



DENGUE INFECTION IN A PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT

INFECCIÓN POR DENGUE EN UN PACIENTE CON LUPUS ERITEMATOSO SISTÉMICO: REPORTE DE CASO

Carlos Alberto Franco-López ^{1,a}, Roberto Arreguín-Reyes ^{1,b}, Arturo García-Galicia ^{1,c}, Deyaneira Palacios-Figueroa ^{1,d}, Miguel Sánchez-Solís ^{1,a}, Nancy Rosalía Bertado-Ramírez ^{1,e}, Álvaro José Montiel-Jarquín ^{1,f}

ABSTRACT

Introduction: Systemic Lupus Erythematosus (SLE) is an autoimmune disease caused by an autoreactive B and T cell response with loss of immune tolerance to self-antigens. It manifests with asthenia, fever, myalgias, arthralgias, skin rash and fatal organ damage. Dengue is a zoonotic disease caused by the dengue virus (DENV), transmitted by mosquitoes of the *Aedes aegypti* species. Diagnostic suspicion is made in the presence of acute febrile syndrome with clinical manifestations and demographic history. Confirmation is by detection of the virus by PCR-RT, or of the structural protein Ns1. **Clinical case:** The present case report is a 58-year-old woman with data of lupus exacerbation and with clinical manifestations suggestive of Dengue fever, with a history of travel to an endemic area. The confirmatory PCR-RT test leads to appropriate medical treatment. The importance of the case lies in differentiating the diagnosis in a timely manner.

Keywords: Systemic lupus erythematosus; Cutaneous lupus erythematosus; Dengue; Viral zoonoses; Fever. (Source: MESH-NLM)

RESUMEN

Introducción: El lupus eritematoso sistémico (LES) es una enfermedad autoinmune por respuesta autorreactiva de células B y T con pérdida de la tolerancia inmunitaria frente a autoantígenos. Se manifiesta con astenia, fiebre, mialgias, artralgias, erupción dérmica y daño fatal a órgano. El dengue es una enfermedad zoonótica por el virus de dengue (DENV), transmitida por mosquitos de la especie *Aedes aegypti*. La sospecha diagnóstica se realiza en presencia de síndrome febril agudo con manifestaciones clínicas y antecedentes demográficos. La confirmación es por la detección del virus mediante PCR-RT o de la proteína estructural NS1. **Caso clínico:** El presente caso clínico se trata de una mujer de 58 años con datos de exacerbación lúpica y con manifestaciones clínicas sugerentes de dengue; al interrogatorio evidenció el antecedente de viaje a zona endémica. La prueba confirmatoria de PCR-RT conduce a adecuación del tratamiento médico. La importancia del caso recae en diferenciar el diagnóstico oportunamente.

Palabras clave: Lupus eritematoso sistémico; Lupus eritematoso cutáneo; Dengue; Zoonosis virales; Fiebre. (Fuente: DeCS- BIREME)

¹ High Speciality Medical Unit, Speciality Hospital, National Medical Center "Gral. de Div. Manuel Ávila Camacho", Mexican Institute of Social Security, Puebla de Zaragoza, Puebla, Mexico.

^a General Physician specializing in Internal Medicine.

^b Rheumatology Specialist.

^c Pediatrics Specialist.

^d General Physician.

^e Neurology Specialist.

^f General Surgery Specialist.

Cite as: Franco-López CA, Arreguín-Reyes R, García-Galicia A, Palacios-Figueroa D, Sánchez-Solís M, Bertado-Ramírez NR, Montiel-Jarquín AJ. Dengue infection in a patient with systemic lupus erythematosus: A case report. Rev Fac Med Hum. 2024;24(4):214-220. doi 10.25176/RFMH.v24i4.6519

Journal home page: <http://revistas.urp.edu.pe/index.php/RFMH>

Article published by the Journal of the Faculty of Human Medicine of the Ricardo Palma University. It is an open access article, distributed under the terms of the Creative Commons License: Creative Commons Attribution 4.0 International, CC BY 4.0 (<https://creativecommons.org/licenses/by/4.0/>), which allows non-commercial use, distribution and reproduction in any medium, provided that the original work is duly cited. For commercial use, please contact revista.medicina@urp.edu.pe





INTRODUCTION

Systemic lupus erythematosus (SLE) is a chronic, inflammatory, autoimmune disease characterized by an autoreactive response of B and T cells, leading to a loss of immune tolerance to self-antigens. Its clinical manifestations can be mild, moderate, or, in more severe cases, life-threatening. It is characterized by symptoms such as asthenia, fever, myalgia, arthralgia, skin rash, and potentially fatal organ damage both at the onset and during disease activity⁽¹⁾. Dengue is a zoonosis transmitted by *Aedes aegypti* mosquitoes and causes fever, headache, myalgia, arthralgia, and transient skin rashes. In severe cases, it can lead to respiratory difficulties, hemorrhage, and multiple organ failure⁽²⁾. The objective of this case report is to describe the clinical presentation of dengue in a patient with SLE.

CLINICAL CASE

A 58-year-old woman, originally from the state of Chiapas, and a resident of the state of Puebla for the last 10 years, was diagnosed with lupus involving mucocutaneous and joint manifestations since 2019.

At the time of this report, the patient was undergoing treatment with chloroquine 150 mg, azathioprine 90 mg, and prednisone 7.5 mg every 24 hours. She had also been diagnosed with systemic arterial hypertension since 2019, for which she was being treated with valsartan, amlodipine, and hydrochlorothiazide (5 mg/160 mg/12.5 mg) every 24 hours. On January 9, 2023, she presented with a fever of 38.9°C, holocranial headache, hyporexia, asthenia, and arthralgia. She self-medicated with 500 mg of acetaminophen, resulting in partial improvement. Two days later, her fever returned (38.9°C), accompanied by nausea and one episode of gastrointestinal vomiting. She was hospitalized for febrile syndrome under study, and her maintenance treatment for SLE was suspended. Upon admission, she had a fever of 38.9°C and knee pain.

Physical examination revealed erythematous papules on the eyelids and malar region, with no ulcers in the nasal or oral mucosa. A maculopapular rash with erythematous papules and mild confluent scaling was noted on the anterior chest and the right posterior hemithorax. No cardiopulmonary or abdominal involvement was observed. The upper limbs showed a maculopapular rash, and the lower limbs exhibited limited flexion and extension due to knee pain. The results of blood count, blood chemistry, and coagulation tests are shown in Table 1. The general urinalysis reported: cloudy brown appearance, 100 leukocytes/ μ L, negative nitrites, 150 mg/dL proteins, 250 erythrocytes/ μ L, 30-41 leukocytes per field, 40-50 erythrocytes per field, 2+ bacteria, 1+ epithelial cells, 0-1 hyaline casts, and 0-1 granular casts. A rapid antigen test for SARS-CoV-2 was negative.

The patient received treatment with acetaminophen 1 g every 8 hours and Hartmann solution 1000 ml IV every 24 hours. She had a slow evolution with persistent fever and increased arthralgia and edema in her lower limbs. Upon further questioning, the patient reported a recent trip to an endemic area (state of Chiapas) one week before the onset of symptoms. The Rumpel-Leede test was performed and reported positive. Epidemiology was notified of a probable dengue diagnosis with warning signs (thrombocytopenia). A real-time polymerase chain reaction (RT-PCR) test for dengue was performed.

Treatment with chloroquine 150 mg every 24 hours and acetaminophen was resumed; azathioprine was not restarted. The patient showed improvement, without hemorrhage despite severe thrombocytopenia. The RT-PCR result, three days after the sample was taken, was positive for dengue (DENV-3 serotype). With the resolution of symptoms and no warning signs, she was discharged home after five days of hospitalization.



**Table 1.** Laboratory results obtained during the hospital stay.

	Parameter	12/03/2024	13/03/2024	14/03/2024
COMPLETE BLOOD COUNT (CBC)	Hemoglobin (g/dL)	14.6	15.62	14.86
	Hematocrit	44.3	47.99	45.26
	Platelets	79 800	53 000	34 000
	Citrated platelets			
	Leukocytes (cel/uL)	4100	3290	5060
BLOOD CHEMISTRY	Glucose (mg/dL)		101	
	Creatinine (mg/dL)		0.71	
	Na+ (mmol/L)		135	
	K+ (mmol/L)		4.4	
	Cl- (mmol/L)		103	
	AST (mg/dL)		82	
	ALT (mg/dL)		19	
	Total Bilirubin (mg/dL)		0.31	
	Direct Bilirubin (mg/dL)		18	
	Indirect Bilirubin (mg/dL)		0.13	
COAGULATION TIMES	Albumin (mg/dL)			
	LDH (UI/L)		601	
	Prothrombin Time (PT) (seconds)		12.5	
	Control Prothrombin Time (seconds)		11.5	
	Partial Thromboplastin Time (PTT) (seconds)		35.6	
	International Normalized Ratio (INR)		1.09	

CLINICAL CASE

DISCUSSION

Systemic lupus erythematosus (SLE) has a global incidence of 6.73 per 100,000 individuals in Caucasian populations and 31.4 per 100,000 in African American populations annually⁽³⁾. The clinical findings of SLE are shown in Table 2⁽⁴⁾. The criteria of the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) allow for the classification of the clinical presentation of SLE by systems and organs (Table 3)⁽⁵⁾. The SLEDAI (Systemic Lupus Erythematosus Disease Activity Index), later modified

as MEX-SLEDAI for the Mexican population, evaluates disease activity during lupus exacerbation⁽¹⁵⁾, though the patient did not meet the criteria for exacerbation. Initial treatment for SLE includes antimalarials, while glucocorticoids are recommended for controlling acute attacks and maintenance therapy⁽⁶⁾. Dengue is a zoonotic disease caused by the dengue virus (DENV), transmitted by *Aedes aegypti* mosquitoes⁽⁸⁾. In Mexico, 12,671 cases were reported in 2022 (with an incidence of 9.74 per 100,000 inhabitants); 57% of these cases were concentrated in the states of Sonora, Veracruz, Estado de

México, Tabasco, and Chiapas, with serotypes DENV-2 (56.03%) and DENV-3 (24.93%) being the most prevalent⁽⁷⁾. According to the World Health Organization (WHO), dengue is classified as: 1) Dengue without warning signs (suspected dengue due to residence in or travel to endemic areas, fever, and at least two symptoms such as nausea, vomiting, myalgia, arthralgia, leukopenia, or a positive tourniquet test); 2) Dengue with warning signs (same as the previous

definition, plus any warning symptom such as abdominal pain, serositis, hemorrhages, altered mental status, visceromegaly, or a sudden drop in platelet count); and 3) Severe dengue (includes the previous signs plus evidence of organ or system damage, including multiple organ failure)⁽⁷⁾. In this case, the patient fell under the category of dengue with warning signs due to the presence of thrombocytopenia.

Table 2. Spectrum of clinical symptoms in Systemic Lupus Erythematosus (measurement of lupus activity and cumulative damage in patients with Systemic Lupus Erythematosus)⁽⁴⁾.

Affected system	Symptom	% of occurrence	
		At presentation	During lupus activation
General	Fatigue	50	74 to 100
	Fever	36	40 to 80
	Weight changes	21	44 to 60
	Myalgia and Arthralgia	62 al 67	83 to 95
Tegumentary	General	73	80 to 91
	Malar rash	73	80 to 91
	Photosensitivity	29	41 to 60
	Mucosal Membrane Lesions	10 al 21	27 to 52
	Alopecia	32	18 to 71
	Raynaud's Phenomenon	17 al 33	22 to 71
	Purpura	10	15 to 34
	Urticaria	1	4 to 8
Renal	General	16 al 38	34 to 73
	Nephrosis	5	11 to 18
Gastrointestinal	Esophagitis, Pseudo-obstruction	18	38 to 44
	Splenomegaly	5	9 to 20
	Hepatomegaly	2	7 to 25
Pulmonary	General	2 al 12	24 to 98
	Pleuritis	17	30 to 45
	Effusion		24
	Pneumonia		29
Cardiovascular	General	15	20 to 46
	Pericarditis	8	8 to 48
	Murmurs		23
	ECG Changes		34 to 70
	Lymphadenopathy	7 al 16	21 to 50
Central Nervous System	General	12 al 21	25 to 75
	Functional		Majority
	Psychosis	1	5 to 52
	Seizures	0.5	2 to 20



Table 3. Classification criteria of the European Alliance of Associations for Rheumatology (EULAR)/American College of Rheumatology (ACR) for Systemic Lupus Erythematosus (SLE) 2019

Entry Criterion (Required for classifying SLE)	
ANA (antinuclear antibodies) at a titer >1:80 on Hep-2 cells or an equivalent positive test (at any time).	
Domains and Clinical Criteria	Score
Constitutional	
Fever (>38 °C)	2
Hematologic	
Leukopenia (<4,000 cells/L)	3
Thrombocytopenia (<100,000 cells/L)	4
Autoimmune hemolysis (confirmed)	4
Neuropsychiatric	
Delirium (characterized by changes in consciousness or reduced ability to concentrate; development of symptoms <2 days; symptom fluctuation throughout the day; acute/subacute changes in cognition or behavior)	2
Psychosis (characterized by hallucinations and in the absence of delirium)	3
Seizures (generalized or focal)	5
Mucocutaneous	
Non-scarring alopecia (confirmed by a physician)	2
Oral ulcers (confirmed by a physician)	2
Subacute cutaneous lupus or discoid lupus (confirmed by a physician. If a skin biopsy is performed, typical changes must be present)	4
Acute cutaneous lupus (confirmed by a physician. If a skin biopsy is performed, typical changes must be present)	6
Serosal	
Pleural or pericardial effusion (evidenced by imaging)	5
Acute pericarditis (2 or more than 1) Pericardial chest pain, 2) Pericardial rub, 3) ECG showing new generalized ST elevation or PR depression, 4) New or worsening pericardial effusion confirmed by imaging)	6
Musculoskeletal	
Joint involvement (either: 1) Synovitis involving two or more joints; or 2) Tenderness in two or more joints with at least 30 minutes of morning stiffness)	6
Renal	
Proteinuria (>0.5 g in 24 hours)	4
Renal biopsy reporting lupus nephritis class II or V	8
Renal biopsy reporting lupus nephritis class III or IV	8

Domains and immunology criteria	Score
Antiphospholipid antibodies	
Anticardiolipin antibodies [IgA, IgG, or IgM at medium or high titer (>40 phospholipid units A (APL), GPL, or MPL, or >99th percentile)] or	2
Positive anti-B2GP1 antibodies (IgA, IgG, or IgM) or	
Positive lupus anticoagulant	
Complement Proteins	
Low C3 or low C4	3
Low C3 and low C4	4
SLE-Specific Antibodies	
Anti-dsDNA antibodies or	6
Anti-Smith antibodies	

Classification of SLE requires: 1) an entry criterion + 2) a total score of ≥ 10 points, and 3) at least one clinical criterion. A criterion should not be counted if there is a more likely explanation than SLE. The occurrence of a criterion on one or more occasions is sufficient, and the criteria do not need to occur simultaneously. Within each domain, only the highest-weighted criterion is counted toward the total score if more than one is present (Clinical manifestations and diagnosis of systemic lupus erythematosus in adults)⁽⁵⁾.

The diagnostic suspicion is based on acute febrile syndrome with clinical manifestations and demographic history. The Rumpel-Leede or tourniquet test is recommended by the WHO due to its ease of application and utility in decision-making. The test involves inflating the sphygmomanometer cuff on the upper arm to a point midway between the individual's systolic and diastolic pressures and maintaining it inflated for five minutes. After deflation and two minutes of rest, the number of petechiae below the antecubital fossa is counted. The test is considered positive if more than 10 petechiae are present within a square inch of skin on the arm⁽¹⁶⁾.

Although the test has documented low sensitivity and specificity (58%, 95% CI: 43%-71%; and 71%, 95% CI: 60%-80%, respectively), it remains recommended as a decision-support tool in resource-limited areas⁽¹⁶⁾. Confirmation of dengue is achieved through the detection of the virus via RT-PCR or the identification of the NS1 structural protein or specific IgM⁽¹⁷⁾. Treatment is symptomatic, and depending on the severity, most cases are managed on an outpatient basis. Patients with comorbidities or signs of severe disease should be hospitalized⁽⁸⁾.

In the clinical case presented, the patient, who had an exacerbation of lupus, revealed a recent trip to an endemic dengue area during the medical history interview. Diagnostic suspicion was based on the positive Rumpel-Leede test, which supported the decision to perform the confirmatory RT-PCR test, alongside laboratory results and patient history. The use of immunosuppressants such as azathioprine and prednisone may have facilitated the severity of dengue in this case, as both drugs are known to cause bone marrow toxicity.

The variations in thrombocytopenia further supported the classification of the patient's case as dengue with warning signs, which led to the management with intravenous fluids, up to 1000 milliliters in addition to oral intake. The patient experienced third-space fluid leakage, primarily in the lower limbs, during the first 48 hours of hospitalization, which resolved by the time of discharge. Distinguishing between lupus exacerbation and dengue infection can be challenging due to their overlapping clinical presentations. A thorough medical history is always essential to guide clinical suspicion and differentiate the diagnosis in a timely manner.



Author contributions: JC participated in the collection of patient data, writing of the clinical case, introduction, discussion, conclusions. RA in writing the summary, discussion and final review of the case. LM in data collection, images, preparation of the timeline, table of results.

Financing: Self-financed.

Conflicts of interest: The authors declare that they have no conflict of interest.

Received: May 17, 2024.

Approved: August 20, 2024.

Correspondence: Jessica Milagros Calcino Cuela.

Address: Jr. Huiracocha 1770, Jesús María, Lima-Perú.

Telephone: (+51) 912749947

Email: jessica_milcc@hotmail.com

REFERENCES

- Kiriakidou M, Ching CL. Systemic Lupus Erythematosus. *Ann Intern Med.* 2020 Jun 2;172(11):ITC81-ITC96. doi:10.7326/AITC202006020. PMID: 32479157.
- Harapan H, Michie A, Sasmono RT, Imrie A. Dengue: A Minireview. *Viruses.* 2020 Jul 30;12(8):829. doi:10.3390/v12080829. PMID: 32751561; PMCID: PMC7472303.
- Rees F, Doherty M, Grainge MJ, Lanyon P, Zhang W. The worldwide incidence and prevalence of systemic lupus erythematosus: a systematic review of epidemiological studies. *Rheumatology (Oxford).* 2017 Nov 1;56(11):1945-1961. doi:10.1093/rheumatology/kex260. PMID: 28968809
- Wallace JD, Gladman Dafna D. Clinical manifestations and diagnosis of systemic lupus in adults. UpToDate [Internet]. Uptodate.com. [citado el 9 de abril de 2024]. Disponible en: <https://www.uptodate.com/contents/clinical-manifestations-and-diagnosis-of-systemic-lupus-erythematosus-in-adults>
- Aringer M, Costenbader K, Daikh D, Brinks R, Mosca M, Ramsey-Goldman R, Smolen JS, et al. 2019 European League Against Rheumatism/American College of Rheumatology Classification Criteria for Systemic Lupus Erythematosus. *Arthritis Rheumatol.* 2019 Sep;71(9):1400-1412. doi:10.1002/art.40930. Epub 2019 Aug 6. PMID: 31385462; PMCID: PMC6827566.
- Sifuentes Giraldo WA, García Villanueva MJ, Boteanu AL, Lois Iglesias A, Zea Mendoza AC. New therapeutic targets in systemic lupus. *Reumatol Clin.* 2012 Jul-Aug;8(4):201-7. English, Spanish. doi:10.1016/j.reuma.2012.01.012. Epub 2012 Apr 6. PMID: 22483661.
- Panorama Epidemiológico de Fiebre por Dengue y Fiebre Hemorrágica por Dengue con información del Sistema Especial de Vigilancia Epidemiológica de Dengue. Publicación por Semana Epidemiológica a cargo de la Dirección de Vigilancia Epidemiológica de Enfermedades Transmisibles. *Semana Epidemiológica 52.* Gob.mx. [citado el 05 de enero de 2023]. Disponible en: https://www.gob.mx/cms/uploads/attachment/file/878786/Pano_dengue_52_2023.pdf
- Frantchez V, Fornelli R, Graciela Pérez S., Arteta Z., Cabrera S., Sosa., et al. Dengue en adultos: diagnóstico, tratamiento y abordaje de situaciones especiales. *Rev. Méd. Urug.* [Internet]. 2016 Abr [citado 2023 Mar 23]; 32(1): 43-51. Disponible en: http://www.scielo.edu.uy/scielo.php?script=sci_arttext&pid=S1688-03902016000100006&lng=es.
- Aringer M, Costenbader K, Johnson SR. Evaluación de los criterios de clasificación EULAR/ACR para pacientes con lupus eritematoso sistémico. *Experto Rev Clin Immunol.* 2022 febrero; 18 (2):135-144.
- Dima A, Jurcut C, Chasset F, Felten R, Arnaud L. Hydroxychloroquine in systemic lupus erythematosus: overview of current knowledge. *Ther Adv Musculoskelet Dis.* 2022;14:1759720X211073001.
- Muller DA, Depelensenaire AC, Young PR. Clinical and Laboratory Diagnosis of Dengue Virus Infection. *J Infect Dis.* 2017 Mar 1;215(suppl_2):S89-S95. doi:10.1093/infdis/jiw649. PMID: 28403441.
- Guzman MG, Harris E. Dengue. *Lancet.* 2015 Jan 31;385(9966):453-65. doi:10.1016/S0140-6736(14)60572-9. Epub 2014 Sep 14. PMID: 25230594.
- Medina F, Medina JF, Colón C, Vergne E, Santiago GA, Muñoz-Jordán JL. Dengue virus: isolation, propagation, quantification, and storage. *Curr Protoc Microbiol.* 2012 Nov;Chapter 15:Unit 15D.2. doi:10.1002/9780471729259.mc15d02s27. PMID: 23184594.
- Soo KM, Khalid B, Ching SM, Chee HY. Meta-Analysis of Dengue Severity during Infection by Different Dengue Virus Serotypes in Primary and Secondary Infections. *PLoS One.* 2016 May 23;11(5):e0154760. doi:10.1371/journal.pone.0154760. PMID: 27213782; PMCID: PMC4877104.
- Vera-Rivero DA, Chirino-Sánchez L, Martínez Lastre A. Medición de la actividad lúpica y daño acumulado en pacientes con lupus eritematoso sistémico. *Rev Cuba Reumatol [Internet].* 2019 Ago [citado 2024 Abr 09]; 21 (2): e88. Disponible en: http://scielo.sld.cu/scielo.php?script=sci_arttext&pid=S1817-59962019000200007&lng=es.
- Grande AJ, Reid H, Thomas E, Foster C, Darton TC. Tourniquet Test for Dengue Diagnosis: Systematic Review and Meta-analysis of Diagnostic Test Accuracy. *PLoS Negl Trop Dis.* 2016 Aug 3;10(8):e0004888. doi:10.1371/journal.pntd.0004888. PMID: 27486661; PMCID: PMC4972435.