Search for Aetiological Factors of Non-Cirrhotic Portal Fibrosis

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Abstract
A study of gut ecology was undertaken on 16 patients with non-cirrhotic portal fibrosis (NCPF), 18 patients of cirrhosis and 6 patients of extra-hepatic portal obstruction (EH0). Bacteriological and fungal examination of jejunal and ileal aspirates, stool or small intestinal fluid examination for parasitic infections revealed no significant differences between NCPF, EHO and cirrhotic patients. Non-specific changes in the jejunal mucosa were noticed in 7 out of 8 NCPF and 6 out of 10 cirrhotic patients. Jejunal biopsy showed non-specific changes of uncertain significance in 3 out of 9 NCPF, 4 out of 12 cirrhotics and 4 out of 5 cases of EHO. Our results therefore do not implicate bacterial flora, fungi or gut morphology changes in the pathogenesis of NCPF.

Key words: Non-cirrhotic portal fibrosis—autoimmune gastritis; Cirrhosis; Extrahepatic obstruction.

Introduction
Non-cirrhotic portal fibrosis (NCPF) is an important cause of intractable obstruction in our country1,2, but its aetiological and pathogenic mechanisms are obscure.3 It has been postulated that some exogenous factors absorbed from the gut enter the portal circulation to produce these changes.1 These factors may include hepatic toxins, microbial or parasitic agents and/or their products, chemical agents e.g. arsenic,4 etc. We studied gut ecology and biopsy materials from small and large bowel in patients suffering from NCPF, cirrhosis of liver and extrahepatic portal obstruction (EHO) to detect any specific causative factor in the production of NCPF.

Materials and Methods
Forty patients (16 NCPF, 18 cirrhosis, 6 EHO) having moderate to gross splenomegaly and proved portal hypertension with or without history of hematemesis and melena were studied. Patients having definite cause for splenomegaly e.g. haemoglobinopathy, kala azar etc. were excluded. The diagnosis of portal hypertension was confirmed by splenportal venography and recording intrasplenic pressure. Routine liver function tests including 45 minutes BSP retention test, and liver biopsy (needle biopsy in all and wedge biopsy in the majority of cases) were done. The biopsy diagnosis of NCPF or cirrhosis was based on the criteria outlined earlier.5 The aetiopathological diagnosis of portal hypertension was based on clinical, histological, biochemical and splenoportographic criteria as outlined in the workshop on NCPF.6 Stool examination was done by conventional method in each case. None of the patients had been treated with any antibiotics in the recent past. Intra-gastric instillation with a sterile radio-opaque polyvinyl double lumen tube was done under fluoroscopic control. Intestinal contents were aspirated from jejunum and ileum and cultured in appropriate media in serial dilutions to ascertain bacterial and fungal flora quantitatively and qualitatively.6 Samples of jejunal and ileal fluid were also examined under the microscope for parasites. Multiple jejunal biopsies were done in 22 cases of portal hypertension using Quinton’s hydraulic machine. The tissues obtained were processed and stained with haematoxylin and eosin and PAS. Sigmoidoscopic biopsy specimens of 6 cases were also similarly studied.

Results
Patients studied were aged between 10 to 50 years. Mean age of patients of NCPF, cirrhosis and EHO were 33, 32 and 26 years respectively. Males predominated in all groups (12 NCPF, 12 cirrhosis and 5 EHO). History of gastrointestinal bleeding was obtained in 7 patients of NCPF, 11 cirrhotics and 5 EHO. The coliform counts of jejunal and ileal aspirates of NCPF, cirrhosis and EHO patients and control subjects (Figure) revealed no differences between the groups (Wilcoxon signed rank test; P>0.05 for all) but patients with cirrhosis or NCPF had significantly higher count than simultaneously studied control subjects (P<0.05). Coliform counts of ileal fluid were similar in three groups. Parasitic infection in the jejunal or ileal aspirates or in the stool samples was found in 10/16 (62.5%) with NCPF, 8/18 (44.4%) cirrhotic patients and 2/6 (33.3%) EHO patients. No significant differences were observed by x² testing (P>0.05 for all). The number of cases with parasitic infection in NCPF, cirrhosis and EHO groups respectively were: E. histolytica—2, 0, 0; G. lamblia—1, 1, 0; round worms—4, 0, 2; hook worms—2, 3, 0; Strongyloides—0, 4, 0 and mixed infections—1, 0, 0. Abnormal fungi (Table) could be isolated in 3/16 with NCPF, 3/18 with cirrhosis and none of the EHO cases. These were not statistically significant. Jejunal biopsy was done in 8 NCPF, 10 cirrhotic and 4 EHO patients. Normal or mild changes7 were found in all the EHO, 4 cirrhotic and one NCPF

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patients. Moderate changes were noticed in 7 NCPF (87%) and 6 cirrhosis (60%). Non-specific changes in the colonic mucosa such as moderate excess of lymphocytes, plasma cells, few eosinophils and macrophages were found in 3/9 (33.3%) NCPF, 4/12 (33.3%) cirrhosis and 4/5 (80%) EHO patients \( (P > 0.05) \).

**Discussion**

Bacteriological examination of jejunal aspirate revealed no significant difference in coliform overgrowth in all groups and thus are unlikely to be a major factor in the production of NCPF. Intestinal parasitic infestation was found in 10/16 cases with NCPF, of which *Ascaris* was seen in 4/16, but in none with cirrhosis. These differences were significant at 10% level of probability, but not at 5% level. This study therefore does not justify labelling *Ascaris* as the causative agent for NCPF, but association with this parasite needs further larger study. *Ascaris* extracts have previously been shown to be associated with portal venospasm.\(^4\) Patchy thickening of the intrahepatic portal vein branches observed in NCPF has been believed to arise from incorporation of thrombi.\(^5\) *Aspergillus* or any other fungi are unlikely to produce NCPF. The finding of unusual fungi from 7 cirrhosis (40%) could be explained due to an impaired immune response.\(^1\) Histological study of jejunal and rectal mucosa did not reveal any specific abnormality.

**Table: Fungal isolation from the small intestine (most distal ileal) of patients suffering from portal hypertension**

<table>
<thead>
<tr>
<th></th>
<th>Aspergillus</th>
<th>Penicillium</th>
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<tbody>
<tr>
<td></td>
<td>Cirrhosis</td>
<td>EHO</td>
</tr>
<tr>
<td>NCPF</td>
<td>10 (1)</td>
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<tr>
<td></td>
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<td>10 (1)</td>
<td>10 (1)</td>
</tr>
<tr>
<td>1/16</td>
<td>2/18</td>
<td>5/18</td>
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\( ^* \) Total No. of cases with isolates: 7; 6EHO cases examined.

**References**