Original Article

Association of Progression of Pulmonary Fibrosis with Severity of Liver Cirrhosis

Muhammad Masood, Shahid Hamid, Sajid Nisar, Fawad Ahmed Randhawa, Ambreen Butt and Faisal Masud

Background: It has been found that frequency of pulmonary fibrosis increases in patients with cirrhosis of liver. We hypothesized that as the stage of cirrhosis advances, the frequency of pulmonary fibrosis should increase. We used child's pugh classification to stage the cirrhosis of liver.

Material & Methods: Fifty five patients of age range 16 to 80 years, both males and females having established cirrhosis of liver on ultrasonography, regardless of etiology, visiting the outpatient and inpatient department for treatment were selected. Patients were divided into three groups according to child's criteria i.e group A, group B, and group C. HRCT of chest was performed on patients in all three groups to look for pulmonary fibrosis.

Results: 27 (49%) patients were found to have pulmonary fibrosis on HRCT. The frequency of pulmonary fibrosis in different groups of child's classification was also assessed and it was found that class C and class B, are affected more than A.

Conclusion: Pulmonary fibrosis progresses with severity of liver cirrhosis

Keywords: Cirrhosis, Child's classification, pulmonary fibrosis

Introduction

Liver cirrhosis is a worldwide health problem. Alcoholism and viral hepatitis are the most common causes worldwide, whereas viral hepatitis and especially hepatitis C is the most common cause of cirrhosis in Pakistan.[1]

Liver cirrhosis is characterized by liver injury followed by regeneration and fibrosis. Liver fibrosis is the wound healing response of liver to repeated injuries. After injury, parenchymal cells regenerate and fibrosis occurs due to interaction between different cell types and cytokines. Profibrotic agents include type-2 CD4 positive lymphocytes, CD40 receptor and ligand interaction and cytokines like IL 4, TGF beta, platelet derived growth factor.[2,3,4]

Pulmonary complications are frequently observed in liver cirrhosis.[5] As the blood from the liver passes to the lungs, lungs are exposed to similar profibrotic agents as the liver, in patients with cirrhotic liver disease. So pulmonary fibrosis is the likely outcome. We in another study conducted earlier, documented the increased frequency of pulmonary fibrosis in patients with liver cirrhosis.[6] Similarly other studies have shown relationship between liver cirrhosis and interstitial lung disease.[7,8] As the liver cirrhosis progresses and increases in severity, lungs are more and more exposed to profibrotic agents and severity of pulmonary fibrosis is likely to increase. So it was hypothesized that as the stage of cirrhosis of liver advances, the frequency of pulmonary fibrosis should increase. We used the child pugh turcotte (CPT) classification to stage the cirrhosis of liver.

Objective

The study was conducted to find out the association of progression of pulmonary fibrosis with severity of cirrhosis according to child's classification.

Material and Methods

This study was conducted at Medical Unit-IV of Services Hospital, Lahore. Total study period was 06 months, starting from November 2003 till April 2004 & total 55 patients were recruited.

Inclusion Criteria

Patients between 16 to 80 years of age presenting to medical outpatient department or admitted to Medical Unit-IV having established cirrhosis of liver on the basis of ultrasonography regardless of etiology were included in study.

Exclusion Criteria

1. Patients with pulmonary tuberculosis
2. Patients with history suggestive of chronic obstructive air way disease

3. Patients with primary lung tumor or lung metastasis
4. Patients with sarcoidosis.
5. Patients with history suggestive of autoimmune disorders
6. Patients with history of exposure to asbestos
7. Patients on interferon or chemotherapy

Material and Methods

Patients were recruited according to inclusion criteria and informed consent was taken. Patients were assessed clinically for jaundice, ascites, grade of hepatic encephalopathy and laboratory tests were performed for serum bilirubin, serum albumin and prothrombin time to define the child's class. Patients were then subdivided into three groups i.e. A, B and C according to child's criteria. Child's class was assigned to each patient based on two clinical and three laboratory criteria as defined in (CTP) classification. HRCT was done on each patient to look for the pulmonary fibrosis. Each HRCT was reported by the same radiologist.

Results

This study included 55 patients. Age range of patients was between 16 to 80 years. Patients of both sexes were included in the study. Out of 55 patients 30 (55%) were males and 25 (45%) were females.

HRCT scan of the lungs was performed on all 55 patients. 27 patients (49%) showed evidence of pulmonary fibrosis on HRCT **(Table 1)**.

Table-1: Pulmonary fibrosis in cirrhosis on HRCT

Tests	Number	Percentage
Present	27	49.0%
Absent	28	51.0%

Fifteen of these 27 patients with pulmonary fibrosis were male while 12 were females **(Table 2).**

Table-2: Sex distribution of pulmonary fibrosis in cirrhosis

Sex	Number	Percentage
Male	15	55.0%
Female	12	45.0%

Out of 27 patients with pulmonary fibrosis 6 patients were from child group A, 10 from child group B and 11 from child group C **(Table 3)**.

Table-3: Child group distribution of pulmonary fibrosis in cirrhosis

Child's group	Total No.	Pulm. Fibrosis	Percentage
Group A	20	06	30.0%
Group B	16	10	62.0%
Group C	19	11	58.0%

Discussion

Viral hepatitis is major cause of cirrhosis in Pakistan. Prevalence of hepatitis C is more than hepatitis B.[9] In western world, alcoholic liver disease accounts for 60-70% cases of cirrhosis. Other causes of cirrhosis include cryptogenic cirrhosis (10-15%), biliary disease (5-10%), genetic haemochromatosis (5%), Wilson's disease and alpha-1 anti trypsin deficiency.[1]

In cirrhosis there is increased hepatic deposition of collagen (type I & type II). It is now recognized that hepatic stellate cells, portal fibroblasts and myo-fibroblasts of bone marrow origin are primarily responsible for this collagen deposition and hepatic fibrosis and subsequent progression to cirrhosis.[1,2,3] These cells are activated by fibrogenic cytokines such as transforming growth factor beta (TGF-B), angiotensin II and leptin, as well as proliferative cytokines like platelet derived growth factor and cytokines produced by chronic inflammation like tumor necrosis factor (TNF) alpha, TNF beta and interleukin-1 (IL-1).[4,5,6]

The frequency of interstitial lung disease in chronic liver disease of different etiologies varies between 13-60%. The present study shows pulmonary fibrosis in 49% of the patients with cirrhosis as compared to 3% frequency of pulmonary fibrosis in general (western population). Idiopathic pulmonary fibrosis has been associated with cirrhosis due to hepatitis C virus and various studies have shown high prevalence of anti HCV antibodies (28.8% and 13%).[9,10] However these studies have not established any cause and effect relationship between pulmonary fibrosis and cirrhosis of liver. Interstitial lung disease appears medially 4.5 ± 3.2 years after clinical onset of chronic hepatitis and abnormalities in pulmonary function have been reported in association with chronic liver disease of varied etiology.[11] In the present study we looked for progression of pulmonary fibrosis with severity of cirrhosis according to child's class. It is found that frequency of pulmonary fibrosis is more in child class B & C than in Class A.

Reversibility of advanced liver fibrosis has been recently documented. This has stimulated the

researchers to develop new anti-fibrotic drugs. So treatment of cirrhosis with anti-fibrotic agents will probably reduce the severity of fibrosis in the lungs and treatment of Hepatitis C with interferon at an early stage of chronic liver disease will possibly prevent the pulmonary fibrosis. Further studies are required to establish the cause and effect relationship between cirrhosis and pulmonary fibrosis and to establish the relation of severity of pulmonary fibrosis with severity of cirrhosis, duration of cirrhosis or both.

Conclusion

The study has shown strong association between cirrhosis of liver and pulmonary fibrosis but it does not show clear cause and effect relationship and also does not show definite relation between severity of cirrhosis of liver and frequency of pulmonary fibrosis. For this further research work is needed.

Department of Medicine
SIMS/Services Hospital, Lahore
theesculapio@hotmail.com
www.sims.edu.pk/esculapio.html

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