CASE REPORT AND LITERATURE REVIEW

Rheumatology Quarterly

DOI: 10.4274/qrheumatol.galenos.2023.18209
Rheumatology Quarterly 2023;1(3):121-3

A DILEMMA IS WIDESPREAD BETWEEN RHEUMATOLOGY AND INFECTIOUS DISEASES, AS EVIDENCED BY A CASE

Tuba Demirci Yıldırım, Efe Erbay, Gerçek Şen, Fatoş Önen

Dokuz Eylül University Faculty of Medicine, Department of Rheumatology, İzmir, Turkey

Abstract

Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by multisystem organ involvement and various symptoms. Many diseases present with laboratory and clinical features similar to those of SLE, for example, malignancies and infections that are termed "lupus mimickers". This article presents a case of visceral leishmaniasis in which clinical characteristics and laboratory profiles imitated SLE in our hospital.

Keywords: Systemic lupus erythematosus, visceral leishmaniasis, splenomegaly

INTRODUCTION

Systemic lupus erythematosus (SLE) is an autoimmune connective tissue disease with a wide variety of clinical manifestations that predominantly affects women (1). Considering the variable manifestations of SLE, the differential diagnosis is broad. In this article, we share our case of visceral leishmaniasis (VL), which we considered a preliminary diagnosis of SLE.

CASE REPORT

A 23-year-old female patient with no history of disease was examined for diffuse myalgia, arthralgia, and fever. She was referred to our clinic because of anti-nuclear antibody (ANA) positivity, pancytopenia, high acute phase reactant, and splenomegaly (Table 1). In the examination of the patient, it was determined that splenomegaly, which was 170 mm, was detected incidentally; her complaints had increased gradually for three months; and she lost nearly ten percent of her body weight in this process. It was learned that the patient had been evaluated in terms of hematological malignancies before but could not get any diagnosis. At the physical examination, her body temperature was 38.5 °C, her arterial blood pressure was 90/60 mm/Hg, and her heart rate was 110 beats/min. She had hepatosplenomegaly (19 cm hematometry and a palpable spleen 9 cm from the left costal border). She had no lymphadenopathy or skin lesions. The most frequent infectious diseases were eliminated, including leptospirosis, tuberculosis, human immunodeficiency virus, Epstein-Barr virus, and viral hepatitis B and C. Laboratory tests revealed pancytopenia, elevated levels of C-reactive protein, and sedimentation (Table 1). Abdominal tomography confirmed splenomegaly, with the spleen on its largest axis measuring 24.6 cm. Laboratory results showed ANA 1/320-1000 dilution with a speckled pattern, pancytopenia with lymphopenia, and polyclonal hypergammaglobulinemia (Table 1). The diagnostic hypothesis at that time was an autoimmune disease or hematological malignancy. No atypical cells were detected in the peripheral smear, and bone marrow aspiration and biopsy were performed. In the infectious examinations of the patient, leishmaniasis enzyme-linked immunosorbent assay: Positive

Address for Correspondence: Tuba Demirci Yıldırım, Dokuz Eylül University Faculty of Medicine, Department of Rheumatology, İzmir, Turkey
Phone: +90 506 269 72 71 **E-mail:** tubademirci87@gmail.com **ORCID ID:** orcid.org/0000-0003-3186-0591
Received: 13.09.2023 **Accepted:** 17.09.2023 **Epub Date:** 26.09.2023 **Publication Date:** 29.09.2023

Table 1. Laboratory findings

Tests	Results	Normal range
Hemoglobin, g/dL	6.9	12-16
Leukocytes/(10^3/uL)	1.1	4-10.3
Lymphocytes/(10^3/uL)	0.4	1-3.5
Platelets, (10^3/uL)	120	156-373
Aspartate aminotransferase, µ/L	28	0-35
Alanine aminotransferase, µ/L	17	0-50
Creatinine, mg/dL	0.62	0.6-1.1
Rheumatoid factor, IU/mL	10↓	-
C-reactive protein, mg/L	68	0.2-5
Sedimentation rate (mm/h)	25	-
Anti-nuclear antibody	1/320-1000 speckled	Negative <1/100< titer
Anti-dsDNA	Negative	1/10< titer
Hematuria	Negative	-
Urine protein	Negative	-
Complement C3, mg/dL	64	90-180
Complement C4, mg/dL	23	10-40
Protein electrophoresis	Hypergammaglobulinemia	-

(serum was studied at 1/100 dilution) and leishmaniasis indirect fluorescence antibody test: 1/256 positive were detected. A bone marrow biopsy was reported as having polytypic staining with more plasma cells close to each other with kappa and lambda in the appearance found in myelodysplastic syndrome (MDS) cases and thought to be reactive. After clinical information, sections were also evaluated for leishmania, but no specific findings were observed. In the patient's history, VL was diagnosed due to multiple mosquito contacts during her stay in Manisa, all other anamneses, physical examination, laboratory, and leishmaniasis serology positivity. From the time of diagnosis, treatment with intravenous liposomal amphotericin B on 3 mg/kg/day was initiated on days 0-5,14, and 21. The clinical and laboratory findings improved. The patient's splenomegaly decreased, and she was discharged with an improved general condition.

DISCUSSION

When diagnosing rheumatologic disease, it is always important to distinguish between mimicrs. This dilemma is very common in rheumatology and infectious diseases. There are reports in the literature that leishmaniasis can mimic or trigger an autoimmune disease such as SLE and rheumatoid arthritis (2). Because of the clinical heterogeneity of SLE and the lack of pathognomonic testing, it can usually be diagnosed after alternative diagnoses have been excluded (3). VL, or kala-azar, is a systemic disease that is potentially fatal to humans. Infection caused by a protozoan of the genus *Leishmania* causes death in 95% of cases if left untreated (4). Our country is reported as an endemic region for cutaneous leishmaniasis by the World Health Organization, but VL is sporadically seen in the Aegean region (4). Fever, myalgia, arthralgia, and pancytopenia are common in VL cases, and the diagnosis of SLE was investigated when clinically combined with the ANA positivity detected in our case. The mechanisms involved in the pathophysiology of autoantibody production are not yet fully understood (5). However, a negative anti-dsDNA test, normal levels of C3 and C4 complement proteins, and massive splenomegaly made the diagnosis of infection stronger. In areas endemic to VL, SLE diagnosis can be a clinical dilemma. At the same time, VL may present as an opportunistic disease in immunocompromised patients with SLE, and thus, this differential diagnosis should be considered (6). In addition, pancytopenia is remarkable in patients with VL. Clinicians usually encounter VL as an opportunistic infection in patients with cell-mediated immunosuppression or, because the clinical presentation is not specific, in the differential diagnosis of myeloproliferative diseases. Recent advances, for example, in manipulation of the PI3K/Akt/HIF1 axis, which may contribute to the MDS features of VL, have enhanced our understanding of the role of the liver, spleen, and bone marrow microenvironments in shaping host-parasite interactions and their defining effect

on clinical expression and infection outcome (7). In this study, early diagnosis of VL and initiation of treatment prevented misdiagnosis and inadequate treatment.

Ethics

Informed Consent: Information of informed consent from the patient.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Concept: T.D.Y., E.E., G.Ş., Data Collection or Processing: T.D.Y., E.E., G.Ş., Literature Search: T.D.Y., E.E., G.Ş., Writing: T.D.Y., E.E., F.Ö.

Conflict of Interest: The authors have no conflicts of interest to declare.

Financial Disclosure: The authors declared that this study received no financial support.

REFERENCES

1. Zucchi D, Elefante E, Schilirò D, et al. One year in review 2022: systemic lupus erythematosus. Clin Exp Rheumatol 2022;40:4-14.
2. Bueno GCL, Koerich ATS, Burg LB, Kretzer SL, Moral JÂGD, Pereira IA. Visceral leishmaniasis mimicking systemic lupus erythematosus. Rev Soc Bras Med Trop 2019;52:e20180208.
3. Narváez J. Systemic lupus erythematosus 2020. Med Clin (Barc) 2020;155:494-501.
4. World Health Organization (WHO). Leishmaniasis. Available from: URL: https://apps.who.int/neglected_diseases/ntddata/leishmaniasis/leishmaniasis.html
5. Liberopoulos E, Kei A, Apostolou F, Elisaf M. Autoimmune manifestations in patients with visceral leishmaniasis. J Microbiol Immunol Infect 2013;46:302-5.
6. Fernández-Guerrero ML, Aguado JM, Buzón L, et al. Visceral leishmaniasis in immunocompromised hosts. Am J Med 1987;83:1098-102.
7. Poulaki A, Piperaki ET, Voulgarelis M. Effects of Visceralising Leishmania on the Spleen, Liver, and Bone Marrow: A Pathophysiological Perspective. Microorganisms 2021;9:759.