King Saud University
College of Medicine
Second year – GIT block

Complications of Liver Cirrhosis

Lecture 11

430 Pathology Team

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Complications of liver cirrhosis:

- Portal hypertension.

    1. Ascites.
    2. Hepatic encephalopathy.
    3. Porto-systemic shunt (including variceal bleeding)
    4. Splenomegaly

- Jaundice and cholestasis
- Spontaneous bacterial peritonitis.
- Hepatorenal syndrome.
- Hepatocellular carcinoma.

Portal Hypertension:

Definition: is a condition of increased pressure in hepatic blood flow.

Causes:

- Prehepatic (affecting the portal vein before it enters the liver, e.g. portal vein thrombosis)
- Intrahepatic (causes from the liver itself e.g. Cirrhosis)
- posthepatic

The dominant intrahepatic cause is cirrhosis, accounting for most cases of portal hypertension.

Others causes of hepatic portal hypertension *:* massive fatty liver - Hepatic schistosomiasis

- Portal hypertension in cirrhosis results from:
    1. increased resistance to portal flow at the level of the sinusoids
    2. compression of central veins by perivenular fibrosis
    3. expanded parenchymal nodules.
- Anastomoses between the arterial and portal systems in the fibrous bands also contribute to portal hypertension by imposing arterial pressure on the normally low-pressure portal venous system.

Clinical consequences of portal hypertention:

1. Ascites:

Definition: it is the accumulation of excess fluid in the peritoneal cavity that exceeds the expected volume of about 25 ml.

85% caused by cirrhosis

It is generally a serous fluid having less than 3 gm/dL of protein.

Pathogenesis of Ascites: Three mechanisms are involved:

- Portal hypertension leads to vasodilatation in the splanchnic vessels, reducing blood volume and activating the renin-angiotensin-aldosterone system. This causes sodium and water retention.
- Increased transudation of fluid takes place because of increased hydrostatic pressure in the splanchnic vascular bed.
- Increased transudation of fluid is predisposed to by low plasma oncotic pressure (associated with hypoalbuminemia due to reduced albumin synthesis by damaged liver cells).

2. Splenomegaly :

Long-standing congestion may cause congestive splenomegaly usually up to (1000 gm)

hematologic abnormalities attributable to hypersplenism, such as thrombocytopenia or pancytopenia (an abnormal deficiency in all blood cells) may occur.

Cause:

- Results from elevated portal venous pressure, that causes congestion of blood in the spleen.

3. Porto-systemic shunt (including esophageal varices):

Normally:

Instead of returning directly to the heart, venous blood from the GI tract is delivered to the liver via the portal vein before reaching the inferior vena cava.

This circulatory pattern is responsible for the first-pass effect in which drugs and other materials absorbed in the intestines are processed by the liver before entering the systemic circulation.

In diseases that impede this flow cause portal hypertension and can lead to the development of esophageal varices, an important cause of esophageal bleeding.

Pathogenesis:

Portal hypertension results in the development of collateral channels at sites where the portal and caval systems communicate. Although these collateral veins allow some drainage to occur, they lead to development of a congested subepithelial and submucosal venous plexus within the distal esophagus. (*varices):* 90% of cirrhotic patients

With the rise in portal venous pressure, bypasses develop wherever the systemic and portal circulations share capillary beds.

Principal sites are:

1 veins around and within the rectum (manifest as hemorrhoids)

2 Veins at the cardioesophageal junction (producing esophageal varices),

3 Veins of the retroperitoneum

4 Veins of the falciform ligament of the liver (involving periumbilical and abdominal wall collaterals, producing caput medusea).

— Caput medusea are abdominal wall collaterals which appear as dilated subcutaneous veins extending outward from the umbilicus.

Causes:

1. Acohol (most common)
2. Hepatic schistosomiasis (2nd most common)

Morphology:

- Varices can be detected by venogram : tortuous dilated veins lying primarily within the submucosa of the distal esophagus and proximal stomach. Venous channels directly beneath the esophageal epithelium may also become massively dilated.
- Varices may not be grossly obvious in surgical or postmortem specimens, because they collapse in the absence of blood flow .
- Variceal rupture results in hemorrhage into the lumen or esophageal wall, in which case the overlying mucosa appears ulcerated and necrotic. If rupture has occurred in the past, venous thrombosis, inflammation, and evidence of prior therapy may also be present.

Clinical features:

While varices are often asymptomatic, they may rupture, causing massive hematemesis.

Causes of the hematemesis: The factors that lead to rupture are not well defined, but these are likely to contribute

- Inflammatory erosion of thinned overlying mucosa
- Increased tension in progressively dilated veins
- Increased vascular hydrostatic pressure associated with vomiting

Treatment:

It is a medical emergency because:

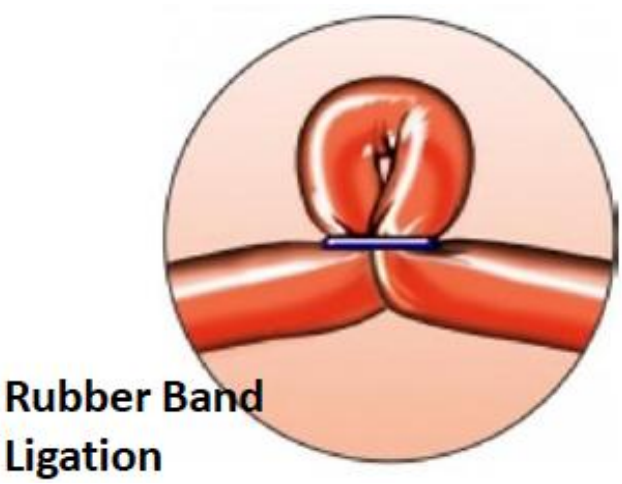
1. These vessels are easily ruptured
2. After bleeding they had to tamponade
3. Concomitant coagulopathies.

Coagulopathy is a condition where blood cloating is abnormal or impaired. It happens in patients with liver cirrhosis and causes impaired coagulation mainly due to:

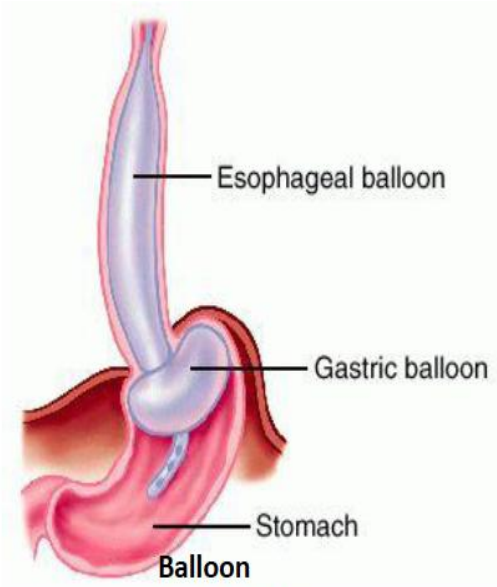
A) loss of hepatic synthesis of cloating factors
B) impaired absorption vitamin K (a fat soluble vitamin), which is a result of improper bile formation and absorption.

It is treated by any of several methods:

- Sclerotherapy by injecting some sclerotic materials inside vessels to dry it up and close it.
- Endoscopic balloon tamponade (mechanical method)
- Endoscopic rubber band ligation



Rubber Band Ligation



Balloon Tamponade

Prognosis:

- Half of patients die from the first bleeding episode either as a direct consequence of hemorrhage or following hepatic coma triggered by hypovolemic shock.
- Additional 50% within 1 year.
- Each episode has a similar rate of mortality.
- Over half of deaths among individuals with advanced cirrhosis result from variceal rupture.

4. Hepatic encephalopathy:

- Hepatic encephalopathy: is a number of liver related disturbances in brain function.
- They range from subtle behavioral abnormalities to deep coma and death.
- Some muscular and neuromuscular abnormalities maybe present. Particularly characteristic is *asterixis* (also called flapping tremor)
- In most instances there are only minor morphologic changes in the brain, such as edema and an astrocytic reaction.

Two physiologic conditions seem to be important in the genesis of this disorder:

(1) severe loss of hepatocellular function

(2) shunting of blood from portal to systemic circulation around the chronically diseased liver.

- The underlying causes of this derangement:
- In the acute setting: elevated blood ammonia
- In the chronic setting: deranged neurotransmission arises from alterations in amino acid metabolism in the brain.

Spontaneous bacterial peritonitis:

Spontaneous bacterial peritonitis (SBP) is an infection of the ascitic fluid without obvious intra-abdominal source of sepsis; usually complicates advanced liver disease.

Jaundice (icterus):

Definition: a yellow discoloration of skin and sclerae *(icterus, the first sign),* occurs when systemic retention of bilirubin leads to elevated serum levels above 2.0 mg/dL (the normal in the adult is <1.2 mg/dL).

Causes: there are many causes of jaundice, but the causes of elevated bilirubin in cirrhosis are as flows:

1) Reduced hepatic uptake that happens with hepatocellular disease such in cirrhosis or hepatitis
2) Reduced hepatocellular excretion of bilirubin or bilirubin overproduction
3) Impaired hepatic bile flow

Because there is more than one mechanism that contributes the formation jaundice in cirrhosis, which may show different levels unconjugated and conjugated bilirubin levels.

Cholestasis:

It is characterized by systemic retention of not only bilirubin but also other solutes eliminated in bile such as bile salts and cholesterol. Cholestasis also arises from many causes, but hepatocellular dysfunction or hepatic biliary tree (intrahepatic causes) is the main reasons that related to cirrhosis.

Hepatorenal syndrome:

It is the appearance of renal failure in individuals with severe chronic liver disease in whom there are no intrinsic morphologic or functional causes for the renal failure.

Hepatorenal syndrome does not include damage that may happen as concomitant toxicity occur with exposure to certain substances.

Also excluded are instances of advanced hepatic failure in which circulatory collapse leads to acute tubular necrosis and renal failure.

Incidence:

It is about 8% per year among patients who have cirrhosis and ascites.

Causes:

- Decreased renal perfusion pressure due to systemic vasodilation
- Activation of the renal sympathetic nervous system with vasoconstriction of the afferent renal arterioles
- Increased synthesis of renal vasoactive mediators that decrease glomerular filtration because of the (periglomerular fibrosis + wrinkling of capillaries)

Kidney function promptly improves if hepatic failure is reversed.

Hepatocellular Carcinoma:

Especially with chronic HBV infections.

Treatment: liver transplantation.