Clinical and immunological features of Systemic Lupus Erythematosus complicated by Hepatitis "C" virus infection

Thesis

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بسم الله الرحمن الرحيم

قالوا سبحانك لا علم لنا الا ما علمتنا انك انت العليم الحكيم

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List of Abbreviations

- **ACL** : Anti cardiolipin antibody
- **ACR** : American Collage of Rheumatology
- **AECA** : Anti-Endothelial-cell antibodies
- **AH** : Autoimmune hepatitis
- **ALP** : Alkaline phosphatase
- **ALT** : Alanine Transaminase.
- **ANA** : Anti-nuclear antibodies.
- **Anti-**Sm : Anti-Smith antibody
- **AST** : Aspartate Transaminase.
- **AZA** : Azathioprine.
- **BAFF** : B cell activating factor of the tumor necrosis factor family
- **B cells** : B lymphocytes
- **BCP** : B cell receptor
- **C** : Complement component
- **CAC** : coronary artery calcification
- **CBC** : Complete blood count.
- **CCP** : Cyclic citrullinated peptide.
- **Cg** : Cryoglobulinemia.
- **CHC** : Chronic hepatitis C.
- CLE : Chronic cutaneous Lupus Erythematosus
- **CLU** : Carolina Lupus Study
- **CRP** : C-reactive protein.
- **Cryo +ve** : Cryoglobulin +ve.
- **Cryo -ve** : Cryoglobulin –ve.
- **Dcs** : dendritic cells
- **DILE** : Drug - induced Lupus Erythematosus
- **DM** : Dermatomyositis
- **DNA** : Deoxy ribonucleic acid
- **ds-DNA** : Double stranded- Deoxy ribonucleic acid
- **EBVNA** : Epstein-Barr virus nuclear antigens

- **ELISA** : Enzyme linked immunosorbant assay.
- **EMC** : Essential mixed cryoglobulinemia
- **ESR** : Erythrocyte sedimentation rate.
- **FS** : Fibromyalgia syndrome
- **GI** : Gastrointestinal.
- **Hb** : Hemoglobin.
- **HBV** : Hepatitis B virus.
- **HCC** : Hepatocellular carcinoma.
- **HCV** : Hepatitis C virus.
- **HIV** : Human immunodeficiency virus.
- **HLA** : Human Leucocytic Antigen
- **IFN** : Interferon.
- **Ig G** : Immunoglobulin G.
- **Ig M** : Immunoglobulin M.
- **IL** : Interleukin.
- **ISN** : International Society of Nephrology
- **LE cells** : Lupus erythematosis cells
- **LKM1** : Liver kidney microsomal 1.
- **LN** : lupus nephritis
- **LP** : Lichen planus.
- **MHC** : Major Histocompitapility Complex
- **MC** : Mixed cryoglobulinemia.
- **MN** : Membranous nephropathy.
- **MPGN** : Membranoproliferative glomerulonephritis.
- **MZ** : Marginal zone
- **NHL** : Non Hodgkin lymphoma.
- **NK cells** : natural killer cells
- **NSAIDs** : Non steroidal anti-inflammatory drugs.
- **PAN** : polyarteritis nodosa.
- **PCR** : Polymerase chain reaction.
- **PCT** : Porphyria cutanea tarda.
- **PLT** : Platelets.
- **PM** : Polymyositis

- **PT** : prothrombine time.
- **RA** : Rheumatoid arthritis.
- **RF** : Rheumatoid factor.
- **RPS** : Renal Pathology Society
- **S** : Significance.
- **S. albumin** : Serum albumin.
- **SCLE** : Subacute Cutaneous Lupus Erythematosus
- **SD** : Standard deviation.
- **SLE** : Systemic lupus erythematosus.
- **SnRNP** : Small nuclear ribonucleoprotein
- **SS** : Sjogren's syndrome.
- **T cells** : T lymphocytes
- **Th** : T helper cells.
- **TLC** : Total leucocytic count.
- **TNF** : Tumour necrosing factor.
- **WHO** : World Health Organization
- **WBC** : White blood corpuscles.

Introduction and Aim of the work

Systemic lupus Erythematosus (SLE) is a chronic, inflammatory disease that can affect every organ system of the body. SLE is a protean in its manifestations and follows a relapsing and remitting course. ***(Bartels et al., 2006).***

SLE is an autoimmune disorder that involves multi-system microvascular inflammation with the generation of auto antibodies. Although the specific cause of SLE is unknown, multiple factors are associated with the development of this disease. These include genetic, racial, hormonal and environmental factors. Many immune disturbances, both innate and acquired, occur in SLE. ***(Hahn et al., 2005).***

Hepatitis C virus (HCV) is a spherical, enveloped, single stranded RNA virus belonging to the flaviviridae family and flavivirus genus. It has extensive genomic variability resulting in six major genotypes and numerous subtypes. ***(Mukherjee and Dhawan, 2006).***

The prevalence of HCV infection varies throughout the world. Egypt has the highest number of reported infections, largely attributed to the use of contaminated parenteral antischistosomal therapy. This has led to a mean prevalence of HCV antibodies in Egyptian population of 22%. ***(Frank et al., 2000)***.

Viruses might be one of the elements that trigger SLE. Steroid therapy may influence the natural history of virus infections. The most

frequent extra hepatic manifestations of HCV include arthralgia, myalgia, sicca syndrome and antinuclear antibodies ***(Perlemuter et al., 2003).***

Hepatitis C virus (HCV) infection is associated with various auto immune disorders and can mimic Systemic Lupus Erythematosus (SLE) clinically and serologically ***(Ahmed et al., 2006)***

Aim of work

The aim of this work is to study the prevalence of hepatitis C virus infection in patients with Systemic Lupus Erythematosus, also to study the clinical and immunological features of SLE patients complicated by HCV.

Systemic Lupus Erythematosus

Definition:

Systemic Lupus Erythematosus is an inflammatory connective tissue disease with variable manifestations. SLE may affect many systems with immune complexes and a large array of auto antibodies, particularly anti nuclear anti bodies (ANA_s). ***(Greenspun, 2005).***

Epidemiology:

The Prevalence of SLE in USA is approximately 50 cases per 100.000 populations. Worldwide, the prevalence of SLE is variable, from 12 cases per 100.000 populations in Britain to 39 cases per 100.000 populations in Sweden. Although African Americans have high prevalence of this disease, SLE is rare among blacks who live in Africa. ***(Bartels et al., 2006).***

SLE is more prevalent in women in their reproductive period, published ratios of women to men vary from 9: 1 to 15: 1, with a higher incidence among African-American than whites and has a mean age at diagnosis of 30 to 39 years. ***(Tamir and Brenner, 2003).*** Among children, SLE occurs three times more commonly in the females than males. ***(Lahita, 1997).***

Cause and pathology:

Systemic Lupus Erythematosus (SLE) is an autoimmune disorder that affects multiple organ systems. The cause of the disease is unclear. ***(Dall'Era et al., 2003).***

The hallmark of the disease is production of antibodies to the cell nucleus. These antibodies are referred to as antinuclear antibodies (ANA) and are seen in 95% of patients with SLE. ***(Criscione and Pisetsky, 2004).***

ANA are not unique to SLE and can occur in other autoimmune disorders, such as rheumatoid arthritis, scleroderma, mixed connective tissue disease, and poly myositis; ANA also occur in up to 5% of the normal population. Some patients with SLE may not have a positive ANA titer***. (Criscione and Pisetsky, 2004).***

ANA bind to several different molecules in the nucleus, including DNA, RNA, histones, and small nuclear ribonucleoproteins. Antibodies to double-stranded DNA (anti-ds-DNA) and to the Sm nuclear antigen (anti-Sm) are found only in patients with SLE. ***(Klipple et al., 2001).***

The pathogenic findings related to SLE are mainly related to inflammation and blood vessel abnormalities, including bland vasculopathy, vasculitis, and immune-complex deposition. ***(Klipple et al., 2001).***

The pathologic findings of SLE-related nephritis are best understood

and involve immune complex deposition in the glomerulus with anti-ds-DNA playing a key role, which leads to the activation of the complement system. ***(Criscione et al., 2004).***

Skin lesions demonstrate inflammation at the dermal-epidermal junction that is likely due to immune complex deposition and activation of the complement pathway. ***(Klipple et al., 2001).***

Autoantibodies may play a role in cytopenias that are often seen SLE patients. Venous and arterial thrombosis is related to occlusive vasculopathy, which is related to general inflammation, and inflammation in association with antiphospholipid and anticardiolipin antibodies and lupus anticoagulant. ***(Taylor and Gill, 2005).***

Systemic Lupus Erythematosus is a multifactorial disease in which the relative contribution of each factor increases the relative risk of disease susceptibility. Significant factors arise from genetic components, together with environmental elements. Genetic predisposition may be so strong that relatively minor environmental insult may be sufficient to trigger a disease. ***(Theo Filopoulos and Kono, 2002).***

I- Genetic predisposition:

Susceptibility to SLE depends on multiple genes. Susceptibility genes are defined as genes that increase the relative risk for a disease, even though most individuals with that gene are healthy. The number of