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Харківський національний медичний університет

Кафедра Внутрішньої медицини №3
Факультет VI по підготовці іноземних студентів

ЗАТВЕРДЖЕНО
на засіданні кафедри внутрішньої медицини №3
29 серпня 2016 р. протокол № 13
Зав. кафедри _____д.мед.н., професор Л.В. Журавльова

МЕТОДИЧНІ ВКАЗІВКИ
для студентів

з дисципліни «Внутрішня медицина (в тому числі з ендокринологією)
студенти 4 курсу I, II, III медичних факультетів, V та VI факультетів по підготовці іноземних студентів

Цирози печінки

Харків 2016

KHARKOV NATIONAL MEDICAL UNIVERSITY DEPARTMENT

OF INTERNAL MEDICINE N3

METHODOLOGICAL RECOMMENDATIONS FOR STUDENTS

Liver cirrhoses

Kharkiv 2016

Practical class "Liver cirrhoses" (LC), 4 hours

Despite of considerable success in diagnosis of diseases of digestive tract sometimes it is impossible to make a certain diagnosis on practice. This basically applies to the chronic diffuse diseases of liver (CDDL)-(LC) that occur with relatively nonspecific clinical symptoms (discomfort in the right upper quadrant, fatigue, jaundice, hepatomegaly, biochemical changes, etc.). Often a doctor, not being able to perform morphological study of the liver, i.e. the fine needle biopsy (FNB), formulates diagnosis empirically, and thus diagnosis has insufficient evidentiary level. About 2 million people die annually all over the world from cirrhosis and viral hepatocarcinoma. Mortality associated with alcoholic LC in developed countries is similar to that of viral LC.

Aims of teaching:

- To teach students to recognize basic symptoms and syndromes of LC.
- To acquaint students with physical methods of study in CL.
- To acquaint students with methods of study which are used for the diagnosis of LC, indications and contra-indications for their conducting, techniques of their performance, diagnostic value of each of them.
- To teach students to interpret the results of the conducted studies independently.
- To teach students to recognize and diagnose complications of LC.
- To teach students to prescribe treatment for LC.

What should a student know?

- Incidence of LC.
- Etiologic factors of LC.
- Pathogenesis of LC.
- Basic clinical syndromes of LC.
- General and alarm symptoms of CL.
- Physical symptoms of LC.
- Diagnosis of LC.
- Morphological studies of liver (biopsy) in LC.
- Instrumental methods of LC diagnosis.
- Differential diagnosis of LC.
- Classification of LC.
- Complications of LC.
- Treatment of LC (change of lifestyle, a balanced diet, medicinal therapy).

What should a student be able to do?

- To distinguish basic clinical and physical syndromes of LC.
- To interpret the results of biochemical and immunoenzyme assays.
- To interpret the data of liver biopsy.
- To interpret the results of instrumental methods of study of liver.
- To estimate the accordance of a certain patient to the criteria of successful therapy.
- To perform the differential diagnosis.
- To prescribe the treatment to patients with LC.

The list of practical skills, which a student should possess:

- Inspection of abdomen.
- Examination of abdomen.
- Superficial palpation of stomach.
- Deep methodical sliding palpation of abdomen according to Obraztsov- Strazhesko method.
- Examination of skin and mucosa.
- Physical data of liver inspection.

Topics content:

LIVER CIRRHOSIS

Cirrhosis represents the final common histologic pathway for a wide variety of chronic liver diseases. The term cirrhosis was first introduced by Laennec in 1826. It is derived from the Greek term *scirrhus* and refers to the orange or tawny surface of the liver seen at autopsy.

Cirrhosis is defined histologically as a diffuse hepatic process characterized by fibrosis and the conversion of normal liver architecture into structurally abnormal nodules. The progression of liver injury to cirrhosis may occur over weeks to years. Indeed, patients with hepatitis C may have chronic hepatitis for as long as 40 years before progressing to cirrhosis.

Etiology

Most common causes of cirrhosis are:

- Chronic viral hepatitis (B or C)
- Alcoholic liver disease
- Non-alcoholic fatty liver disease
- Immune
  - Primary sclerosing cholangitis
  - Autoimmune liver disease
- Biliary
  - Primary biliary cirrhosis
  - Secondary biliary cirrhosis
  - Cystic fibrosis
- Genetic
  - Haemochromatosis
  - Wilson's disease
  - $Alpha_1$-antitrypsin deficiency
- Cryptogenic (unknown—15%)
- Chronic venous outflow obstruction

Pathophysiology

Many forms of liver injury are marked by fibrosis, which is defined as an excess deposition of the components of the extracellular matrix (ie, collagens, glycoproteins, proteoglycans) in the liver. This response to liver injury potentially is reversible. By contrast, in most patients, cirrhosis is not a reversible process.

The development of hepatic fibrosis reflects an alteration in the normally balanced processes of extracellular matrix production and degradation. The extracellular matrix, the normal scaffolding for hepatocytes, is composed of collagens (especially types I, III, and V), glycoproteins, and proteoglycans.

Stellate cells, located in the perisinusoidal space, are essential for the production of extracellular matrix. Stellate cells, which were once known as Ito cells, lipocytes, or perisinusoidal cells, may become activated into collagen-forming cells by a variety of paracrine factors. Such factors may be released by hepatocytes, Kupffer cells, and sinusoidal endothelium following liver injury. Distruction of the liver architecture causes distortion and loss of the normal hepatic vasculature with with the development of portosystemic vascular shunts and the formation of nodules. Cirrhosis evolves slowly over years to decades, and normally continues to progress even after removal of etiological agent. Cirrhosis is a histological diagnosis characterized by diffuse hepatic fibrosis and nodule formation. These changes usually affect the whole liver, but in primary biliary cirrhosis they can be patchy.
Cirrhosis can be classified histologically into two types:

- *Micronodular cirrhosis*, characterized by small nodules about 1 mm in diameter
- *Macronodular cirrhosis*, characterized by larger nodules of various size. Areas of previous collapse of the liver architecture are evidenced by large fibrous scars.

Clinical presentation

The clinical features of cirrhosis result from hepatocyte dysfunction, portosystemic shunting, and portal hypertension. Patients may have no symptoms for long periods. The onset of symptoms may be insidious or, less often, abrupt. Weakness, fatigue, disturbed sleep, muscle cramps, and weight loss are common. In advanced cirrhosis, anorexia is usually present and may be extreme, with associated nau- sea and occasional vomiting. Abdominal pain may be present and is related either to hepatic enlargement and stretching of Glisson capsule or to the presence of ascites. Menstrual abnormalities (usually amenorrhea), erectile dysfunction, loss of libido, sterility, and gynecomastia in men may occur. Hematemesis is the presenting symptom in 15–25%.
Skin manifestations consist of spider angioma (invariably on the upper half of the body), palmar erythema (mottled redness of the thenar and hypothenar eminences), and Dupuytren contractures. Evidence of vitamin deficiencies (glossitis and cheilosis) is common. Weight loss, wasting, and the appearance of chronic illness are present. Jaundice—usually not an initial sign—is mild at first, increasing in severity during the later stages of the disease. In 70% of cases, the liver is enlarged, pal- pable, and firm if not hard and has a sharp or nodular edge; the left lobe may predominate. Splenomegaly is present in 35–50% of cases and is associated with an increased risk of complications of portal hypertension. The superficial veins of the abdomen and thorax are dilated, reflecting the intrahepatic obstruction to portal blood flow, as do rectal varices. The abdominal wall veins fill from below when compressed. Ascites, pleural effusions, peripheral edema, and ecchymoses are late find- ings. Encephalopathy characterized by day–night reversal, asterixis, tremor, dysarthria, delirium, drowsiness, and ultimately coma also occurs late except when precipitated by an acute hepatocellular insult or an episode of gastrointestinal bleeding. Fever may be a presenting symptom in up to 35% of patients and usually reflects associated alcoholic hepatitis, spontaneous bacterial peritonitis, or intercurrent infection.

Portal Hypertension

The normal liver has the ability to accommodate large changes in portal blood flow without appreciable alterations in portal pressure. Portal Hypertension results from a combination of increased portal venous inflow and increased resistance to portal blood flow. Patients with cirrhosis demonstrate increased splanchnic arterial flow and, accordingly, increased splanchnic venous inflow into the liver. Increased splanchnic arterial flow is explained partly by decreased peripheral vascular resistance and increased cardiac output in the patient with cirrhosis. Nitric oxide appears to be the major driving force for this phenomenon. Increased resistance across the sinusoidal vascular bed of the liver is caused by fixed factors (formation of regenerating nodules and, after the production of collagen by activated stellate

cells, deposition of the collagen within the space of Disse) and dynamic factors (vasoconstriction of the hepatic sinusoid).

The portal hypertension of cirrhosis is caused by the disruption of hepatic sinusoids. However, portal hypertension may be observed in a variety of noncirrhotic conditions.

Portal hypertension can have prehepatic, intrahepatic, or posthepatic causes. Budd-Chiari syndrome, a posthepatic cause, is characterized by the following symptoms:

- Hepatomegaly
- Abdominal pain
- Ascites

Ascites is suggested by the following findings on physical examination:

- Abdominal distention
- Bulging flanks
- Shifting dullness
- Elicitation of a "puddle sign" in patients in the knee-elbow position

Diagnosis

During angiography, a catheter is placed selectively via either the transjugular or transfemoral route into the hepatic vein to measure portal pressure.

Hepatic encephalopathy

The symptoms of hepatic encephalopathy may range from mild to severe and may be observed in as many as 70% of patients with cirrhosis. Symptoms are graded on the following scale:

- Grade 0 - Subclinical; normal mental status but minimal changes in memory, concentration, intellectual function, coordination
- Grade 1 - Mild confusion, euphoria or depression, decreased attention, slowing of ability to perform mental tasks, irritability, disorder of sleep pattern (ie, inverted sleep cycle)
- Grade 2 - Drowsiness, lethargy, gross deficits in ability to perform mental tasks, obvious personality changes, inappropriate behavior, intermittent disorientation (usually with regard to time)
- Grade 3 - Somnolent, but arousable state; inability to perform mental tasks; disorientation with regard to time and place; marked confusion; amnesia; occasional fits of rage; speech is present but incomprehensible
- Grade 4 - Coma, with or without response to painful stimuli

Diagnosis

An elevated arterial or free venous serum ammonia level is the classic laboratory abnormality reported in patients with hepatic encephalopathy.

Electroencephalography may be helpful in the initial workup of a patient with cirrhosis and altered mental status, when ruling out seizure activity may be necessary.

Computed tomography (CT) scanning and MRI studies of the brain may be important in ruling out intracranial lesions when the diagnosis of hepatic encephalopathy is in question.

Hepatorenal Syndrome

This syndrome represents a continuum of renal dysfunction that may be observed in patients with a combination of cirrhosis and ascites. Hepatorenal syndrome is caused by the vasoconstriction of large and small renal arteries and the impaired renal perfusion that results.

Hepatorenal syndrome progression may be slow (type II) or rapid (type I). Type I disease frequently is accompanied by rapidly progressive liver failure. Hemodialysis offers temporary support for such patients. These individuals are salvaged only by performance of liver transplantation. Exceptions to this rule are the patients with fulminant hepatic failure (FHF) or severe alcoholic hepatitis who spontaneously recover liver and kidney function. In type II hepatorenal syndrome, patients may have stable or slowly progressive renal insufficiency. Many such patients develop ascites that is resistant to

management with diuretics.

Diagnosis

Hepatorenal syndrome is diagnosed when a creatinine clearance rate of less than 40 mL/min is present or when a serum creatinine level of greater than 1.5 mg/dL, a urine volume of less than 500 mL/day, and a urine sodium level of less than 10 mEq/L are present. Urine osmolality is greater than plasma osmolality.

Diagnosis

Laboratory abnormalities are either absent or minimal in early or compensated cirrhosis.

- Anemia, a frequent finding, is often macrocytic; causes include suppression of erythropoiesis by alcohol as well as folate deficiency, hemolysis, hypersplenism, and occult or overt blood loss from the gastrointestinal tract.
- The white blood cell count may be low, reflecting hypersplenism, or high, suggesting infection;
- thrombocytopenia, the most common cytopenia in cirrhotic patients, is secondary to alcoholic marrow suppression, sepsis, folate deficiency, or splenic sequestration. Prolongation of the prothrombin time may result from reduced levels of clotting factors (except factor VIII). However, bleeding risk correlates poorly with the prothrombin time because of concomitant abnormalities of fibrinolysis, and among hospitalized patients under age 45, cirrhosis is associated with an increased risk of venous thromboembolism.

Blood chemistries reflect hepatocellular injury and dysfunction, manifested by modest elevations of AST and alkaline phosphatase and progressive elevation of the bilirubin. Serum albumin decreases as the disease progresses; γ-globulin is increased and may be as high as in autoimmune hepatitis. The risk of diabetes mellitus is increased in patients with cirrhosis, particularly when associated with HCV infection, alcoholism, hemochromatosis, or NAFLD. Vitamin D deficiency has been reported in as many as 91% of patients with cirrhosis. Patients with alcoholic cirrhosis may have elevated serum cardiac troponin I and brain natriuretic peptide levels. Blunted cardiac inotropic and chronotropic responses to exercise, stress, and drugs, as well as systolic and diastolic ventricular dysfunction (“cir- rhotic cardiomyopathy”) and prolongation of the QT interval in the setting of a hyperkinetic circulation, are common in cirrhosis of all causes, but overt heart failure is rare in the absence of alcoholism. Relative adrenal insufficiency appears to be common in patients with advanced cirrhosis, even in the absence of sepsis.

Liver biopsy may show inactive cirrhosis (fibrosis with regenerative nodules) with no specific features to suggest the underlying cause. Alternatively, there may be additional features of alcoholic liver disease, chronic hepatitis, NASH, or other specific causes of cirrhosis. Combinations of routine blood tests (eg, AST, platelet count), including the FibroSure or FibroMax tests, and serum markers of hepatic fibrosis (eg, hyaluronic acid, amino-terminal propeptide of type III collagen, tissue inhibitor of matrix metalloproteinase 1) are potential alternatives to liver biopsy for the diagnosis or exclusion of cirrhosis.

Imaging

Ultrasonography is helpful for assessing liver size and detecting ascites or hepatic nodules, including small hepatocellular carcinomas. Together with a Doppler study, it may establish patency of the splenic, portal, and hepatic veins. Hepatic nodules are characterized further by contrast-enhanced CT or MRI. Nodules suspicious for malignancy may be biopsied under ultrasound or CT guidance.

Other Examinations

Esophagogastroduodenoscopy confirms the presence of varices and detects specific causes of bleeding in the esophagus, stomach, and proximal duodenum. Liver biopsy may be performed by laparoscopy or, in patients with coagulopathy and ascites, by a transjugular approach. In selected cases, wedged hepatic vein pressure measurement may establish the presence and cause of portal hypertension. Transient

elastography, which uses ultrasound to determine liver stiffness, and magnetic resonance elastography are available in a limited number of centers as noninvasive tests for cirrhosis and portal hypertension.

Assessment of the Severity of Cirrhosis

Child-Turcotte-Pugh Scoring System for Cirrhosis

Clinical Variable	1 Point	2 Points	3 Points
Encephalopathy	None	Grade 1-2	Grade 3-4
Ascites	Absent	Slight	Moderate or large
Bilirubin (mg/dL)	< 2	2-3	>3
Bilirubin in PBC* or PSC** (mg/dL)	< 4	4-10	10
Albumin (g/dL)	>3.5	2.8-3.5	< 2.8
Prothrombin time(seconds prolonged or INR)	< 4 s or INR < 1.7	4-6 s or INR 1.7-2.3	>6 s or INR >2.3

*PBC = Primary biliary cirrhosis
**PSC = Primary sclerosing cholangitis

Child Class A = 5-6 points, Child Class B = 7-9 points, Child Class C = 10-15 points

Epidemiologic work shows that the Child-Turcotte-Pugh (CTP) score may predict life expectancy in patients with advanced cirrhosis. A CTP score of 10 or greater is associated with a 50% chance of death within 1 year.
Model for End-Stage Liver Disease (MELD) scoring system exists to assess the relative severity of patients' liver disease. Patients may receive a MELD score of 6-40 points. The 3-month mortality statistics are associated with the following MELD scores. The MELD is more difficult to calculate at the bedside, but unlike the CTP system, includes renal function; if this is impaired it is known to be a poor prognostic feature in end-stage liver disease.

Complications

Upper gastrointestinal tract bleeding may occur from varices, portal hypertensive gastropathy, or gastroduodenal ulcer. Varices may also result from portal vein thrombosis, which may complicate cirrhosis. Liver failure may be precipitated by alcoholism, surgery, and infection. Hepatic Kupffer cell (reticuloendothelial) dysfunction and decreased opsonic activity lead to an increased risk of systemic infection, which increase mortality fourfold. Osteoporosis occurs in 12–55% of patients with cirrhosis. The risk of hepatocellular carcinoma is increased greatly in persons with cirrhosis.

Treatment

The most important principle of treatment is abstinence from alcohol. The diet should be palatable, with adequate calories (25–35 kcal/kg body weight per day in those with compensated cirrhosis and 35–40 kcal/kg/d in those with malnutrition) and protein (1–1.2 g/kg/d in those with compensated cirrhosis and 1.5 g/kg/d in those with malnutrition) and, if there is fluid retention, sodium restriction. In the presence of hepatic encephalopathy, protein intake should be reduced to no less than 60–80 g/d. Vitamin supplementation is desirable. Patients with cirrhosis should receive the HAV, HBV, and pneumococcal vaccines and a yearly influenza vaccine.

Specific medical therapies may be applied to many liver diseases in an effort to diminish symptoms and to prevent or forestall the development of cirrhosis. Examples of such treatments include the following:

- Prednisone and azathioprine - For autoimmune hepatitis
- Interferon and other antiviral agents - For hepatitis B and C
- Phlebotomy - For hemochromatosis
- Ursodeoxycholic acid - For primary biliary cirrhosis
- Trientine and zinc - For Wilson disease

Once cirrhosis develops, treatment is aimed at the management of complications as they arise. Examples include the following:

- Hepatorenal syndrome - Kidney function usually recovers when patients with cirrhosis and hepatorenal syndrome undergo liver transplantation; patients with early hepatorenal syndrome may be salvaged by aggressive expansion of intravascular volume with albumin and fresh frozen plasma and by avoidance of diuretics
- Hepatic encephalopathy - Pharmacologic treatment includes the administration of lactulose and antibiotics
- Ascites - Treatment can include sodium restriction and the use of diuretics, large-volume paracentesis, and shunts (peritoneovenous, portosystemic, transjugular intrahepatic portosystemic)

Ascites

Salt restriction is the first line of therapy. In general, patients begin with a diet containing less than 2000 mg of sodium daily. Some patients with refractory ascites require a diet containing less than 500 mg of sodium daily.

Diuretics should be considered the second line of therapy. Spironolactone blocks the aldosterone receptor at the distal tubule. It is dosed at 50-300 mg once daily. Adverse effects of spironolactone include hyperkalemia, gynecomastia, and lactation. Other potassium-sparing diuretics, including amiloride and triamterene, may be used as alternative agents, especially in patients complaining of gynecomastia. Furosemide may be used as a solo agent or in combination with spironolactone. The drug blocks sodium reuptake in the loop of Henle. It is dosed at 40-240 mg daily in 1-2 divided doses. Patients infrequently need potassium repletion when furosemide is dosed in combination with spironolactone. Aggressive diuretic therapy in hospitalized patients with massive ascites can safely induce a weight loss of 0.5-1kg daily, provided that patients undergo careful monitoring of renal function. Diuretic therapy should be held in the event of electrolyte disturbances, azotemia, or induction of hepatic encephalopathy.

Albumin may increase the efficacy and safety of diuretics.

Large-volume *paracentesis* is thought to be safe in patients with peripheral edema and in patients not currently treated with diuretics.

Hepatic encephalopathy

Lactulose is helpful in patients with an acute onset of severe encephalopathy symptoms and in patients with milder, chronic symptoms. This nonabsorbable disaccharide stimulates the passage of ammonia from tissues into the gut lumen and inhibits intestinal ammonia production. Initial lactulose dosing is 30 mL orally once or twice daily. Dosing is increased until the patient has 2-4 loose stools per day. Dosing should be reduced if the patient complains of diarrhea, abdominal cramping, or bloating.

Neomycin and other antibiotics (eg, metronidazole, oral vancomycin, paromomycin, oral quinolones) serve as second-line agents. They work by decreasing the colonic concentration of ammoniagenic bacteria. Neomycin dosing is 250-1000 mg orally 2-4 times daily. Treatment with neomycin may be complicated by ototoxicity and nephrotoxicity.

Other chemicals capable of decreasing blood ammonia levels are *L-ornithine L-aspartate* and sodium benzoate.

Low-protein diets were recommended routinely in the past for patients with cirrhosis. High levels of aromatic amino acids contained in animal proteins were believed to lead to increased blood levels of the false neurotransmitters tyramine and octopamine, with resultant worsening of encephalopathic symptoms. In this author's experience, the vast majority of patients can tolerate a protein-rich diet (>1.2 g/kg daily) that includes well-cooked chicken, fish, vegetable protein, and, if needed, protein supplements. Protein restriction is rarely necessary in patients with symptoms of chronic encephalopathy. Many patients with cirrhosis have protein-calorie malnutrition at baseline; the routine restriction of dietary protein intake increases their risk for worsening malnutrition.

Zinc deficiency

Zinc deficiency commonly is observed in patients with cirrhosis. Treatment with zinc sulfate at 220 mg orally twice daily may improve dysgeusia and can stimulate appetite. Furthermore, zinc is effective in the treatment of muscle cramps and is adjunctive therapy for hepatic encephalopathy.

Pruritus

Pruritus is a common complaint in cholestatic liver diseases (eg, primary biliary cirrhosis) and in noncholestatic chronic liver diseases (eg, hepatitis C). Although increased serum bile acid levels once were thought to be the cause of pruritus, endogenous opioids are more likely to be the culprit pruritogen. Mild itching complaints may respond to treatment with antihistamines and topical ammonium lactate.

Osteoporosis

Supplementation with calcium and vitamin D is important in patients at high risk for osteoporosis, especially patients with chronic cholestasis or primary biliary cirrhosis and patients receiving corticosteroids for autoimmune hepatitis.

Liver transplantation

Patients should be referred for consideration for liver transplantation after the first signs of hepatic decompensation.

Patient Monitoring

Patients with cirrhosis should undergo routine follow-up monitoring of their complete blood count, renal and liver chemistries, and prothrombin time. The policy is to monitor stable patients 3-4 times per year (surveillance of esophageal varices, surveillance for hepatocellular carcinoma).

The control of an initial level of knowledge:

1. Which of the listed below factors promote the development of liver cirrhosis?

   A. Viruses, alcohol abuse
   B. Bacteria, fungi
   C. Influence of vitamin supplements
   D. Rickettsia, mycoplasma
   E. Gallbladder diseases

2. What clinical symptoms are typical for the initial stage of liver cirrhosis?
   A. Nausea, vomiting, loss of body weight
   B. Loss of body weight, meteorism, feeling of heaviness in right hypochondrium
   C. Bitter taste in mouth, heartburn
   D. Enlargement of a liver, spleen, liver stigmata
   E. Xanthelasma, palmar erythema, ascitis

3. What causes the enlargement of a spleen in liver cirrhosis?
   A. Venous stasis
   B. Diffuse fibrosis of a red pulp
   C. Portal hypertension
   D. All of the mentioned above factors
   E. Increased number of arterio-venous shunts

4. What changes of CBC are typical for hypersplenism?
   A. Reduction of number of erythrocytes, thrombocytes , leukocytes
   B. Reduction of number of erythrocytes, leukocytes, increased number of thrombocytes
   C. Lymphocytosis, leucopenia
   D. Eosinopenia, increase of ESR
   E. Lymphocytosis, leukocytosis, reduction of eosinophils number

5. What changes in blood are the most typical for liver cirrhosis?
   A. Iron-deficiency anemia
   B. B12- folic acid deficiency anemia
   C. Hemolytic anemia
   D. None of the listed
   E. All of the listed

6. What influences the rise of the body temperature in liver cirrhosis?
   A. Inflammatory changes in hepatocytes
   B. Inflammation of bile ducts
   C. Associated gastroduodenitis
   D. Passage of pyrogenic intestinal flora through the liver
   E. Associated cholecystitis

7. What biochemical changes are typical for the syndrome of cytolisis?

A. Increase of alkaline phosphatase, decrease of the common protein and cholesterol
B. Decrease of iron content and prothrombin in the blood serum, increase of cholesterol
C. Increase of AST, ALT, LDG, bilirubin
D. Increase of bilirubin, alkaline phosphatase, prothrombin
E. Decrease of prothrombin and transaminases, increase of bilirubin

8. What biochemical changes are typical for the syndrome of cholestasis?
A. Increase of cholesterol and alkaline phosphatase, decrease of fibrinogen
B. Decrease of cholesterol and bile acids, increase of unconjugated bilirubin
C. Increase of cholesterol, alkaline phosphatase, the conjugated bilirubin
D. Decrease of the general bilirubin, cholesterol, increase of transaminases
E. Decrease of alkaline phosphatase, increase of ceruloplasmin and albumin

9. What are the findings on palpation when examining the patient with liver cirrhosis?
A. Enlarged, firm, rounded edge
B. Enlarged, doughy, rounded edge
C. Reduced, bumpy, pointy end
D. Enlarged, firm, pointy end
E. Reduced, doughy, rounded edge

10. The syndrome of a portal hypertension is?
A. Enlargement of a liver, meteorism, skin itch
B. Enlargement of a liver and a spleen, jaundice
C. Enlargement of a liver, ascites, varicose veins
D. Reduction of a liver, edemas, jaundice
E. Enlargement of a liver, ascitis, edemas, cardiomyopathy

Correct answers:
1 A
2 B
3 D
4 A
5 C
6 D
7 C
8 C
9. D
10. C

Liver cirrhosis. The control of final level of knowledge

1. How many clinical stages are there in the course of hepatic coma?

A. 2
B. 3
C. 4
D. 1
E. None

2. What groups of medications are used for the treatment of liver cirrhosis?

A. Antibiotics, hepatoprotectors, vitamins
B. Hepatoprotectors, cytostatics, immunosuppressants
C. Hepatoprotectors,choleretics, spasmolytics
D. Hepatoprotectors, cholekinetics, anabolics
E. Sulfanilamides, hepatoprotectors , nitrates

3. What are the most informative methods for diagnosis of hepatic jaundice?

A. Biochemical blood assay
B. Duodenal probe
C. Cholecystography
D. Ultrasonography
E. Endoscopic retrograde pancreatocholangiography

4. What signs are the least typical for portal hypertension?

A. Development of collaterals
B. Hemorrhage from varicose veins
C. Ascites
D. Fever
E. Splenomegalia

5. The most probable sign of the hemorrhage from esophageal varices are:

A. Stomachache
B. Heartburn
C. Scarlet blood in emetic masses
D. Dark blood in emetic masses
E. Defecation of black color

6. The peculiarity of portal hypertension development in case of macronodular LC is:

A. It precedes the development of functional insufficiency of a liver
B. Occurs at exacerbation
C. Occurs early
D. Has stable course
E. All of the listed above are true

7. What medicines are prescribed for the treatment of ascites/edemas syndrome?

A. ACE inhibitors
B. Diuretics

C. Glucocorticoids
D. Interferons

8. Complications of LC include:

A. Chronic constipation
B. Acute intestinal impassability
C. Hepatic coma
D. An acute gastric hemorrhage
E. Chronic diarrhea

9. The leading clinical syndrome in macronodular LC is:

A. The syndrome of hepatic-cellular insufficiency
B. The syndrome of a portal hypertension
C. The syndrom of a jaundice and cholestasis
D. Asthenovegetative syndrome
E. Mesenchymal -inflammatory syndrome

10. The indication to application of glucocorticosteroids in LC is:

A. Mesenchymal-inflammatory syndrome
B. Splenomegalia
C. Hemorrhage from the varicose veins of a gullet
D. Marked asthenovegetative syndrome
E. Jaundice

The final level of knowledge:

1C	**6. B**
2 B	**7. C**
3. A	**8. C**
4. D	**9. A**
5. D	**10. A**

Case-based questions.

1. The patient, who had suffered from LC for 5years, complaints on marked fatigue, skin pallor, cold sweats, thirst, vomiting with a touch of dark red blood. What is the most probable reason for occurrence of this type of hemorrhage?
   A. Portal hypertension.
   B. Thrombosis of hepatic veins
   C. Malignization
   D. Heart failure
   E. Pulmonary embolism

2. The patient had been suffering from viral hepatitis B during past 4 years. He reports an alcohol abuse for many years. He complains on heartburn and burning pain behind the breastbone, which he has been feeling during the last 2 months. There was a vomiting with fresh dark blood in the morning after meals and lifting of weight. At examination – the skin is pale and wet, heartbeat rate - 92/min, BP 90/60 mm. Scleras are icteric, abdomen is enlarged due to ascites, hepatosplenomegalia. List the most probable reasons for the hemorrhage:

A. Achalasia of the esophagus
B. Malory-Weiss syndrome
C. Rupture of esophageal varices
D. Bud-Chiari syndrome
E. Duodenal ulcer

3. Patient with cirrhosis had recently complained on moderate pain in epigastrium, constant bloating, which increases after eating. Objective data: distended subcutaneous veins of abdomen, signs of free fluid in the abdomen, enlarged liver and spleen. Ultrasonography of abdomen: distention of portal vein, enlargement of liver and spleen. What kind of cirrhosis complication has developed in this patient?
   A. Peritonitis
   B. Dysbacteriosis
   C. Portal hypertension
   D. Hepatic failure
   E. Thrombosis of a portal vein

4. Patient has micronodular liver cirrhosis. During last 2 months he noticed the development of dyspnea, edemas of lower extremities, ascites. Patient was taking hepatoprotectors and glucocorticoids. What combination of medicines should be added to the treatment, which is already conducted?

A. Spironolactone + ascorutine
B. Nerabol + furosemide
C. Lidokain + hydrochlorothiazide
D. Albumin + ascorutine
E. Spironolactone + furosemide

5. A 49 years old man is the handicapped person of the II group. He has been treated for liver cirrhosis for several years. During the last month his abdomen became noticeably enlarged, the general weakness has increased. During 2 weeks he has been taking furosemide on daily basis. He was directed to the hospital for treatment. What changes can be revealed in electrolyte blood assay?

A. Hypocalcemia
B. Hypokalemia
C. Hypernatremia
D. Hypercalcemia
E. Hypokalemia

6. A 46 years old man complains on vomiting containing bright red blood. He had been suffering from micronodular liver cirrhosis of viral etiology for 5 years. During last 6 months there is an enlargement of the abdomen due to ascites. What should be the first measure of the urgent therapy?

A. Vasopressin 20 units i/v
B. Cordiamin 2 ml. i/m
C. Mesatone 1 % - 2 ml i/m
D. Prednisolone 30 mg i/v
E. Swallowing pieces of ice.

7. A woman of 42 years old suffers from micronodular cryptogenic liver cirrhosis. During the last week her condition has worsened: there were cramps, dizziness, and increase of the jaundice. What laboratory assay should be done in order to explain the reason of deterioration of her condition?

A. Determination of ammonia level in serum.
B. Determination of cholesterol level in blood.
C. Determination of α-fetoprotein contents in blood
D. Determination of ALT and AST
E. Determination of alkaline phosphatase level

8. A patient with a background of liver cirrhosis, after the use of alcohol complains on headache, vomiting, disgust for meals, sleeplessness, jaundice, hepatic smell from a mouth, and bloating. What complication of liver cirrhosis has developed?

A. Hepatic failure
B. Hemorrhage from varices
C. Portal hypertension
D. Acute stomach ulcer
E. Mesenteric venous thrombosis

9. A patient, who had been suffering from LC for a long time, recently complains on the moderate pain in epigastrium, bloating after meals. Objective data: the distention of subcutaneous abdominal veins, the signs of a free liquid in the abdominal cavity, the enlargement of the liver

and the spleen. Ultrasonography: distended portal vein, enlargement of liver and spleen. What is the most serious complication of LC in this patient?

A. Portal vein thrombosis
B. Hepatic failure
C. Portal hypertension
D. Peritonitis
E. Disbacteriosis of intestines

10. A woman of 24 years old complains on intensive skin itch, which worsens in the evenings and a dull pain in right side of the abdomen. She became sick 2 years ago after delivery. Objective data: jaundice, xanthelasmas on the eye lids. The liver is 6 cm enlarged above normal, dense, the edge is smooth, painless. The spleen is 3 cm enlarged above normal. The reaction to a superficial antigen of hepatitis B virus is negative. What form of a liver disease does the patient suffer from?

A. Fatty hepatosis
B. Chronic hepatitis
C. Chronic cholecystitis
D. Hemochromatosis
E. Primary biliary cirrhosis

Correct answers:

1. A	**5. B**	**9.C**
2. B	**6. A**	**10. E**
3. C	**7. D**	
4. E	**8. B**	

Control questions.

1. Definition of LC.
2. The basic clinical syndromes of LC
3. The characteristics of biochemical syndromes of LC
4. The characteristics of physical data of LC.
5. The peculiarities of viral LC.
6. The peculiarities of toxic LC
7. Methods of diagnosis of LC.
8. Complications of LC.
9. Principles of treatment of viral LC
10. Principles of treatment of autoimmune LC
11. Lifestyle changes and diet in LC
12. Pharmacological therapy in LC
13. Prevention of LC

Practical tasks.

1. To supervise a patient with LC
2. To give interpretation for the laboratory assays.
3. To give interpretation for the insrtumental methods of study.
4. To perform differential diagnosis of LC
5. To list complications of LC
6. To write recipes concerning therapy of LC.

The report of clinical examination of the patient (the uniform form)

Name, Surname_____

Age_____ **Profession**_____

Complaints_____

Anamnesis morbi

Last exacerbation_____

Anamnesis morbi

1.

Results of physical examination of the patient:

The preliminary diagnosis:

The examination plan:

Results of additional studies:

_____
_____
_____
_____
_____

Substantiation of the clinical diagnosis:
_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

The clinical diagnosis:
Main disease: _____
_____

Accompanying diseases:
_____
_____
_____

Complication
_____
_____

Treatment:
1. Regimen _____
2. Diet _____
3. _____
4. _____
5. _____

Further reading:

1. Davidson's "Principles and Practice of Medicine" 21st edition, Alimentary tract and pancreatic disease, p. 835-919.
2. Current Medical Diagnosis and Treatment, Gastrointestinal disorders, 2014, p. 564-662
3. Harrison's, Principles of Internal Medicine, 19th edition, Gastoenterology and Hepatology, p.257-398
4. Beers MH, Berkow R, eds. Merck Manual Second Home Edition 2004–2005. "Clinical Manifestations of Liver Disease." Available at: http://www.merck.com/mmhe/sec10/ch135/ch135e.html?qt=portal%20hypertension&alt=sh.
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Інформаційні ресурси

сайт кафедри внутрішньої медицини № 3 ХНМУ http://www. vnmed3.kharkiv.ua/, встановлене інформаційно-освітнє середовище Moodle на піддомен сайта http://distance-training. vnmed3.kharkiv.ua

Методична вказівка складена: асистентом А.К. Журавльовою

Методична вказівка переглянута і затверджена на засіданні кафедри: _____

З доповненнями (змінами) _____

Завідувач кафедри Л.В. Журавльова