THE
MICHIGAN SOCIETY OF
PATHOLOGISTS

presents

**A SEMINAR**

on

**DISEASES OF THE LIVER**

moderated by

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on

Thursday, October 11, 1973
Sheraton Cadillac
Detroit, Michigan

CASE 1

This 17 year old male had acute onset of massive hematemesis. On admission he was found to have ascites and prominent abdominal veins. Laboratory studies included: hematocrit, 18%; albumin, 2.8 gms/100 ml.; bilirubin, 1.5 mgm%; prothrombin, 43%.

An emergency porto-caval shunt was performed. On the third postoperative day he developed asterixis, became delerious and then comatose. Because he developed localized seizures, a neurologist was consulted who noted corneal pigment rings. A serum ceruloplasim level was low. The patient died on the ninth postoperative day.

At autopsy the liver weighed 1460 gm, was coarsely nodular with fine intervening septations and was bile-stained. Esophageal varices and splenomegaly were present. The brain was normal.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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CASE 2

This nine year old boy was the product of a full term pregnancy to a primiparous 23 year old female. At one month of age he manifested jaundice. Liver biopsy at laparatomy was reported to show neonatal hepatitis. He was maintained on prednisone for one year. His jaundice dissappeared at the age of eight to nine months, but he continued to have hepatosplenomegaly and his subsequent growth was below the third percentile for his age. The patient had a younger sister who also had jaundice in infancy. She also had had a liver biopsy diagnosed as neonatal hepatitis. After a year of steroid therapy, she had remained clinically well, but had slight abnormalities of hepatic function tests.

At the age of seven years the boy's liver was felt 5 cm. below the right costal margin. Tests of liver function at that time showed a total bilirubin of 3.2 mg.% (direct 1.6), an alkaline phosphatase of 60 KA units, SGOT/SGPT 178/63 units, and cholesterol of 204 mg.% Ascites and esophageal varices were noted shortly thereafter. The patient's final admission was for abnormal behavior, disorientation and early liver failure. Bilirubin was 11.3 mg.% and peaked at 24 mg.% prior to death. The SGOT was 116 units and later increased to 250 units. E. coli was cultured from the blood. He manifested progressive deterioration with bloody diarrhea.

CASE 2 (cont'd)

The liver at necropsy weighed 450 g. It was firm, yellow-tan with nodules up to 4 cm. A representative area is included in the seminar. The common bile duct below the cystic duct was narrowed and fibrotic. The spleen weighed 230 g.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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CASE 3

This 63 year old black housewife was admitted on 4/28/73 with pruritus vulvae, weakness, lethergy, fever and vomiting. She had been well until February, 1973, when a diagnosis of diabetes mellitus was established and the patient received Diabinese and Aldomet. Diabinese was discontinued 4 weeks prior to admission. There was no history of alcoholism.

On examination the patient had a temperature of 102° F. There was mild abdominal distention with no organomegaly. The admitting diagnoses: Diabetes mellitus, hypertensive cardiovascular disease, and vaginitis. Rectal examination was performed on the following day and "snow-white" stools were noted.

Laboratory investigations at the time of admission included: Hemoglobin, 13.1 g%; WBC, 19,300/cu. mm; Differential, 30% neutrophils, 47% lymphocytes, and 15% atypical lymphocytes. Pyruia was present but urine culture was negative. STS-non-reactive; GBAg-negative (RIA); tests for serum antibodies against mitochondria, smooth muscle and nuclei were negative. Upper G.I. series showed a small duodenal diverticulum; IVP showed a left stag-horn calculus with left hydronephrosis. A liver scan showed hepatocellular damage with no evidence of billiary obstruction.

CASE 3 (cont'd)

Following admission the patient remained febrile. On May 7, 1973 a laparotomy disclosed no evidence of extrahepatic bile duct obstruction. An operative cholangiogram was interpreted as normal. Cultures of the bile were negative. The patient remained slightly febrile following surgery. On May 10,11973 a small amount of white fecal material was noted.

Summary of chemistry results:

| | 4-30 | 5-3 | 5-8 | 5-10 | 5-14 |
|---|---|---|---|---|---|
| LDH | 274 | 143 | 153 | 121 | N |
| SGPT | 214 | 132 | 132 | 92 | 61 |
| SGOT | 175 | 82 | 48 | 23 | N |
| Alk-P (K.S. units) | 132 | 156 | 130 | 75 | 60 |
| Bilirubin - total | 4.2 | 4.5 | 2.5 | 1.9 | N |
| Cholesterol | 316 | 309 | 141 | 131 | 114 |
| Glucose | 266 | 272 | 286 | 250 | 233 |

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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CASE 4

A 54 year old woman underwent a cholecystectomy with halothane anesthesia. Three weeks later a subphrenic abcess was drained, also using halothane anesthesia. One week later she was noted to be icteric. The bilirubin was 14 mg percent and SGOT was 433 units. Within three days she became lathargic, comatose, and developed rectal bleeding and cutaneous ecchymoses. At this time the bilirubin was 18 mg percent, SGOT was 101 units, SGPT was 272 units, and prothrombin time was less than 10%. The BUN and creatine became elevated, and she died 15 days after the second operation.

At autopsy the liver weighed 1480 gm. It was soft, yellow and bile-stained, and had a prominene accentuation of the lobular architecture with punctate depressions apparently corresponding to the centrolobular zones.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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CASE 5

This 15 year old girl had a transient episode of peripheral edema and abdominal swelling in June, 1970. The following month she became lethargic and fatigued, and in late August, manifested icterus and ascites.

Bilirubin was 23 mg per 100 ml; SGOT, 500 u.; HBAg, negative; alkaline phosphatase, 32 u. Physical examination revealed icterus, ascites and peripheral edema.

Her SGOT fell to 150, but she developed asterixis and then coma. Hypoglycemia and renal failure supervened, and she died approximately 4 weeks after the onset of jaundice. In the last several days, she was given high doses of steroids.

At autopsy, the liver weighed 500 gms. The capsule was wrinkled. The parenchyma had broad dark brown tracts separating yellow nodular masses. There were 2000 ml of ascitic fluid.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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CASE 6

This 22 year old white male reported to an outpatient clinic complaining of generalized malaise, myalgia and a mild cough. Physical examination was within the limits of normal. A white blood count showed relative lymphocytosis. The clinical diagnosis was influenza. The patient was treated with Declomycin 150 m.g.t.i.d. and aspirin and instructed to return if he did not improve.

Three days later the patient reported to the emergency room complaining of severe malaise, abdominal pain and emesis of reddish-colored vomitus. His temperature was 101.60°F, pulse was 80 per min. and the blood pressure was 90/40 mm. Hg. There was pallor of skin and mucus membranes and mild tenderness in the left palpable and there was no lymphadenopathy. The hematocrit was 44% and WBC was 11,000 cells per cu. mm. (60% lymphocytes, 10% of which were atypical). Three hours after admission the patient went into irreversible shock and died.

At necropsy the peritoneal cavity contained 3,000 ml of liquid and clotted blood. The spleen weighed 460 g. and had an irregular split in the capsule. The liver weighed 1640 g. and appeared grossly normal except for centrilobular congestion. The sections used for the Seminar are from the necropsied liver.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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CASE 7

This 49 year old white woman had been unwell for several months. She had not been on any drugs other than birth control pills. Physical examination showed xanthelasmas on both eyelids and a large, hard but smooth liver. Upper and lower gastrointestinal series and cholecystogram were normal. Liver scan showed diffuse small defects and three larger defects.

Laboratory data: Total serum protein, 8.0 g.% (albumin 3.5, globulin 4.5); hematocrit - 42%, WBC, 9,600 with normal differential; SGPT 120 (normal 20-55 units); total serum bilirubin, 1.9 mg.% (direct 1.7 mg.%); alkaline phosphatase, 436 u. (normal 20-67 units.).

Exploratory laparotomy was unremarkable except for hepatomegaly. Several biopsy specimens were obtained from 'defects' suggested by the liver scan. Postoperatively, the patient did well except for slight jaundice (total bilirubin, 3.3 mg.%) Tests of liver function one month after laparatomy showed: total serum bilirubin, 2.2 mg.% (direct 1.9); SGPT, 710 units; alkaline phosphatase, 595 units; and serum cholesterol, 422 mg.%.

The sections in the Seminar are from the open biopsy specimen.

Your diagnosis:_____

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Dr. Ishak's diagnosis:_____

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CASE 8

A 46 year old man had been consuming one pint of whiskey daily for 20 years. In the two months prior to admission, he developed progressive dyspnea and weakness.

On admission the patient was intoxicated. Ascites, hepatomegaly and spider angiomata were noted on the chest.

Laboratory studies included bilirubin, 4.2 mgm%; SGOT, three times normal; alkaline phosphatase, twice normal; WBC, 10,000; serum protein, 6.3 gm per 100 ml. with 3.2 gm of albumin.

During the next 18 days the bilirubin progressively rose to 14 mgm percent with the direct reacting fraction accounting for 75%. The stools became pale, and bilirubinuria was noted. Obstructive jaundice was diagnosed, and the bilirary tract was explored but was found to be normal. Postoperatively he developed renal and hepatocellular failure, and he died several days later.

At autopsy the liver weighed 2570 gms, was finely nodular, firm, and light yellow to brown. The spleen weighed 320 gm.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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CASE 9

This 14 month old male child was admitted for evaluation of a protuberant abdomen. Physical examination revealed a large mass occupying the entire upper abdomen and extending 3 cm. below the umbilicus. The mass could be moved laterally and moved with respiration. The kidneys could be palpated behind the mass.

Liver scan showed a large filling defect thought to be within the right lobe of the liver. An intravenous pyelogram was interpreted as normal except for calcification outside the renal outline

Serum electrolytes, BUN and tests of hepatic function of hemostasis were in the normal range. Hepatitis B antigen was not detectable, and postoperative Alpha fetoglobulin determinations were negative.

Celiotomy revealed an 8 cm. mass extending out of the left lobe of the liver. Multiple enlarged lymph nodes were present in the porta hepatis and along the lesser curvature of the stomach. Frozen sections of three of the lymphnodes showed no neoplasm. A left hepatic lobectomy was performed. The patient made an uneventful recovery and was discharged one month later. He remains well 17 months following hepatic lobecotomy.

The resected left lobe weighed 520 g. Its surface was distorted by a gray-tan multinodular mass, measuring 10 x 7 x 6 cm. Calcific areas were noted in the tumor.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

CASE 10

This 29 year old woman noted an upper abdominal mass three weeks prior to admission. She was otherwise asymptomatic. She had taken birth control pills for the preceding five years.

Physical examination was unremarkable except for a 15 cm., smooth right upper quadrant mass extending the costal margin to the umbilicus. All laboratory studies were within normal livits.

At operation, a 10 cm. mass was found in the quadrate lobe. This was widely resected. The tumor was somewhat lobulated, tan to yellow and contained a large central hemorrhagic zone.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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CASE 11

This 66 year old white male was admitted to the hospital with a five week history of a constant bloating sensation, anorexia, nausea, yellow stools and dark urine. There was no history of exposure to hepatitis or ethanol ingestion. The patient was a non-smoker, but claimed that he had been exposed to 'noxious chemical vapors' at work for many years.

Physical examination showed jaundice, ascites, and a large firm liver. A cholecystogram showed non-visualization. A liver scan showed a few vaguely defined defects.

Laboratory data: Total serum bilirubin, 5.5 mg% (direct 4.2); SGOT/SGPT, 159/75 (normal 40); alkaline phosphatase, 100 units (normal 12-40 units); prothrombin time, 61%.

The patient died on the day after admission. The liver weighed 2,720 g. and was nodular. Approximately one-third of the right lobe was replaced by a dark red, sponge-like mass (Seminar slide). Similar smaller nodules were scattered throughout the rest of the liver. Five yellow-tan to hemorrahagic nodules, up to 2 cm. in diameter, were scattered in the spleen.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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## CASE 12

This six year old white girl was admitted because of fatigue, poor appetite and occasional abdominal discomfort of one to two months duration. The past history was negative except for the usual childhood illnesses.

Physical examination revealed a firm nodular mass (the size of a lemon) in the right upper quadrant of the abdomen. This was felt to be part of the liver. The hemoglobin on admission was 13.6 g. All other laboratory tests, including the total serum protein, serum bilirubin, alkaline phosphatase and transaminase, were within normal limits. At laparotomy a 6 cm. in diameter mass was found in the inferior portion of the right lobe of the liver. The surgeon's gross diagnosis was carcinoma. A right hepatic cobectomy was performed. The patient was discharged three weeks postoperatively.

She was last followed up in January, 1972, seven years after her hepatic lobectomy. She had developed normally and was asymptomatic. There were no signs of liver disease and the liver was not palpable. Tests of hepatic function (serum bilirubin, serum alkaline phosphatase, SGOT/SGPT) were within the limits of normal. Hepatitis B antigen was not detected in the serum.

CASE 12 (cont'd)

Gross examination of the resected right lobe of the liver showed a 5 x 4 cm. firm nodular mass which was well-demarcated from the surrounding liver. The cut surface had a central gray area from which fibrous septa radiated to the periphery, subdividing the main nodule into smaller lobules. The lobules were light brown in color.

Your diagnosis: _____

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Dr. Ishak's diagnosis: _____

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MICHIGAN SOCIETY OF PATHOLOGISTS

Seminar, Oct. 1973

Kamal G. Ishak, M.D., Ph.D.

Armed Forces Institute of Pathology

Washington, D.C.

## DIAGNOSES

Case 1 - Multilobular cirrhosis associated with hepatolenticular degeneration (Wilson's disease)

Case 2 - a. Multilobular cirrhosis associated with alpha-1 antitrypsin deficiency.

b. Cholestasis, marked and reduction in intrahepatic bile ducts ?etiology.

Case 3 - a. Hepatocellular injury associated with methyldopa therapy.
b. Non-caseating granulomas probably related to anthracosilicosis.
c. Fatty metamorphosis and glycogen nuclei consistent with diabetes mellitus.

Case 4 - a. Centrilobular necrosis associated with halothane anesthesia.
b. Cholestasis and other changes ?related to extrahepatic biliary tract disease.

Case 5 - Massive necrosis consistent with fulminant viral hepatitis.

Case 6 - Infectious mononucleosis hepatitis.

Case 7 - Primary biliary cirrhosis.

Case 8 - Nutritional (alcoholic) liver disease.

Case 9 - Hepatoblastoma, mixed epithelial and mesenchymal type.

Case 10 - Hepatocellular adenoma.

Case 11 - Hemangiosarcoma.

Case 12 - Focal nodular hyperplasia.

CASE 1

Histopathology:

1. Multilobular (macronodular; postnecrotic) cirrhosis. Large pseudolobules with substructure separated by fibrous septa of varying thickness.

2. Septa contain many cholangioles and are heavily infiltrated with inflammatory cells (lymphocytes, neutrophils, plasma cells). Portal areas are incorporated in some of septa.

3. Junction between pseudolobules and septa 'moth-eaten' due to unicellular necrosis -- acidophilic degeneration, sinusoidal acidophilic bodies and Mallory bodies. Degenerating cells with Mallory bodies surrounded by neutrophils.

4. Accumulation of lipofuscin pigment in many hepatocytes within pseudolobules.

5. Accumulation of a large quantity of copper in hepatocytes of many but not all pseudolobules.

6. Presence of numerous glycogen ('hydropic') nuclei, particularly at pseudolobular peripheries.

7. Marked hepatocellular unrest with anisocytosis, anisonucleosis and bi- and trinucleation.

References:


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4. Lindquist, R. R.: Studies on the pathogenesis of hepatolenticular degeneration. II. Cytochemical methods for the localization of copper. Arch. Path. 87:370-379, 1969.

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7. Sternlieb, I. and Scheinberg, I. H.: Chronic hepatitis as a first manifestation of Wilson's disease. Ann. Intern. Med. 76: 59-64, 1972.

8. Sternlieb, I.: Evolution of the hepatic lesion in Wilson's disease (hepatolenticular degeneration). In Progress in Liver Diseases, Vol. IV, New York, Grune and Stratton, 1972, p. 511-525.

CASE 2

Histopathology:

1. Multilobular cirrhosis. Large pseudolobules with substructure encircled by septa of varying thickness. One large area of scarring completely devoid of pseudolobules.

2. Septa composed of acellular and somewhat hyalinized collagen. Very few inflammatory cells (lymphocytes and few plasma cells). Relatively few medium and large interlobular ducts seen; some contain bile plugs in the lumen. Septal macrophages hypertrophied and packed with light-tan pigment (PAS-positive, but diastase resistant).

3. Cholangiolar proliferation at junction of pseudolobules and septa, but somewhat patchy in distribution. Many cholangioles contain bile plugs and are surrounded and infiltrated by neutrophils.

4. Moderate cholestasis, mainly at the periphery of pseudolobules. Associated changes include pseudoxanthomatous transformation and occasional pseudoglands.

5. Presence of numerous, mainly globular, eosinophilic bodies in cytoplasm of hepatocytes, particularly at pseudolobular peripheries. Bodies intensely PAS-positive but diastase-resistant, and vary in diameter from less than 1 to over 30 micra.

6. Occasional sinusoidal acidophilic bodies.

7. Minimal copper accumulation in hepatocytes at pseudolobular peripheries.

8. Minimal focal fatty metamorphosis.

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Case 2 Cont'd.

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7. Palmer, P. E., Wolfe, H. J. and Gherardi, G. J.: Hepatic changes in adult $\alpha_1$-antitrypsin deficiency. Gastroenterology 65:284-293, 1973.

Histopathology:

1. Marked unrest with anisocytosis, anisonucleosis, binucleation and mitoses.

2. Ballooning degeneration, mainly para- or peri-central.

3. Focal necrosis with infiltration by lymphocytes and some plasma cells.

4. Haphazardly-distributed sinusoidal acidophilic bodies.

5. Minimal fat (medium and large) vacuolization.

6. Occasional glycogen nuclei at limiting plates.

7. Minimal centrilobular cholestasis.

8. Multiple varying-sized, non-caseating granulomata distributed intralobularly (mainly around central veins) and in a portal-periportal location. Most contain a coarsely-granular nonpolarizable black pigment and occasional birefringent needle-like particles.

9. Moderate Kupffer cell hypertrophy with hemosiderin and lipofuscin accumulation.

10. Marked portal and periportal inflammation (lymphocytes, plasma cells, eosinophils and neutrophils). There is patchy disruption of the limiting plates with occasional separation of a liver cell.

11. Patchy minimal to moderate periportal fibrosis with occasional linkage of two portal areas.

References:

1. Bloodworth, J. M. B.: Morphologic changes associated with sulfonylurea therapy. Metabolism 12:287-301, 1963.

2. Elkington, S. G., Schreiber, W. M. and Conn, H. O.: Hepatic injury caused by ∝-alpha-methyldopa. Circulation 40:589-595, 1969.

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Case 3 Cont'd.

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9. Rehman, O. U., Keith, T. A. and Gall, E. A.: Methyldopa-induced submassive hepatic necrosis. J.A.M.A. 224:1390-1392, 1973.

CASE 4

Histopathology:

1. Centrilobular necrosis (with some extension into mid-zones). Adjacent areas of necrosis often linked together ('bridging'). Changes include drop-out of cells, sinusoidal dilatation, collapse of reticulum stroma, moderate inflammation (neutrophils, lymphocytes) and Kupffer cell hypertrophy with pigment (lipofuscin and some hemosiderin) accummulation.

2. Ballooning degeneration of hepatocytes at edges of zones of necrosis.

3. Occasional sinusoidal acidophilic bodies in mid-lobular zones.

4. Minimal fat (small and medium) vacuolization of hepatocytes in mid- and peripheral zones.

5. Moderate cholestasis, with occasional pseudogland-formation and a rare bile-lake, in mid- and peripheral zones. Some Kupffer cells show pseudoxanthomatous transformation.

6. Minimal patchy periportal cholangiolar proliferation. Some contain bile plugs and are surrounded and infiltrated by neutrophils (acute cholangiolitis).

7. Moderate periportal and portal inflammation. Most of inflammatory cells are neutrophils but some lymphocytes and eosinophils are also seen.

8. Minimal acute cholangitis and presence of bile plugs in some interlobular ducts.

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CASE 5

Histopathology:

1. Massive (panlobular) hepatocellular necrosis. Lobules appear smaller than normal due to dropping out of all hepatocytes. Reticulum stroma is condensed and sinusoids are full of erythrocytes. Numerous inflammatory cells are present in the stroma and sinusoids (lymphocytes, plasma cells, neutrophils and eosinophils). Kupffer cells are markedly hypertrophied and contain a moderate amount of lipofuscin pigment.

2. Cholangiolar proliferation, mainly in peripheral lobular zones.

3. Endophlebitis of some central veins (infiltration with lymphocytes and plasma cells, subintimal edema and endothelial swelling).

4. Moderate to marked portal inflammation - cells qualitatively similar to those in lobules.

References:


1. Lucké, V., and Mallory, T.: The fulminant form of epidemic hepatitis. Am. J. Pathol. 22:867-945, 1946.

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4. Zuckerman, A. J.: Virus Diseases of the Liver. New York, Appleton - Century-Crofts, 1970.

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CASE 6

Histopathology:

1. Marked hepatocellular unrest with anisocytosis, anisonucleosis, increased numbers of binucleated cells and many mitotic figures. (Dissociation of liver plates probably a postmortem artefact).

2. Occasional acidophilic degeneration and sinusoidal acidophilic bodies.

3. Presence of a large number of lymphocytes in sinusoids.

4. Moderate Kupffer cell hypertrophy.

5. Marked portal and periportal inflammation (lymphocytes and occasional eosinophils and plasma cells). Inflammatory cells are seen to infiltrate the wall of an occasional vein in a portal area.

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8. Sutton, R. N. P.: The EB virus in relation to infectious mononucleosis. J. Clin. Path. 25 (Suppl.): 58-64, 1973.

Histopathology:

1. Moderate cholestasis throughout the lobule but patchy in distribution. Associated changes include pseudogland formation and pseudoxanthomatous transformation. Latter change involves hepatocytes (particularly at lobular periphery), cholangiolar cells and Kupffer cells. Pseudoxanthomatous cells have a reticulated or foamy cytoplasm and some are bile-stained.

2. Moderate but patchy periportal cholangiolar proliferation; cholangioles often surrounded and infiltrated by neutrophils (acute cholangiolitis). There is also associated periportal fibrosis with occasional linkage of portal areas.

3. Unicellular peripheral hepatocytic degeneration (piecemeal necrosis); this includes cytoplasmic dissociation, occasional sinusoidal acidophilic bodies and separation of single or groups of hepatocytes and their incorporation into the expanded portal areas.

4. Accumulation of a moderate quantity of copper in periportal hepatocytes.

5. Marked portal and periportal inflammation. Cells include lymphocytes, plasma cells, neutrophils and eosinophils. Some portal macrophages are hypertrophied and contain a tan-colored (PAS-positive but nonglycogenic) pigment.

6. Absence of bile ducts in many portal areas. Residual bile ducts show "chronic non-suppurative destructive cholangitis" which includes: infiltration of the epithelium by lymphocytes and plasma cells, segmental degeneration of lining cells, and periductal chronic inflammation. Some of the sections show a granulomatous reaction around degenerating ducts.

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CASE 8

Histopathology:

1. Moderate, predominantly large vacuolar fatty metamorphosis with no zonal distribution.

2. Presence of numerous Mallory bodies (alcoholic hyaline) mainly in centrilobular zones. Affected hepatocytes are two to several times the normal size and contain irregular or dendritic eosinophilic masses, which sometimes form a ring around the nucleus (Mallory bodies are PAS-negative). Remainder of cytoplasm of hepatocytes usually empty and nuclei show pyknosis or lysis. Degenerating hyepatocytes harboring Mallory bodies show lysis of cell membrances and are in the process of being scavenged by neutrophils. Liver cell plates in central zones appear fractured due to loss of cells and collagen deposition in spaces of Disse and sinusoids ("capillarization").

3. Occasional sinusoidal acidophilic bodies.

4. Moderate cholestasis, central and midzonal. Associated changes include pseudoxanthomatous change of Kupffer cells and occasional hepatocytes.

5. Presence of a moderate quantity of a coarsely-granular, refractile, brown pigment in hepatocytes in peripheral zones. This stains positively with iron stains.

6. Varying degrees of central vein "sclerosis."

7. Intralobular and periportal fibrosis. In both cases scarring is "stellate" or "arachnoidal" with fine septa separating and isolating the liver plates. Occasional septa link central veins to portal areas or to other central veins, but there is no true pseudolobulation

8. Periportal cholangiolar proliferation with acute inflammation (acute cholangiolitis).

9. Moderate portal and periportal inflammation (neutrophils, lymphocytes).

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Histopathology:

1. Well-circumscribed neoplasm surrounded by pseudocapsule. Occasional fibrous septum extends from surface into depths of neoplasm.

2. Histologic features best separated into those of tissues derived from entoderm or mesoderm, although these are intimately admixed throughout.

3. Entodermal Derivatives: a. Varying sized epithelial areas clearly identifiable as hepatocellular. These have a small (2-3 cells across) trabecular pattern with inconspicuous sinusoids lined by flat endothelial cells. Cells vary from large cells with a pale or vacuolated cytoplasm (containing glycogen and lipid) to smaller ones with an eosinophilic finely-granular cytoplasm. Latter show more nulcear hyperchromasia and pleomorphism than former cells; occasional mitotic figures seen. Clearly-defined canaliculi, occasionally containing a bile-plug, are present between cells in trabeculae. Hematopoietic elements (mainly red cell precursors and megakaryocytes) often seen in sinusoids. Foci of hemorrhage, infarction and necrosis present throughout epithelial hepatocellular areas.

   b. Poorly differentiated epithelial elements merging imperceptibly into hepatocellular elements. These 'embryonal' cells are small, have ill-defined borders, and a relatively large vesicular nucleus. They occasionally form tubular or acinar structures with a central lumen containing a pink-staining homogenous secretion; the cytoplasm and contents of some of the acini is Alcian-blue-positive and mucicarminophilic.

4. Mesodermal Derivatives: a. Cellular very 'primitive' mesenchymal tissue to fibromyxomatous tissue to mature collagen. b. Varying-sized islands of osteoid, mainly within mesenchymal tissue. These show areas of ossification. c. Hematopoietic elements (vide supra).

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CASE 10

Histopathology:

1. Well-circumscribed neoplasm surrounded by pseudocapsule, but showing area of growth outside capsule. Latter area merges imperceptibly into adjacent liver.

2. Neoplasm composed of narrow trabeculae (2 to several cells thick) with inconspicuous slit-like sinusoids lined by flat endothelial cells. Numerous varying-sized veins are scattered throughout and an occasional small arteriole can be identified. The reticulum pattern is well-developed in some areas but not in others. An occasional fibrous septum is present but no bile ductules are identified. Foci of recent hemorrhage and one large infarcted area are seen.

3. Clearly defined canaliculi are seen between hepatocytes. These are occasionally dilated by a plug of bile.

4. Neoplastic cells are several times normal size and generally have an empty cytoplasm except for some pericanalicular condensation. Empty appearance due to large content of glycogen, which is much greater in quantity than in non-neoplastic hepatocytes. Some of these cells also contain fat vacuoles. Cytoplasm of some cells has bile in it. Nuclei of neoplastc cells are 2 to 4 times larger than normal and, while slightly hyperchromatic, show very inconspicuous nucleoli. Most cells contain one nucleus but scattered bi- and trinucleated cells are occasionally seen. No mitoses are present.

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CASE 11

Histopathology:

1. Hepatic lobules replaced by multiple, irregular, varying-sized cavities containing blood. The larger spaces are supported by collagenous tissue, and show multiple papillary tufts or polypoid ingrowths with a fibromyxomatous core.

2. The lining of the cavities and covering of the tufts consists of flattened or fusiform cells apparently forming a syncytium which rests on a reticulum network. Most of the cells are arranged in a single layer but foci of multilayering are seen. The cells have poorly defined outlines and a scanty amount of eosinophilic cytoplasm. They show moderate pleomorphism and nuclear hyperchromasia. The nuclei are round, oval or irregular, have a fine chromatin network and inconspicuous nucleoli. Mitoses are very rare. An occasional multinucleated cell is noted.

3. Cells similar to those noted above are seen to directly invade and grow along sinusoidal spaces and in so doing causing separation and isolation of liver plates. The hepatocytes in these fragmented plates show varying degrees of atrophy and cholestasis; occasional cells show coagulative degeneration presumed to be anoxic in etiology. Ductular elements appear to be proliferating in the fibrous stroma between vascular spaces.

4. Presence of neoplastic cells lining vascular channels which are interpreted as portal vein branches or central veins.

5. Presence of foci of chronic inflammatory cells (mainly lymphocytes) in the fibrous stroma around the cavities comprising the neoplasm.

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CASE 12

Histopathology:

1. Well-circumscribed tumor directly abutting on Glisson's capsule.

2. Tumor subdivided into irregularly-shaped nodules by fibrous septa of varying thickness. These converge upon several stellate-shaped scars. Small delicate fibrous septa extend into the main nodules for varying distances, and some of these which are cut horizontally are round or irregular and appear to be isolated deep within the nodules.

3. Presence of multiple vascular channels, more prominent in the stellate scars and thicker septa. Most of these are veins but arteries and arterioles can also be identified. Some of the larger vessels show eccentric or concentric thickening due to subintimal fibroplasia. In some of the sections large veins are noted between the periphery of the tumor and the adjacent liver.

4. Proliferation of many ductules (cholangioles) in the fibrous septa, particularly along those extending deep into the nodules.

5. Presence of inflammatory cells in the septa. Many of those in relation to the ductules are neutrophils, but lymphocytes are seen deep in the fibrous tissue.

6. The nodules are composed of hepatocytes arranged in randomly oriented plates which are thicker than normal. Sinusoidal spaces lined by endothelial cells are present as well as varying-sized veins. The hepatocytes show moderate anisocytosis and anisonucleosis and have an empty on occasionally vacuolated cytoplasm. This appearance is due to the large quantity of glycogen in the cytoplasm as well as a moderate amount of fine droplet fat. A canalicular network is present throughout but is difficult to identify in the hematoxylin and eosin-stained preparation. No bile stasis is evident

7. Presence of occasional sinusoidal acidophilic bodies, particularly at the junction of hepatocellular elements with the septa.

8. Absence of lipofuscin pigment in hepatocytes.

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