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INTERSTITIAL PULMONARY DISEASE IN HEPATITIS C VIRUS PATIENTS

Thesis
Submitted for Partial Fulfillment of the M. Sc. Degree
In Chest Diseases

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Abstract

Chronic hepatitis C virus infection has been reported in association with several extrahepatic manifestations. Included in this list is interstitial lung involvement. This study aimed to elucidate the association of HCV infection with interstitial pulmonary involvement and to investigate the relationship of severity of hepatic affection and respiratory functional and radiological changes among involvement. Thirty patients with proved hepatitis C virus (HCV) infection from the outpatient clinic of tropical department of Kasr El-Aini hospital were enrolled in this study. High resolution CT (HRCT) chest was performed to all the patients. Pulmonary changes were detected in HRCT of 14 patients (46.6%). Lung spirometry was done to all of them. FVC%, and FEV1% were abnormal in 6 patients (20%), FEF25-75% were abnormal in 3 patients (10%).

Key Words:

- Interstitial Lung Disease
- Hepatitis C virus
- Pulmonary Manifestations of HCV

List of Abbreviations

ACE	Angiotensin-converting enzyme
AFP	Alpha feto protein
AIP	Acute interstitial pneumonia
ALT	Alanine aminotransferase
ANA	Anti-nuclear antibodies
APRI	AST-to-Platelet Ratio Index
ARDS	Adult respiratory distress syndrome
AST	Aspartate aminotransferase
BOOP	Bronchiolitis obliterans organizing pneumonia
CD8+	Clusters of differentiation (T-suppressor cells)
CDC	Centers for Disease Control and Prevention
CHF	Congestive heart failure
CMV	Cytomegalo virus
COPD	Chronic obstructive pulmonary disease
CT	Computed tomography
CVD	Collagen vascular diseases
DIP	Desquamative interstitial pneumonia
DPLD	Diffuse parenchymal lung diseases
EBV	Epstian Bar virus
ECG	Electrocardiogram
EG	Eosinophilic granuloma
EIA	Enzyme Immunoassay
ELF	European Liver Fibrosis
ELISA	Enzyme linked immunosorbant assay
EMC	Essential mixed cryoglobulinemia
EP	Eosinophilic pneumonia
Gamma-GT	Gamma-glutamyltranspeptidase
HCC	Hepatocellular carcinoma

HCV	Hepatitis C virus
HIV	Human immunodeficiency virus
HPS	Hepatopulmonary syndrome
HRCT	High-resolution computed tomography
HSP	Hypersensitivity pneumonitis
IFN	Interferon
IIPs	Idiopathic interstitial pneumonia
IL-8	Interluekin-8
ILD	Interstitial lung diseases
IPF	Idiopathic pulmonary fibrosis
IVDUs	Intravenous drug users
KHAI	Knodel histological activity index
LAM	Lymphangioleiomyomatosis
LDH	Lactate dehydrogenase
M2	Muscarinic receptors No. 2
MC	Mixed cryoglobulins
MN	Membranous nephropathy
MPGN	Membranoproliferative glomerulonephritis
NAD	No abnormality detected
NAFLD	Non alcoholic fatty liver disease
NASBA	Nucleic acid amplification system
NIH	National Institutes of Health
NSIP	Nonspecific interstitial pneumonia
PAP	Pulmonary Artery Pressure
PAT	Parenteral antischistosomal therapy
PBMC	Peripheral blood mononuclear cells
PCP	Pneumocystis carinii pneumonia
PCR	Polymerase chain reaction
PCT	Porphyria cutanea tarda
PEG	Pulmonary eosinophilic granuloma

PFT	Pulmonary function test
PPHTN	Portopulmonary Hypertension
RA	Rheumatoid arthritis
RB-ILD	Respiratory bronchiolitis-associated ILD
RIBA	Recombinant Immunoblot Assay
RNA	Ribonucleic acid
STPD	Standard temperature and pressure
SVR	Sustained virological response
Tc-labeled	Technetium
UIP	Usual interstitial pneumonia

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INTRODUCTION

Hepatitis C virus (HCV) is a common infectious agent, and it is estimated that 3% of the world population are infected with HCV. It was reported that HCV caused 20% of acute hepatitis and 70% of chronic hepatitis **(Hoofnagle, 1997)**. HCV could be stimulated chronically by immune system **(Pawlotsky et al., 1995)**.

HCV being both a hepato and lymphotropic virus can represent a chronic stimulus for the immune system **(Zignego et al., 1995)**.

In the general population of HCV positive patients the appearance of various organ involvement can be related to different immunological factors namely various autoantibodies and immune complex production secondary to B lymphocyte expansion **(Ferri et al**., **1991)**.

Since HCV is well known to induce chronic inflammation and fibrosis in the liver, it was thought that HCV may play a similar role in the lung and be involved in the pathogenesis of pulmonary fibrosis **(Moorman et al., 2005)**.

An association between HCV infection and IPF was initially supported by seroepidemiological data, which revealed a higher prevalence of anti-HCV antibodies in patients with IPF **(Ueda et al., 1992)**.

Although idiopathic pulmonary fibrosis is considered to be idiopathic, inhaled substances are suggested to be responsible for the manifestation of this clinical presentation **(Hubbard et al., 1996)**. Onset of symptoms following a viral infection or common cold in some patients suggests that development of the disease may be due to the injury related to the infection. There is evidence that hepatitis C virus, Epstein-Barr virus (EBV), and adenoviruses may be responsible for the fibrosis **(Kuwano et al., 1997)**.

AIM OF THE WORK

The aim of this study is to elucidate the association of HCV infection with interstitial pulmonary involvement and to investigate the relationship of severity of hepatic affection and respiratory functional and radiological changes among involvement.

Interstitial Lung Disease

Introduction:

Many acute and chronic lung disorders with variable degrees of pulmonary inflammation and fibrosis are collectively referred to as interstitial lung diseases (ILDs) or diffuse parenchymal lung diseases (DPLD) **(McAnulty and Laurent, 1995)**.

The term diffuse (interstitial) lung disease embraces a large number of disorders characterised by distinct cellular and extracellular infiltrates in the acinar regions of the lung (that is, distal to the terminal bronchiole). Some of these diseases present acutely whereas others have a subacute or chronic course: the infiltrate may result in tissue injury, as in cryptogenic fibrosing alveolitis, or cause little damage to the lung architecture, as in pulmonary eosinophilia **(Du Bois, 1994)**.

By the beginning of the 20th century, the gross and microscopic pathology of chronic ILD was well described. The focus turned to identifying occupational or environmental causes of ILD. Efforts from around 1950 to 1970 were aimed at understanding the radiographie, physiologic, and pathologic features of these diseases. By the 1960s, progress in categorizing ILDs was made: connective tissue diseases, drugs, occupational and environmental exposures, sarcoidosis, and inherited conditions were recognized as distinct entities. Those conditions that either remained unassociated