was positive for antinuclear ribonucleoprotein (anti-nRNP) antibodies by double immunodiffusion.[3] Antibodies to native deoxyribonucleic acid (nDNA) by the Crithidia luciliae method, Smith antigen, SS-A(Ro) and SS-B(Ha,La) by double immunodiffusion[3] were negative. A rheumatoid factor and lupus erythematosus prep were negative. Complements consisting of C3, C4, and properdin factor B all were within normal limits. An erythrocyte sedimentation rate was elevated at 72 mm/hr (normal range 0 to 15 mm/hr).

A rheumatologic consultation was obtained and noted the presence of bilateral knee and ankle effusions, sclerodactyly, and a history consistent with Raynaud's phenomenon. In view of the patient's positive antinuclear antibody, anti-nRNP antibody, and other clinical and laboratory findings, a diagnosis of mixed connective tissue disease was proposed.

The patient was started on prednisone, 1 mg/kg/day in three divided doses with marked improvement in his cardiopulmonary symptoms. Eight days later a computerized tomography (CT) scan was performed of his chest to exclude other possible causes of the pericardial effusion. No lesions were found, and only a trace amount of pericardial fluid was noted. His pleural effusions had completely resolved. A 24-hour urine test

obtained before his discharge showed a decrease in total protein to 2 g/24h. The patient was discharged on a slow tapering course of prednisone.

One month later, a repeat CT scan of the chest and echocardiogram showed complete resolution of the pericardial effusion and no other pulmonary lesions.

DISCUSSION

Mixed connective tissue disease has been described as a rheumatic disease syndrome characterized by features that resemble SLE, rheumatoid arthritis, progressive systemic sclerosis (scleroderma), and polymyositis/dermatomyositis, with high titers of circulating antibodies against nRNP.[4]

Since the first description of 25 people with mixed connective tissue disease,[4] the disease entity has been described extensively, including cases with cardiac involvement. A clinical evaluation of 16 patients with mixed connective tissue disease, by Oetgen et al,[5] reported a 38% incidence of cardiac abnormalities including pericarditis, asymmetric septal hypertrophy, and left ventricular dilatation. In a study by Alpert et al[6] of 38 patients with the disease, symptoms potentially attributed to the cardiovascular system were noted in 32 patients. Cardiovascular examination revealed abnormalities in 30 of 38 patients. Such abnormalities included acute pericarditis with or without pericardial effusion, mitral valve prolapse, intimal hyperplasia of the coronary arteries, perivascular and myocardial lymphocytic infiltrates including clinical myocarditis, and pulmonary hypertension.

Cardiac involvement in children with mixed connective tissue disease also was found not to be unusual. In one study, an evaluation of 14 children with the disease revealed six with pericarditis and nine with aortic insufficiency.[7]

Pericarditis has been the most frequent cardiac finding in mixed connective tissue disease.[8] In a study by Oetgen et al,[5] 25% had evidence of pericarditis. Alpert et al[6] noted 29% with pericardial abnormalities detected by clinical and laboratory findings. A 43% incidence of pericarditis was detected by Singsen et al.[7] Leung et al[9] reported 4 of 17 (24%) patients with pericardial abnormalities by echocardiography. Two (12%) of these patients had small pericardial effusions. Nunoda et al[10] described a 55-year-old female with mixed connective tissue disease who developed perimyocarditis and pericardial effusion. Pericardiocentesis was performed, and 300 mL of straw-yellow colored fluid was removed.

The pathogenesis of pericarditis in mixed connective tissue disease is unclear, but Negoro et al[11] suggest it is attributable to the activation of the complement system by locally formed ribonucleic protein immune complexes. Although there is a high frequency of pericardial involvement in mixed connective tissue diseases, the incidence of cardiac tamponade is very rare. In a review of the English literature, only two other cases in addition to the current case have been reported. In a study by Alpert et al,[6] postmortem examination of four patients with mixed connective tissue disease was performed. Pericardial abnormalities were noted in three out of four patients. A large quantity of serosanguinous pericardial fluid and diffuse inflammation of the epipericardial surface were noted during pathologic examination of the patient with cardiac tamponade. There were widespread fibrin deposition and infiltration with polymorphonuclear leukocytes on histologic examination of this case. In another report,[9] a patient with a 6-year history of mixed connective tissue disease had purulent pericarditis and cardiac tamponade caused by *Nocardia asteroides.* However, no information was given detailing other symptoms of the disease at the time of her tamponade or when the diagnosis was made in relationship to the event.

TABLE. FREQUENCY OF PERICARDIAL INVOLVEMENT IN VARIOUS CONNECTIVE TISSUE DISORDERS

Disorders	%
Mixed connective tissue disease[5-7,9]	30.3
Systemic lupus erythematosus[1,12-17]	44
Rheumatoid arthritis[18-21]	24
Scleroderma[22-26]	58.6
Polymyositis/dermatomyositis[27-32]	11.4

*Percentage represents average of referenced studies.

The incidence of pericardial involvement has been found to be high in SLE,[1,12-17] rheumatoid arthritis,[18-21] and scleroderma,[22-26] but not in dermatomyositis/polymyositis.[27-32] Pericardial abnormalities were noted to be much more frequent when using echocardiography or at autopsy compared to clinical evaluation alone.[6,15,18,19,22,33,34] However, the occurrence of tamponade was rare in all these diseases. The table represents averages of clinical, echocardiographical, and pathological studies of pericardial disorders in various connective tissue diseases.

There have been a few reports of tamponade presenting as the initial manifestation of SLE.[12-14,16,17] Studies of patients with SLE have reported a 20% to 50% incidence of clinical pericarditis.[12] Pericardial

fluid ranged in color from serous to hemorrhagic. Pericardial effusions were detected in 50% by echocardiography, and up to 80% had pericardial involvement at autopsy.[13-15] Askari et al[12] reviewed several reports on pericarditis and tamponade in SLE. Of 1116 cases of SLE, pericarditis was found in 321 (28.7%) and tamponade in five (0.45%). In the individual series reviewed, the incidence of tamponade ranged from 0% to 2%. In a report by Swaak et al,[35] a weak association was found between the presence of anti-nRNP antibodies and pleuropericarditis.

In necropsy studies on patients with rheumatoid arthritis, the incidence of pericarditis varied from 11% to 50%.[18] In a study by MacDonald et al,[19] 16 of 51 patients (31%) had echocardiographic evidence of pericardial effusion. Two other patients were noted to have pericardial thickening. Bacon and Gibson[20] found echocardiographic evidence of pericardial effusion in 50%, 15%, and 0% of patients with chronic nodular rheumatoid arthritis, typical non-nodular rheumatoid arthritis, and osteoarthritis, respectively. In a review of the literature on cardiac tamponade and constrictive pericarditis in rheumatoid arthritis, pericardial tamponade has been documented in association with it in 20 cases[18]; at the time of the tamponade, 84% of the patients had moderate to severe rheumatoid arthritis. Escalant et al[21] noted the prevalence of cardiac compression with tamponade in rheumatoid arthritis varied from 0.22% to 0.5%.

McWhorter and Leroy[22] reviewed records of 210 patients with scleroderma and identified two patterns of pericardial disorders in 15 patients. One pattern of chronic pericardial effusion in 11 of 15 patients occurred in association with chest pain, dyspnea, cardiomegaly, and symptoms of congestive heart failure. Another pattern found in four patients consisted of acute pericarditis with fever, pericardial friction rub, dyspnea, and chest pain. Early evidence of tamponade was reported in three patients, but no emergency intervention was required. Autopsies were performed on 34 of the 210 patients. Pericardial involvement (defined as fibrinous or fibrin adhesions or pericardial effusion of 50 cc or greater) was found in 19 patients (56%). Sackner et al[23] noted pathology of the pericardium as a common feature in 18 of 25 (72%) postmortem examinations of patients with scleroderma. D'Angelo et al[24] compared 58 autopsied patients with scleroderma with 58 matched controls and found pericardial lesions in 55% compared with only 12% of the controls. However, the incidence of pericardial effusion was the same as in controls.

There has been an increasing number of reports of cardiac involvement in polymyositis and dermatomyositis.[27-32] However, the incidence of pericardial involvement appears small, which may be due in part to underutilization of echocardiography in evaluation of patients with these disorders. In a study by Bitnum et al,[30] 2 of 13 children had a friction rub and one had a history of pericardial effusion. Askari and Huettner[27] reported two cases of pericardial effusion out of eight patients evaluated with cardiac abnormalities. In a study of 21 patients with polymyositis, Gottdiener et al[31] detected 16 (76%) with evidence of cardiac abnormalities, but pericardial effusion was detected in only one case. In another study,[28] 67 of 134 (50%) patients were found to have an abnormal cardiac finding, but no evidence of pericardial involvement was detected. No cases of tamponade were reported in the above studies of patients with polymyositis or dermatomyositis.

The treatment of pericarditis included the use of nonsteroidal anti-inflammatory drugs with or without corticosteroids, or removal of the pericardial fluid if cardiac tamponade existed.[6,12,15-17,21,22,36,37] Occasionally, resection of the pericardium was required when constriction of the pericardium was present.[18] In most cases, acute pericarditis was self-limiting and treatment was primarily symptomatic, using nonsteroidal anti-inflammatory drugs to relieve the pain. In instances of effusion without tamponade, corticosteroids were usually effective in resolving symptoms and eliminating pericardial fluid. The treatment of cardiac tamponade was to remove the pericardial fluid and lower pericardial pressure toward normal. This was usually done by pericardiocentesis or a surgical procedure.

CONCLUSION

Pericardial disorders can occur in various connective tissue diseases and may be fatal rarely. Pericardial effusions commonly go undetected clinically in connective tissue diseases and are not found until autopsy. If pericardial effusion is suspected upon evaluation of a patient, an echocardiogram should be performed and followed serially to determine if the effusion is progressive and to monitor response of the effusion to therapy. One should be prepared to treat cardiac tamponade if a patient deteriorates suddenly.

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