Case Report
Volume 10:9, 2020
DOI: 10.37421/jccr.2020.10.1379

Clinical Case Reports

ISSN: 2165-7920 Open Access

Systemic Lupus Erythematosus: An Autoimmune Disease with Multiple Clinical Ways of Presentation

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Abstract

Systemic Lupus Erythematosus (SLE) is a chronic autoimmune disease that can affect any organ in the body. Therefore, the clinical manifestations that patients present are highly variable, they can have mild conditions such as localized skin or joint manifestations, up to more serious conditions, such as kidney, hematological or central nervous system conditions. The SLE is characterized by abnormal production of autoantibodies; the most characteristic are Antinuclear Antibodies (ANA), and their specificities, and antiphospholipid antibodies. In this review, we present a clinical case of SLE with particular clinical manifestations, with the aim of providing the reader with key findings in this pathology to improve the precision of the diagnosis early and thus initiate treatment in a timely manner.

Keywords: Systemic lupus erythematosus • Antinuclear antibodies

Introduction

A 19-year-old female patient with no personal or family history of autoimmune diseases. In childhood, she presented an arteriovenous malformation in the left thigh treated with sclerotherapy, without any other important data in her medical history. Six months prior to her emergency admission, she presented asthenia, and she came with hematology and the diagnosis of unspecified anemia was integrated, was treated with oral iron, without improvement in symptoms or hemoglobin levels, 4 weeks prior to her admission, she presented throat pain and cervical lymphadenopathy, she went to otorhinolaryngology, and was treated with NSAIDs and antibiotics without improvement of the symptoms. She went to the emergency department for oppressive chest pain, which was exacerbated when lying down and improved when sitting, in addition to unquantified fever that did not improve with NSAIDs, dyspnea, and profuse diaphoresis [1,2].

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On physical examination she presented tachycardia, tachypneic, and fever of 39°, retroauricular and cervical, asymmetric, bilateral, mobile, soft and non-painful lymphadenopathy on palpation, diameter varied from 0.5 to 2 cm, splenomegaly was palpated 2 cm per below the rib margin. Complementary studies were requested as part of their initial approach (Table 1) with normal cardiac enzymes, liver function tests, and a highlighted normochromic normocytic anemia, leukopenia, lymphopenia, with elevated ferritin, moderately elevated PCR, the microscopic examination of urine with presence of blood and proteins (three crosses), was approached by internal medicine, which requested virus serology Epstein Barr, Cytomegalovirus, Hepatitis A, B and C, which was negative. A chest X-ray was requested, in which a left pleural effusion was observed, and a neck echo where multiple lymphadenopathy was observed, the largest being 18 by 10 mm at the two left cervical level, and an abdominal echo where the presence of splenomegaly of 750 grams. It was evaluated by an oncologist surgeon who performed an excisional biopsy of the cervical nodes, with a histopathological result of lymphocytic hyperplasia and a bone marrow aspirate with a report of lymphocytic hyperplasia (Table 2). M:E ratio 2:1.

Rheumatology interconsultation was performed, requesting 24-hour antibody and protein studies, antinuclear antibodies was positive, rheumatoid

Table 1. Laboratory studies.

Laboratory Studies	
Leukocytes	3830 mm^3
Neutrophils	2750 mm^3
Lymphocytes	689 mm^3
Hemoglobin	8.7 g /dl
CVM	26.9 fl
CHM	33.8 g/ dl
Platelets	208 103 / mm^3
Creatinine	0.5 mg / dl
Alanine aminotransferase	18 U/L
Aspartate Aminotransferase	27 U/L
Total bilirubin	0.1 U/L
24-hour urinary protein	1689 mg
24-hour urinary creatinine	1056 mg
Immunological studies	
Coombs Direct	Positive
Coombs Indirect	Positive
Protein C Reactive	19.2 mg/dL
Rheumatoid factor	108.8 IU/mL (0-14)
C3	44 mg/dL (90-180)
C4	1.0 mg/dL (16.5-38)
Anti-DNA	200 IU/mL (0-20)
Cardiolipin IgG	14.0 U/ml (<10)
Cardiolipin IgM	80.0 (<10))
Antinuclear antibodies	4.6 U/mL (<1.2)
Anti B2 glycoprotein IgG	45 U/ml (<10)
Anti B2 glycoprotein IgM	51 (<10)
Lupus Anticoagulant positive	51

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Received 16 August 2020; **Accepted** 24 August 2020; **Published** 31 August 2020

factor positive, complement C3 and C4 consumed, anti-DNA positive at high titers, anti-cardiolipin antibodies IgG and IgM, positive at high titers, antibodies anti beta 2 glycoproteins IgG and IgM positive, direct and indirect Coombs positive, in a 24-hour urine study, creatine 1056 and protein 1689 mg stood out, with a protein-creatinine ratio of 1.6, a computed tomography of the chest was request, with bilateral pleural effusion and pericardial effusion (Figure 1), and a renal biopsy was performed, where lupus proliferative membranous glomerulonephritis was observed, Class III +V, activity index 8 and chronicity of 4 (Figures 2 and 3). The diagnosis of systemic lupus erythematosus with renal, hematological, serositis and serological activity was integrated. In the treatment 3 pulses of methylprednisolone 1 gram were administered every 24 hours for 3 days, continuing with reductive doses of prednisone of 1 mg per kilogram of weight orally, remission induction therapy with mycophenolate was started progressively until reaching 3 grams, hydroxychloroquine, calcium and vitamin D were added, achieving remission of the symptoms, at 3 months antiphospholipid antibodies were again performed, which confirmed positivity, and in laboratory studies there was a decrease in proteinuria from 24 hours to 0.5 grams in 24 hours, that is, the patient is having a total response and a favorable evolution.

Discussion

Lupus erythematosus is an inflammatory autoimmune disease of the connective tissue [3,4]. Skin and mucosal lesions appear in 80% of patients.

Table 2. Medulogram.

Medulogram	
Erythroid series	Hypoplastic. Erythroblasts are seen in all forms of ripening predominantly polychromatic
Megakaryocytic series	Hypoplastic. Megakaryocytes are not observed. Platelet production decreased but sufficient for function
Myeloid series	Hypoplastic. Precursor and mature forms of normal but diminished morphology.
Lymphoid series	Predominant. Morphology shows cell maturity
Ferric coloration	Iron uptake by sideroblasts
Leukocyte formula	Myelocytes 3%
	Metamyelocytes 3%
	Dropped 8%
	Neutrophils 36%
	Basophils 1%
	Eosinophils 2%
	Monocytes 0%
	Lymphocytes 47%

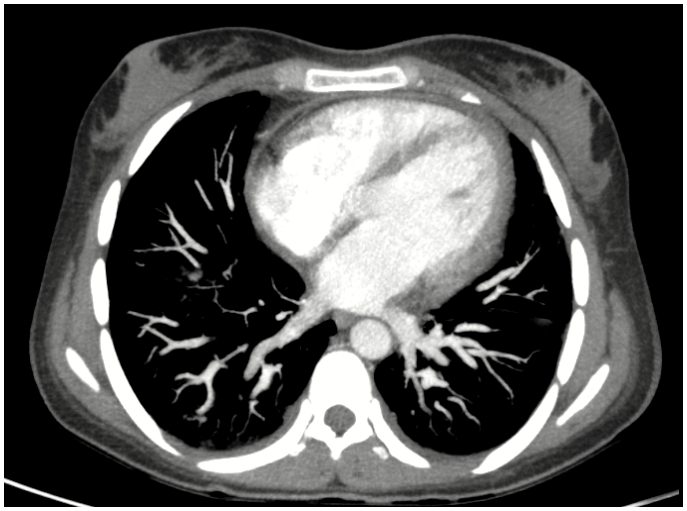

Figure 1. Chest CT with contrast I.V. in the axial axis, pericardial effusion with a greater amount in the LV postero-lateral wall area, without evident pericardial enhancement. It is associated with a small bilateral pleural effusion.

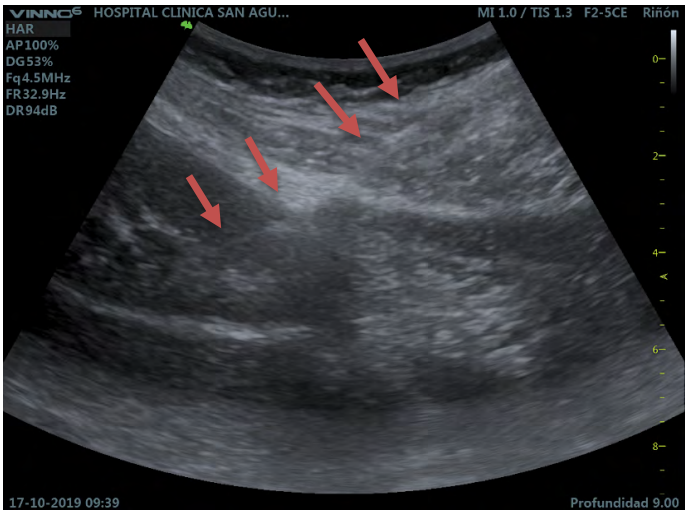

Figure 2. Ultrasound-guided percutaneous biopsy, Ultrasonographic vision of the needle as an echogenic linear image in the renal cortex of the lower pole and with an adequate angle of attack (50º to 70º).

Figure 3. Renal biopsy. Membranous and mesangial IgG and IgM deposits.

However, we did not find malar rash in our patient, which is a characteristic sign of this disease [5]. It is important to mention that the patient had previously been treated for a clinical picture of iron deficiency anemia, for which she received iron VO 100 mg every 12 hours, causing metrorrhagia. However, when requesting blood chemistry, the results suggested in this patient, anemia of chronic disease, therefore it was important to rule out an associated inflammatory disorder like SLE. Subsequently, due to the presence of asymmetric lymphadenopathies in the cervical region, the echographic sonographic shows multiple mix nodules of variable sizes distributed in both sides in the neck. Polyadenopathy syndrome is a frequent manifestation in Systemic Lupus Erythematosus (SLE). Adenopathy's are generally small in size and are found in the cervical, inguinal, and axillary region. They are present in up to 25% of patients and usually appear in the early stages of the disease or in relapses [6]. The differential diagnosis of polyadenopathy syndrome in SLE includes necrotizing histiocytic lymphadenitis or Kikuchi-Fujimoto disease (EKF), Castleman's disease, syphilis, tuberculosis, sarcoidosis, mononucleotide syndromes, herpes simplex, human immunodeficiency virus, hepatitis B virus and hepatitis, other infections and lymphoma. So, in order to rule out other infectious processes or a hematologic proliferative disease, tests for Epstein-Barr virus, hepatitis A and C viruses and a biopsy was performed, the results of these were negative [7].

The American College of Rheumatology (ACR) and the European

League Against Rheumatism (EULAR) have established new criteria for the classification of Systemic Lupus Erythematosus (SLE), in which Antinuclear Antibodies (ANA) are required for classification and are divided into 7 clinical domains (constitutional, hematological, neuropsychiatric, mucocutaneous, serous, musculoskeletal and renal) and three immunological (antiphospholipid, complement and specific antibodies), with their respective scores and at least 10 points are required to classify the patient with SLE. In the case of this patient, these criteria are met, reaching a score of 48 points [8,9]. There is no a general treatment for SLE due to the heterogeneity of its behavior and the management must be individualized based on the characteristics of the patient and the activity of the disease and even with the possibility of access to some drugs such as biological therapies. Treatment is based on the use of Glucocorticoids (GC), Non-Steroidal Anti-Inflammatory Drugs (NSAIDs), antimalarials and various immunosuppressants. Most rheumatologists agree with the use of immunomodulators for moderate to severe SLE during a period of intense immunosuppressive therapy known as induction therapy, followed by a longer period of maintenance therapy. The 3 main goals of induction therapy are to stop damage, regain function, and control immune activity.

The patient had renal activity, evidenced by biopsy. To treat it, among the least toxic regimens recommended by the ACR EULAR/ERA-EDTA guidelines, Mycophenolate Mofetil (MMF) is an excellent choice. According to several randomized controlled trials (RCTs) a dose of 2 gr daily of MM, is not inferior to the National Institute of Health (NIH) regimen, based of doses of cyclophosphamide for induction therapy in patients with nephritis due to proliferative or pure membranous lupus. And mycophenolate is an excellent option in Latin Americans, as some studies have shown. 8 In a trial, ALMS (Aspreva Lupus Management Study), 370 patients with ISN/RPS (International Society of Nefrology / Renal Pathology Society) class III, IV, or V of lupus nephritis were randomized to receive intravenous pulse cyclophosphamide monthly 0.5-1.0 g/m^2 or mycophenolate mofetil 3 g daily. Both groups also received high doses of prednisone (60 mg daily). The overall clinical response rate was similar in both treatment groups, subgroup analyzes revealed that mycophenolate mofetil was associated with a significantly higher response rate than cyclophosphamide. For these reasons we chose MMF in our patient. In SLE, there is a high prevalence of non-optimal levels of vitamin D. A prevalence of 25 (OH) D insufficiencies is reported from 15 to 75% and the deficiency is from 15 to 27%. It has been observed that the use of glucocorticoids, antimalarials and immunosuppressants can accelerate catabolism, alter the absorption of 25 (OH) D and condition resistance at the nuclear vitamin D receptor. There are predictive factors for deficiency and deficiency of 25 (OH) D in patients with SLE. Lupus nephritis has been shown to be a predictor of vitamin D deficiency in SLE patients. 9Antimalarials have been used in the treatment of SLE since the 19th century, current evidence suggests the use of hydroxychloroquine (HCQ) or chloroquine. Antimalarials have photoprotective, hypolipidemic, antiangiogenic, antithrombotic effects and, in addition, inhibit the function of the activating factor of B cells and phospholipase A2, which allows them to be indicated in the treatment of cutaneous lupus, of SLE with mild to moderate activity, as a concomitant treatment to prevent relapses and damage to major organs.

Conclusion

For all the aforementioned in the studies, the patient was administered 3 pulses of methylprednisolone 1 gram every 24 hours for 3 consecutive days, continuing with reductive doses of prednisone of 1 mg per kilogram of oral weight, induction therapy was started to remission with mycophenolate progressively until reaching 3 grams, hydroxychloroquine, calcium and vitamin D were also added, achieving remission of symptoms. At 3 months, antiphospholipid antibodies were performed again, which were positive, and in laboratory studies there was a decrease in proteinuria from 24 hours to 0.5 grams in 24 hours, that is, the patient is having a total response and a favorable evolution. The optimal duration of maintenance therapy in lupus nephritis is unclear. The EULAR/ERA-EDTA guidelines recommend that maintenance immunosuppression be continued for at least 2-3 years in patients who respond to induction therapy (GC or immunosuppressant).

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How to cite this article: Guzmán-García Santiago, Rodriguez-Maya Felipe, Chamba Pineda Lizbeteh, and Flores Amay Thalía. "Systemic Lupus Erythematosus: An Autoimmune Disease with Multiple Clinical Ways of Presentation." *Clin Case Rep* 10 (2020): 1379. DOI: 10.3742/jccr.2020.10.1379