LIVER AND RHEUMATIC DISEASES

Essay

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List of Abbreviations

γGT ..... Gamma glutamyl transferase

aCL ..... Anticardiolipin antibodies

ACR ..... American College of Rheumatology

AIH ..... Autoimmune hepatitis

ALP..... Alkaline phosphatase

ANA ..... Antinuclear antibody

aPL..... Antiphospholipid antibodies

AZA ..... Azathioprine

CYP ..... Cyclophosphamide

CSA..... Cyclosporine

CXR ..... Chest radiograph

DEXA ..... Dual-energy x-ray absorptiometry

DMARDS .. Disease modifying antirheumatic drugs

EHM ..... Extrahepatic manifestations

ENA ..... Extractable nuclear antigen

FBC..... Full blood count

HBV ..... Hepatitis B virus

HCC..... Hepatocellular carcinoma

HCV..... Hepatitis C virus

HIV..... Human immunodeficiency virus

HPS..... Hemophagocytic syndrome

IFN..... Interferon

LEF..... Leflunomide

LFT..... Liver function test

MTX ..... Methotrexate

NRH..... Nodular regenerative hyperplasia

NSAID ..... Non steroidal anti-inflammatory drugs

P3NP..... Procollagen III amino terminal peptide

PAN ..... Polyarteritis nodosa

PBC..... Primary biliary cirrhosis

RA..... Rheumatoid arthritis

RF ..... Rheumatoid factor

SLE ..... Systemic lupus erythematosus

SS ..... Sjögern's syndrome

SSc ..... Systemic sclerosis

TCZ ..... Tocilizumab

TNFa..... Tumor necrosis factor

WBC ..... White blood cell count

Introduction

The liver is the largest gland in the body weighing 1500 gm with many complex functions. These functions of the liver allow the body maintenance of homeostasis. A wide variety of rheumatic diseases affect the liver and their prevalence, significance and specific hepatic pathology varies with each disease ***(Abraham et al., 2004).*** Also rheumatic features are common in liver diseases ***(Albert et al., 2007)***.

Rheumatoid arthritis causes extra articular manifestations which are rare and exceptionally serious in the liver. The most important hepatic disorders associated with rheumatoid arthritis are intrahepatic portal hypertension without cirrhosis, amyloidosis and drug hepato-toxicity ***(Diouf et al., 2001).***

Nodular Regenerative hyperplasia (NRH) is made of diffuse nodules of hepatocytes without fibrosis and it is closely associated with felty's syndrome ***(Diouf et al., 2001).***

Although symptomatic liver involvement is rare in Sjögren's Syndrome (SS), asympotomatic liver involvement is common in the form of primary biliary cirrhosis (PBC), autoimmune hepatitis (AIH), hepatitis C virus (HCV) infection and fatty liver. Clinicians must be aware of the possibility of liver involvement so that it can be treated as soon as possible ***(Aoki et al., 2004).***

Systemic lupus erythematosus (SLE) is an immune mediated systemic disease associated with diverse abnormalities of the skin, kidneys, hematological and muscloskeletal systems. Abnormalities of the liver function are not included in the diagnostic criteria of SLE, and the liver is generally not regarded as a major target organ for damage in patients with SLE ***(Lu et al., 2006).*** However hepatic disease may be more common in systemic lupus erythematosus (SLE) than is usually thought ***(Abraham et al., 2004).***

There is no characteristic histological feature present in the liver of patients with SLE. A variety of histological lesions have been observed on liver biobsy in patients with SLE including cholestasis with prominent bile plugs, steatosis, acute or chronic hepatitis and cirrhosis. A form of cholestasis described as canalicular cast of bile was reported to be peculiar to SLE patients with liver disease ***(Chow et al., 1997).***

As regard extrahepatic manifestations of liver diseases there are many rheumatological manifestations associated with chronic hepatits C virus (HCV) infection including arthralagia, myalgia, arthritis, vasculitis and sicca syndrome. The picture may mimic rheumatoid arthritis (RA), particularly as rheumatoid factor is present in 50- 80 % of cases, also sicca syndrome is common in patients with chronic HCV infection and shares similarities with primary sjögren syndrome ***(Lormeau et al., 2006)***.

Pimary biliary cirrhosis (PBC) is often associated with other non - hepatic autoimmune diseases, especially primary sjögren's syndrome, which may favour articular involvement. PBC and rheumatoid arthritis (RA) have been suggested to coexist in 1.8 to 5.6% of patients with PBC ***(Caramella et al., 2007)***.

Autoimmune hepatitis has clinical manifestations, serological markers, pathogenic mechanisms, genetic predispositions and therapies similar to the rheumatic diseases. The rheumatic manifestations may mask the underlying liver disease and vice versa ***(Czaja, 2007)*.**

Aim of the Work

The aim of this work is to review recent studies that clarify the hepatic involvement in rheumatic diseases as well as the rheumatic manifestations of hepatic diseases.

Hepatic Manifestations in Rheumatic Diseases

Liver Structure and Function

The liver is the largest organ of the body, weighing 1 to 1.5 kg and representing 1.5 to 2.5% of the lean body mass. The size and shape of the liver vary and generally match the general body shape, long and lean or squat and square. The liver is located in the right upper quadrant of the abdomen under the right lower rib cage against the diaphragm and projects for a variable extent into the left upper quadrant ***(Ghany and Hoofnagle, 2005)***.

The liver is held in place by ligamentous attachments to the diaphragm, peritoneum, great vessels and upper gastrointestinal organs. It receives a dual blood supply; approximately 20% of the blood flow is oxygen-rich blood from the hepatic artery and 80% is nutrient-rich blood from the portal vein arising from the stomach, intestines, pancreas and spleen ***(Ghany and Hoofnagle, 2005)***.

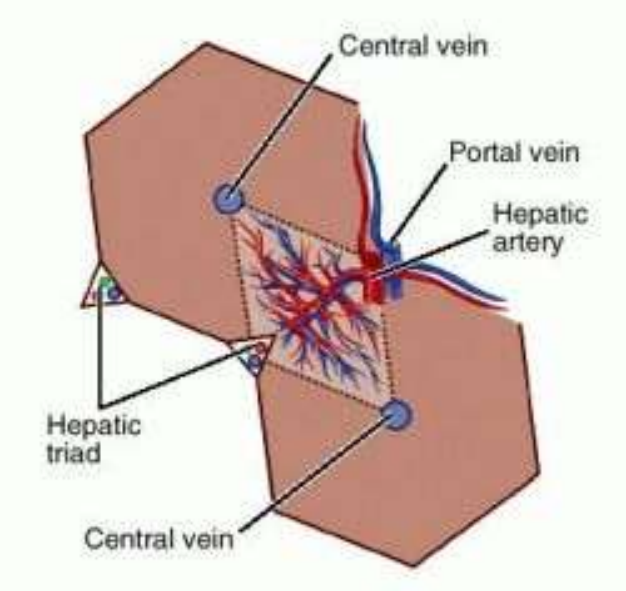

Figure (1): Liver acinus: hepatic lobules are represented by hexagons (solid lines); liver acinus is represented by rhombus (dotted line).

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The majority of cells in the liver are hepatocytes, which constitute two third of the mass of the liver. The remaining cell types are Kupffer cells (members of the reticuloendothelial system), stellate (Ito or fat-storing) cells, endothelial cells and blood vessels, bile ductular cells and supporting structures. Viewed by light microscopy, the liver appears to be organized in lobules, with portal areas at the periphery and central veins in the center of each lobule. However, from a functional point of view, the liver is organized into acini, with both hepatic arterial and portal venous blood entering the acinus from the portal areas (zone 1) and then flowing through the sinusoids to the terminal of hepatic veins (zone 3); the intervening hepatocytes