Hepatic Abnormalities in Congestive Heart Failure

Needle Biopsy Studies

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Needle biopsies of the liver were performed on 30 patients with heart failure and correlated with clinical features and biochemical liver function studies. Hepatic biopsy served as a useful adjunct to other methods in deciding the status of the liver in this group. Type of heart disease, degree of heart failure and length of heart failure could not be correlated with the observed histology. Neither history, physical examination, nor biochemical functional studies provided sufficient information to predict anatomy with certainty. A histologic diagnosis improved both therapeutic and prognostic perspective.

The demonstrated value of needle biopsy makes an evaluation of its use in studying the liver in congestive heart failure desirable. This is a report of needle biopsies of the liver correlated with clinical features and biochemical studies in 30 patients with heart failure, evaluated after maximum response to a cardiac therapeutic regimen.

Material and Methods

The selected patients were taken from routine ward admissions with congestive heart failure in whom initial appraisal revealed hepatomegaly and/or jaundice. Patients with viral hepatitis, biliary obstruction, malignancy, and hemolytic disease were excluded from these studies. Each patient received cardiotherapy consisting of rest, sodium restriction, diuretics and digitalization. When maximum response to this regimen was obtained as determined by weight changes, venous pressure and circulation time, liver biopsies were performed.

Ages of patients ranged from 30 to 78 years. Eighteen were male and 12 female. Fourteen had rheumatic heart disease; 7 had hypertensive heart disease; 6 had arteriosclerotic heart disease; 2 had constrictive pericarditis; and 1, thyrotoxic heart disease. Congestive failure had been present from 6 months to 10 years. Ten patients had grades II and III functional capacity and 20 had grade IV functional capacity according to American Heart Association standards. Fourteen had auricular fibrillation; 16 had regular sinus rhythm. Hepatomegaly was persistent in 25 patients; in 5 cardiotherapy led to its disappearance. Splenomegaly was present in 11 and jaundice in 6. Ascites refractory to diuretics was present in 14. History revealed alcoholism in 12 patients and poor dietary intake in 15 others.

Biochemical liver function studies consisted in the determination of serum bilirubin, bromsulfalein excretion, total serum cholesterol and cholesterol esters, cephalin cholesterol flocculation, thymol turbidity, serum albumin and globulin, prothrombin time and alkaline phosphatase. Serum bilirubin of more than 1.0 mg. per cent and retention of bromsulfalein of 5.0 per cent or more were considered abnormal. Total cholesterol above or below 150 to 240 mg. per cent with less than 50 to 70 per cent of the total being esterified was classified as abnormal. Three plus or plus cephalin flocculation in 48 hours, thymol turbidity of 5 units or more, serum alkaline phosphatase greater than 5 Bodansky units per 100 cc., and total serum protein of less than 6.8 Gm. per 100 cc, or reversal of the albumin-globulin ratio were considered abnormal.

Liver biopsies were performed with the Vim Silverman needle without complications. Seven patients had serial biopsies. A histologic diagnosis of portal cirrhosis (diffuse fibrosis) was made on the basis of periportal fibrosis, bile duct proliferation, and pseudolobulation with or without hyaline changes, fatty metamorphosis, and lymphocytic infiltration. The diagnosis of hepatic focal infiltration was based on the presence of small intralobular foci of lymphocytes or polymorphonuclear leukocytes not in relation to the central vein, or portal area. Central necrosis was diagnosed by the presence of dead cells or absence of hepatic cells along with condensation of the reticulum around the central vein. Pericentral vein fibrosis was diagnosed by the appearance of condensed reticulum around the central vein. These were interpreted as stages of the classical lesions attributed to congestive failure. The only biopsy specimen showing passive congestion as seen
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* Abnormal values in italics.
in routine autopsy material was the one showing central necrosis. Absence of passive congestion in needle biopsy specimens is due to decrease of blood stasis by needle pressure and tissue tension, and lack of the agonal dilatation of sinusoidal spaces in post-mortem liver sections. Lack of fat in needle biopsy specimens was attributed to the long periods of bed rest prior to the liver studies during which time fat may have been mobilized.

**Observations**

Seventeen of the 30 needle biopsies showed normal liver histology, 1 with a slight amount of fat. Some of those with normal histology had slight degrees of blood stasis. Six biopsies showed portal cirrhosis. Five biopsies showed focal areas of infiltration with 1 showing a slight amount of fat. One biopsy showed central necrosis with chronic passive congestion and 1 biopsy showed pericentral vein fibrosis.

Of the 17 patients with normal liver on biopsy, 7 had rheumatic heart disease, 4 hypertensive heart disease, 4 arteriosclerotic heart disease and 2 constrictive pericarditis. Of the 6 patients with portal cirrhosis, 3 had rheumatic heart disease, 2 had hypertensive heart disease and 1 had arteriosclerotic heart disease. Of 5 patients with focal infiltration, 3 had rheumatic heart disease, 1 had thyrotoxic heart disease and 1 had arteriosclerotic heart disease. The patient with central necrosis had rheumatic heart disease, and the patient with pericentral vein fibrosis had hypertensive heart disease.

Hepatomegaly disappeared with cardiology in the patient with central necrosis and in 4 of the patients with normal liver histology. Patients with hepatomegaly regressing on cardiology had a greater degree of liver tenderness prior to treatment, and pressure on the liver evoked a more substantial increase in distention of the neck veins.

**Correlation of Histology with Clinical Features**

Alcoholism and dietary deficiency seemed to be important causes of abnormal histology although such histories were associated with normal liver biopsies in many instances. Four (66.6 per cent) patients with portal cirrhosis, 2 (40 per cent) patients with focal infiltration and 6 (35.3 per cent) patients with normal histology had histories of alcoholism. Prolonged poor dietary intake was present in each of the patients with portal cirrhosis, 2 (40 per cent) patients with focal infiltration, 6 (35.3 per cent) patients with normal histology and the patient with pericentral vein fibrosis.

Neither clinical jaundice, splenomegaly nor ascites could be correlated with biopsy findings. Four of the 6 patients with jaundice had clinical and roentgenologic evidences of lung infarcts. Three of the jaundiced patients had normal liver histology, 2 had portal cirrhosis and 1 had central necrosis associated with congestion. Of 11 patients with splenomegaly, auricular fibrillation was present in 9, with possible embolization to account for splenic enlargement. The spleen was palpably enlarged in only 1 (16.6 per cent) of the patients with portal cirrhosis, whereas 3 (90 per cent) of the patients with focal infiltration and 7 (41.4 per cent) of the patients with normal histology (6 of whom had auricular fibrillation) had splenomegaly. Ascites was present in 7 (41.4 per cent) patients with normal histology, 5 (83.3 per cent) patients with portal cirrhosis, and 2 (40 per cent) patients with focal infiltration. Spider angiomas were present in 2 patients with portal cirrhosis.

The type of heart disease did not determine the type of histology and the degree of heart failure had little influence on the hepatic lesion (table 1). A functional grade of III or IV was given to 12 (70.5 per cent) patients with normal histology, to 3 (50 per cent) patients with portal cirrhosis and to 3 (60 per cent) patients with focal infiltration. Severe failure with grade IV functional capacity was present in the 2 patients with central necrosis and pericentral vein fibrosis.

Heart size, electrocardiographic findings and type of rhythm could not be correlated with liver histology. The duration of heart failure did not apparently determine histopathology. Signs and symptoms of some degree of heart failure had been present continuously for more than one year in 11 (64.7 per cent) patients with normal liver histology and in 3 (50 per cent) patients with portal cirrhosis. Persistent failure was noted for more than eight years in 2 (11.7 per cent) patients with normal liver biopsies and in 1 (16.6 per cent) patient with portal cirrhosis.
Correlation of Histology and Biochemical Functional Studies

Biochemical studies did not provide a clue to the observed histology. Individual patients with normal liver histology had functional patterns closely resembling those of patients with portal cirrhosis, focal infiltration, and pericentral vein necrosis. Serum bilirubin elevation was present in 8 (47 per cent) patients with normal histology, 3 (50 per cent) with portal cirrhosis and 1 (20 per cent) with focal infiltration. Abnormal bromsulfalein retention was present in 8 (47 per cent) patients with normal histology, 5 (83.3 per cent) with portal cirrhosis and 2 (40 per cent) with focal infiltration. Cholesterol disturbances were present in 5 (29.4 per cent) of the normal group, in 3 (50 per cent) of the patients with portal cirrhosis, and in 3 (60 per cent) of those with focal infiltration. Protein disturbances were present in 14 (82.3 per cent) of those with normal liver histology, in all (100 per cent) of the patients with portal cirrhosis, and in 4 (80 per cent) of the group with focal infiltration. Positive cephalin flocculation was present in 4 (23.5 per cent) of the normal group, in 2 (33.3 per cent) of the patients with portal cirrhosis, and in 2 (40 per cent) of those with focal infiltration (table 1).

The following case histories illustrate the difficulties in correlating clinical features, biochemical function and histology:

**Case 11.** A 47 year old unemployed man with rheumatic heart disease, an enlarged heart, mitral stenosis and insufficiency, auricular fibrillation and with a functional classification of grade IV, had been followed for three and one-half years for recurrent bouts of congestive heart failure. His diet had been adequate and there was no history of alcoholism. He had persistent hepatomegaly and splenomegaly despite disappearance of ankle edema and of pulmonary congestion. Liver function studies revealed intermittent hyperbilirubinemia, increased bromsulfalein retention and abnormal protein patterns. A clinical diagnosis of portal cirrhosis was considered. Two liver biopsies revealed normal histology.

**Case 22.** A 53 year old housewife with rheumatic heart disease, enlarged heart, aortic stenosis and insufficiency, mitral stenosis and insufficiency, regular sinus rhythm, right bundle branch block and a functional classification of grade IV, had been followed over a period of 14 years for congestive heart failure. There was no history of alcoholism but her diet had been inadequate since the onset of symptoms of congestive heart failure. She was fairly well controlled by digitalis, salt restriction and diuretics. Persistent hepatomegaly without splenomegaly was attributed to chronic passive congestion or "cardiac cirrhosis." Biochemical liver function studies showed elevation of the serum bilirubin with cholesterol and protein changes. Needle biopsy showed portal cirrhosis (fig. 1).

**Case 24.** A 57 year old laborer with arteriosclerotic heart disease associated with angina pectoris, enlarged heart, regular sinus rhythm and grade II functional classification, was admitted with congestive heart failure which had been present for one year. His diet had been good; in early adulthood he had consumed large amounts of whiskey for prolonged periods. Examination showed liver enlargement 8 cm. below the costal margin which persisted after his response to diuretics. Electrocardiograms
showed evidence of an old posterior wall infarction. Biochemical liver function studies were normal except for slight elevations of serum cholesterol and alkaline phosphatase. Needle biopsy revealed small focal collections of lymphocytes as the only abnormality.

Case 29. A 78 year old laborer was admitted for hypertensive heart disease, enlarged heart, auricular fibrillation and grade IV functional classification. Congestive heart failure had been present during hemoptysis, fever, and jaundice associated with congestive heart failure. He had rheumatic heart disease, enlarged heart, aortic stenosis and insufficiency, mitral insufficiency and auricular fibrillation. The functional classification was grade IV. His diet had been adequate and there was no history of alcoholism. Chest x-ray films were characteristic of pulmonary infarction. He responded to cardiotherapy and antibiotics with disappearance of hepatomegaly. Biochemical function studies revealed hyperbiliru-

Fig. 2. Case 29. Pericentral vein fibrosis.

Fig. 3. Case 30. Central necrosis with passive congestion.

the preceding two years. There was no history of alcoholism but his diet had been inadequate for several years. Hepatomegaly, 6 cm. below the costal margin, remained after treatment and it was suspected the patient might have portal cirrhosis. Liver function studies revealed a hypoalbuminemia, total cholesterol and ester ratio disturbance and a 3 plus cephalin flocculation. A needle biopsy showed pericentral vein fibrosis (fig. 2).

Case 30. A 77 year old man was admitted for binemia, hypocholesterolemia, hypoalbuminemia and a 4 plus cephalin flocculation. Needle biopsy showed central necrosis with passive congestion (fig. 3). He improved and was discharged to the cardiac clinic. Nine months later he was readmitted with recurrence of congestive failure, fever and jaundice. He failed to respond to therapy and postmortem examination revealed subacute bacterial endocarditis of the aortic valve. Postmortem liver histology showed central necrosis with passive congestion.
Correlation of Histology with Therapeutic Response

Sixteen (94.1 per cent) of the patients with normal histology, all of the 5 patients with focal infiltration and the 1 patient with pericentral vein fibrosis responded to diuretics with disappearance of ankle edema, ascites and pulmonary congestion although hepatomegaly persisted. Failure to respond to the diuretic regimen in the presence of normal liver histology led to further scrutiny. Renal dysfunction, electrolyte disturbances or infection were then found to be the underlying cause for temporary resistance. On the other hand, despite intensive cardiotherapy the patient with central necrosis and the 6 patients with portal cirrhosis continued to have fluid retention non-responsive to cardiotherapy. Prognosis in the group with portal cirrhosis was related to the degree of the liver disease; in the others it was determined by the type of heart disease and the severity of congestive failure.

Comment

The limitations of needle biopsy have been fully recognized throughout this investigation. Postmortem examinations of 3 patients in this series corroborated needle biopsy diagnoses. These studies demonstrated a surprisingly high degree of error in the diagnosis of liver changes based on physical and biochemical evaluation. A clinical diagnosis of portal cirrhosis was made in only 3 of the 6 patients proven to have this disorder. Six of 17 patients found to have normal histology and 2 of 5 patients found to have focal infiltration had a diagnosis of portal cirrhosis before biopsy. Diagnostic difficulty arose from attaching undue significance to the type of heart disease, the degree and duration of heart failure, the presence of splenomegaly and the type of biochemical changes seen.

The importance of determining the nature of liver changes in patients with heart failure is illustrated in a review of the cirrhotic group. Continued sodium and protein restriction had been employed in an effort to reduce fluid accumulation. The discovery of a cirrhotic process led to use of a higher carbohydrate and protein food intake. Improvement in diuresis followed although fluid retention persisted. Knowledge of existing cirrhosis also furnished an objective basis for the presenting clinical picture.

Summary and Conclusions

1. Needle biopsies of the liver were performed on 30 patients with congestive heart failure and correlated with clinical features and biochemical function studies. Biopsy revealed normal (histologic) sections in 17 patients, portal cirrhosis in 6, focal infiltration in 5, central necrosis in 1, and pericentral vein fibrosis in 1.

2. Histories of dietary deficiency and alcoholism were related to the observed hepatic changes but were often present with normal histology. Physical examination permitted an accurate diagnosis when correlated with history in some instances, but led the clinician astray in others. Neither jaundice, splenomegaly nor ascites could be correlated with histology. Spider angiomas were seen only in 2 patients with portal cirrhosis. Type of heart disease, degree of heart failure, and duration of heart failure could not be correlated with the observed histology.

3. Biochemical liver function studies did not provide a clue to encountered histology. The dissociation of biochemical tests and histology suggested that the latter was not responsible for the observed liver function changes.

4. Diuretic therapy was more effective in patients with normal histology, focal infiltration and pericentral vein fibrosis. Fluid accumulation was resistant to treatment in patients with cirrhosis and in a patient with central necrosis. Prognosis was related to the degree of liver disease in the patients with portal cirrhosis and to the type of heart disease and severity of congestive failure in the others.

5. Needle biopsy of the liver is a useful adjunct to the history, physical examination and biochemical function studies in determining the state of the liver in congestive heart failure. It permits an anatomic diagnosis and improves prognostic and therapeutic perspective in patients with persistent hepatomegaly associated with heart failure.

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