The Liver in Sickle Cell Disease

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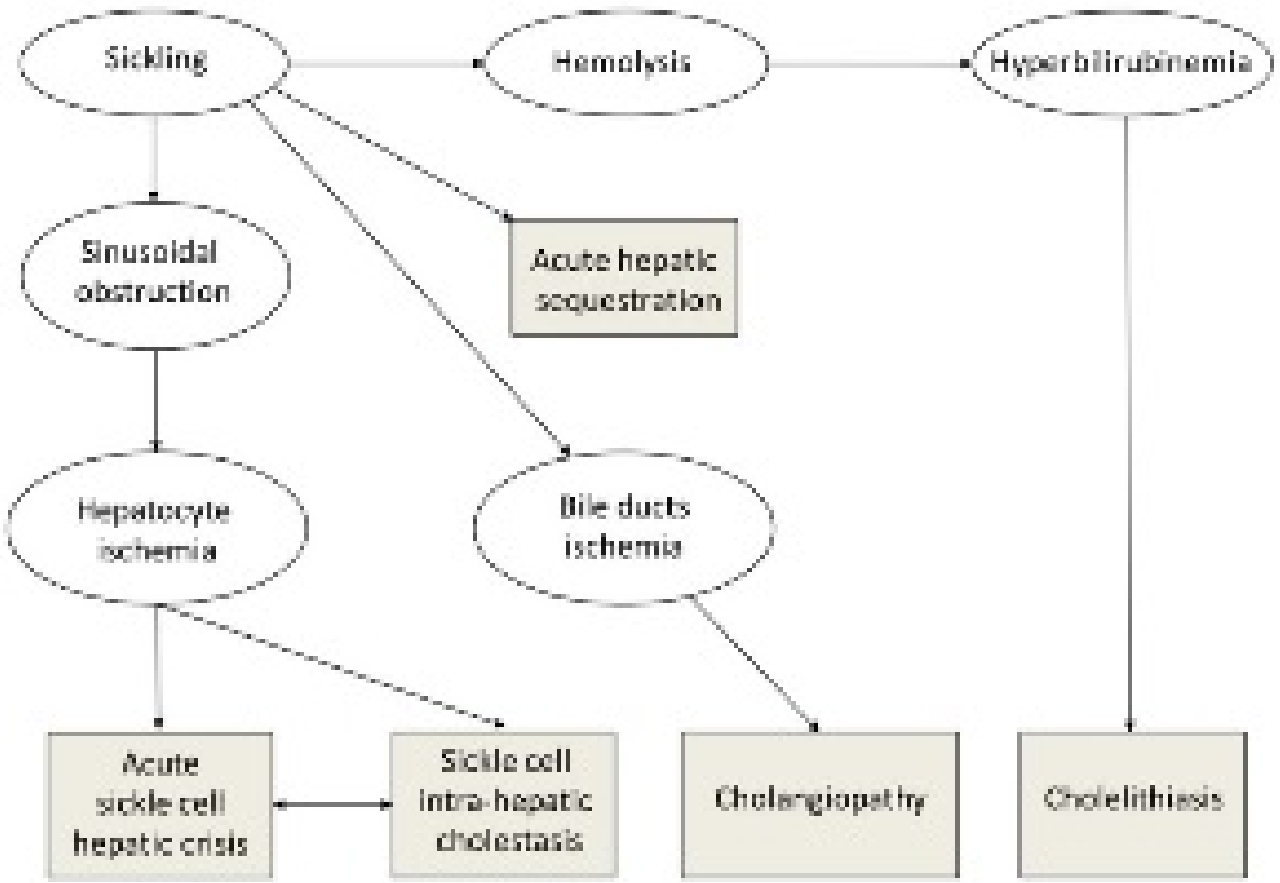
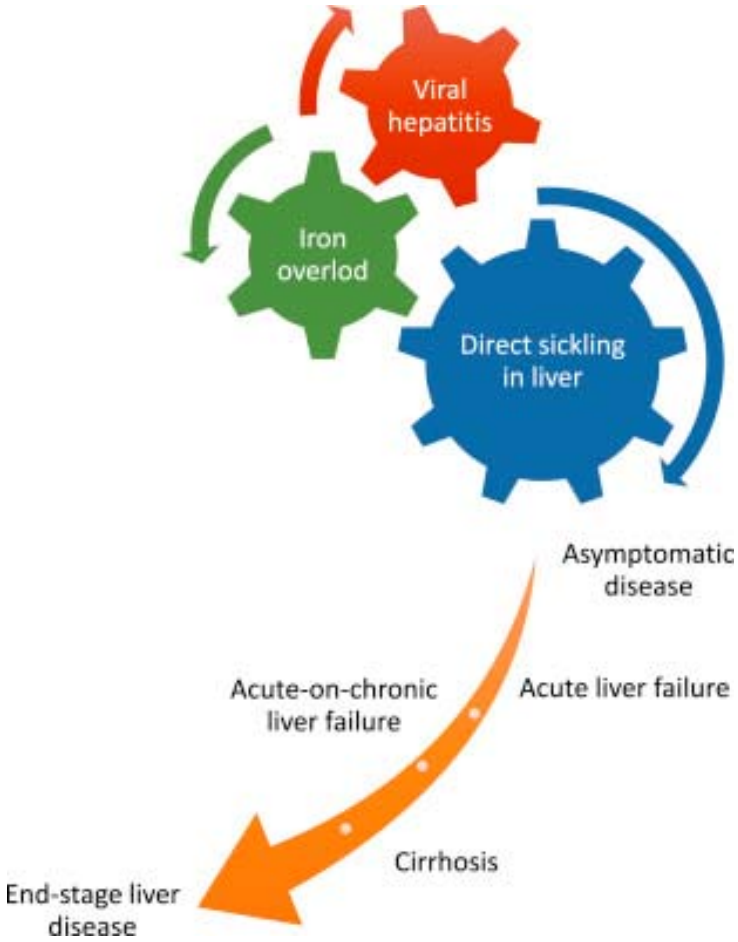
Pathophysiology of Liver Diseases

- Presence of HbS
  - Valine for glutamic acid at position 6 on the beta chain
- If both chains have the mutation → SCD
- More common in African Americans (1:365 have trait)
- Intravascular sickling → vaso-occlusive crisis → tissue/end organ damage
- “Sickle Hepatopathy” is an umbrella term
- Can occur in 10-40% in crisis


Sickling
Hemolysis
Hyperbilirubinemia
Sinusoidal obstruction
Acute hepatic sequestration
Hepatocyte ischemia
Bile ducts ischemia
Acute sickle cell hepatic crisis
Sickle cell intra-hepatic cholestasis
Cholangiopathy
Cholelithiesis


Viral hepatitis
Iron overlod
Direct sickling in liver
Asymptomatic disease
Acute-on-chronic liver failure
Acute liver failure
Cirrhosis
End-stage liver disease

Classification of hepatobiliary disease in SCD

Acute Liver Diseases	Chronic Liver Diseases
Related to sickling	
Acute sickle hepatic crisis (ischemia)	Chronic cholestasis
Acute sickle intrahepatic cholestasis	Biliary cirrhosis
Acute hepatic sequestration	
Complications of treatment (transfusions)	
HCV	HCV
HBV	HBV
	Secondary hemochromatosis
Other	
Cholelithiasis/cholangitis	Cholelithiasis
Budd-Chairi syndrome	Co-existing other liver disease
Hepatic abscess	

Acute Hepatic Sickle Crisis

- Can occur in up to 10% of those with SCD
- Transient hepatic ischemic injury
- Low grade fever, RUQ pain, jaundice
- AST/ALT usually up to 3x ULN and < 1000 IU/L
- Alkaline phosphatase normal
- Total bilirubin < 15 mg/dL (mostly conjugated)
- Usually resolves within 2 weeks
- Try to avoid liver biopsy (high complications)

Acute Hepatic Sequestration in SCD

- Sequestration of sickle cells in hepatic sinusoids
- Rare
- RUQ pain, low fever, jaundice
- Rapid enlargement of organ
- Mild increased AST/ALT (usually normal)
- ALP can be very high (>500 IU/L) from compression
- Bilirubin can be very high (20-25 mg/dL), mostly conjugated
- Usually resolves in a few days

Acute Sickle Intrahepatic Cholestasis

- Intrahepatic sickling -> hepatocyte ballooning and canalicular cholestasis
- Fever, RUQ pain, leukocytosis
- Very High bilirubin (>15 mg/dL), can exceed 50 mg/dL
  - Conjugated > unconjugated
- AST and ALT can > 1000 IU/L
- ALP can range from normal to 1000 IU/L
- Can have increased INR, PSE, organ failure (high mortality)
- May require EBT to target HbS <20-30%

Chronic liver diseases

- Recurrent ischemic insults can lead to hepatic fibrosis
- Cirrhosis has been reported in 16-29% in autopsy studies
- HBV, HCV, secondary hemochromatosis precipitating etiologies
- Sickle cholangiopathy
  - Bile duct ischemia
  - Ascending cholangitis
  - Bilomas
  - Biliary abscesses
  - MRCP diagnostic test of choice
  - ERCP if stone/obstruction
  - Ursodeoxycholic acid (UDCA) may be helpful
- Budd-Chiari syndrome (BSC)
- Veno-occlusive disease (VOD)
- Nodular regenerative hyperplasia (NRH)

Cholelithiasis

- Increased risk of pigmented stones from chronic hemolysis
- Usually multiple small stones (usually pigmented)
- Prevalence of stones: 50% by age 22
- CBD stones in 18%
- Many develop symptoms of stones
- RUQ pain, cholestasis, fever
- ERCP to remove stone/relieve obstruction
- Laparoscopic cholecystectomy treatment of choice along with EBT

Management of hepatobiliary disease in SCD

Liver pathology	Treatment
Acute sickle hepatic crisis	Hydration, O2, EBT (target HbS 20-30%)
Hepatic sequestration	Hydration, O2, EBT
Acute intrahepatic cholestasis	Hydration, O2, EBT
Chronic cholestasis	EBT, UDCA, ERCP if dominant stricture or stone
Hepatic hemosiderosis	Chelation
HBV	Nucleoside/tide analogue
HCV	DAA
Cirrhosis	Manage complications
Cholelithiasis	Lap Cholecystecomy
CBD stones	ERCP, consider Lap Chole

References

- E Theocharidou et al. Clin Liv Dis 2019;23: 177-189
- S Allsli et al. J Clin Med 2019;8:1481
- R Shah et al. WJ Gastrointestinal Pathophysiology 2017;8:108-116

References

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