Evaluation Of Needle Biopsy Of The Liver: 1950-1958

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Even though the technique of needle biopsy of the liver was reported as early as 1895, the first impetus for its use in this country came from the report of Iversen and Roholm in Sweden in 1939. The early reports on the use of needle biopsy of the liver in the United States were by Hoffbauer and Volwiler and Jones in 1947. All of Hoffbauer’s cases consisted of patients with hepatomegaly. On the other hand, 68 of 234 biopsies reported by Volwiler and Jones were through the transthoracic approach and in patients with apparently normal-sized livers. In these early reports, needle biopsy of the liver was recognized as an aid in understanding the pathogenesis of disordered hepatic function and for guidance in therapy.

Four major indications for needle biopsy of the liver were outlined in an earlier report:

1. To define the stage of known liver disease for treatment and prognosis.
2. To diagnose certain hepatic pathologic conditions in which examination of the tissue is indispensable.
3. To disclose the presence of systemic disease in the liver.
4. To investigate and understand the pathogenesis of clinical liver disease.

The following case reports have been selected as examples to illustrate the value of needle biopsy under these criteria.

I. To define the stage of known liver disease.

CASE 1.

A 16 year old white female was referred by her local physician because of progressive jaundice of four months’ duration thought to be due to viral hepatitis. The patient had been hospitalized three times before coming to Detroit. Her only complaint was malaise. There was considerable tenderness over the liver, which was enlarged three centimeters below the right costal margin. The serum iron was 178 mcg. percent. The liver flocculations were 4 plus. The zinc sulfate turbidity was 40 units. The total bilirubin was 4.2 mg. percent with a direct of 1.7 mg. SGOT-transaminase was 546 units and decreased to 34 units after cortisone therapy was started. One month following admission a needle biopsy of the liver was done and mild to moderate periportal infiltrates were seen. The hepatic wedge pressure was elevated. Several L. E. tests were negative. The roentgen-study of the esophagus and stomach was normal.

Comment: During the following two years, the patient was followed with serum bilirubin determinations and steroid therapy was decreased gradually. Icterus increased when the steroid therapy was withdrawn. She was considered to be developing a post-necrotic cirrhosis with hyperglobulinemia and hypoalbuminemia. Heavy fibrous tissue in the portal areas was seen in a second needle biopsy done eighteen months after the first admission.

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CASE 2.

A ten year old boy was admitted with a three year history of Legg-Calvé-Perthes disease (osteochondritis deformans juvenilis) involving the left hip. The patient had been placed in a body cast for one month. One year later he was hospitalized on two occasions with a diagnosis of infectious hepatitis. The patient began to tire easily and had occasional epistaxis during the following two years. There were spider angiomata over the upper extremities and the anterior chest. No lymphadenopathy was found. The left lobe of the liver was enlarged, hard, and non-tender. The spleen extended 10 cm. below the left costal margin.

Laboratory studies included a white blood cell count of 4,150, serum bilirubin 0.65 mg., reticulocyte count 1.6 percent, albumin 3.3 gm., globulin 3.7 gm., cephalin cholesterol 3 plus, thymol turbidity 16 units, thymol flocculation 2 plus, bromsulfalein 17 percent and serum cholesterol 149 mg. percent. There was no bilirubinuria. The bone marrow was compatible with lupus erythematosus, but was not diagnostic. Two peripheral L. E. tests were suggestive but non-conclusive. A peripheral blood smear was normal. X-ray of the gallbladder was normal.

One month later the patient was re-admitted with severe left hip pain of 12 hours duration, pharyngeal injection and a temperature of 101 degrees. Hepatosplenomegaly was present. There was marked spasm of the left lower extremity with difficulty in movement of the hip. The leukocyte count was 8,500. The patient improved gradually and was discharged with a diagnosis of probable rheumatoid arthritis of the hip. During the following year the patient was observed as an out-patient. He gained weight and the liver and spleen were smaller in size. A few spider angiomata were present over the chest wall. The total proteins were 6.7 gm.; the white blood count was 3,550; bromsulfalein was 15 percent. The cephalin cholesterol was 4 plus, thymol turbidity was 6 units, and the thymol flocculation was 4 plus. Esophageal varices were seen in the x-ray of the esophagus. A liver biopsy was done and widespread fibrosis and lymphocytic infiltration were seen in the portal spaces. Re-duplicated bile ducts were prominent.

Comment: The stage of liver disease in this 10 year old boy was clarified by needle biopsy. The final diagnosis was post-necrotic cirrhosis.

II. To diagnose certain hepatic pathologic conditions in which examination of the tissue is indispensable.

CASE 3.

A 59 year old white male was admitted with a diagnosis of diabetes mellitus. There was a past history of peptic ulcer disease and mild icterus which was due to cholelithiasis. The patient's symptoms improved after dietary fat restriction. One year later the patient was re-admitted because of gradual weight loss. He appeared well-nourished but the skin had a sallow tint. The body hair was sparse and the skin was dry, atrophic and dusky. The chest was emphysematous. The lungs were clear. No cardiomegaly was present. The liver was palpable two centimeters below the right costal margin and was non-tender. The testicles were atrophied.

The complete blood count was normal. The fasting blood sugar was 283 mg. The urine had 2 plus glycosuria. The 24 hour urine sugar was 23 gm. Serum calcium
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was 10.4 mg., serum phosphorus 3.6 mg. and the bromsulfalein was 5 percent. Free acid was present in the stomach. Kidney function was good. X-rays of the esophagus, stomach, duodenum, gallbladder and chest were normal. The kidneys appeared normal in intravenous pyelograms. The diabetes was controlled with protamine zinc insulin 20 units and an 1800 calorie diabetic diet.

The following year the patient was admitted with ankle edema, dyspnea, and fatigue. There were congestive changes in the chest. The heart was enlarged to the left. P was greater than A. The liver was palpable 5 cm. below the right costal margin. Moderate pedal edema was present. The skin was pigmented over the exposed surfaces and had a brownish-gray cast. Right heart failure was thought to be due either to a myocardial infarct or to pericardial effusion. The venous pressure was 88 mm. of water and the decholin circulation time was 32 seconds. Flattening of the T waves was seen in the electrocardiogram indicating coronary atherosclerosis. There was fluid present in the right pleural cavity and left ventricular hypertrophy. The fasting blood sugar was 84 mg., the non-protein nitrogen 48 mg. and zinc sulfate 10 units. The serum bilirubin and liver flocculations tests were normal. The bromsulfalein test was 7 percent. The complete blood count was normal. Following slow digitalization the patient lost 10 pounds during a ten-day period. Liver biopsy at this time was diagnostic of hemochromatosis. Two venesections were done at monthly intervals following discharge from the hospital. Three months later the patient expired and at necropsy was found to have hemochromatosis involving the skin, liver, pancreas, myocardium, stomach and adrenals.

Comment: This disease was unsuspected initially. Tissue diagnosis is indispensable in hemochromatosis.

Case 4.

A 42 year old housewife was admitted with a history of good health all of her life. She complained of fullness in the abdomen and pain in the right side radiating to the inguinal area. This discomfort was increased by sneezing and coughing. The present history began one month previously when she had developed an upper respiratory infection associated with generalized aching, fever, chills and cough. Because of prolonged asthenia following this illness, the patient was admitted to a local hospital where hepatic disease was suspected. Regenerating liver tissue had been seen in a liver biopsy.

At the time of her admission to Ford Hospital there was neck vein distention in the recumbent position. Spider angiomata were seen over the right shoulder and chest. No icterus was present. The breath sounds and resonance were decreased over the right lung base. The blood pressure was 120/80. A slight systolic apical murmur was present with a protodiastolic gallop. The liver was enlarged 4-5 cm. below the right costal margin and was not nodular.

The hemoglobin was 12.2 gm. and a leukocyte count of 12,650. The urine, non-protein nitrogen, and fasting blood sugar were normal. The liver flocculation tests were normal. The total proteins were 8.3 gm. with an albumin of 4.6 mg. The prothrombin time was normal. The stools for parasites were negative. The bromsul-
falein test was markedly abnormal (54 percent). Urea clearance indicated renal impairment (35 standard clearance). The Bence-Jones protein was negative. Cryoglobulins were negative. The L.E. test was negative. Diffuse amyloidosis was seen in a liver biopsy and a bone marrow biopsy was confirmatory of amyloidosis.

Comment: An unsuspected lesion was found in the liver biopsy of this patient in whom tissue diagnosis was indispensable to identify the hepatic pathology.

III. To disclose the presence of systemic disease.

CASE 5.

A 65 year old negro male was referred from another hospital. He had back pain of four months duration, anemia, and a 50 pound weight loss. The low back pain was non-radiating and interfered with walking and sleeping. The patient had been hospitalized four weeks previously. He was emaciated. There was moderate tenderness over the lumbar spine. Grade III arteriosclerotic changes were present in the eye grounds. The heart was enlarged to the left. A grade II apical systolic murmur was present. The liver was enlarged and the prostate also was enlarged with a nodule in the left lobe. There were nucleated red blood cells and young myeloblasts in the peripheral blood. The spine had osteoblastic changes. Acid phosphatase was 4.5 mg. A prostate biopsy was negative for pathology. Agnogenic myeloid metaplasia was diagnosed by needle biopsy of the liver.

CASE 6.

A 31 year old male Arab was admitted because of the acute onset of headache, arthralgias in the hands, elbows, shoulders, neck, right hip, knees and ankles. He had been vomiting and had developed diarrhea with a fever of 102 degrees. Schistosomiasis mansoni ova were identified in the stool examination. This infestation was found also in the biliary drainage. The patient stated that previously he had been swimming in contaminated water in his native country of Yemen. The bromsulfalein test was 6 percent. The hemoglobin and leukocyte count were normal. A Schistosome ovum was found in the liver biopsy with marked tissue reaction around the ovum.

IV. To investigate and understand the pathogenesis of clinical liver disease.

CASE 7.

A 47 year old negro male was admitted with a right lobar pneumonia. Sputum cultures with sensitivity studies were done and a coagulase positive staphylococcus was found with sensitivity to penicillin and streptomycin. The patient's course after two weeks was unimproved. Novobiocin was added to the antibiotic therapy. Ten days later the patient's temperature returned to normal but he was noted to be icteric and obstructive jaundice was present. A transduodenal drainage was normal with no evidence of biliary calculi. During the subsequent four months the jaundice cleared and the patient was improved. At this time bile stasis was seen in the needle biopsy of the liver. Six months later a repeat liver biopsy was interpreted as normal. The patient has remained well.

Comment: This patient represents an obstructive jaundice concomittant with Novobiocin therapy recently reported by Haubrich.
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The development of the hepatic changes were demonstrated by needle biopsy. Histologic evidence that the liver had healed was secured by a second needle biopsy of the liver after a period of convalescence.

COMMENT

From 1950 through 1958 there were 741 biopsies performed. Of these 64 percent confirmed the clinical impression, 9 percent corrected an erroneous clinical diagnosis, and an unsuspected lesion was found in 6 percent. Needle biopsy of the liver was helpful in establishing the diagnosis in 79 percent of the patients studied. Biopsy findings were non-specific in 13 percent, neither confirming nor correcting the clinical diagnosis. Misleading biopsy findings were found in 5.5 percent. An unsuccessful biopsy or inadequate specimen was obtained in eighteen patients (2.5 percent).

Gamble and Sullivan have reported 81 percent diagnostic value in 323 needle biopsies. Ward et al found that needle biopsy indicated the proper diagnosis in 74 percent of 1114 biopsies on 1000 patients. Fisher and Faloon have reported the biopsy to be not consistent with the initial clinical diagnosis in 30.2 percent. We have found the number of unsuspected lesions discovered by needle biopsy to have increased since an earlier report. Hemochromatosis has been found in several patients in whom the clinical diagnosis had been suspected of cirrhosis, nephrosis and amyloidosis.

Table I

<table>
<thead>
<tr>
<th>Pathologic Diagnoses</th>
<th>No. Cases</th>
</tr>
</thead>
<tbody>
<tr>
<td>Portal Cirrhosis</td>
<td>294 (11)*</td>
</tr>
<tr>
<td>Normal Liver</td>
<td>108 (4)</td>
</tr>
<tr>
<td>Malignancy</td>
<td>65</td>
</tr>
<tr>
<td>Metastatic carcinoma, hepatoma, lymphoma</td>
<td></td>
</tr>
<tr>
<td>Hepatitis</td>
<td>52 (6)</td>
</tr>
<tr>
<td>Fatty Liver</td>
<td>42 (2)</td>
</tr>
<tr>
<td>Bile Stasis</td>
<td>41</td>
</tr>
<tr>
<td>Hemochromatosis</td>
<td>26 (9)</td>
</tr>
<tr>
<td>Inadequate Specimen</td>
<td>18</td>
</tr>
<tr>
<td>Biliary Cirrhosis</td>
<td>11</td>
</tr>
<tr>
<td>Sarcoid</td>
<td>7 (1)</td>
</tr>
<tr>
<td>Chronic Passive Congestion</td>
<td>6</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>38</td>
</tr>
<tr>
<td>Including granulomata, miliary tuberculosis, glycogen storage disease, agnogenic myeloid metaplasia, postnecrotic cirrhosis, amyloid, polyaneritis, Schistosomiasis, et al.</td>
<td>708 (33)*</td>
</tr>
</tbody>
</table>

*Second biopsies, duplicate diagnoses.

In Table I are tabulated the pathologic diagnoses from 741 biopsies. The incidence of various anatomic lesions has remained about the same since 1954. The diagnosis of normal liver tissue in 112 biopsies is attributed to the use of this diagnostic technique in various systemic disorders which occasionally may involve the liver. These have included lupus erythematosus, subacute bacterial endocarditis, polyarteritis, 'cardiac' cirrhosis in chronic congestive failure, metastatic malignancy in the liver and attempts to diagnose early hemochromatosis in patients with diabetes mellitus. Approximately two-thirds of the 294 patients with portal cirrhosis have been classified as mild or moderate.
Needle biopsy of the liver has continued to be an important technique in 'looking for' metastatic disease. Needle biopsy was diagnostic of metastatic carcinoma in 53 patients (74 percent) of 71 patients in the series who were proven to have carcinoma in the liver. Subsequent laparotomy or necropsy in 18 patients proved that there had been no metastases to the liver. Hence the diagnostic accuracy in 'looking for' metastatic disease in the liver was 79 percent. Eight of twelve lymphoma's were found by liver biopsy. Although two or three penetrations might have been made at the time of the initial biopsy, the percentage of accuracy reported includes only a single biopsy in each patient. An increase in the diagnostic accuracy in finding metastases is to be expected if a second biopsy is done after a progress interval of time.

Of the patients biopsied in this series, 84 percent had hepatomegaly, 28 percent were icteric, 18 percent had splenomegaly and 9 percent had ascites. This diagnostic test is done with its specific indications balanced against the possible risk. We have had one death (0.13 percent mortality) from bile peritonitis in a geriatric patient with obstructive jaundice. Back pressure of bile or blood in the liver is a precise contraindication for the procedure. Purulent infection in the area of approach to the liver is also an absolute contraindication. In one patient with systemic actinomycosis the biopsy needle entered a liver abscess without serious sequelae. Relative contraindications include the uncooperative patient, bleeding tendencies, impaired blood coagulation and ascites. Occasionally patients have pleural pain following the procedure and require intercostal block anesthesia. We have had one patient develop pneumothorax after the biopsy procedure and three patients had a mild subcutaneous emphysema. The intercostal approach was used in 702 biopsies and the anterior subcostal approach in 39.

**SUMMARY**

The value of needle biopsy of the liver has been evaluated from an experience of nine years. The technique has aided in a proper diagnosis in 79 percent of the patients studied. Case reports have illustrated the precise indications and value of the procedure.

**BIBLIOGRAPHY**