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Effusive Constrictive Tuberculous Pericarditis —Report of a Case

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Abstract：A 62–year–old man was admitted with the chief complaint of dyspnea associated with orthopnea. In addition, cardiac tamponade and right pleural effusion were also observed. The polymerase chain reaction findings for *Mycobacterium tuberculosis* were positive, and a culture of *Mycobacterium tuberculosis* from the pericardial fluid was positive. The bacillus was strepomycin resistant. Antituberculous drugs combined with prednisolone were administered. In addition, pericardiocenteses were also performed several times. However, the symptoms of dyspnea subsequently continued.

An echo–free space and a thick serous pericardium with frond－like structures protruding into the pericardial cavity were observed. The intracardiac right ventricular pressure curve showed a dip and plateau pattern. A preoperative diagnosis of effusive constrictive tuberculous pericarditis was thus made.

A partial pericardiectomy and epicardiotomy were thus carried out. The pathology of the excised pericadium revealed granulomatous changes with Langhans' type giant cell infiltration. The patient well tolerated surgery and has since been doing well for longer than 3 years postoperatively.

Key words：**Effusive constrictive tuberculous pericarditis, Pericardiectomy, Epicardiotomy, Frond–like structures**

Introduction

In a 62–year–old man demonstrating massive effusion both in the pericardium and right pleural cavity, both positive polymerase chain reaction (PCR) findings and the echoardiographic characteristics of tuberculous (TB) pericarditis were observed. Good results were obtained using antituberculous drugs and by performing a pericardiectomy. Our findings indicate the importance of PCR in making an accurate a preoperative diagnosis of tuberculosis in combination with the preoperative echocardiographic findings and the postoperative pathological findings of excised pericardial specimens. We herein describe a surgical case with effusive constrictive TB pericarditis. We also discuss the diagnosis and treatment of such patients.

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Table 1. Details of the aspirated pleural and pericardial fluid specimens

Date 2000	April 28	June 8	July 4	August 8	October 24	October 27
Sites of aspiration	PLE	PE	PE	PE	PE	PLE
Outlook	unknown	Serosanguineous	Serosanguineous	Yellow turbidity	Yellow	unknown
Amount of aspirated fluids (mml)	unknown	650	1,200	900	900	unknown
Specific gravity	1.033	1.041	NP	NP	NP	1.026
Protein content (g/dl)	NP	7.1	NP	7	7.4	3.5
LDH	NP	NP	NP	3,476	3,940	NP
Sugar (mg/dl)	1.9	34	NP	24	18	NP
Cell count (mm^3)	700	3,400<	NP	2,940	3,000<	3,600
Polynuclearcyte (%)	85	55	NP	90	85	25
Mononuclearcytes (%)	15	45	NP	10	15	75
Staining for acid-fast bacilli (Gaffky)	2	0	0	0	1	0
Culture for Mycobacterium tuberculosis	(+)	(+)	(−)	(−)	(−)	(−)
Polymerase chain reaction	(+)	NP	NP	NP	NP	NP
ADA (IU/l 37℃)	79.4	189	223	194	116	23.3

ADA : Adenosine deaminase LDH : Lactate dehydrogenase PLE : Pleural effusion PE : Pericardial effusiorn
NP : Not performed

A case report

A 62-year-old man was admitted with the chief complaint of dyspnea with orthopnea. Regarding his past history, he had been suffering from cough and anorexia since January 2000. He was admitted to Hagiwara Chuou Hospial on April 21, 2000, because of mild fever and a progression of anorexia. After admission, both right pleural effusion (PLE) and pericardial effusion (PE) were detected. The polymerase chain reaction (PCR) findings for *Mycobacterium tuberculosis* (*M. tuberculosis*) of fluid aspirated from the right pleural cavity were positive. He was thereafter transferred to Moji Municipal Hospital on April 27, 2000. He was given four antituberculous drugs (isoniazid, 400 mg ; rifampicin, 450 mg ; ethanbutol, 750 mg orally a day and streptomycin (SM), 0.75 g intramuscularly a day) and corticosteroids (prednisolone, 50 mg orally a day in a tapered dosage). SM was replaced with pyrazinamide, 1.5 g orally a day due to drug resistance to SM. In addition, pericardiocenteses for cardiac tamponade were performed 4 times during a six-month period (Table 1). A pericardial fluid culture was positive for *M. tuberaulosis*. He was later transferred to our hospital because of a progression of dyspnea on December, 12, 2000. On admission, he demonstrated severe orthopnea. On physical examination, he was 185 cm tall and weighed 86.7 kg. His jugular veins were distended. Hepatomegaly and pretibial pitting edema were present. His blood pressure was 110/80 mmHg and pulse rate 110 /minute with a regular rhythm. His body temperature was 37.1℃. His heart sounds were weak without any abnormal murmurs.

A chest radiograph revealed severe cardiomegaly with a cardiothoracic ratio of 0.68 and bilateral PLE. An electrocardiogram showed sinus tachycardia of 120/ minute and a low QRS voltage. A two dimensional echocardiogram demonstrated the end-diastolic LV diameter to be 40 mm, the end-systolic LV diameter to be 30 mm, and the ejection fraction to be 58%. The pericardium was diffusely thickened. An echo-free space was observed. The serous pericardium was thickened with frond-like structures protruding in the pericardial cavity. The inferior vena cava was dilated to a size as large as 28 mm without any significant respiratory movement (Fig. 1).

Computed tomography of the chest revealed a dif-

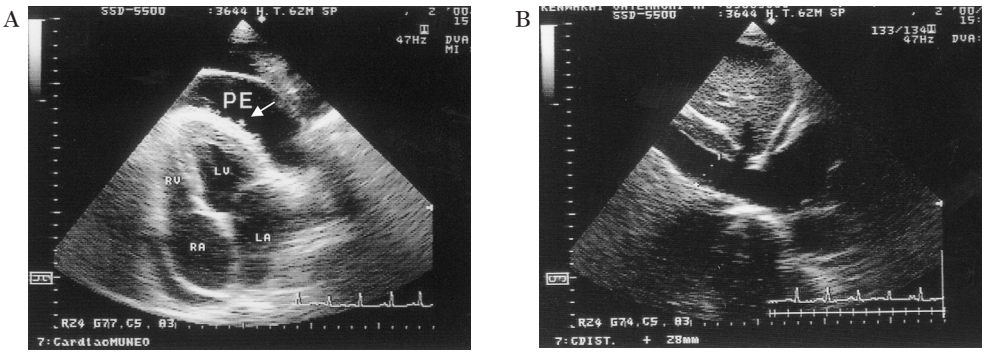

Fig. 1. A : A preoperative transthoracic wall echocardiogram (four chamber view from the subxyhoid approach). The visceral pericardium was thickened with frond-like structures protruding in the pericardial cavity (arrow). PE=pericardial effusion, RV=right ventricle, LV=left ventricle, RA=right atrium, LA=left atrium.
B : The inferior vena cava was distended to 28 mm without any significant respiratory movement.

fusely thickened pericardium with a large amount of PE and bilateral PLE (Fig. 2).

The preoperative hemodynamics are shown in Table 2. The right ventricular pressure (RVP) curve showed a dip and plateau pattern. The right atrial mean pressure (RAmP) was 19 mmHg, the RVP was 40/11 mmHg, the end-diastolic right ventricular pressure (RVEDP) was 21 mmHg, and the pulmonary artery pressure (PAP) was 38/16 mmHg. The cardiac index was 1.4 L/min/m^2. Effusive constrictive TB pericarditis was diagnosed.

On December 16, 2000, surgery was performed. A median sternotomy was carried out. The pericardium was opened longitudinally and a 400 ml of serous yellow fluid were sucked out. The pericardium was measured to be about 5-6 mm in thickness (Fig. 3). The epicardium was covered with a fibrous coating. An anterior pericardiectomy was performed from the right to left phrenic nerves in order to avoid the injury of the nerves and an epicardiotomy using a golf knife (multiple longitudinal and transverse incisions)[1] was also partially done on the fibrous epicardium of the RA, RV and LV. In addition, a longitudinal left pleurotomy was performed. A total of 900 ml of serous yellow fluid were aspirated from the left pleural cavity. Next 2 g of Kanamycin was spread over the residual pericardial cavity.

A pathological study revealed fibrin accumulation on the thickened fibrous pericardium and the epithelioid granulomas with Langhans' giant cells in the excised pericardium (Fig. 3). *M. tuberculosis* was demonstrated neither by Ziehl-Neelsen staining nor by a culture of the pericardium.

Postoperatively, antituberculous drugs were given for 10 months.

The hemodynamics were found to have improved at the 6 month follow-up (Table 2). The dip and plateau pattern on the RV pressure curve disappeared. The RAmP was 7 mmHg, the RVP was 34/2 mmHg, the RVEDP was 10 mmHg, and the PAP was 30/10 mmHg. The cardiac index was 3.4 L/min/m^2.

Although an echo free space still remains in the posterior wall of LV, the patient is doing well after surgery under a careful follow-up for more than 3 years.

Discussion

The incidence of tuberculosis in Japan at the present time is much higher than that in the USA or some European countries.[2)3)] It is reported that TB pericarditis is seen in 1-2% of all patients with tuberculosis, and it is now seen most frequently in patients with acquired immunodeficiency syndrome (AIDS).[4)] Though still very small in number in Japan, the number of tuberculosis patients co-infected with HIV is gradually increasing.[3)] Furthermore, the number of newly registered cases of tu-

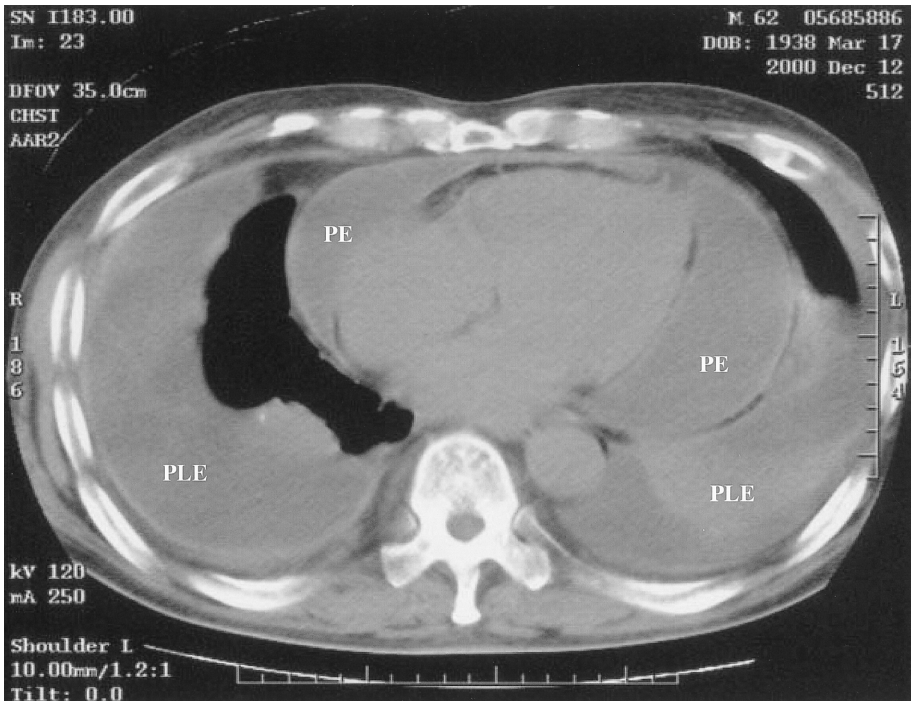

Fig. 2. Computed tomography of the chest on admission : A diffusely thickened pericardium with a large amount of pericardial effusion and pleural effusion was seen. PE : pericardial effusion, PLE : pleural effusion.

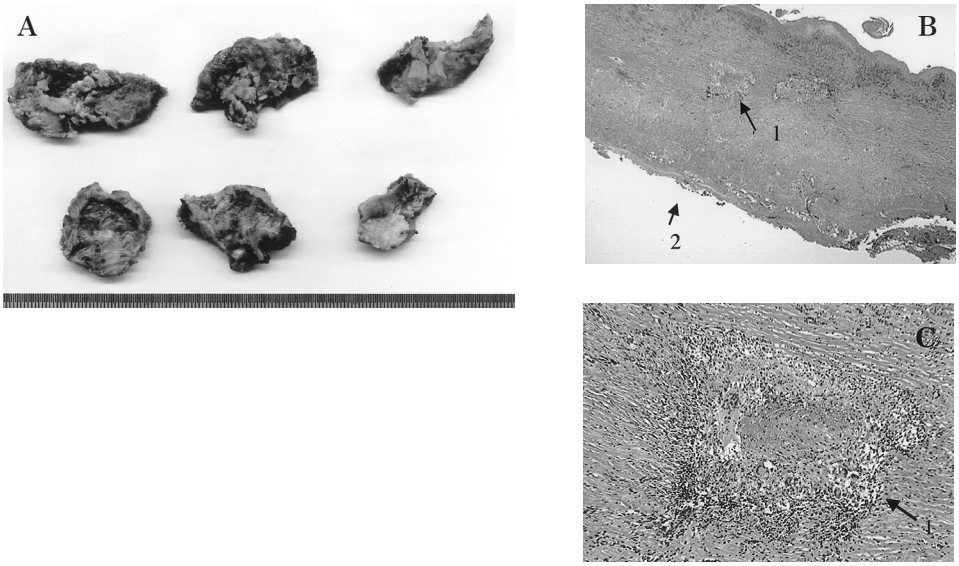

Fig. 3. Pannel A : The resected pericardium was markedly thickened.
Pannel B : Arrow 1 indicates epithelioid granulomas with Langhans' giant cells. Arrow 2 indicates the areas of fibrin accumulation.
Pannel C : enlarged picture B. Arrow 1 indicates epithelioid granulomas with Langhans' giant cells.

berculosis among socioeconomically poor people is also increasing in Japan.[3] TB pericarditis still carries a 20% to 40% mortality even when the most effective antituberculous drugs are administered.[5] In addition, some reports have also showed the possibility of constrictive pericarditis developing from acute TB pericarditis in Japan.[2)6)]

Pathogenesis

TB pericarditis has been shown to usually develop by a retrograde spread from peribronchial, peritracheal and/or mediastinal lymph nodes. Less commonly, it occurs during miliary tuberculosis, and it may also develop from a focus in the lung, spine or sternum.[7)8)] Ryoke et al.[2] also described that pericardial infection rarely arises from a direct spread from the lung or pleura. In our case, the swelling of mediastinal lymph nodes was detected by a CT scan taken on May 5, 2000. As a result, TB pericarditis is considered to develop due to a retrograde spread from the mediastinal lymph nodes.

Diagnosis

The criteria for the diagnosis of TB pericarditis by Trautner et al.[9] are as follows : (1) a culture of either pericardial tissue or fluid specimens that is positive for *M. tuberculosis*, (2) granulomas and acid-fast bacilli seen on a histopathological examination of pericardial tissue, or (3) granulomas in the pericardial tissue and a positive culture for *M. tuberculosis* from another site.

The difficulty of making an early diagnosis of TB pericarditis

The symptoms of TB pericarditis are nonspecific.[10] Ortbals et al.[5] described the frequency of symptoms to be as follows : cough 48-94% , dyspnea 74-88%, chest pain 39-76%, night sweating 14-58%, orthopnea 39-66%, weight loss 40-85%, ankle edema 36-55%, hemoptysis 14-17%, and ascites 3-14%. However, in the advanced stages of this illness, some patients present the findings of typical constrictive pericarditis, such as peripheral edema and ascites, which may sometimes be incorrectly attributed to other etiologies, such as liver cirrhosis.[11]

The purified protein derivative of tuberculin is not a reliable indicator of TB pericarditis, since this test may be negative in as many as 30% of patients with tuberculosis owing to anergy.[2)8)]

Table 2. Hemodynamics

	Before surgery 12/16/2000	After surgery 6/18/2001
RAmP (mmHg)	19	7
RVP (mmHg)	40/11	34/2
RVEDP (mmHg)	21	10
PAP (mmHg)	38/16	30/10
CI (L/min/m^2)	1.4	3.4

RAmP ; right atrial mean pressure, RVP ; right ventricular pressure, RVEDP ; end-diastolic right ventricular pressure, PAP ; pulmonary artery pressure, CI ; cardiac index.

Acid-fast bacilli in pericardial effusion and tissue specimens are rarely found by direct Ziehl-Neelsen staining.[8]

The source of the *mycobacterium* in TB pericarditis remains uncertain, with less than half of all patients having evidence of pulmonary tuberculosis.[4)12)]

According to Sagrista-Sauleda J. et al.[12] the mean delay between hospital admission and diagnosis is 5.2 weeks because of the slow growth of *M. tuberculosis* in culture.

M. tuberculosis was grown from the pericardial fluid in 50% of all obtained samples.[10]

Ortbals and Avioli[5] described that an open pericardial biopsy appears to be the most reliable diagnostic tool, particularly in a seriously ill febrile patient with evidence of active disease for one to two weeks in whom a diagnosis has yet to be established.

Other diagnostic techniques are PCR, testing to determine the adenosine deaminase activity (ADA) and interferon-γ level.[4] *M. tubercurosis* complex DNA by PCR had a sensitivity of 75% and a specificy of 100%.

Pericardial fluid with a high ADA activity (> 40/L) greatly helps in making an early diagnosis of TB pericarditis, with a sensitivity of 83% and a specificity of 78%.[13]

In our case, the presence of PLE was quite helpful in making an early diagnosis of TB pericarditis, because PCR for *M. tubercurosis* from PLE was positive at Hagiwara Chuo Hospital. Therefore, TB pericarditis was successfully diagnosed during

the early stages of admission.

Treatment

The goal of therapy of TB pericarditis is not only to relieve the acute symptoms of tamponade, but also to prevent a progression from the effusive stage to a constrictive one.[9)]

Regarding medical treatment, O'Brien[14)] reported 6– to 9–month of short–course chemotherapeutic regimens to be effective.

The four–drug regimen should be given immediately, when TB pericarditis is either diagnosed or a presumptive clinical diagnosis of TB pericarditis is made in severely ill patients with a massive accumulation of PE and systemic symptoms.[8)]

Corticosteroids are administerd at a dose of 80 mg a day of prednisolone or its equivalent in tapered dosages for 6 to 8 weeks.[9)] If necessary, steroids should be given before any irreversible constriction takes place.[9)]

Pericardiocentesis is often carried out as a diagnostic or therapeutic procedure, or both as ancillary measures to control heart failure.[10)] In our case, corticosteroids may not have prevented the development of rigid constriction of the serous pericardium.

Pathologically, the four stages of TB pericarditis have been described and are referred as follows : stage 1;dry or fibrinous, stage 2 ; effusive, stage 3; absorptive or early fibrous, and stage 4 ; constrictive or late fibrous.[15)]

Prompt treatment given in the first two stages may prevent constriction in more than half of all patients. Beyond stage 3 with the clinical signs and symptoms of cardiac tamponade, surgical intervention is needed, because constrictive pericarditis occurs in 30－50% of all patients despite prompt antituberculous treatment. It is now suggested that in cases in whom pericardial constriction is suspected, a pericardiectomy should be performed as soon as possible to allow for easier surgical techniques with a low surgical mortality and the ability to better preserve of the myocardial function.[15)] In patients with acute or subacute TB pericarditis, the risk of developing constrictive pericarditis is high if there are any clinical manifestations of cardiac tamponade.[9)]

When a hemodynamic compromise persists for 6 to 8 weeks, a pericardiotomy is usually indicated, and there is general agreement that it should be done earlier rather than later.[4)] Echocardiography is important for evaluating the progression of PE. The risk of developing constriction has been suggested to be higher in patients with "shaggy" effusion on echocardiography than in those with "non–shaggy" effusion.[4)]

Particularly, a surgical operation should be carried out as soon as possible when the epicardium is found to be thickened with frond–like structures[16)] protruding in the pericardial cavity due to the existence of fibrin accumulation or adhesion between epicardium and fibrous pericardium with a decreasing PE. In our case, the epicardium was thickened with frond－like structures protruding in the pericardial cavity based on the echocardiography findings. Furthermore, the RVP curve revealed a dip and plateau pattern at preoperative cardiac catheterization. Therefore, the cardiac hemodynamics indicated a rigid constriction developing from the elastic constriction. Therefore, our case demonstrated both stage 2 and stage 4 characteristics.

Though there was a risk of postoperative local infection due to *M. tubercurosis*, Gooi et al.[17)] reported that surgery in combination with adequate chemotherapy is not contraindicated early in the course of the disease since a dissemination of tuberculosis or a failure of wound heeling did not occur in their cases. Quale et al.[18)] also advocated early surgical intervention for patients with TB pericarditis. Pericardiocentesis is often a lifesaving procedure. However, a recurrence of tamponade occurred in all 3 patients following pericardiocentesis, and a diagnosis was not immediately made (none of the 7 smears of pericardial fluid contained any acid–fast bacilli). As a result, they proposed that a pericardial window should be performed in patients with suspected effusive TB pericarditis, since effective drainage can be established, and the pericardial biopsy specimen can often confirm the diagnosis. They proposed a formal pericardiectomy for pericardial thickening, even in the absence of tamponade.[19)] In our case, though it was possible to have made an early diagnosis, the use of a pericardial window was considered to be better a treatment option rather than pericardiocentesis which was re-

peatedly performed.

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