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CIRRHOSIS: PATHOPHYSIOLOGY, DIAGNOSIS, AND THERAPEUTIC APPROACHES

Abdakiova Baxtigul Ilhomiddin qizi,
Tashkent Medical Academy

Abstract
Cirrhosis is a late stage of liver disease in which healthy liver tissue is gradually replaced by scar tissue (fibrosis). This scarring blocks the flow of blood through the liver and impairs its ability to function properly. The liver plays a critical role in detoxifying harmful substances, producing proteins important for blood clotting, and processing nutrients, so when cirrhosis develops, these functions are compromised.

Keywords: Hepatic fibrosis, Portal hypertension, Liver function tests, Ascites, Liver biopsy, Non-invasive diagnostic tools, Liver transplantation, Alcoholic cirrhosis, Viral hepatitis-related cirrhosis, Non-alcoholic fatty liver disease (NAFLD).

Introduction

Causes of Cirrhosis

Cirrhosis can result from a variety of chronic liver diseases, including:

1. Chronic alcohol abuse – Long-term excessive alcohol consumption is a common cause.
2. Chronic viral hepatitis (Hepatitis B, C, or D) – These infections cause ongoing inflammation that can lead to liver damage over time.
3. Non-alcoholic fatty liver disease (NAFLD) – Fat buildup in the liver, especially in people with obesity or metabolic syndrome, can lead to cirrhosis.
4. Autoimmune liver diseases – Conditions like autoimmune hepatitis where the body's immune system attacks liver cells.
5. Inherited diseases – Conditions like hemochromatosis (excess iron accumulation) or Wilson's disease (copper accumulation).
6. Biliary diseases – Conditions like primary biliary cholangitis (PBC) or primary sclerosing cholangitis (PSC) can block bile ducts, causing liver damage.

Symptoms of Cirrhosis

Early-stage cirrhosis often has no symptoms. As the disease progresses, symptoms can include:
Fatigue and weakness
Jaundice (yellowing of the skin and eyes)
Itching (due to bile build-up)
Loss of appetite and weight loss
Nausea
Swelling in the abdomen (ascites) or legs (edema)
Spider-like blood vessels on the skin

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Easy bruising or bleeding

Complications of Cirrhosis

Cirrhosis can lead to life-threatening complications, including:

1. Portal hypertension – Increased pressure in the portal vein, leading to complications like varices (enlarged veins) in the esophagus or stomach, which can bleed.
2. Hepatic encephalopathy – A buildup of toxins (such as ammonia) in the bloodstream that can affect brain function, causing confusion or coma.
3. Ascites – Accumulation of fluid in the abdomen.
4. Hepatocellular carcinoma (HCC) – Patients with cirrhosis are at increased risk for liver cancer.
5. Liver failure – The liver loses its ability to function, which can be fatal without a liver transplant.

Diagnosis

Cirrhosis is diagnosed through a combination of:

Medical history and physical examination

Blood tests to check liver function, including liver enzymes, bilirubin, and clotting factors.

Imaging tests such as ultrasound, CT scan, or MRI to assess liver damage and fibrosis.

Liver biopsy to confirm cirrhosis and determine the extent of liver scarring.

Liver elastography (Fibro Scan) to measure liver stiffness, indicating fibrosis.

Treatment

There is no cure for cirrhosis, but treatment focuses on managing the underlying cause and preventing further liver damage. Key treatments include:

Avoiding alcohol completely if alcohol-related liver disease is the cause.

Medications to treat viral hepatitis or autoimmune liver diseases.

Lifestyle changes such as weight loss and management of diabetes for NAFLD-related cirrhosis.

Diuretics to reduce fluid retention and lactulose to manage hepatic encephalopathy.

Endoscopic treatment to prevent variceal bleeding and beta-blockers to manage portal hypertension.

In advanced cases of cirrhosis or liver failure, liver transplantation is the only definitive treatment.

Prevention

Preventing cirrhosis involves managing risk factors such as:

Limiting alcohol consumption

Vaccination against hepatitis B and screening for hepatitis C

Maintaining a healthy weight and managing conditions like diabetes and high cholesterol

Avoiding exposure to toxins that can damage the liver, such as certain chemicals or unregulated supplements

Diagnosis and Monitoring

1. **Early Diagnosis and Screening:**

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Liver Elastography (FibroScan) is recommended for assessing liver stiffness and fibrosis, especially in patients with chronic liver diseases like hepatitis B, hepatitis C, or alcohol-related liver disease.

Regular **screening for hepatocellular carcinoma (HCC)** in patients with cirrhosis through ultrasound every 6 months is advised, with or without alpha-fetoprotein (AFP) testing.

2. **Non-Invasive Biomarkers:**

The use of non-invasive biomarkers, such as the Fibrosis-4 (FIB-4) index or AST-to-Platelet Ratio Index (APRI), can help in identifying advanced fibrosis or cirrhosis, reducing the need for liver biopsies.

3. **Routine Surveillance:**

Patients with cirrhosis should undergo routine monitoring for varices and portal hypertension using endoscopy or non-invasive tests.

Regular blood tests to monitor liver function (bilirubin, albumin, INR), kidney function (creatinine), and electrolytes (sodium) are essential to assess disease progression

Management of Complications

1. **Portal Hypertension**:Non-selective beta-blockers (like propranolol or carvedilol) are recommended to prevent variceal bleeding in patients with significant portal hypertension.

Endoscopic variceal ligation (EVL) should be used for those who cannot tolerate beta-blockers or have large varices.

2. **Ascites Management**:

First-line treatment includes dietary sodium restriction and diuretics (spironolactone and furosemide).

Albumin infusion is recommended for patients with spontaneous bacterial peritonitis (SBP) or large-volume paracentesis.

For refractory ascites, transjugular intrahepatic portosystemic shunt (TIPS) may be considered.

3. **Hepatic Encephalopathy**:

Lactulose remains the first-line treatment to reduce ammonia levels, with rifaximin as an add-on therapy for recurrent cases.

Regular monitoring of serum ammonia is not required unless clinically indicated.

4. **Hepatorenal Syndrome** (HRS):

Albumin infusion, along with vasoconstrictors such as terlipressin (where available) or midodrine and octreotide, is recommended for managing type 1 HRS.

Early detection and management of renal dysfunction are critical to improve outcomes.

Lifestyle Modifications and Prevention

1. Alcohol Abstinence:

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Complete abstinence from alcohol is crucial for patients with alcohol-related cirrhosis.
For those struggling with alcohol dependence, integrating behavioral therapy and medications (e.g., naltrexone, acamprosate) is recommended.

2. Vaccination:
Patients with cirrhosis should be vaccinated against hepatitis A, hepatitis B, influenza, and pneumococcus to prevent additional infections that can worsen liver function.

3. Nutritional Support:
Protein restriction is no longer recommended for cirrhosis patients unless they have severe hepatic encephalopathy. Instead, adequate protein intake (1.2-1.5 g/kg/day) is advised to prevent muscle wasting (sarcopenia).
Small, frequent meals with late-night snacks rich in complex carbohydrates can help prevent fasting-related hypoglycemia and muscle loss.

Treatment of Underlying Causes
1. Hepatitis B and C:
Antiviral therapy for hepatitis B or C is essential to prevent further progression of liver disease. Direct-acting antivirals (DAAs) for hepatitis C can lead to viral eradication and improve liver function.

2. Non-Alcoholic Fatty Liver Disease (NAFLD):
For cirrhosis related to NAFLD, weight loss through diet and exercise is recommended.
Patients with metabolic syndrome should manage underlying conditions like diabetes, obesity, and dyslipidemia.

Liver Transplantation
1. Transplant Referral:
Patients with decompensated cirrhosis, refractory complications, or hepatocellular carcinoma (HCC) within transplant criteria should be referred for liver transplant evaluation.

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