Cardiac Tamponade as Initial Presentation of Systemic Lupus Erythematosus in Third-Trimester Pregnancy

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Patient: Female, 21-year-old
Final Diagnosis: Cardiac tamponade • lupus nephritis • preeclampsia • systemic lupus erythematosus
Symptoms: Chest pain • depression • rash • sore throat
Medication: —
Clinical Procedure: —
Specialty: Rheumatology

Objective: Rare coexistence of disease or pathology
Background: Systemic lupus erythematosus (SLE) is a common autoimmune disorder in women of childbearing age. It can present during pregnancy and can lead to poor maternal and fetal outcomes, with a higher risk of preterm birth and pre-eclampsia. Women are at a higher risk of lupus flares during pregnancy, especially if undiagnosed or if disease is poorly controlled. Cardiac tamponade is a rare complication of SLE and can be fatal.

Case Report: A 21-year-old primigravida African American woman with a history of asthma presented with progressive pleuritic left shoulder pain. She had a recent history of sore throat, facial rash, and depressed mood after sun exposure. A work-up was strongly positive for antinuclear antigen, anti-Smith, anti-Smith/ribonucleoprotein, anti-chromatin, anti-SSA, anti-SSB, anti-dsDNA, and low C3. Echocardiogram showed hemodynamically stable cardiac tamponade. The patient also had proteinuria and hypertension attributed to pre-eclampsia. However, a renal biopsy confirmed lupus nephritis. The patient was treated with pericardiocentesis, prednisone, azathioprine, and hydroxychloroquine. There was significant clinical improvement with resolution of cardiac tamponade and improvement in renal function.

Conclusions: Cardiac tamponade is a rare and life-threatening manifestation of SLE. Prompt work-up and treatment with immunosuppressants and pericardiocentesis is needed to improve maternal and fetal outcomes. SLE patients are at higher risk of exacerbations of the disease during pregnancy. It is also important to rule out lupus nephritis in an SLE patient with pre-eclampsia. This report shows the importance of accurate diagnosis of SLE in pregnancy and the appropriate management to ensure the best outcomes for the mother and fetus.

Keywords: Cardiac Tamponade • Lupus Erythematosus, Systemic • Lupus Nephritis • Pre-Eclampsia • Pregnancy Trimester, Third

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Background

Systemic lupus erythematosus (SLE) is an autoimmune disease affecting the skin and organs of the body. Globally, the incidence of SLE ranges from 0.3 to 23.3 per 100 000 person years [1]. It is more common in women and non-White individuals. Epidemiological studies have demonstrated racial disparities, with African American patients developing SLE at an earlier age and more severe disease with increased mortality [2]. Cardiac manifestations of SLE include myocarditis, pericarditis, valvular disease, thrombosis, and cardiac conduction defects [3].

Cardiac tamponade is a life-threatening complication of SLE that presents with chest pain, shortness of breath, palpitations, and, in more severe cases, dizziness and syncope. In a retrospective study of 409 patients with SLE, cardiac tamponade was diagnosed in 5.9% (24/409) of patients and can be fatal without treatment [4]. Of these 24 patients, 12 had cardiac tamponade as the initial presenting feature of SLE [4]. Pericardial effusion is seen in about 50% of SLE and usually has no significant clinical relevance [5]. There have been 2 reported cases of cardiac tamponade presenting in new-onset SLE that developed post-partum [6,7].

The 2019 European Alliance of Associations for Rheumatology (EULAR) classification for SLE include clinical and serologic with a positive antinuclear antibody titer of at least 1: 80 [8]. Clinical criteria include hematologic, musculoskeletal, serosal, renal, mucocutaneous, constitutional, and neuropathic elements. Treatment for all SLE patients involves hydroxychloroquine with a dose up to 5 mg/kg. Steroids can be used as adjuncts to immunosuppressive therapy. Steroid-sparing agents that can be used are methotrexate, azathioprine, mycophenolate, or cyclophosphamide. In pregnancy, hydroxychloroquine and azathioprine are safe, while methotrexate, mycophenolate, and cyclophosphamide are teratogenic. Benefits and risks in the mother and the fetus need to be considered, especially in cases of life-threatening disease of the mother, which would take precedence, such as alveolar hemorrhage [8,9].

A PubMed search using the keywords “SLE or systemic lupus erythematosus,” AND “cardiac tamponade” AND “pregnancy” was performed. This case report presents a 21-year-old African American woman with pericardial effusion, and cardiac tamponade as initial manifestations of systemic lupus erythematosus in the third trimester of pregnancy.

Case Report

A 21-year-old primigravida African American woman at 28-weeks’ gestation with past medical history of obesity, exercise-induced asthma, and pre-diabetes presented to the University Hospitals Cleveland Medical Center Emergency Department (ED) with left shoulder pain. She had initially presented to the labor and delivery triage with severe chest pain for 10 days. At that time, the chest pain was worse when lying flat with inspiration and improved leaning forward. Computed tomography (CT) pulmonary embolism protocol, troponins, amylase, lipase, and COVID-19 swab were all negative and pain resolved with nonsteroidal anti-inflammatory drugs. CT chest showed no evidence of pericardial effusion. Eight days after going to the labor and delivery triage, the patient presented again to the ED with worsening pleuritic pain. The pain was constant, worse with lying flat, and was slightly relieved with acetaminophen. The patient’s medications were aspirin 81 mg daily, which was started at 12 weeks’ gestation for pre-eclampsia prophylaxis and a prenatal vitamin. The family history was significant for supraventricular tachycardia in her mother and hypertension in her father, with no history of autoimmune diseases. The patient denied any tobacco, alcohol, or illicit drug use.

Review of symptoms was positive for a recent sore throat 1 month prior, insomnia, loss of appetite, depressed mood, and malar rash that was erythematous when it started and became hypochromic, having developed after prolonged sun exposure. The patient denied hair loss or oral ulcers. Vital signs in the ED were blood pressure 140/78 mmHg, pulse 106 beats per minute, respiratory rate 18 breaths per minute, temperature 36.2°C, and oxygen saturation 99% on room air. A physical exam was notable for tachycardia, with cardiac, respiratory, and skin unremarkable. There was no jugular venous distension or peripheral edema. The patient was noted to have depressed mood, anxiety, and minimal verbal interaction. The troponin level and electrocardiogram (EKG) were unremarkable, with no evidence of pulsus alternans. A point-of-care ultrasound revealed a pericardial effusion. Transthoracic echocardiography showed evidence of pericardial tamponade, with a large pericardial effusion with right diastolic collapse and preserved ejection fraction (Figure 1, Video 1). The patient underwent a pericardiocentesis with 600 cm³ of serosanguinous fluid removed. The patient was transferred to the cardiac intensive care unit (ICU) for hemodynamic monitoring.

The differential diagnosis included infection, connective tissue disease, and hypothyroidism. Pericardial fluid analysis showed glucose of 67 mg/dL, LDH 166 U/L, and total protein of 4.7 g/dL, consistent with an exudative effusion. An autoimmune work-up (Table 1), thyroid-stimulating hormone, Coxsackie B virus, and Adenovirus labs were performed. QuantIFERON gold testing was negative for tuberculosis and pericardial fluid was negative for adenosine deaminase, ruling out tuberculosis, which is important to exclude. The patient was empirically started on prednisone 20 mg daily and followed-up and evaluated at 7 days with improvement.
by the Maternal-Fetal Medicine. The initial urine spot protein level was 100 mg/dL and > 500 mg/dL the following day. The patient’s blood pressures were monitored for pre-eclampsia. Blood cultures were negative

On hospital day 3, an autoimmune work-up (Table 1) showed ANA 1: 5120 in a speckled pattern, C4 <8 mg/dL (decreased), C3 92 mg/dL (normal), anti-Smith antibody greater than 8, anti-Smith/ribonucleoprotein antibody greater than 8, anti-chromatin antibody greater than 8, anti-centromere antibody normal, anti-ribosomal P protein antibody normal, anti-Ro/SSA >8 AI (Ref <1 negative), anti-La/SSB >8 AI (Ref <1 negative), anti-double-stranded DNA 61 IU/mL (Ref <4 negative, >10 positive).

The patient exhibited confusion and was diagnosed with ICU delirium. She was started on 1 mg haloperidol by mouth as needed. Given the patient’s prior depressed mood and anxiety prior to ICU admission, neuropsychiatric lupus (NSL) was also in the differential diagnosis. However, the patient’s anti-ribosomal P and anti-phospholipid antibodies, which are associated with NSL, were negative.

The patient then developed atrial fibrillation and was given digoxin 500 μg i.v. and 250 μg i.v., with improvement of her atrial fibrillation. Throughout her hospitalization, the patient had rising urine total protein and creatinine with urine total

### Table 1. Autoimmune work-up.

| Autoimmune workup                          | Results                                      |
|--------------------------------------------|----------------------------------------------|
| ANA                                        | 1: 5120 (Ref <1: 40)                         |
| ANA pattern                                | Speckled                                     |
| Anti-smith antibody                        | >8 Al (Ref <1 negative)                      |
| Smith/RNP antibody                         | >8 Al (Ref <1 negative)                      |
| Anti-chromatin antibody                    | >8 Al (Ref <1 negative)                      |
| Anti-centromere antibody                   | Normal                                       |
| Anti-ribosomal P protein antibody           | Normal                                       |
| Anti-Ro/SSA                                | >8 Al (Ref <1 negative)                      |
| Anti-La/SSB                                | >8 Al (Ref <1 negative)                      |
| Anti-double-stranded DNA                   | 61 IU/mL (Ref <4 negative, >10 positive)    |
| Serum C3 complement (mg/dL)                | <8 mg/dL (Ref 87-200)                        |
| Serum C4 complement (mg/dL)                | 92 mg/dL (Ref 10-50)                         |
| Lupus anticoagulant                        | Negative                                     |
| Anti-cardiolipin antibody                  | Negative                                     |
| Anti-beta-2-glycoprotein                   | Negative                                     |
| CRP                                        | Negative                                     |
| ESR                                        | 40 mm/h (Ref: 0-20)                          |

ANA – anti-nuclear antibody; RNP – ribonucleoprotein; SSA – anti-Sjögren’s-syndrome-related antigen A autoantibodies; SSB – anti-Sjögren’s-syndrome-related antigen B autoantibodies; DNA – deoxyribonucleic acid; CRP – C-reactive protein; ESR – erythrocyte sedimentation rate.
protein 590 mg/dL and urine creatinine 191 mg/dL. Urinary analysis (UA) showed 3+ mg/dL protein, 1+ blood, 2+ mg/dL ketones, 3+ granular casts, 3+ hyaline casts, red blood cells (RBC) 22, and white blood cells (WBC) 15. The total protein-to-creatinine ratio increased from 1.91 on admission to 3.39 during hospitalization. Due to worsening kidney function, Nephrology was consulted, and lupus nephritis was suspected; therefore, a with renal biopsy was recommended. Bilateral renal ultrasound was done to rule out obstruction and showed no hydronephrosis. She was started on prednisone 80 mg daily based on 1 mg/kg recommendations from Rheumatology. The patient was stable for discharge on day 8 with a regimen of prednisone 80 mg daily and hydroxychloroquine 200 mg daily with outpatient follow-up with Maternal-Fetal Medicine and Rheumatology.

Four days after discharge, the patient was sent to the labor and delivery ward from the Maternal-Fetal Medicine Clinic due to orthopnea. Vitals were notable for a blood pressure of 153/86 mmHg. A physical exam was notable for mild crackles bilaterally on lower lung fields. Laboratory test results were notable for a protein-to-urine creatine ratio of 0.8 and brain natriuretic peptide (BNP) of 192 pg/mL. The uric acid level was normal at 5.3 mg/dL (reference range 2.3-6.7). A 24-h urine calcium was not done. The patient was prescribed 20 mg i.v. furosemide daily for symptoms. Pre-eclampsia could not be ruled out and 2 doses of 12 mg intramuscular (i.m.) betamethasone 24 h apart was given for fetal lung maturation. She was also given labetalol 20 mg i.v. on admission and then started on labetalol 200 mg twice daily (BID) by mouth. She developed worsening dyspnea, left shoulder pain, and tachypnea, with a respiratory rate of 33 breaths per minute, but improved with 0.4 mg i.v. hydromorphone and 20 mg i.v. furosemide. Cardiology was consulted and an EKG was consistent with stage 3 pericarditis. She was started on colchicine 0.6 mg daily and 40 mg i.v. furosemide daily.

The patient clearly met the diagnostic criteria for SLE, with strongly positive ANA, ant-dsDNA, chromatin, SSA, SSB, RNP, Sm/RNP, Smith, low C3, and elevated ESR. Clinical manifestations included pericarditis/pericardial effusion, proteinuria with RBCs, cutaneous, hematologic (normocytic anemia), and (probably) neuropsychiatric. On hospital day 6, the patient developed an acute headache. Labetalol was discontinued, and she was started on 2 g/h i.v. magnesium overnight, given the concern for pre-eclampsia in the context of hypertension. The patient reported resolution of headache and was started on benazepril 10 mg daily. She had sudden onset of headache again and with blood pressures of 160/90 s and administered another 2 g/h i.v. magnesium infusion, with resolution of headache, and was discharged with stable blood pressure.

At Rheumatology follow-up, the patient was continued on prednisone 60 mg daily and hydroxychloroquine 200 mg BID, with a plan to start azathioprine as she planned to breastfeed, given the safety during breastfeeding compared to mycophenolate. One week later, the patient presented to the ED with pleuritic chest pain. The patient was normotensive with heart rate of 125 beats per minute. A complete metabolic panel was unremarkable, and the complete blood count was notable for leukocytosis of 12.5 K/dL. Initial troponins were 0.76 ng/ml and 0.66 ng/ml, and BNP was 126 pg/mL. EKG was normal. A chest X-ray showed cardiomegaly with left pleural effusion. An ultrasound showed ejection fraction of 55%, large pericardial effusion with multiple fibrous strands, restrictive pattern of left ventricular diastolic filling, and mild-to-moderate tricuspid regurgitation. The patient was diagnosed with pericarditis and large pleural effusion and admitted to the cardiac ICU.

A subxiphoid pericardial window was surgically created and prednisone dose was increased to 80 mg daily per Rheumatology, with plans to taper by 5 mg per week. She was started on colchicine 0.6 mg BID. The patient was also prescribed Pneumocystis jiroveci prophylaxis with trimethoprim/sulfamethoxazole 3 times weekly and peptic ulcer prophylaxis with pantoprazole 20 mg daily. The patient underwent follow-up ultrasound, which showed improvement in pericardial effusion. A UA showed a protein-to-creatinine ratio of 6.97, and Nephrology was consulted to assess for kidney biopsy. Nephrology recommended outpatient follow-up for biopsy, as lupus flare was unlikely. The patient developed thrombocytosis of 700×10^4 L, and a peripheral blood smear showed thrombocytosis, likely secondary to inflammation. The patient had a cardiac MRI to rule out constrictive pericarditis and the result was unremarkable. She was discharged on prednisone 75 mg daily with taper of 5 mg per week and short course of colchicine 0.6 mg BID.

On follow-up, azathioprine was started with a maintenance dose of 150 mg daily (2 mg/kg), and hydroxychloroquine 200 mg BID and prednisone taper were continued. She was advised to discard breast milk for 4 h after her prednisone and azathioprine doses in the morning. The patient had a kidney biopsy 3 months later, consistent with class V lupus nephritis with minimal activity and chronicity scores and no glomerulosclerosis.
Discussion

This case emphasizes early diagnosis and management of cardiac tamponade and lupus nephritis in a third trimester pregnancy with a new diagnosis of SLE that responded well to high-dose steroids and azathioprine. The patient’s age, race, and pregnancy status were important risk factors for the development of SLE, which can exhibit severe complications, including cardiac tamponade. This is an extremely rare case of cardiac tamponade as a presenting symptom of SLE in pregnancy, and 2 cases have been reported post-partum. In 2009, Ketata et al described the case of a 29-year-old woman in France who presented with post-partum cardiac tamponade and was diagnosed with SLE based on anemia, leukopenia, and positive ANA, and anti-dsDNA antibodies [6]. The patient had a favorable outcome after treatment with pericardiocentesis and glucocorticoids. Another case was published by Averbuch et al in 1986 of a woman who developed tamponade 1 week after delivering a healthy child and was diagnosed with SLE [7].

Early recognition of tamponade is key to making a complete recovery, as the disease can be fatal if untreated. Patients often present with chest pain, dyspnea, and dizziness. Physical exams include Beck’s triad with hypotension, jugular venous distension, and muffled hearts sounds [10]. While the diagnosis of cardiac tamponade can be suspected based on results of history and physical exam, EKG and chest X-ray should be done [10]. The characteristic EKG finding is electrical alternans, which shows an alternating QRS amplitude on the rhythm strip, which is rare. The more common EKG finding is sinus tachycardia. If a prior chest X-ray is available for comparison, an enlarged heart on chest X-ray aids the diagnosis. However, echocardiography is the best and first-line imaging modality to determine the size of the pericardial effusion and to assess of diastolic function, as this can be compromised [10].

The etiologies of cardiac tamponade in pregnancy are broad and include iatrogenesis, trauma, malignancy, collagen vascular diseases, and connective tissue diseases. It is important to consider SLE as an autoimmune-related cause of tamponade in pregnancy, as it can lead to congenital heart block. Additionally, prompt diagnosis and treatment of SLE is key to preventing further development of pericarditis and flares during pregnancy. Pregnant patients with SLE are at increased risk for pre-eclampsia, gestational diabetes, and lupus nephritis [11]. Fetal risks include congenital heart block, miscarriage, intrauterine fetal demise, preterm rupture of membranes, preterm birth, and intrauterine growth restriction [12].

This case was further complicated by hypertension as a concern for the development of pre-eclampsia. The patient’s proteinuria can be seen in her pre-eclampsia and lupus nephritis. The diagnostic criteria for pre-eclampsia by the American Congress of Obstetricians and Gynecologists is a rise in systolic blood pressure greater than or equal to 140 mmHg or a diastolic blood pressure greater than or equal to 90 mmHg in a patient that was previously normotensive on 2 separate occasions 4 h apart, in addition to proteinuria of either ≥300 mg in a 24-h urine collection or protein/creatinine ratio of 0.3 (mg/mg) (30 mg/mmol), occurring after 20 weeks of pregnancy. Proteinuria is not required for the diagnosis if end-organ damage is indicated by marked thrombocytopenia, impaired liver function, new renal insufficiency, or new cerebral or visual dysfunction [13]. The presentation of lupus nephritis varies from no symptoms to severe proteinuria, and the diagnosis is confirmed with renal biopsy, with the threshold for recommending biopsy ranging from 500 mg/day to 1 g/day [14].

Our patient likely had both pre-eclampsia and SLE, leading to renal dysfunction. During her first admission, the protein/creatinine ratio decreased after treatment with steroids, implying that her underlying lupus was causing kidney dysfunction. However, during later admissions, the patient continued to have hypertension and required treatment with magnesium for pre-eclampsia. The patient also developed a headache, supporting a diagnosis of pre-eclampsia in addition to SLE. The patient’s repeated accumulation of a pericardial effusion further supports the presentation of pre-eclampsia, as her lupus laboratory test results were stable at that time. Therefore, this patient’s presentation demonstrates the importance of recognizing concomitant SLE and pre-eclampsia in pregnancy. In contrast to the existing literature, both this patient and the neonate had good outcomes, highlighting the importance of early diagnosis and prompt treatment of both conditions.

Treatment of SLE during pregnancy is directed toward disease remission by evaluating clinical and laboratory parameters. It is recommended that SLE patients planning to become pregnant should be in disease remission 6 months prior to conception. Hydroxychloroquine is a safe medicine used in SLE patients unless there is a contraindication. It should be continued during pregnancy and can help reduce the risk of flare, pre-eclampsia, and neonatal heart block [9]. Immunosuppressants used to treat lupus that are contraindicated during pregnancy include mycophenolate and cyclophosphamide, making lupus nephritis more difficult to treat. Azathioprine is safe in pregnancy and can be effectively used for lupus nephritis. Low-dose aspirin can be used in SLE and/or antiphospholipid antibody syndrome to reduce the risk of pre-eclampsia and should be started at 12 weeks’ gestation [9]. Steroids can be used, especially in life-threatening cases such as cardiac tamponade, lupus nephritis, and alveolar hemorrhage. EULAR guidelines recommend checking lab parameters such as Ro/SSA, La/SSB, and antiphospholipid antibody laboratory rest results. Ro/SSA and La/SSB are associated with congenital heart block and it is therefore important to check these in SLE patients during...
pregnancy. Collaboration with Rheumatology and high-risk obstetrics/maternal fetal medicine is important, especially in high-risk pregnancies, such as the case presented [9].

Furthermore, this patient’s case stresses the importance of choosing an appropriate pharmacological agent for breastfeeding mothers with SLE. Commonly employed immunosuppressants for SLE that are safe due to minimal to no excretion in breast milk are azathioprine and hydroxychloroquine. Cyclophosphamide should be avoided while breastfeeding due to the potential for developing neutropenia. Glucocorticoids only enter the breast milk in small quantities and are generally not contraindicated. However, women on higher doses (usually 50 mg or greater) should wait 4 h after dosage to breastfeed, thereby reducing the concentration of glucocorticoid in the breast milk [15].

Although cardiac tamponade during pregnancy has a high risk for complications, we present a case where both the patient and the newborn had a good outcome. This can be attributed to a large multidisciplinary team of Rheumatology, Nephrology, Maternal-Fetal Medicine, Thoracic Surgery, and Cardiology.

Conclusions

Cardiac tamponade is a life-threatening condition that can be fatal without intervention. Patients with SLE who are not treated are more likely to have maternal and fetal complications. Early recognition and close monitoring are key to improving outcomes. This case report demonstrates a unique presentation of SLE in a patient, where pericardial effusion leading to tamponade was the initial presentation. A collaborative multidisciplinary approach was essential for good maternal and fetal outcomes. This report shows the importance of accurate diagnosis of SLE in pregnancy and appropriate management to ensure the best outcomes for the mother and fetus.

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