FUNCTIONAL ANATOMY OF LIVER AND BILIARY SYSTEM AND FOCUSING ON A CASE REPORT: METABOLIC LIVER DISEASE

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ABSTRACT

Metabolic liver diseases comprise a heterogeneous group of disorders characterized by abnormalities in hepatic metabolism, often leading to progressive liver injury. We report a case of metabolic liver disease presenting with nonspecific symptoms and abnormal liver function tests. This case highlights the importance of early recognition, systematic evaluation, and timely management to prevent long-term complications.

Liver is a dual organ having both secretary and excretory functions. It is the largest gland in the body, weighing about 1.5 kg in man. It is located in the upper and right side of the abdominal cavity, immediately beneath dia phragm.Fatty liver disease (now often called MASLD - Metabolic dysfunction-associated steatotic liver disease) is when excess fat builds up in the liver, often without symptoms in early stages, but can progress to inflammation (MASH/NASH) and liver damage, linked to obesity, diabetes, and alcohol use. Treatment focuses on lifestyle changes like weight loss, healthy diet, exercise, and avoiding alcohol, with potential to reverse damage

KEY WORDS; Metabolic liver disease, Health, Management, Liver

INTRODUCTION

Metabolic liver diseases include inherited and acquired conditions such as non-alcoholic fatty liver disease (NAFLD), Wilson disease, hemochromatosis, and alpha-1 antitrypsin deficiency. These disorders are increasingly recognized as major causes of chronic liver disease worldwide. Early diagnosis is essential, as many metabolic liver diseases are treatable and progression to cirrhosis or liver failure can be prevented.

FUNCTIONAL ANATOMY OF LIVER AND BILIARY SYSTEM

Liver

Hepatic Lobes

Liver is made up of many lobes called hepatic lobes (Fig. 40.1). Each lobe consists of many lobules called hepatic lobules.

Hepatic Lobules

Hepatic lobule is the structural and functional unit of liver. There are about 50,000 to 100,000 lobules in the liver. The lobule is a honeycomb-like structure and it is made up of liver cells called hepatocytes.

Hepatocytes and Hepatic Plates

Hepatocytes are arranged in columns, which form the hepatic plates. Each plate is made up of two columns of cells. In between the two columns of each plate lies a bile canaliculus . In between the neighboring plates, a blood space called sinusoid is present. Sinusoid is lined by the endothelial cells. In between the endothelial cells some special macrophages called Kupffer cells are present.**PortalTriads**

Each lobule is surrounded by many portal triads. Each portal triad consists of three vessels:

1. A branch of hepatic artery
2. A branch of portal vein
3. A tributary of bile duct.

BILIARY SYSTEM

Biliary system or extrahepatic biliary apparatus is formed by gallbladder and extrahepatic bile ducts (bile ducts outside the liver). Right and left hepatic bile ducts which come out of liver join to form common hepatic duct. It unites with the cystic duct from gallbladder to form common bile duct (Fig.). All these ducts have similar structures.

Common bile duct unites with pancreatic duct to form the common hepatopancreatic duct or ampulla of Vater, which opens into the duodenum. There is asphincter called sphincter of Oddi at the lower part of common bile duct, before it joins the pancreatic duct. It is formed by smooth muscle fibers of common bile duct. It is normally kept closed; so the bile secreted from liver enters gallbladder where it is

stored. Upon appropriate stimulation, the sphincter opens and allows flow of bile from gallbladder into the intestine.

BLOOD SUPPLY TO LIVER

Liver receives maximum blood supply of about 1,500 mL/minute. It receives blood from two sources, namely the hepatic artery and portal vein.

HEPATIC ARTERY

Hepatic artery arises directly from aorta and supplies oxygenated blood to liver. After entering the liver, the hepatic artery divides into many branches. Each branch enters a portal triad.

PORTAL VEIN

Portal vein is formed by superior mesenteric vein and splenic vein. It brings deoxygenated blood from stomach, intestine, spleen and pancreas. Portal blood is rich in monosaccharides and amino acids. It also contains bile salts, bilirubin, urobilinogen and GI hormones.

However, the oxygen content is less in portal blood. Flow of blood from intestine to liver through portal vein is known as enterohepatic circulation. The blood from hepatic artery mixes with blood from portal vein in hepatic sinusoids. Hepatic cells obtain oxygen and nutrients from the sinusoid.

HEPATIC VEIN

Substances synthesized by hepatic cells, waste products and carbon dioxide are discharged into sinusoids. Sinusoids drain them into central vein of the lobule. Central veins from many lobules unite toform bigger veins, which ultimately form hepatic veins (right and left) which open into inferior vena cava.

SECRETION OF BILE

Bile is secreted by hepatocytes. The initial bile secreted by hepatocytes contains large quantity of bile acids, bile pigments, cholesterol, lecithin and fatty acids. From hepatocytes, bile is released into canaliculi. From here, it passes through small ducts and hepatic ducts and reaches the common hepatic duct. From common hepatic duct, bile is diverted either directly into the intestine or into the gallbladder. Sodium, bicarbonate and water are added to bile when it passes through the ducts. These substances are secreted by the epithelial cells of the ducts. Addition of sodium, bicarbonate and water increases the total quantity of bile.

STORAGE OF BILE

Most of the bile from liver enters the gallbladder, where it is stored. It is released from gallbladder into the intestine whenever it is required. When bile is stored in gallbladder, it undergoes many changes both in quality and quantity such as:

1. Volume is decreased because of absorption of a large amount of water and electrolytes (except calcium and potassium)
2. Concentration of bile salts, bile pigments, cholesterol, fatty acids and lecithin is increased because of absorption of water and electrolytes
3. The pH is decreased slightly
4. Specific gravity is increased
5. Mucin is added to bile .

BILE SALTS

Bile salts are the sodium and potassium salts of bile acids, which are conjugated with glycine or taurine.

FORMATION OF BILE SALTS

Bilesalts are formed from bile acids. There are two primary bile acids in human, namely cholic acid and chenodeoxycholic acid, which are formed in liver and enter the intestine through bile. Due to the bacterial action in the intestine, the primary bile acids are converted into secondary bile acids: Cholic acid → deoxycholic acid Chenodeoxycholic acid → lithocholic acid Secondary bile acids from intestine aretransported back to liver through enterohepatic circulation. In liver, the secondary bile acids are conjugated with glycine (amino acid) or taurin (derivative of an amino acid) and form conjugated bile acids, namely glycocholic acid and taurocholic acids. These bile acids combine with sodium or potassium ions to form the salts, sodium or potassium glycocholate and sodium or potassium taurocholate

FUNCTIONS OF BILE SALTS

Bile salts are required for digestion and absorption of fats in the intestine. The functions of bile salts are:

1.Emulsification of Fats Emulsification is the process by which the fat globules are broken down into minute droplets and made in the form of a milky fluid called emulsion in small intestine, by the action of bile salts. Lipolytic enzymes of GI tract cannot digest the fats directly because the fats are insoluble in water due to the surface tension.

2.Absorption of Fats Bile salts help in the absorption of digested fats from intestine intoblood. Bile salts combine with fats and make complexes of fats called micelles. The fats in the form of micelles can be absorbed easily.

3. Choleretic Action Bile salts stimulate the secretion of bile from liver. This action is called choleretic action.

4. Laxative Action Laxative is an agent which induces defecation. Bile salts act as laxatives by stimulating peristaltic movements of the intestine.

5. Prevention of Gallstone Formation Bile salts prevent the formation of gallstone by keeping the cholesterol and lecithin in solution. In the absence of bile salts, cholesterol precipitates along with lecithin and forms gallstone.

BILE PIGMENTS

Bile pigments are the excretory products in bile. Bilirubin and biliverdin are the two bile pigments and bilirubin is the major bile pigment in human beings.

Bile pigments are formed during the breakdown of hemoglobin, which is released from the destroyed RBCs in the reticuloendothelial system.

FORMATION AND EXCRETION OF BILE PIGMENTS

Stages of formation and circulation of bile pigments:

1. Senile erythrocytes are destroyed in reticulo-endothelial system and hemoglobin is released from them
2. Hemoglobin is broken into globin and heme
3. Heme is split into iron and the pigment biliverdin
4. Iron goes to iron pool and is reused
5. First formed pigment biliverdin is reduced to bilirubin.
6. Bilirubin is released into blood from the reticulo-endothelial cells
7. In blood, the bilirubin is transported by the plasma protein, albumin. Bilirubin circulating in the blood is called free bilirubin or unconjugated bilirubin
8. Within few hours after entering the circulation, the free bilirubin is taken up by the liver cells
9. In the liver, it is conjugated with glucuronic acid to form conjugated bilirubin
10. Conjugated bilirubin is then excreted into intestine through bile.

FATE OF CONJUGATED BILIRUBIN

Stages of excretion of conjugated bilirubin:

1. In intestine, 50% of the conjugated bilirubin is converted into urobilinogen by intestinal bacteria. First the conjugated bilirubin is deconjugated into free bilirubin, which is later reduced into urobilinogen.
2. Remaining 50% of conjugated bilirubin from intestine is absorbed into blood and enters the liver through portal vein (enterohepatic circulation). From liver, it is re-excreted in bile
3. Most of the urobilinogen from intestine enters liver via enterohepatic circulation. Later, it is reexcreted through bile
4. About 5% of urobilinogen is excreted by kidney through urine. In urine, due to exposure to air, the urobilinogen is converted into urobilin by oxidation
5. Some of the urobilinogen is excreted in feces as stercobilinogen. In feces, stercobilinogen is oxidized to stercobilin.

NORMAL PLASMA LEVELS OF BILIRUBIN

Normal bilirubin (Total bilirubin) content in plasma is 0.5 to 1.5 mg/dL. When it exceeds 1mg/dL, the condition is called hyperbilirubinemia. When it exceeds 2 mg/dL, jaundice occurs

FUNCTIONS OF BILE

Most of the functions of bile are due to the bile salts.

1. DIGESTIVE FUNCTION
2. ABSORPTIVE FUNCTIONS
3. EXCRETORY FUNCTIONS
4. LAXATIVE ACTION
5. ANTISEPTIC ACTION
6. CHOLERETIC ACTION
7. MAINTENANCE OF pH IN GASTROINTESTINAL TRACT
8. PREVENTION OF GALLSTONE FORMATION
9. LUBRICATION FUNCTION
10. CHOLAGOGUE ACTION

FUNCTIONS OF LIVER

Liver is the largest gland and one of the vital organs of the body. It performs many vital metabolic and homeostatic functions, which are summarized below.

1. METABOLIC FUNCTION

Liver is the organ where maximum metabolic reactions such as metabolism of carbohydrates, proteins, fats, vitamins and many hormones are carried out.

2. STORAGE FUNCTION

Many substances like glycogen, amino acids, iron, folic acid and vitamins A, B12 and D are stored in liver.

3. SYNTHETIC FUNCTION

Liver produces glucose by gluconeogenesis. Itsynthesizes all the plasma proteins and other proteins (except immunoglobulins) such as clotting factors, complement factors and hormonebinding proteins. It also synthesizes steroids, somatomedin and heparin.

4. SECRETION OF BILE

Liver secretes bile which contains bile salts, bile pigments, cholesterol, fatty acids and lecithin. The functions of bile are mainly due to bile salts. Bile salts are required for digestion and absorption of fats in the intestine. Bile helps to carry away waste products and breakdown fats, which are excreted through feces or urine.

5. EXCRETORY FUNCTION

Liver excretes cholesterol, bile pigments, heavy metals (like lead, arsenic and bismuth), toxins, bacteria and virus (like that of yellow fever) through bile.

6. HEAT PRODUCTION

Enormous amount of heat is produced in the liver because of metabolic reactions. Liver is the organ where maximum heat is produced.

7. HEMOPOIETIC FUNCTION

In fetus (hepatic stage), liver produces the blood cells . It stores vitamin B12 necessary for erythropoiesis and iron necessary for synthesis 256 Section 4 t Digestive Systemof hemoglobin. Liver produces thrombopoietin that promotes production of thrombocytes.

8. HEMOLYTIC FUNCTION The senile RBCs after a lifespan of 120 days are destroyed by reticuloendothelial cells (Kupffer cells) of liver.

9. INACTIVATION OF HORMONES AND DRUGS Liver catabolizes the hormones such as growth hormone, parathormone, cortisol, insulin, glucagon and estrogen. It also inactivates the drugs, particularly the fatsoluble drugs. The fatsoluble drugs are converted into watersoluble substances, which are excreted through bile or urine.

10.DEFENSIVE AND DETOXIFICATION FUNCTIONS

Reticuloendothelial cells (Kupffer cells) of the liver play an important role in the defense of the body. Liver is also involved in the detoxification of the foreign bodies.

GALLBLADDER

Bile secreted from liver is stored in gallbladder. The capacity of gallbladder is approximately 50 mL. Gallbladder is not essential for life and it is removed (cholecystectomy) in patients suffering from gallbladder dysfunction. After cholecystectomy, patients do not suffer from any major disadvantage. In some species, gallbladder is absent.

FUNCTIONS OF GALLBLADDER

Major functions of gallbladder are the storage and concentration of bile.

1. Storage of Bile Bileis continuously secreted from liver. But it is released into intestine only intermittently and most of the bile is stored in gallbladder till it is required.
2. Concentration Bile Bile is concentrated while it is stored in gallbladder. The mucosa of gallbladder rapidly reabsorbs water and electrolytes, except calcium and potassium. But the bile salts, bile pigments, cholesterol and lecithin are not reabsorbed. So, the concentration of these substances in bile increases 5 to 10 times
3. AlterationofpHofBile The pH of bile decreases from 8 –8.6 to 7 –7.6 and it becomes less alkaline when it is stored in gallbladder.
4. Secretion of Mucin Gallbladder secretes mucin and adds it to bile. When bile is released into the intestine, mucin acts as a lubricant for movement of chyme in the intestine.
5. Maintenanceof Pressure in BiliarySystem Due to the concentrating capacity, gallbladder maintains a pressure of about 7 cm H2O in biliary system. This pressure in the biliary system is essential for the release of bile into the intestine.

FILLING AND EMPTYING OF GALLBLADDER

Usually, the sphincter of Oddi is closed during fasting and the pressure in the biliary system is only 7 cm H2O. Because of this pressure, the bile from liver enters the gallbladder. While taking food or when chyme enters the intestine, gallbladder contracts along with relaxation of sphincter of Oddi. Now, the pressure increases to about 20 cm H2O. Because of the increase in pressure, the bile from gallbladder enters the intestine. enters the intestine. Contraction of gallbladder is influenced by neural and hormonal factors.

1.Neural Factor : Stimulation of parasympathetic nerve

(vagus) causes contraction of gallbladder by releasing acetylcholine. The vagal stimulation occurs during the cephalic phase and gastric phase of gastric secretion.

2. Hormonal Factor: When a fatty chyme enters the intestine from stomach, the intestine secretes the cholecystokinin, which causes contraction of the gallbladder.

REGULATION OF BILE SECRETION

Bile secretion is a continuous process though the amount is less during fasting. It starts increasing after meals and continues for three hours. Secretion of bile from liver and release of bile from the gallbladder are influenced by some chemical factors, which are categorized into three groups:

1. Choleretics
2. Cholagogue
3. Hydrocholeretic agents.

Choleretics Substances which increase the secretion of bile from liver are known as choleretics. Effective choleretic agents are:

i. Acetylcholine
ii. Secretin
iii. Cholecystokinin
iv. Acid chyme in intestine
v. Bile salts.

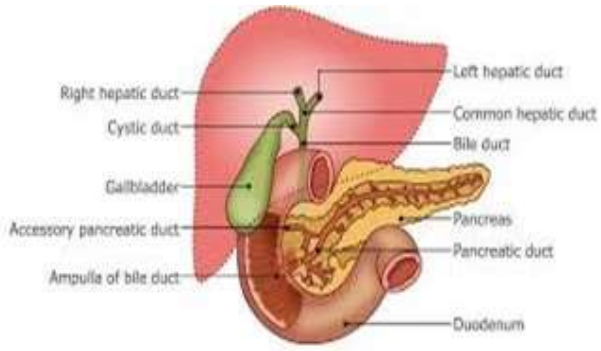
Cholagogues Cholagogue is an agent which increases the release of bile into the intestine by contracting gallbladder.

Common cholagogues are:

i. Bile salts
ii. Calcium
iii. Fatty acids
iv. Amino acids
v. Inorganic acids

All these substances stimulate the secretion of cholecystokinin, which in turn causes contraction of gallbladder and flow of bile into intestine.

Hydrocholeretic Agents Hydrocholeretic agent is a substance which causes the secretion of bile from liver, with large amount of water and less amount of solids. Hydrochloric acid is a hydrocholeretic agent.



CASE PRESENTATION / RESULTS

A 35-year-old male presented with fatigue, mild right upper quadrant abdominal discomfort, and unintentional weight gain over six months. There was no history of alcohol abuse, viral hepatitis, or hepatotoxic drug use. Physical examination revealed mild hepatomegaly without stigmata of chronic liver disease.

Laboratory investigations showed elevated alanine aminotransferase (ALT) and aspartate aminotransferase (AST) levels with normal bilirubin. Lipid profile demonstrated hypertriglyceridemia, and fasting blood glucose was elevated. Viral hepatitis markers were negative. Abdominal ultrasound revealed increased hepatic echogenicity consistent with fatty infiltration. Based on clinical, laboratory, and imaging findings, a diagnosis of metabolic liver disease consistent with non-alcoholic fatty liver disease was made. The patient was managed with lifestyle modification, including dietary changes, weight reduction, and regular physical activity.

DISCUSSION

Metabolic liver diseases are often underdiagnosed due to their insidious onset and nonspecific clinical presentation. NAFLD, the most common metabolic liver disease, is closely associated with obesity, insulin resistance, dyslipidemia, and metabolic syndrome. Persistent metabolic insults can lead to non-alcoholic steatohepatitis (NASH), fibrosis, cirrhosis, and hepatocellular carcinoma.

The cornerstone of management remains early identification and correction of underlying metabolic risk factors. Lifestyle modification is the first-line therapy and has been shown to improve liver enzymes and histology. Pharmacological therapies may be considered in selected patients. Regular follow-up is crucial to monitor disease progression and treatment response.

CONCLUSION

This case emphasizes the need for a high index of suspicion for metabolic liver diseases in patients with abnormal liver enzymes and metabolic risk factors. Early diagnosis and intervention can significantly alter disease course and reduce morbidity.

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