Systemic Lupus Erythematosus and Autoimmune Hepatitis: A Case Report

Lúpus Eritematoso Sistémico e Hepatite Autoimune: A Propósito de um Caso Clínico

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ABSTRACT

Systemic lupus erythematosus is a multisystem autoimmune disorder. Liver involvement is normally not a part of the systemic lupus erythematosus spectrum, but is seen in up to 60% of patients. The clinical presentation of autoimmune hepatitis ranges from asymptomatic disease, recognized only by incidentally biochemical abnormalities, to an acute or even fulminant hepatitis. It is important to distinguish systemic lupus erythematosus associated hepatitis from autoimmune hepatitis since complications and therapies are different in the two conditions. The co-occurrence of systemic lupus erythematosus and autoimmune hepatitis is rare, and few cases are reported in the literature so far.

The authors present a case report of a 30-year-old female patient from Angola, diagnosed for systemic lupus erythematosus in 2005 in immunosuppressive therapy for almost 10 years with methotrexate and cyclosporine. In 2014, she presents recent aggravating complaints for knee and elbow arthralgia, with morning rigidity over 2 hours, abdominal pain with episodic fever and fatigue are described. In a recent laboratory test evaluation, besides the homogeneous antinuclear antibodies pattern with rising titers, we found a citoplasmatic filamentous pattern suggestive of anti-smooth muscle antibodies found to be F-actine antibodies confirmed in VSM 47 transfected cells that with borderline liver function tests made de diagnosis of autoimune hepatitis in a patient with previous systemic lupus erythematosus.

KEYWORDS: Actins; Antibodies, Antinuclear; Hepatitis, Autoimmune; Lupus Erythematosus, Systemic

RESUMO

O lúpus eritematoso sistémico é uma doença autoimune sistémica. O envolvimento hepático não é habitual no espectro de lúpus eritematoso sistémico, mas ocorre em cerca de 60% dos doentes. A apresentação clínica da hepatite autoimune é variável, desde uma doença assintomática, reconhecida apenas por alterações dos parâmetros bioquímicos da função hepática, até manifestações de uma hepatite aguda que, em casos raros, pode ser fulminante. É importante distinguir hepatite asso-

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ciada ao lúpus de hepatite autoimune, já que a intervenção farmacológica e eventuais complicações são diferentes nas duas condições. A co-ocorrência de lúpus eritematoso sistémico e hepatite autoimune é rara, e poucos casos estão atualmente descritos na literatura.

Os autores apresentam um caso clínico de uma doente do sexo feminino com 30 anos de idade, natural e residente em Angola, com diagnóstico de lúpus eritematoso sistémico desde 2005 e sob terapêutica imunossupressora há quase 10 anos (metotrexato e ciclosporina). Em 2014 refere agravamento recente de gonalgia e artralgias do cotovelo com rigidez matinal superior a 2 horas, dor abdominal acompanhada de febre episódica e fadiga. Numa recente avaliação laboratorial, a par do padrão homogéneo dos anticorpos antinucleares, com títulos crescentes, encontrámos em simultâneo um padrão citoplasmático filamentoso sugestivo da presença em simultâneo de anticorpos anti-músculo liso. Testes confirmatórios com células transfetadas VSM 47 permitiram identificar anticorpos F-actina, que associados a elevações borderline *das transaminases, permitiram fazer o diagnóstico de hepatite autoimune numa doente com lúpus eritematoso sistémico.*

PALAVRAS-CHAVE: *Actinas; Anticorpos Antinucleares; Hepatite Autoimune; Lúpus Eritematoso Sistémico*

INTRODUCTION

Systemic lupus erythematosus (SLE) is a multisystem autoimmune disorder involving various organs such as kidneys, skin and the central nervous system. Liver involvement is normally not part of the spectrum of SLE, but is seen in up to 60% of SLE patients. Hepatotoxic drugs, coincident viral hepatitis and non-alcoholic fatty liver disease (often induced by steroids) are the most commonly described causes of elevated liver enzymes in SLE.[1,2] Liver diseases that accompany SLE disease activity generally have good prognosis and do not progress to cirrhosis.[1,2]

The clinical presentation of autoimune hepatitis (AIH) ranges from asymptomatic disease recognized only by incidentally biochemical abnormalities to an acute or even fulminant hepatitis. Female predominance and occurrence peaks in early adult life and in the 4th decade of life are characteristic. In symptomatic cases patients are often affected by non-specific symptoms such as nausea, anorexia, abdominal discomfort and jaundice. A common extrahepatic manifestation of AIH may be arthralgia, which is also often seen in SLE.[2,3]

The laboratory criteria for the diagnosis of SLE may overlap on those for AIH, as the antinuclear antibodies (ANA) positive in high titers and the hypergammaglobulinemia, but if a patient already diagnosed for SLE presents transaminase elevation and aggravating complaints from the gastrointestinal tract, it is mandatory for the rheumatologist to investigate for other autoimmune diseases.[3,4]

CASE REPORT

The authors present a case report of a 30-year-old female patient from Angola, diagnosed for SLE in 2005 in immunosuppressive therapy for almost 10 years with methotrexate and cyclosporine, with recent aggravating complaints for knee and elbow arthralgia with morning rigidity over 2 hours, abdominal pain with episodic fever and fatigue. In recent laboratory test evaluation, besides the homogeneous ANA pattern with rising titers, we found a citoplasmatic filamentous pattern suggestive of anti-smooth muscle antibodies (ASMA), found to be F-actine antibodies confirmed in VSM 47 transfected cells, with borderline liver function tests.

Investigation for infectious diseases including hepatitis A and B, tuberculosis, malaria, Dengue and Chikungunya virus, *Entamoeba histolytica* and *Rickettsia conorii* was made, without any relevant findings, excluding the infectious origin for mild hepatitis.

As the patient is becoming intolerant to growing doses of cyclosporine, and is planning a pregnancy in 2017, she is being evaluated to start rituximab.

DISCUSSION

The changing patterns on ANA obligates the laboratory investigation to be orientated towards specific markers for AIH, which usually do not occur in SLE, like soluble liver antigen (SLA), liver-pancreas, smooth-muscle antibody (SMA) with specificity for F-actin and microsomal autoantigens, such as anti-liver kidney antibodies (anti--LKM antibody).[1-4]

As the diagnosis of AIH is relevant in SLE patients with regards to choices of immunosuppressant, long term outcome and optimal surveillance of the patients, adequate attention should be taken to differentiate between "true additional" AIH or non-specific liver involvement.[2]

Elevated liver enzymes are common in SLE. Lupus-related hepatic disease must be distinguished from hepatitis caused by drugs, toxins, and viral and other autoimmune illnesses. The clinical distinction is not always an easy one.

TABLE 1. Laboratory findings.

Laboratory Findings	2013	2014	2015
Hematology			
Hemoglobin (g/dL)	9.4	9.6	9.2
WBC (10^3/mm^3)	6.9	7.7	11.2
SR (mm/h)	79	**100**	55
Liver Function			
AST (U/mL)	18	17	16
ALT (U/mL)	25	**71**	72
GGT (U/mL)	30	**21**	-
Immunology			
Gama Globulins (g/dL)	2.20	2.2	**2.8**
C3 (mg/dL)	101	**115**	109.57
C4 (mg/dL)	20.8	**24.40**	23.80
ANA (IFI)	Positive, Homogeneous 640, Pos. Mitosis and Nucleoli. Negative Citoplasmatic pattern	**Positive, Homogeneous >640, Pos. Mitosis and Nucleoli + Citoplasmatic filamentous pattern sug. ASMA**	**Positive, Homogeneous >640, Pos. Mitosis and Nucleoli + Citoplasmatic filamentous pattern**
ASMA F-actine Ab (IFI)		**Positive**	**Positive**
ds DNA-FEIA (Ui/mL)	Negative (4.91)	**Negative (2.70)**	Negative (3.0)
ENA	RNP positive	**All negative**	All negative
SLA, AMA, LKM,LC-1	-	**All negative**	All negative
Virology Markers			
Hbs Ag			Negative (<0.1)
Hbs Ab (mUi/mL)			Negative (<3.10)
Ac HV TotalAb (mUi/mL)			Positive (>100.00)
Anti Dengue Ab			Ig G pos; Ig M neg
Anti Chikungunia Ab			Ig G pos; Ig M neg
Other Infectious Markers			
IGRA			Negative
Anti ***Plasmodium falciparum*** Ab			IgG Pos (1/20)
Anti ***Entamoeba histolytica*** Ab			Ig G Neg (<1/320) Ig M Neg (<1/40)
Ant ***RicKettsia conorii*** Ab			Ig G Neg (1/40)

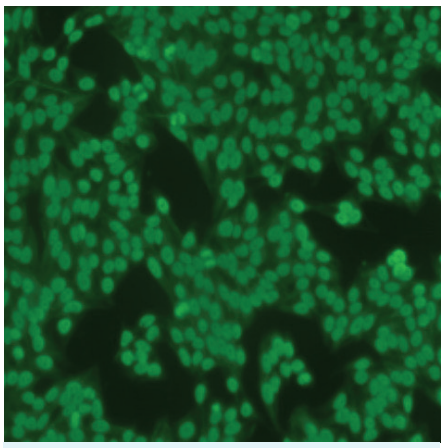

FIGURE 1. ANA Hep. 2 cells IFI: homogeneous nuclear pattern with citoplasmatic filamentous pattern suggestive of ASMA antibodies directed against the target antigen F-actin that react with the cytoskeleton of HEp-2 cells.

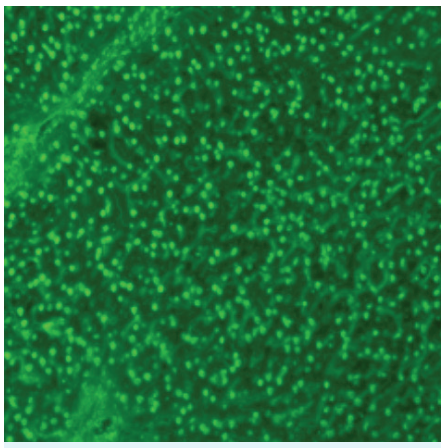

FIGURE 2. ANA liver mosaic IFI: liver hepatocytes revealing homogeneous nuclear pattern with autoantibodies against smooth muscles (ASMA) directed against the target antigen F-actin that react with bile canaliculi on primate liver.

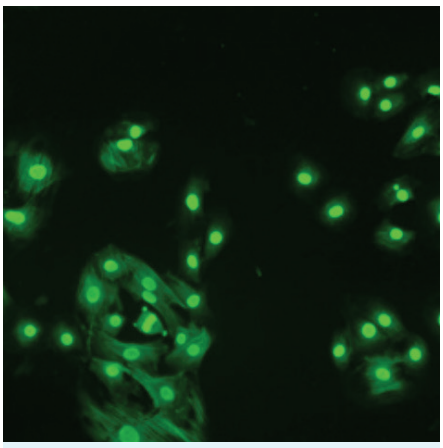

FIGURE 3. VSM 47 transfected cells on liver mosaic 9. The substrate VSM 47 reacts very specifically, showing a filamentous, needle-like fluorescence citoplasmatic filamentous pattern suggestive of F-actine.

Treatment strategies are determined by the predominant disease. The recommended treatment for both, AIH and SLE, are immunosuppressive strategies with therapeutic success. There is no data available for the prognosis of AIH with concomitant SLE but publications suggest that achievement of complete remission is crucial not only for long-term survival in these patients but also regarding quality of life.[1]

CONCLUSION

Differential diagnosis of elevated liver enzymes in patients with SLE as non-specific hepatic involvement or as AIH is demanding. Histology may be essential to distinguish AIH in SLE from non-specific hepatic involvement in SLE.

To distinguish whether the patient has primary liver disease with associated autoimmune clinical and laboratory features resembling SLE - such as AIH - or if the elevation of liver enzymes is a manifestation of SLE remains a difficult challenge for the treating physician.

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