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CARDIAC TAMPONADE, FIRST SIGN OF ONSET OF SYSTEMIC LUPUS ERYTHEMATOSUS

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Abstract
Lupusul eritematos sistemic (LES) este o boală autoimună cu manifestări clinice variate, ce poate afecta multiple organe și sisteme. Una dintre complicațiile severe asociate LES este tamponada cardiacă, o complicație rară, amenințătoare de viață. În această lucrare, prezentăm cazul unei femei în vârstă de 36 de ani, ce a fost diagnosticată cu LES după un episod de tamponadă cardiacă. Tamponada cardiacă este rar întâlnită în LES, mai ales ca debut al bolii.
Acest caz subliniază importanța recunoașterii precoce a afectării cardiace și dorește să pună în evidență faptul că LES poate debuta cu tamponadă cardiacă. Îngrijirea multidisciplinară ce implică reumatologi, cardiologi și alți specialiști este esențială în gestionarea LES cu complicații cardiace.
Cuvinte cheie: *tamponadă cardiacă, lupus eritematos systemic.*

Abstract
Systemic lupus erythematosus (SLE) is an autoimmune disease with various clinical manifestations that can affect multiple organs and systems. One of the severe complications associated with SLE is cardiac tamponade, a rare and life-threatening complication. In this paper, we present the case of a 36-year-old woman who was diagnosed with SLE after an episode of cardiac tamponade. Large pericardial effusions with cardiac tamponade are rarely encountered in SLE, particularly as the onset of the disease. This case highlights the importance of early recognition of cardiac tamponade and raises awareness of the fact that SLE can present with cardiac involvement, such as cardiac tamponade, at the onset of the disease. Multidisciplinary care involving rheumatologists, cardiologists, and other specialists is essential in the management of SLE with cardiac complications.
Key words: *cardiac tamponade, systemic lupus erythematosus.*

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Introduction

Systemic lupus erythematosus (SLE) is an autoimmune disease that can involve any organ or system, exhibiting great diversity in presentation. One common manifestation of SLE is pain, stiffness and swelling of the joints. Cutaneous manifestations of SLE include a malar rash, a butterfly-shaped rash that appears on the cheeks and bridge of the nose. Photosensitivity is another common symptom of SLE, where exposure to sunlight can trigger or worsen skin rashes[1]. SLE signs and symptoms can vary in frequency and severity, making it challenging to diagnose it accurately.

Cardiac tamponade as the initial presentation of SLE is very rare, therefore, we are presenting the case of a 36 years old woman and showcasing the differential diagnosis and treatment process of this patient.

Case presentation

A 36 years-old woman presented to the emergency unit in April 2019 with a three-months history of progressive dyspnea, cough and chest pain, that significantly worsened in the last few days. In the past month, she developed fatigue and intermittent fever (37.5 - 38.3°C) but denies having chills, myalgia, arthralgia/arthritis, hair loss, oral or nasal ulcers. She had no history suggestive of heart failure, renal failure, liver disease, diabetes mellitus, hypertension, irrational speech or behavior. She had no medical history or family history of autoimmune diseases. She did not travel recently or had any contact with a tuberculosis patient. She doesn't drink alcohol, smoke cigarettes, or use illicit drugs.

On general examination, the patient showed no signs of trauma, had a temperature of 37.5°C, small petechiae on the lower limbs, cervical and inguinal lymphadenopathy (slightly painful, soft, mobile, non-adherent to deep planes). On cardiovascular examination, the jugular veins were distended, the heart sounds were muffled, she had tachycardia of 125 beats per minute, a blood pressure of 88/56 mmHg. The respiratory examination revealed decreased breath sounds at the right lung base, a respiratory rate of 33 breaths per minute and oxygen saturation of 94% on room air. The abdominal examination revealed hepatomegaly.

The electrocardiogram showed sinus tachycardia and low voltages, excluding acute myocardial infarction. The chest radiograph showed an increased cardiac silhouette. The transthoracic echocardiography revealed a "swinging heart" appearance, large circumferential pericardial effusion of 2.7 cm in the parasternal long axis view and 2.4 cm in the subcoastal view with diastolic collapse of the right ventricle. Cardiac tamponade was

confirmed (inspiratory decrease in the mitral valve E wave velocity on pulse wave Doppler tracing).

A computer tomography (CT) scan of chest, abdomen and pelvis was performed which revealed large pericardial effusion (39 mm adjacent to the left ventricle, 34 mm adjacent to the right atrium, 39 mm at the apex of the heart), moderate ascites, moderate pleural effusion and multiple mediastinal, axillary, lumbo-aortic and inguinal adenopathies. Thoracic CT scan excluded aortic dissection or mediastinal tumors.

The patient underwent an emergency echocardiogram-guided pericardiocentesis, which removed 600 mL of sanguinolent fluid. Additionally, a pericardial drainage tube was kept. Analyses of the pericardial fluid revealed 1400 leucocytes and 100 red blood cells per mm^3, unremarkable levels of protein, glucose and lactate dehydrogenase. The cytology revealed inflammatory cells with no evidence of malignancy. Bacteriologic, fungal cultures and GeneXpert for the detection of Mycobecterium tuberculosis were negative.

Laboratory findings included: hemoglobin of 8.2g/dL (normal value: 12.0-18.5), leucocytes of 3.4 x 10^9/L (normal value: 4-11), platelets of 120 x 10^9/L (normal value: 150-450), erythrocyte sedimentation rate (ESR) of 85 mm/hour (normal value <20mm/h), C-reactive protein (CRP) of 4.2mg/L (normal value: 0-5), normal renal and liver function tests, normal creatine kinase (CK), N-terminal pro b-type natriuretic peptide (NT-proBNP) of 672 pg/ml (normal value <130 pg/ml), normal thyroid-stimulating hormone (TSH) and triiodothyronine (T3) and thyroxine (T4). Serological tests for Human immunodeficiency virus (HIV), hepatitis B and C were negative. Serology for Influenzae virus, Epstein-Barr virus (EBV), Mumps orthorubulavirus, Varicella zoster virus was negative. Blood and urine cultures were negative. Urinalysis by dipstick was normal.

Additional laboratory testing was done to further determine the cause of the poliserositis, bicytopenia, lymphadenopathy, fever and rash. Antinuclear antibodies (ANA) at a titer of 1:1280, anti-double stranded DNA (anti-dsDNA), lupus anticoagulant and circulating immune complexes were all positive. Anti-Smith (anti-Sm) antibodies, rheumatoid factor (RF), anti-cyclic citrullinated peptide (CCP) were negative. Direct Coombs testing was positive. Significantly low serum levels of complement were observed: C3=25 mg/dl (normal levels: 90-180 mg/dl) and C4=0.8 mg/dl (normal levels: 10-40 mg/dl).

Subsequently, an inguinal lymph node biopsy was performed, which showed non-specific lymphadenitis. A few days after the lymph node biopsy, the patient reported a purulent secretion, swelling and increased pain at the incision site. After draining the collection, 8 days of treatment with piperacillin/tazobactam 4/0.5 g was administered. Later, the pathogen was identified as methicillin-resistant staphylococcus aureus.

To further investigate the presence of pancytopenia and lymphadenopathy, a bone marrow biopsy was performed that excluded lymphoproliferative disorders.

During the hospitalization, the patient developed an erythematosus papular rash on the thorax and arms and also complained about arthralgia (wrists and knees) but without signs of swelling and inflammation.

Based on the clinical examination, laboratory tests and cardiac ultrasound, the patient was diagnosed with New York Heart Association (NYHA) class III chronic heart failure, severe aortic regurgitation, moderate mitral regurgitation, stage 2 hypertension very high additional risk group.

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According to the 2019 European Alliance of Associations for Rheumatology/American College of Rheumatology (EULAR/ACR) classification criteria for SLE, the patient had a score of 35, thus helping in establishing the diagnosis of SLE.

The diagnosis of SLE was established based on the positive clinical and immunologic findings. The patient satisfied 9 of the 17 Systemic Lupus International Collaborating Clinics (SLICC) criteria for classifying SLE, namely maculopapular lupus rash, serositis, leukopenia, thrombocytopenia, hemolytic anemia (direct Coomb's test), low serum complement levels, positive serum ANA, positive anti-dsDNA and positive lupus anticoagulant. Supporting the diagnosis, we mention hyperthermia, lymphadenopathy, arthralgia and elevated ESR. The SELENA-SLEDAI (Safety of Estrogens in Lupus National Assessment - Systemic Lupus Erythematosus Disease Activity Index) score was 11, meaning a high activity.

Other potential causes including infection (viral, bacterial, fungal), as well as other medical conditions like cancer and other connective tissue disorders were excluded.

The patient was started on intravenous methylprednisolone at a dose of 1 g/day for three days, followed by oral methylprednisolone at a dose of 32 mg daily (2 tablets of 16 mg per day), which was subsequently tapered. She was also administered 400 mg of hydroxychloroquine daily (2 tablets of 200 mg per day) and azathioprine 100 mg daily (2 tablets of 50 mg per day). The patient had a favorable clinical response.

One year after hospitalization, the dose of methylprednisolone was tapered to 8 mg daily, azathioprine was discontinued and hydroxychloroquine was reduced to 200 mg daily.

In the following years, the patient had a favorable evolution both clinically and biologically, with a low disease activity, maintaining the same therapeutic scheme.

At the moment, the patient's evolution is favorable with a mild disease activity reflected by SELENA-SLEDAI score of 2 and she is on the same drug regimen of 200 mg daily of hydroxychloroquine and 8 mg of methylprednisolone.

Discussion

Cardiac complications are frequently seen in SLE. Pericarditis, myocarditis, valve disorders and conduction system abnormalities are the most frequent cardiac complications in SLE[2-4]. The most prevalent cardiac manifestation of SLE is pericarditis, which has been linked to poor prognosis. Symptomatic pericarditis appears in approximately 25% of SLE patients, often concomitant with pleuritis. Imaging examinations observed that >30% of SLE patients have pericardial

involvement[5-7]. Often, pericardial effusion is small and hemodynamically insignificant in SLE[8]. Rarely, cardiac tamponade can be found in less than 1% of SLE patients and it is considerred an unusual occurrence as the initial manifestation of SLE[9].

Cardiac tamponade is a medical emergency that occurs when there is an accumulation of fluid in the pericardial sac that severely limits the diastolic filling, leading to decreased cardiac output and systemic venous congestion. It is uncommon for cardiac tamponade to be the initial presentation of systemic lupus erythematosus with only a few reported cases in the medical literature. Symptoms of tamponade may include dyspnea with orthopnea, chest pain, irregular heartbeat, jugular venous distension, low blood pressure and muffled heart sounds on cardiac auscultation (last three features describing Beck's triad).

Diagnosis is typically confirmed through echocardiography, which shows specific signs such as pericardial effusion, diastolic right ventricular collapse, systolic right atrial collapse[10].

Other tests, such as electrocardiogram and blood tests, are done to assess the severity of this condition. The low occurrence of tamponade in SLE patients may be attributed to the use of medications like steroids and NSAIDs, which help reduce inflammation in the pericardium.

Cardiac tamponade was found to be more common in women comparing to men, especially those presenting with anemia, renal failure, pleuritis, increased inflammation expressed by high ESR values, and low C4 levels[11], but cases in men were also reported in the specialized literature[12]. Some features such as pleuritis, anti-nucleosome antibodies, and the extent of the pericardial effusion were significant predictors of tamponade[13, 14]. The patient in this case is a female known with some risk factors associated with the development of cardiac tamponade in SLE, including large pericardial effusion, pleuritis, hemolytic anemia, high ESR values and low C3 and C4 levels.

For mild cases of pericarditis, nonsteroidal anti-inflammatory drugs (NSAIDs) might be administered, however high-dose steroids and pericardiocentesis are recommended for cardiac tamponade in SLE patients. Additionally, immunosuppressants like azathioprine, mycophenolate mofetil, and hydroxychloroquine are also recommended[13]. In this case, high-dose steroids and hydroxychloroquine were administered along with pericardiocentesis. After this procedure, the evolution was favorable, the patient had a good therapeutic response and she no longer needed other interventions.

For large effusions, pericardiocentesis is performed, but recurrence is frequent. In addition, pericardiectomy can be useful if pericardiocentesis and steroid therapy are unsuccessful and are followed by a build-up of pericardial fluid.

We excluded additional possible reasons such as infections (bacterial, fungal or viral) and other illnesses like cancer and other connective tissue diseases.

Several cases of infectious pericarditis with cardiac tamponade with EBV, CMV, Mumps virus and Herpes zoster were described in medical literature. However, serology for those viruses were negative[15-18].

Advanced mediastinum tumors can directly invade the organs, resulting in symptoms like dyspnea, coughing and chest pain. Pericardial infiltration can sometimes cause cardiac tamponade[19].

The severity of this condition along with the time of diagnosis and treatment determine

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the prognosis for SLE patients who experience cardiac tamponade. In order to have a better treatment response, early management is essential. Many individuals can fully recover and have a favorable long-term prognosis with proper treatment. Delays in diagnosis and treatment might lead to serious complications including heart failure or death. Cardiac tamponade and other major heart issues can be avoided with regular SLE management and monitoring by medical professionals[20,21].

A few cases of SLE related cardiac tamponade as the first manifestation were found in the medical literature[22-25]. These presentations provide an opportunity for healthcare professionals to learn from each other's experiences. By sharing cases with their colleagues, medical professionals can gain insights, feedback, and perspectives that can help improve their clinical practice.

Conclusions

Cardiac tamponade as the initial presentation of SLE is regarded as an uncommon event. Women are more commonly affected than men and often pericarditis can be present alongside with pleuritis and hematologic abnormalities and low serum complement levels.

Physicians should include SLE as a potential cause in the differential diagnosis of pericarditis and cardiac tamponade and conduct necessary tests for SLE. Early detection of immunological markers for SLE is critical for prompt disease diagnosis. Multidisciplinary care involving rheumatologists, cardiologists, and other specialists is essential in the management of SLE with cardiac complications.

Declaration of interest:

The authors declare no conflict of interest

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