LIVER INVOLVEMENT IN SYSTEMIC LUPUS ERYTHMATOSUS PATIENTS

Thesis

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بسم الله الرحمن الرحيم
قالوا سبحانك لا علم لنا إلا ما
علمتنا إنك أنت العليم الحكيم
سورة البقرة
آية رقم :(٣٢)

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Abstract

Background: Systemic lupus erythematosus (SLE) is a potentially severe, frequently disabling autoimmune disease with multiorgan involvement, liver is less commonly involved.

Objectives: To detect the frequency and nature of liver involvement in SLE patients and to correlate these with other organ involvement and management.

Methods: We reviewed (200) SLE patients who had admitted at Rheumatology and Rehabilitation department, Faculty of Medicine, Cairo university. All patients were subjected to laboratory investigations include (AST, ALT, HCV), abdominal ultrasound, Doppler and liver biopsy when needed.

Results: Regarding the different systems involvement liver involvement was found in 42 SLE patients **(21%)** which is the less commonly affected organ. We classified the 42 patients into 7 major groups: Autoimmune hepatitis in 6 patients **(26%)**, Cholangitis in 1 patient **(4.3%)**, portal venous thrombosis in 2 patients **(8.6%)**, Cirrhosis in 1 patient **(4.3%)**, Liver congestion in 1 patient **(4.3%)**, fatty changes in 13 patients **(56.6%)**, Viral hepatitis in the form of HCV in 6 patients **(26%)**.

We calassified the 200 SLE patients into group A (6 patients with AIH), group B (194 patients without AIH), group C (13 patients with fatty changes), group D (187 patients without fatty changes), group E (6 patients with HCV) ad group F (194 patients without HCV).

The mean age of disease onset and the mean SLICC were significantly higher in group A than group B.

Conclusion: Liver involvement in SLE is the least organ affected. No detected difference considering liver involvement among different cities all over Egypt. The younger the age group of lupus patients with AIH, the more organ damage.

Key words:

(Systemic lupus erythmatosus, liver disease)

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List of Abbreviations

ACL	anticardiolipins
ACR	American college of Rheumatology
AIH	autoimmune hepatitis
ALP	alkaline phosphatase
ALT	Alanine transaminases
ANA	Anti nuclear antibody
Anti dsDNA	Anti double stranded DNA
Anti LKM	Anti liver kidney microsomal antibodies
Anti SLA/LP	Antisoluble liver/antigen pancreas antibodies
APL	antiphospholipids
ASH	alcoholic steatohepatitis
AST	Aspartate transaminases
Blys	B.lymphocyte stimulation
BCs	Budd chiarri syndrome
C3	complement 3
C4	complement 4
CBC	complete blood count
CNS	central nervous system
COX1&2	cyclo oxygenase 1&2
D.Bil.	direct bilirubine
DILE	drug induced lupus erythmatosus
EULAR	European league against rheumatism
ERCP	endoscopy of bile duct and pancreas
ESR	erythrocytic sedemintation rate
FLD	fatty liver disease
HAT	hepatic artery thrombosis
HDL	high density lipoproteins
HLA	human leukocytic antigen
HVOD	hepatic veno-occlusive disease
HVPG	hepatic venous pressure gradient
LDL	low density lipoproteins
LAI	lupus activity index
MRCP	magnetic resonance cholangiopancreatography
Mesna	mercapto ethan esulphonic acid
MRI	magnetic resonance imaging
NASH	non alcoholic staetohepatitis

NRH	nodular regenerative hyperplasia
NSAIDS	non steroidal anti inflammatory drugs
PBC	primary billiary cirrhosis
P.ANCA	perinuclear anti neutrophillic cytoplasmic antibodies
PHT	portal hypertension
PTT	partial thromboplastine time
PSC	primary sclerosing cholangitis
RBCS	red blood cells
SELENA	safety of estrogen in lupus erythmatosus national assessment
SLE	systemic lupus erythmatosus
SLEDAI	systemic lupus erythmatosus disease activity index
SLICC	systemic lupus erythmatosus international collaborating clinic
SLAM	systemic lupus activity measurment
SRI	SLE responder index
SMA	smooth muscle antibodies
TIPS	trans jugular intrahepatic porto systemic shunting
T.Bil.	total bilirubine
TG	triglycerides
UVA	Ultraviolet A
UVB	Ultraviolet B
WBCS	White blood cells

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INTRODUCTION

Systemic lupus erythmatosus (SLE) is a potentialy severe, frequently disabling autoimmune disease with multiorgan involvement and a typically waxing and waning course **(Kamen et al, 2010).**

SLE often harms the heart, joints, lung, blood vessels, liver, kidneys, and nervous system **(Rahman et al, 2008).**

Liver involvement in SLE is not uncommon. It is frequently asymptomatic and limited to liver test abnormalities **(Kalifa et al, 2011).**

Patients with SLE have a 25 – 50% chance of developing abnormal liver tests in their life time **(Van Hoek, 1996).**

Liver diseases in SLE include:

Hepatic congestion, fatty liver, arteritis, cholestasis, peliosis hepatic (numerous small blood-filled cystic lesions throughout the liver), chronic persistent hepatitis, non specific reactive hepatitis, cholangiolitis(inflammation of the small bile capillaries), nodular regenerative hyperplasia of the liver (NRH), and hemangioma **(Matsumoto et al, 1992).**

Autoimmune liver disease (AILD) in patients with lupus SLE, include: autoimmune hepatitis (AIH), primary biliary cirrhosis (PBC), and the AIH / PBC overlape syndrome **(Efe et al, 2011).**

Nodular regenerative hyperplasia (NRH) of liver is uncommon condition, it presents primarily with manifestations of portal hypertension **(Arvanitaki et al, 2001).**

The main cause of liver involvement in SLE patients is previous treatment with hepatotoxic drugs or hepatotropic viral hepatitis **(Kim et al, 2002).**

SLE itself or treated with steroids does not seem to worsen hepatitis C virus (HCV) infection **(Perlemuter et al, 2003).**

Severe liver involvement requiring liver transplantation in SLE, but very few cases have been reported. The patient persisted without reactivation of SLE and with long-term survival **(Zazzetti et al, 2011).**

AIM OF THE WORK

To detect the frequency and nature of liver involvement in SLE patients and to correlate these with other organ affection .

SYSTEMIC LUPUS ERYTHMATOSUS

Systemic lupus erythematosus (SLE) is a multi-organ, autoimmune, inflammatory disease which means the body's immune system mistakenly attacks healthy tissue. This leads to long- term (chronic) inflammation **(Ruiz-Irastorza, 2010).**

SLE predominantly affects adults, usually women of childbearing age (20 to 40 years), at a female to male ratio of 9:1 to 15:1 **(Miah et al., 2008).**

Approximately 8% to 15% of SLE cases occur in children. Older adults diagnosed with SLE, such as postmenopausal women, usually have a milder form **(Amissah-Arthur et al., 2009).**

Genetic and racial factors are also associated with an increased risk of developing SLE. African-American women have a 3 to 4 times higher prevalence of SLE than Caucasian women **(Bae et al., 1998).**

Afro-Caribbean, Asian, Native American, and Hispanic descent have a higher incidence of SLE compared to Caucasian individuals **(Jim Nez et al., 2003).**

This differs from drug-induced lupus erythematosus (DILE), which occurs at similar rates in men and women but with a higher incidence and severity in Caucasian compared to African-American patients **(Marzano et al, 2008)**.

Pathophysiology/Etiology

The development of SLE is a complex immune process that is brought about by dysregulation of B- and T-lymphocytes, the production of auto-antibodies, and the formation of immune complexes **(Suh chet et al., 2008).**

Cytokines are thought to play a key role in SLE; however, the extent to which they affect progression of lupus is not clear. Their involvement may help explain the variations seen in the clinical manifestations of patients **(Bongu et al., 2003).**

While it is known that the immune system plays a role in the development of the disease, what causes the immune system to function abnormally is unknown **(Reidenberg et al., 1998).**

It is speculated that environmental factors play a role, but the data have not consistently supported this theory **(Petri et al., 1992).**

There is, however, evidence to suggest that genetic components play a role **(Bongu et al., 2003).**

Several immunologic gene abnormalities (eg, interferon regulatory factor 5, protein tyrosine phosphatase nonreceptor type 22, and integrin alpha M) have been identified **(Jim Nez et al., 2003).**

Additionally, research in homozygous twins has shown a higher incidence of SLE in families where the prevalence of the disease in other family members was low **(Hess et al., 1995).**