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# Sarcoidosis Manifested as Recurrent Pericardial Effusion with Signs of Impending Tamponade

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**ABSTRACT**

Pericardial effusion is a fatal and life-threatening condition. If it is not addressed thoroughly, complications such as constrictive pericarditis may occur. Etiologies of pericardial effusion varied and one of the most common etiologies is tuberculosis. Other etiologies include inflammation, malignancy or other autoimmune disorder such as sarcoidosis. Sarcoidosis is a diagnosis of exclusion and is confirmed by biopsy result that showed non-caseating epitheloid-cell granuloma, with no other organism or particles. Epidemiology of sarcoidosis in Japan is 1-2 case per 100.000 patients, with the peak incidence between the age of 20 to 39 years old. We reported a case of 37 years old woman presented to our emergency department with shortness of breath and signs of pericardial tamponade. She was previously healthy with no other significant past medical. She was first treated as a case of extrapulmonary tuberculosis and shown no improvement with anti-tuberculosis medications. Several work ups were then done in search of other etiologies of her pericardial effusion. A biopsy form one of her abdominal lymph nodes was performed, which pathologically revealed sarcoidosis. She was placed on corticosteroid and methotrexate with improvement of symptoms. One month followed up showed complete resolution of her pericardial effusion.

## 1. Introduction

Pericardial effusion is an abnormal accumulation of fluid in the pericardial cavity. If it is not addressed thoroughly, pericardial effusion can be fatal and complication such as constrictive pericarditis may arise. Tuberculosis is considered one of the most common etiologies of pericardial effusion in Indonesia. Other etiologies include malignancy, inflammation, autoimmune or other immunocompromised state like HIV. [1-2]

Sarcoidosis can affect any organ, but most commonly presents with pulmonary manifestation. The peak incidence of sarcoidosis is between the ages of 20 to 39 years old, with no preference in race, gender, and age nor certain ethnic. Granuloma accumulation, which occurred as a result of interaction between CD4 T cell and antigen, is the basic pathophysiology of sarcoidosis. [1,3-4]

Trigger factors for sarcoidosis are still unknown. Sarcoidosis is a diagnosis of exclusion and is confirmed by biopsy result that showed noncaseating epitheloid-cell granuloma, with no other organism or particles. We presented an unusual case of sarcoidosis manifested as recurrent pericardial effusion with impending tamponade.

## 2. Case Illustration

A 37 years old widowed-housewife presented to our emergency department with shortness of breath for pass 2 months. Initially, her shortness of breath developed upon climbing up stairs and was relieved

with rest. She also had orthopnea but denies in paroxysmal nocturnal dyspnea. Both of her legs started to swell 3 weeks prior to admission, accompanied by ascites. There's a 3 kg weight lost during the past 2 months but she denies any cough, night sweat, fever or changes in bowel and urinary habit.

She did not have any arthralgia, swelling and skin changes around her face or oral ulcer. There was no history of hypertension, diabetes mellitus nor allergy. The patient then self-consulted to a nearby hospital one months ago where she was diagnosed with congestive heart failure and was given furosemide orally with no resolution of symptoms.

The patient married twice with three children of her own. She had a history of miscarriage 14 years ago. Her late husband died 14 years ago due to colon cancer. She was diagnosed with pulmonary tuberculosis 14 years ago based on her chest-Xray and was given anti-tuberculosis medications for 3 months. Her tuberculosis medications were then discontinued after second opinion with another primary care physician, whom did not consider her case as pulmonary tuberculosis. She was doing well without any complain of her lung.

Upon examination, she was weak but alert with a GCS score of 15. Her blood pressure was 100/80 mmHg; heart rate of 115 beats per minute, with narrow pulse; a respiratory rate of 32 per minutes and body temperature of 36.5$^{o}$C. Her weight was 63 kg with a BMI of 24.6. She had pale palpebral conjunctiva, anicteric sclera with both pupils equal and reactive to light. There was no noted alopecia, lupus hair, rashes on her face nor perioral cyanosis or enlarged lymph nodes. Her trachea was midline with a positive hepato-jugular reflux and a (5+3) cm$H_20$ of jugular venous pressure. Her thorax examination revealed symmetrical chest expansion and her cardiac apex palpated at 6$^{th}$ intercostal 1 cm lateral of left mid-clavicular line, her right cardiac border was at the right sternal border with her left cardiac border at 6$^{th}$ intercostal 1 cm lateral of left midclavicular line. On auscultation, no murmur was noted but positive for muffled sound. Her lung examinations are within normal limits. The patient's abdomen was flabby and soft; bowel sounds was normal with her liver palpated 3 cm below the costal margin and positive for shifting dullness. There was also noted bipedal pitting edema. Patient's neurological examination were within normal limit with no noted muscular atrophy.

A 12-lead electrocardiography of the patient showed sinus tachycardia with low QRS voltage. The patient's initial echocardiography showed normal all chamber, reduced left ventricular systolic function (EF 41%), with global hypokinetik. Other findings are dyastolic dysfunction, mild mitral regurgitation, pulmonary hypertension, good right ventricle contractility with severe pericardial effusion mostly at posterior (1.3-3.8 cm). She underwent abdominal ultrasonography that showed ascites with pelvocaliectasis in both kidneys. Chest CT Scan showed pericardial effusion with cardiomegaly; infiltrates with fibrosis in the right inferior lobe; ground-glass in left lingual and postero-inferior of the left lobe; thickening of interlobular septum in left superior, lingual, antero-inferior of the left lobe, right anterior, medial and antero-inferior of the right lobe; calcification at the right perihilar; right pleural effusion; partial atelectasis in the superior right lobe; centrilobular emphysema at superior and medial of the right lobe. Her abdominal CT Scan showed irregular thickening accompanied by narrowed lumen in the mid abdominal region up to the right pelvic area, which showed inflammation in the ileocecal up to the ascending colon; hepatosplenomegaly; ascites with multiple lymph nodes in the paraorta, right parailiac and mesenterial area.

Table 1. Laboratory examination

| **Blood Examination** | | **Pericardial Fluid** | | **Urine** | |
|---|---|---|---|---|---|
| Hemoglobin (gr/dL) | 11.9 | Total cell | 148 | Colour | Yellow |
| Haematocrit (%) | 36 | PMN (%) | 33 | Turbidity | Clear |
| Leukocyte ($10^3$/uL) | 22.500 | MN (%) | 67 | Mass density | 1.015 |
| Thrombocyte (thousand/uL) | 528.000 | LDH (U/L) | 264 | pH | 6 |
| MCV (fL) | 87.6 | Rivalta | Negative | Nitrite | Negative |
| MCH (pg) | 29 | Albumin (mg/dL) | 1730 | Protein | Negative |
| MCHC (%) | 33.1 | Protein (mg/dL) | 3087 | Glucose | Negative |
| Differential count (%) | 0/0/1/87/9/3 | Triglyceride (mg/dL) | 17 | Ketone | Negative |
| Random blood glucose (mg/dL) | 101 | AFB | Negative | Urobilinogen | Negative |
| Sodium (mEq/L) | 138 | Tuberculosis rapid molecular assay | Negative | Bilirubin | Negative |
| Potassium (mEq/L) | 3.2 | Culture | No organism found | Leukocyte Esterase | Negative |
| Urea (mg/dL) | 35 | Cytology | Chronic inflammation | Blood | Negative |
| Creatinine (mg/dL) | 0.98 | | | Erythrocyte | 2 |
| AST (U/L) | 9 | | | Leukocyte | 2 |
| ALT (U/L) | 10 | | | Epithelial cell | 4 |
| Albumin (gr/dL) | 2.7 | | | Bacteria | Negative |
| LDH (U/L) | 311 | | | Crystal | Negative |
| Total protein (gr/dL) | 5.3 | | | Cylinders | Negative |
| CRP (mg/dL) | 81.3 | | | | |
| HBsAg | Nonreactive | | | **Sputum** | |
| Anti-HCV | Nonreactive | | | AFB | Negative |
| ANA | Nonreactive | | | Gene Expert | Negative |
| Anti-HIV | Nonreactive | | | | |
| PCR-MTB | Negative | | | | |
| PCR-NMTB | Negative | | | | |

MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; MCHC: mean corpuscular hemoglobin concentration; AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase; CRP: c-reactive protein; HBsAg: hepatitis B surface antigen; anti HCV: anti hepatitis C virus; ANA: antinuclear antibody; PCR MTB: polymerase chain reaction; MTB: Mycobacterium tuberculosis; NMTB: non-Mycobacterium tuberculosis; PMN: polumononuclear; MN: mononuclear; AFB: acid fast bacilli;

The patient was diagnosed with severe pericardial effusion with signs of tamponade hence she underwent emergency pericardiostomy, with the initial drainage of 500 cc serous fluid. She was then admitted to our medical ward, with consideration of tuberculosis as a cause of her pericardial effusion. Her pericardial fluid was drained at 200-300 cc per day. She was given second line anti-tuberculosis agents and methylprednisolone of 0.8 mg/kg body weight with a 20% of albumin infusion. After two weeks of anti-tuberculosis medications, her symptoms were not improving. Hence she underwent colonoscopy and biopsy which showed edematous in the periapendicular area, pathology anatomy showed chronic granulomatous. Due to unspecific results, the patient underwent laparotomy biopsy of her abdominal lymph nodes. Biopsy result showed lymphoid follicular, with granulomatous proliferation of epitheloid cell and hemorrhage, consistent with sarcoidosis.

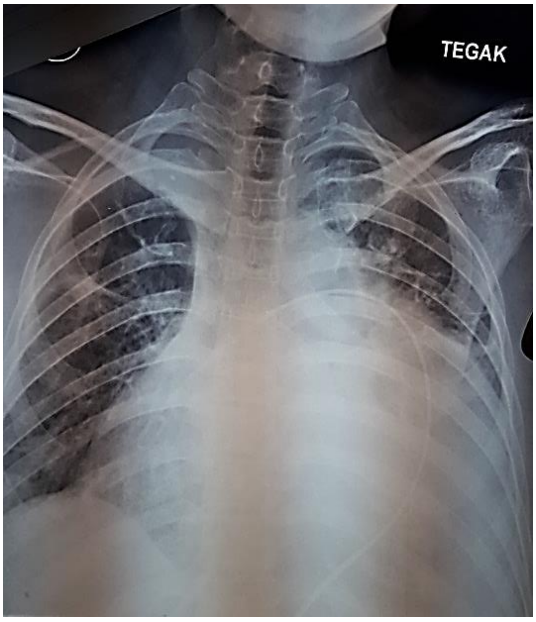


Figure 1. Chest Xray

Her anti-tuberculosis medications were discontinued and methylprednisolone was gradually tapered off. She was started on methotrexate 7.5 mg weekly and 0.5 mg colchicine per oral daily. After two weeks, there was improvement of symptoms, her repeat bedside echocardiography showed minimal pericardial effusion fluid left hence her pericardiostomy was removed. After two months of hospital stayed, the patient was discharged improved with home medication of methotrexate weekly and low dose methylprednisolone. Upon a month follow up, her shortness of breath improved with minimal pericardial effusion on follow up echocardiography.

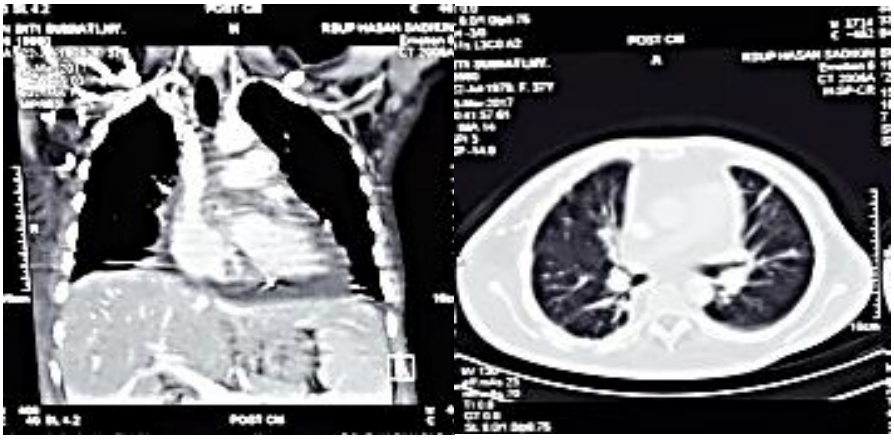

Figure 2. Chest CT Scan

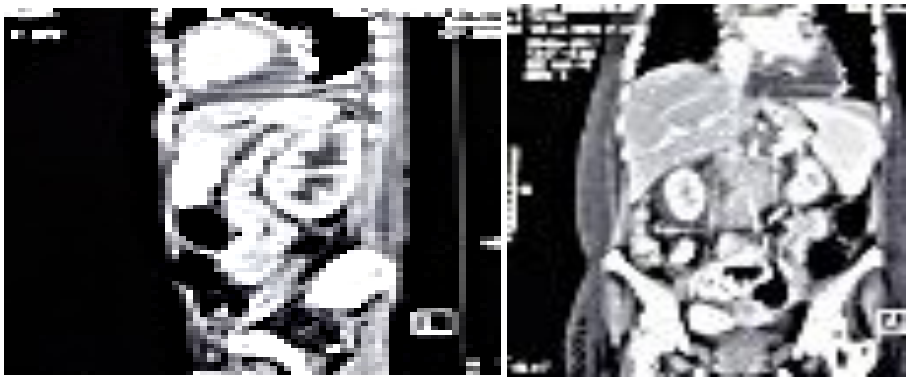

Figure 3. Abdominal CT Scan

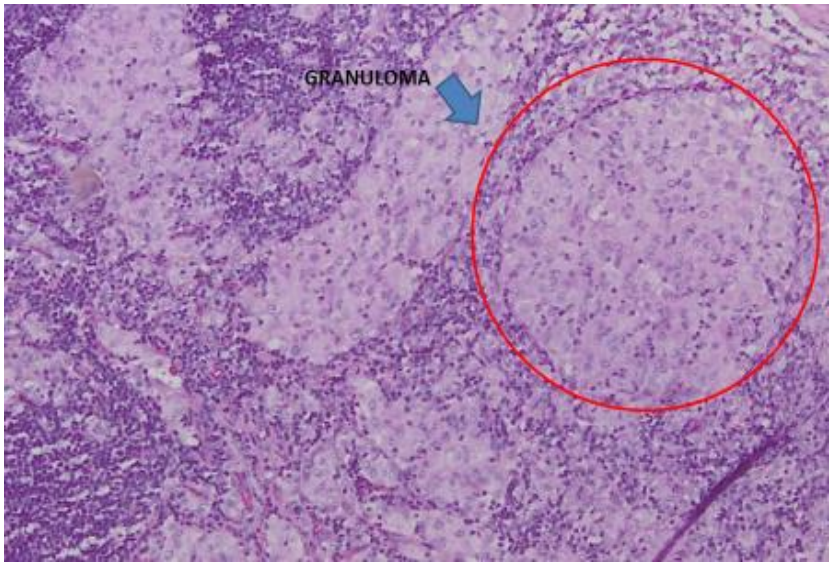


Figure 4. Pathology anatomy taken from one of her abdominal lymph node showed granulomatous proliferation of epitheloid cell and hemorrhage, consistent with sarcoidosis

## 3. Discussion

Tuberculosis is one of the most common etiologies of pericardial effusion in young age adult with no comorbidities in Indonesia. Other etiologies of pericardial effusion are infection, inflammation, malignancy or autoimmune such as systemic lupus erythematosus or immunocompromised such as HIV. [1,2]

Studies stated that PCR MTB has a sensitivity of 76.4%, specificity of 99.8%, positive predictive value of 92.8% and a negative predicative value of 99.2%. While other studies stated that Rapid Molecular Test test for body fluid showed sensitivity of 25 to 95% hence extrapulmonary tuberculosis in this case was hard to exclude. [3]

Chronic granulomatous on pathological anatomy showed that there was a damaged cell, this may include infection, allergic reaction, drug, malignancy and sarcoidosis. Granuloma accumulation, which occurred as a result of interaction between CD4 T cell and antigen, is the basic pathophysiology of sarcoidosis. [1.4-5]

The peak incidence of sarcoidosis was between the ages of 20 to 39 years old, with no preference in race,

gender, age nor certain ethnic. Environmental factor, such as HLA, and genetic factor are thought to play certain role in sarcoidosis, hence explained different epidemiology from one country to another. Epidemiology of sarcoidosis in Japanese was 1-2 case per 100.000 patients. Low social economy status is thought to contribute in the severity of sarcoidosis. [1,4]

Trigger factors for sarcoidosis are still unknown, but overall granuloma accumulation developed as a result to restrict inflammation and pathogen and to protect the surrounding tissue. Granuloma itself composed of macrophage and epitheloid cell, which surrounds by lymphocyte. [1,5,6]

Sarcoidosis is a diagnosis of exclusion and confirmed by biopsy result which showed non-caseating epitheloid-cell granuloma, with no other organism or particles. Biopsy can be done through the skin, lymph nodes, lacrimal glands or conjunctiva. [1.] It is important to rule out other granulomatous diseases such as tuberculosis; hence culture and fast acid staining are usually used. [7,8]

Granuloma in patients with cardiac sarcoidosis, 25% of which was found through autopsy results. Clinical symptoms of cardiac sarcoidosis are only found in 5% of patients; with the most common site of granuloma involvement and scar are the left ventricle, followed by intraventricular septum and the conduction systems. Endomyocardial biopsy has a low sensitivity and specificity (around 20%). This is due to involvement areas of cardiac sarcoidosis are usually specific and not diffuse. The most common location of granuloma in cardiac sarcoidosis is the left ventricle and septum, but endomyocardial biopsy is commonly done on the right ventricle. [1,10]

The risk and benefit of long-term use of steroid should be well calculated in managing patient with sarcoidosis. Some studies suggest giving oral prednisone 20 to 40 mg per day. These studies also suggest evaluation of symptoms after a month to 3 months therapy. If there are improvements of symptoms, prednisone may be continued at a dose of 5 to 15 mg per day 9 to 12 months. [1, 12]

Studies of giving cytotoxic drugs to patients with sarcoidosis are still limited. Some study compared methotrexate and steroid vs placebo and steroid, which showed patients receiving methotrexate has a lower steroid dose compared with placebo after 12 months of therapy. There was no significance difference in the patient's lung function, chest xray or the drug effects. Some case reports have even reported using a TNF-α blocker such as infliximab and etanercept in chronic sarcoidosis or sarcoidosis that was refracter from steroid. As for our patient, she responded well with weekly administration of methotrexate.

## 4. Conclusion

Sarcoidosis might present with recurrent pericardial effusion, clinician should be aware on this manifestation to be addressed thoroughly soon for better outcome of the patients.

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