TUBERCULOSIS ON REGULAR HEMODIALYSIS
—A Case of Pericardial Tamponade—

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The patient presented in this paper had been stable for 3 months after the induction of hemodialysis, when nausea, vomiting and hepatomegaly suddenly developed. A chest film revealed rush cardiomegaly, and massive pericardial effusion was demonstrated by echocardiography. One liter of hemorrhagic fluid was removed by pericardiocentesis and subsequent pericardial drainage under echocardiography.

The patient received chemotherapy against pulmonary tuberculosis 30 years ago and calcification on chest film was apparent. Although sputum smear and pericardial effusion was negative for acid-fast organisms, combination therapy was initiated for suspected tuberculosis. The patient recovered completely and 2 months later it was demonstrated that cultures of sputum grew mycobacterium tuberculosis. Tuberculin skin test (PPD), which was negative 2 months previously, converted to positive.

Tuberculosis must be considered as a potential cause of pericardial tamponade in patients on regular hemodialysis, and prompt therapy for both cardiac tamponade and the occult infection is warranted.

The incidence of tuberculosis in dialyzed patients has been reported to be 1.6–3.3%, which is 6–16 times greater than that in the general population.1–6 The immune deficiencies of chronic renal failure might be suspected to be predisposing factors to the development of tuberculosis.5,6 In addition, it is reported1,2,5,6 that unusual symptoms and a high frequency of extrapulmonary lesions were characteristic of tuberculosis in dialyzed patients. Therefore, a delay in diagnosis might be one of the factors leading to increased mortality in this group3,5,6

We experienced a case in which cardiac tamponade was a first sign of tuberculosis.

CASE REPORT

A 68 year old male was admitted to our hospital in end-stage renal failure in September 1987 for the induction of maintenance hemodialysis treatment. After 3 months of stability, he developed nausea, vomiting and a slight fever. Physical examination revealed hepatomegaly, but no pulmonary rales nor pretibial edema. Heart sound was clear and friction rub was not detected. Emergency laboratory findings disclosed a white blood cell count of 12700/mm³ with 87% neutrophil and 13% lymphocyte, a red blood cell count 223 x 10⁴/mm³, hemoglobin 6.4 g/dl, hematocrit 20.8% and thrombocyte 27.8 x 10⁴/mm³. The serum creatinine and

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blood urea nitrogen level were 11.2 mg/dl and 70 mg/dl respectively before dialysis. The serum levels of GOT, GPT, LDH and CPK were 1530 IU/L, 1290 IU/L, 3010 WU/L and 42 IU/L, respectively. Therefore, initially acute hepatitis was suspected (Fig. 1). However, the patient became dyspeptic and the electrocardiogram showed electrical alternans. R wave showed low voltage. T wave was inverted in lead III and aVF, and right bundle branch block was accelerated. Soon after, atrial fibrillation occurred during hemodialysis. A chest film showed sudden cardiomegaly and a relatively clear pulmonary field (Fig. 2B). Massive pericardial effusion was apparent by using echocardiography. Blood pressure was 120/90 mmHg and pulsus alternans was not demonstrated. Central venous pressure (CVP) increased to the level of 13.5 cmH$_2$O. Blood gas analysis revealed $\text{PCO}_2$ 29.5 mmHg, $\text{PO}_2$ 113.5 mmHg and $\text{HCO}_3$ 20.5 mmol/L under nasal O$_2$ supply (1 L/min).

Seventy milliliter bloody effusion was removed from the pericardial sac by emergency pericardiocentesis. As a result, atrial fibrillation dramatically returned to sinus rhythm. Subsequently, a continuous drainage tube was implanted into the pericardial cavity. A total of 1000 ml of hemorrhagic fluid was withdrawn during that day. The cardiothoracic ratio (CTR) fell from 68% to 47% the following day (Fig. 2C). The character of the pericardial effusion was as follows: Specific gravity was 1024; the hemorrhagic fluid showed a positive Rivalta reaction.

**Fig. 1.** Time courses of serum enzyme levels
All enzymes which were released from congestive liver, were normalized after pericardial drainage.
GOT: glutamic oxaloacetic transaminase
GPT: glutamic pyruvic transaminase
LDH: lactic dehydrogenase

**Fig. 2.** Change in chest x-ray film
A: 21st November 1987
B: 2nd December 1987 (before pericardial drainage)
C: 3rd December 1987 (after pericardial drainage)
arrow: drainage tube
and contained 6.2% protein, red blood cell count 218 x 10^4/mm^3, hemoglobin 6.3 g/dl, hematocrit 19.8%, white blood cell count 4300/mm^3, fibrinogen 355 mg/dl, sugar 101 mg/dl and LDH 3303 U/L. LDH isozyme revealed high level of type V fraction. CEA level was normal. Adenosine deaminase activity (ADA), which is well-known as an effective index in the diagnosis of tuberculosis, was high, namely 25.8 U/L (normal range 9.1-19.1 U/L). Specific microorganisms were not detected from the pericardial effusion. Cytology of pericardial effusion demonstrated no malignancy. Serum viral titers were not significantly changed compared to paired samples taken after 2 weeks. Serum HBs antigen and HA antibody IgM type were negative. Serum HBs, HBe and HA antibody were all positive.

The patient had experienced chemotherapy against pulmonary tuberculosis 30 years previously and calcification was apparent on chest film (Fig. 2A). Therefore, although the tuberculin skin test (PPD) was negative 2 months previously and acid-fast organisms were also negative from a sputum smear and pericardial effusion, combination therapy was started for suspected tuberculosis with isoniazid 200 mg/day, rifampicin 600 mg/day and streptomycin 0.5g intramuscularly twice a week. In addition, hemodialysis was carried out without heparinization. Treatment was temporarily complicated by gastro-intestinal bleeding due to a duodenal ulcer. However, the patient recovered and laboratory data entered within the normal range (Fig. 1). No recurrence of pericardial tamponade was demonstrated on follow-up echocardiography. Two months later mycobacterium tuberculosis was identified from the culture of sputum.

DISCUSSION

Cardiac tamponade in uremic patients has received attention since it was first reported by Goodner and Brown in 1956. The incidence of pericarditis in dialyzed patients is reported to be 6-18% and it is interesting to note that 40% developed within the first three months of dialysis therapy. Although approximately 30% of these pericarditis patients will have no symptoms, cardiac tamponade occurs in about 14-20%, therefore, cardiac tamponade will develop in 2-4% of the total population. It has been reported that up to 90% of patients with pericardial disease in renal failure had preceding infection or a viral prodrome. However, direct microbiologic study results of pericardial effusions are almost always negative. Concerning tuberculous pericarditis, only 15% showed a positive culture. Other factors such as uremic toxin and malnutrition have been suggested to play possible roles in the pathogenesis. However, the etiology of the pericarditis still remains uncertain. We considered that the cause of pericarditis might be tuberculosis in this case for the following reasons. 1) Uremic state was stable and not severe enough for uremic pericarditis. 2) Although specific organisms were not found, ADA level was high and sugar was low in the pericardial effusion. 3) The culture of sputum taken at the same time when pericardial tamponade occurred, demonstrated mycobacterium tuberculosis. 4) Although hemodialysis condition was maintained as before, the pericarditis did not recur after anti-tuberculosis treatment.

The overall mortality in patients who develop dialysis pericarditis is 12-44%. On the other hand, mortality due to tuberculosis in dialyzed patients has been reported to range from 11 to 75%. In patients with pulmonary tuberculosis complicated by extrapulmonary lesions, the mortality is increased to nearly 100%, where there is pericardial involvement. Another factor which determines survival rate is the duration of symptoms prior to initiation of therapy. Therefore, in case of fever of unknown origin even with a negative tuberculin skin test, tuberculosis should be strongly suspected and treated promptly. Early diagnosis and treatment may be the only way of saving the patient's life.

It has been reported that a low grade fever is found in 88% of patients with dialysis pericarditis. Pericardial friction rub and congestive heart failure are present in 90 and 68%, respectively. Dyspnea is found in 93% of those with tamponade. Atrial fibrillation occurs in one fifth of patients. However, liver dysfunction due to congestion was though to be a first clinical sign of pericarditis in the present case. Although CVP 13.5 mmHg was a little low in the considered as congestion, the enzyme released from the liver was dramatically improved after pericardial drainage (Fig. 1). In addition, taking into account that water intake was restricted in the hemodialysis patients, CVP might be usually maintained at a low level. Serum investigation revealed no acute hepatitis A or B infection. Therefore, it was considered that the liver dysfunction was caused by congestion due to
cardiac tamponade. Dyspnea and arrhythmia were suddenly found later. Echocardiography is a good method for the early detection of pericarditis. In order to treat pericarditis, some investigators recommend needle pericardiocentesis13 while others advocate a surgical approach.14,15 Pericardiocentesis sometimes results in unexpected heart perforation and its benefit is often temporary. In the present case, both pericardiocentesis and continuous peri- cardiac drainage were carried out safely and effectively under the guide of echocardiography. Because the possible risk of major surgical procedures are avoided, this method is the most suitable for the treatment of cardiac tamponade in dialyzed patients.

A combination of 2 or 3 drugs may be used to treat tuberculosis in dialyzed patients. Because isoniazid is partly excreted in the urine, its half-life is prolonged. However, the drug is mainly eliminated after acetylation. The dose of 150–300 mg/day could be decided by measuring blood isoniazid level. Pyridoxine 50–100 mg/day might be given to prevent peripheral neuropathy secondary to isoniazid. The dose of streptomycin is recommended to be 0.3–0.5 g after each hemodialysis. In order to avoid permanent hearing loss, the duration of therapy with streptomycin should not exceed 1–2 months or the total dose of streptomycin administered should not exceed 10 g. The ordinary dose of rifampicin (around 600 mg) might be sufficient, since the kinetics of rifampicin are not affected by renal function nor hemodialysis. Ethambutol is excreted by the kidney. The dosage should be around 5 mg/kg/day or 18 mg/kg between dialysis.16,17

In conclusion, tuberculosis might be a potential cause of pericardial tamponade and time must not be wasted in diagnosis. Prompt therapy may be life-saving in tuberculosis complicated with cardiac tamponade. Active treatment is recommended even in doubtful cases. This is especially true in compromised hosts, such as hemodialysis patients.

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