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Pericardial Effusion as A Clue to The Diagnosis of Systemic Lupus Erythematosus: A Case Report

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Abstract

Pericardial effusion (PE) is accumulation of fluid in the pericardial sac. There are broad etiologies of PE, such as inflammation, infection, and malignancy. The etiology must be discovered because the treatment will be focused based on the cause. We present a 40-year-old female who came to the cardiology clinic with exertional dyspnea as the only symptom. The patient had a history of unspecific joint pain two months prior. Physical examination and electrocardiography showed no specific findings but slight cardiomegaly was seen in chest x-ray. Furthermore, moderate circumferential pericardial effusion was revealed from bedside echocardiography. The patient then admitted for further evaluation. Blood counts, peripheral blood smear, urinalysis, and immunoserology examination such as ANA and anti-dsDNA was ordered and the result led to the diagnosis of systemic lupus erythematosus (SLE). High dose steroid injection was given for five days and the symptoms disappeared. Follow-up echocardiography after a week of hospital admission showed significant reduction of pericardial fluid.

***Keywords**: Pericardial Effusion, Systemic Lupus Erythematosus, Inflammatory Disease.*

Introduction

Pericardial effusion happens when abnormal accumulation of pericardial fluid in the pericardial sac and it is a relatively common findings in daily practice. The most common symptoms that appear is dyspneu on exertion that could be worse if left untreated. However, the symptoms also depend on whether the accumulation of pericardial fluid is quick or slow. Clinical findings like classical Beck's triad (hypotension, muffled heart sounds, and increased jugular venous pressure) and changes in electrocardiogram like electrical alternans and microvoltage can only be seen if the PE volume is large (Imazio dan Adler, 2013; Yamani et al., 2022). Thus, diagnosing PE can be challenging especially in limited facilities setting. Additional imaging modalities may be needed to diagnose, especially when it comes to mild to moderate PE with nonspecific sign and symptoms.

Pericardial effusion (PE) has broad etiologic agents ranged from inflammatory diseases like infection and autoimmune to non-inflammatory like neoplastic diseases. It could also be due to cardiac or even systemic complications (Imazio dan Adler, 2013). Although quite challenging, the cause of PE must be discovered because the treatment will be focused based on the etiology. The following is a patient in which pericardial effusion was the only manifestation that lead to the diagnosis of systemic lupus erythematosus (SLE).

Case Report

A 40-year old female came to the cardiology clinic with the primary complaints of exertional dyspnea since a month ago and become worsened in the past few days. The patient had a history of unspecific joint pain all over the extremities two months prior and deny any other diseases. The patient had no history of chest pain, cough, fever, weight loss, close contact with tuberculosis patient, or any kind of trauma. On physical examination, there were no specific findings like signs of right ventricular overload, cardiac murmur, additional heart sounds, pericardial friction rubs, or muffled heart sounds. The lung was clear and didn't indicate any lung disease. There were also no hepatomegaly or splenomegaly. ECG examination **(Figure 1)** revealed sinus rhythm with a heart rate of 80x/minute, normoaxis, and no ST-T changes

or hypertrophy. There were also no low voltage QRS complex or electrical alternans. Echocardiography showed normal left and right ventricular function with ejection fraction of 71%, global normokinetic, no ventricular hypertrophy, and normal cardiac chamber dimension. Subcostal, four-chamber, and parasternal short axis showed echo-free signal with a size of around 15.2-18.4 mm which represent moderate sized PE **(Figure 2)**. There was also no presence of fibrin strands or clots in the pericardial sac.

The patient then admitted for futher evaluation and underwent complete blood counts, chemistry panel, and urinalysis. Complete blood count result was anaemia with hemoglobin level of 7.8g/dL, neutrophil-to-lymphocyte ratio was 11 (high), leukopenia with leukocyte count of 3900/uL, and normal reticulocyte count (1,1%). Peripheral blood smear was ordered with a conclusion of normocytic normochromic anaemia due to chronic disease. The electrolyte count result was within the normal range. Urinalysis showed the presence of blood (+) and protein (++) in the urine. There was also presence of leukocyte (2-3/HPF), erythrocyte (4-5/HPF), and positive epithelial cast in the urine. Chemistry panel examination such as SGOT and SGPT level was normal. However, urea level increased to 87.5mg/dL with normal creatinine level of 1.0mg/dL. Additional immunoserology examination was ordered with positive ANA test with speckled pattern and titer of >1:1000 and high Anti-dsDNA antibody result of 658.3 IU/mL (normal range <100 IU/mL). All the signs, symptoms, and lab results conclude that this patient is diagnosed with SLE.

On hospitalization, this patient was administered with high dose intravenous steroid (Methylprednisolone 125mg three times daily) for five days, two bags of packed red cell, folic acid, amlodipine 10mg, and candesartan 8mg daily. On the day of discharge, the patient's condition improved significantly and no longer have any symptoms. The steroid was tapered off. A week after hospitalization, the patient was followed up both in cardiology and internal medicine clinic and came up in good condition and had no symptoms. A repeat echocardiography was done and there was significant reduction of PE fluid between 0.854-0.875cm **(Figure 3)**. The steroid treatment was also reduced to 8mg daily with addition of mycophenolate mofetil 500mg twice a day.

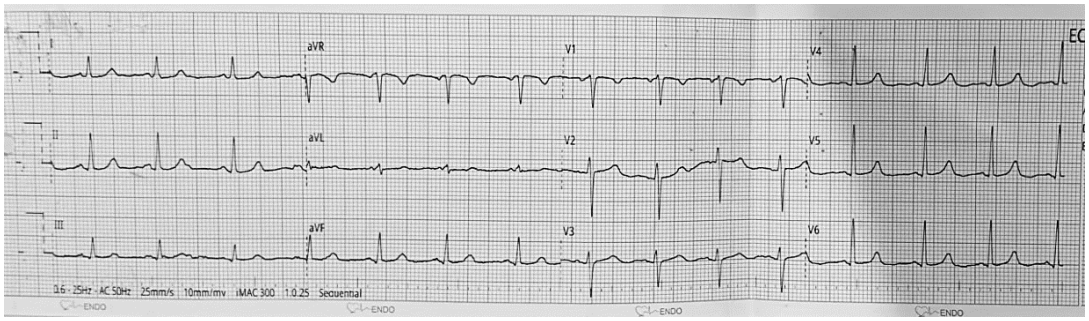

Figure 1. A 12-lead electrocardiogram demonstrating normal findings

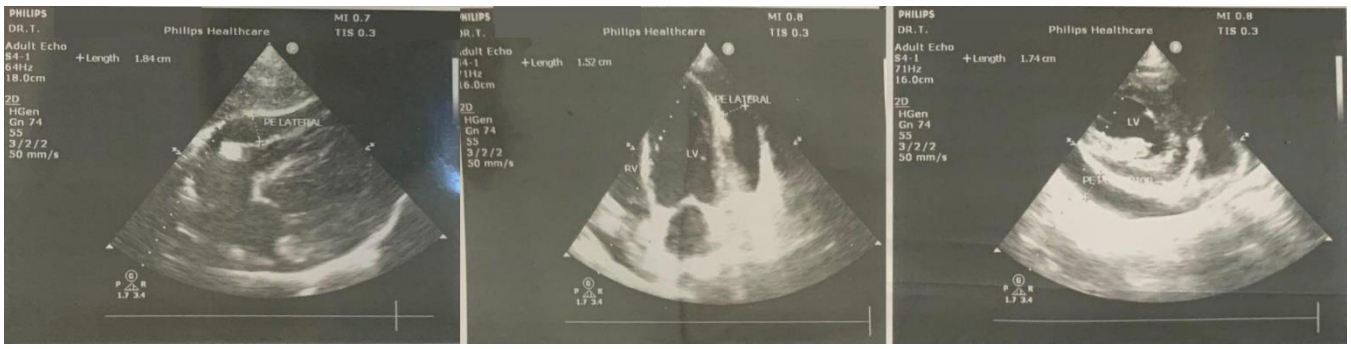

Figure 2. Echocardiography revealed moderate pericardial effusion

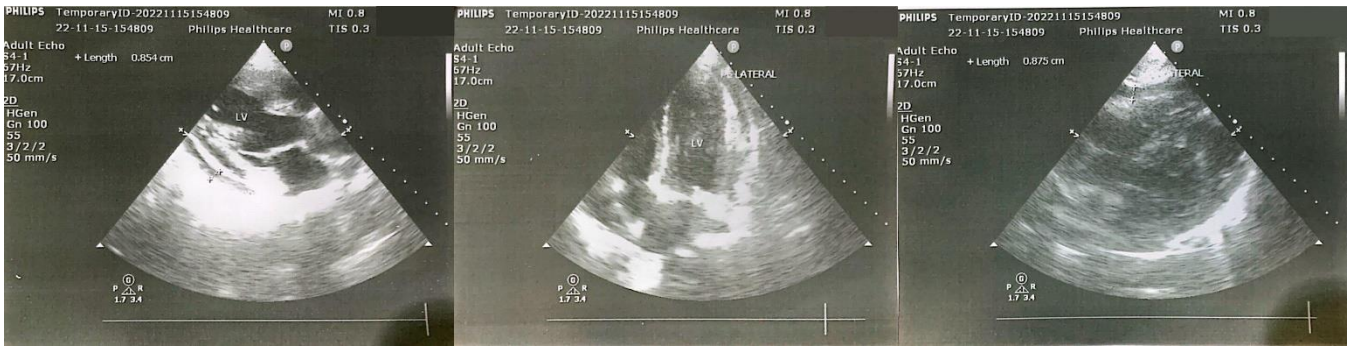

Figure 3. Follow-up echocardiography revealed significant reduction of pericardial effusion

Discussion

The diagnosis of pericardial effusion can be challenging in some cases, especially in mild to moderate size PE because the clinical sign and symptoms may be unclear. The patient in this case only have exertional dyspnea as the symptom when she came to the clinic. On physical examination, we didn't find any findings that lead to the diagnosis of PE such as increased jugular venous pressure, muffled heart sounds, or hypotension. Usually, PE can be seen from electrocardiography that shows low QRS voltage due to abnormal voltage transmission and electrical alternans because of periodic movement of the heart in the fluid-filled pericardial sac (Hannibal, 2014; Kantharia, 2019). However, the ECG of this patient was also normal. The patient was then assessed with echocardiography and moderate PE with a size of 15.2-18.4mm was found circumferentially. The reason why this patient didn't have any specific finding is due to the size of the PE is not large enough and the pericardial fluid might be slowly accumulated. Hence, PE in this patient present without any hemodynamic compromise. Based on pericardial pressure-volume curves, in quickly increasing pericardial effusion, the limit of pericardial stretch is rapidly exceeded even with small accumulation of fluid that cause abrupt rise in pressure that further reduces diastolic compliance leading to decrease in stroke volume and reduced cardiac output (Spodick, 2003).

The use of ultrasound for the diagnosis of pericardial effusion has a lot of advantages. Echocardiography is a rapid, non-invasive, cost effective, widely and readily available examination in almost all healthcare facilities (Klein et al., 2013). Information obtained from echocardiography are the quantity and quality of the pericardial fluid, presence of right atrium and ventricle collapse due to lower chamber pressure compared to pericardial pressure, diastolic ventricular size variability with respiratory cycle, dilatation of inferior vena cava, and the presence of septal bounce (Pérez-Casares et al., 2017).

Once PE is diagnosed, the etiology must be determined. PE has a very broad range of etiology, ranging from infectious agents (viral, bacterial, fungal, or parasitic) to non-infectious such as autoimmune, cancer, metabolic, trauma, or even rarely due to drugs. Thus, history taking and further studies must be done thoroughly (Imazio dan Adler, 2013). In developing countries, pericardial effusion is correlated to tuberculosis (TB) which should be ruled out. This patient denied any features like low-grade fever, weight loss, night sweats, or any contact with tuberculosis or chronic cough patient. Chest x-ray result of this patient was also clear of signs of TB. Thus, we did not suspect tuberculosis as the cause of PE (Cherian, 2004). Another cause of PE is end-stage renal disease that is usually due to high urea level in blood and dialysis-related (Dad dan Sarnak, 2016). However, this is excluded from this patient because the creatinine result was within normal range with only slight increase in urea level in blood. Malignancy can also present as PE in some patients. The most common cause of malignant PE are due to solid malignancy like lung and breast cancer, while primary neoplasms from the pericardium is much less common (Burazor et al., 2013). This patient didn't present any weight loss, chronic cough, change in the shape of the breast with normal physical from head-to-toe. There was also no enlargement of the lymph nodes. Chest x-ray also didn't indicate any signs of mass in the lung and no enlargement of the mediastinum. Thus, TB, kidney disease, and malignancy are excluded from this patient.

From the history taking, this patient had joint pain and stiffness on both upper and lower extremities in the morning without any swelling two months prior. Since then, the patient didn't complain any kind of joint pain anymore. On physical examination, we only found conjunctival pallor that indicate anemia. From the age and gender prevalence with addition of unspecific sign and symptoms from this patient, it could probably lead to autoimmune disease. Women are 10 times more at risk to SLE than men, and age at onset is usually on child-bearing age (Gergianaki et al., 2017). SLE-related pericardial effusion is also seen in around 7.9-16.4% patients with SLE (Chen dan Yu, 2017; Orihuela-Rodríguez dan Carmona-Ruiz, 2019). Hence, this patient then admitted as inpatient for further evaluation. Complete blood counts, chemistry panel, and urinalysis examination revealed anemia, leukopenia and high neutrophil to lymphocyte ratio. Blood smear result was normocytic normochromic anemia due to chronic disease. Hemolytic anemia is also commonly found and one of the classification criteria for SLE (Aringer et al., 2019). However, in this patient, there were no signs of lysis of blood such as splenomegaly and high reticulocyte count. In addition to the blood smear result, this indicate that this patient tends to have chronic disease anemia rather than hemolytic anemia.

There was presence of blood (+), protein (++), leukocyte (2-3/HPF), erythrocyte (4-5/HPF), and positive epithelial cast in the urine. With addition of a history of hypertension and positive Anti-dsDNA result, we suspect this patient had lupus nephritis. Based on WHO classification of lupus nephritis (Kasjmir et al., 2011), these clinical findings suits Class III lupus nephritis. However, further examination such as renal biopsy was unable to be done in the province due to limited facility. Liver function was normal, but urea level increased with borderline result of creatinine. Additional immuno-serology examination revealed positive result of ANA (IF) with speckled pattern and a titer of >1:1000 and positive Anti-dsDNA.

SLE is a complex and multiorgan autoimmune disease that can present with various clinical features (Kaul et al., 2016). The diagnosis of SLE can be made based on the 2019 European League Against Rheumatism/American College of Rheumatology (EULAR ACR) classification criteria that is divided by clinical and immunology domains. A total score of 10 with at least one clinical criterion confirm the diagnosis of SLE (Aringer et al., 2019). This patient fulfilled the entry criterion and had a total score of 19 (leukopenia, pericardial effusion, arthritis, and positive anti-dsDNA). All these findings lead to the diagnosis of SLE. Based on Indonesian Rheumatology Association's guideline of SLE diagnosis and management (Kasjmir et al., 2011) and EULAR recommendation (Fanouriakis et al., 2019), with nephritis, no life threatening conditions, and SLEDAI score of 10, the diagnosis is classified as moderate degree SLE.

On admission, this patient was given high dose intravenous steroid for five days, two bags of packed red cell, folic acid, and her usual hypertension-controlling drugs. There was no rejection reaction after transfusion of PRC was done. The patient showed significant improvement of the symptoms when discharged from the hospital. The steroid was tapered off to a total of 32mg daily. Moderate SLE can be initiated with induction therapy of high

dose steroid for at least three days and followed by azathioprine (2mg/kg/day) or mycophenolate mofetil (2-3gr/day) and tapered off to prednisone (0,5-0,6mg/kg/day) for 4-6 weeks. Maintenance therapy includes azathioprine (1-2mg/kg/day) or mycophenolate mofetil (1-2gr/day) and prednisone (0,125mg/kg/day) (Kasjmir et al., 2011). One week later, she was followed up outpatient in cardiology and internal medicine clinic. The patient reported significant improvement and had no symptoms at all. Repeat echocardiography showed significant reduction of PE fluid. The steroid treatment was reduced to 8mg with addition of mycophenolate mofetil 500mg twice daily by the internist. The goals of SLE treatment are long term survival, prevention of organ damage, and improvement of quality of life of the patient. Maintenance treatment of SLE include the initiation of immunomodulatory agents like methotrexate, azathioprine, and mycophenolate and minimized use of steroid and withdrawal if possible (Fanouriakis et al., 2021; Fava dan Petri, 2019).

Conclusion

This case highlights that not all pericardial effusion can appear with specific signs, symptoms, and electrocardiogram result, especially in minimal to moderate sized PE. Echocardiography can be the most efficient tool to diagnose even with the presence of only minimal PE. Once diagnosed, the etiology must be found. SLE in one of the most common cause of PE, especially in women of child-bearing age. Other signs that presents along with PE like joint pain, mouth ulcers, alopecia, and many other should indicate further laboratory examination that can lead to the diagnosis of SLE.

Conflict of Interest

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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Author contribution

The first author contributes as the data collector, main writer, and prepared the manuscript. The second author drafted the concept and revised the manuscript for publication.

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