Series Editor: Bernard Karnath, MD

Stigmata of Chronic Liver Disease

Bernard Karnath, MD

The liver is the largest internal organ of the body, with blood supplied from both the hepatic artery and the portal vein. The liver performs many functions, including synthesis of most serum proteins, regulation of glucose and lipids, and production of bile. These essential functions become impaired when a liver develops cirrhosis. Cirrhosis is defined pathologically by the loss of normal microscopic lobular architecture with fibrosis and nodular regeneration. Chronic liver disease, including cirrhosis, is currently the twelfth leading cause of death in the United States.[1] Chronic alcoholism and chronic hepatitis C are the leading causes of cirrhosis,[2] and cirrhosis is the most common cause of portal hypertension.

This article reviews the clinical signs, or "stigmata," of chronic liver disease that can be visualized by simple observation of the patient. These include spider angiomas, scleral icterus, jaundice, palmar erythema, gynecomastia, ascites, encephalopathy, and asterixis.[3]

STIGMATA OF CHRONIC LIVER DISEASE

Spider angioma
Jaundice
Scleral icterus
Palmar erythema
Gynecomastia
Ascites
Encephalopathy
Asterixis
Note: Signs listed are not specific to chronic liver disease.

CUTANEOUS MANIFESTATIONS

The cutaneous manifestations of chronic liver disease include spider angiomas, jaundice, pruritus, and palmar erythema. Pruritus is a subjective sign. Although these findings are not specific to chronic liver disease, their presence warrants further investigation, with liver disease being a likely underlying cause.

Spider Angioma

The spider angioma consists of a central arteriole from which radiate numerous small branching vessels (**Figure 1**). Spider angiomas most often occur on the upper trunk. Compression of the lesion causes blanching. Although the pathogenesis of the spider angioma is unclear, its association with chronic liver disease is well established. Spider angiomas are not specific for cirrhosis and may be seen in patients who are taking oral estrogens or are pregnant. Elevated estradiol levels have been associated with the presence of spider angiomas. One study showed that the prevalence of spider angiomas was 50% in alcoholic cirrhotic patients compared to 27% of nonalcoholic cirrhotic patients.[4] Overall, 33% of patients with cirrhosis had spider angiomas.[4]

Jaundice

Jaundice, or icterus, refers to a yellowish discoloration of the skin that results from the deposition of bilirubin and its metabolites in the tissues. It also affects the sclera and mucous membranes (**Figure 2**). Hyperbilirubinemia can result from prehepatic or hepatobiliary dysfunction. Prehepatic dysfunction (eg, hemolytic disorders) results in elevated indirect (unconjugated) bilirubin. Hepatobiliary dysfunction results primarily in elevated direct (conjugated) bilirubin. In chronic liver disease, both conjugated and unconjugated fractions of bilirubin may be elevated.

In general, bilirubin levels of greater than 2.5 mg/dL result in clinically apparent jaundice. However, a study demonstrated that in a sample of medical examiners at various levels of medical training (including medical students), 42% did not detect jaundice in patients with a total serum bilirubin level of 2.5 mg/dL or greater.[5] The level of training of the medical examiners in this study

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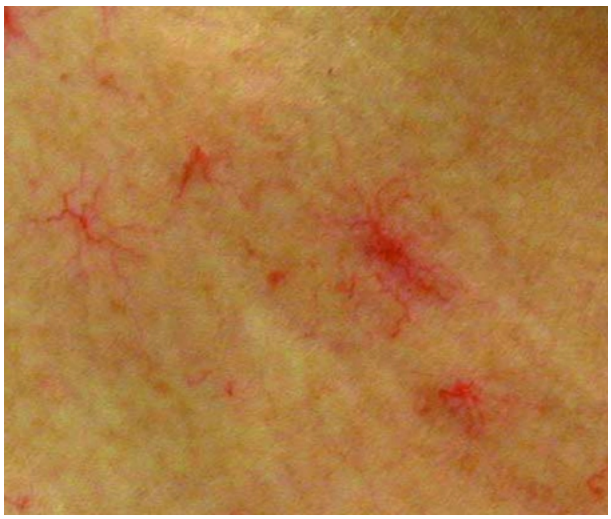

Figure 1. Spider angioma.

affected the specificity but not the sensitivity in the detection of jaundice—that is, medical students had a higher rate of false positives than did other examiners.

Patients with jaundice from liver disease also frequently report a darkening of the urine, which is a sign of elevated conjugated bilirubin. Jaundice without darkened urine indicates elevated unconjugated bilirubin.[6] This is because unconjugated bilirubin binds to albumin in the serum and is not filtered by the kidney.

Other Cutaneous Manifestations

Pruritus is a common complaint in patients with chronic liver disease. Although bile acids have received the most attention as a possible cause,[7,8] the pathogenesis of itching in these patients is still not clear. Patients with pruritus from cholestasis typically describe itching of the palms of the hands and soles of the feet, although diffuse pruritus is common and excoriation may be evident.

Another cutaneous finding that may be present in chronic liver disease is palmar erythema, although it is not specific for liver disease. Palmar erythema may appear as mottling of the palms or as a blanching erythematous patch.

Portal hypertension leads to the development of portosystemic collateral channels. Abdominal wall collateral veins appear as tortuous vessels that radiate from the umbilicus, the so-called *caput medusae*, another clinical sign of chronic liver disease.

GYNECOMASTIA

Gynecomastia is the enlargement of the male breast (**Figure 3**). It can either be a normal physiologic phenomenon or a sign of an underlying disease.[9,10] The prevalence of gynecomastia in cirrhotic patients was reported in one study to be 44%.[10] True gynecomastia is characterized by palpable glandular tissue, especially around the areola. Lipomastia is breast tissue enlargement from adipose tissue and is not a pathologic finding.

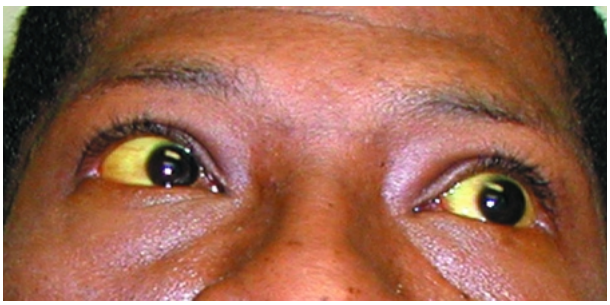

Figure 2. Scleral icterus.

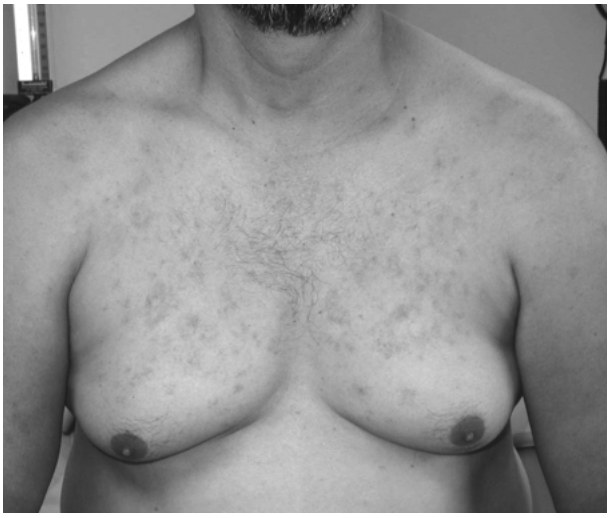

Figure 3. Gynecomastia.

Pathologic gynecomastia can result from deficiency in testosterone activity or from increased estrogen levels. Gynecomastia in chronic liver disease is caused by diminished catabolism of androstenedione, thereby shunting estrogen precursors and increasing plasma levels of estradiol.[9] The resultant elevation in the ratio of free estradiol to free testosterone causes feminization. Additionally, many cirrhotic patients take spironolactone, which is an inhibitor of testosterone synthesis.

ASCITES

Ascites can result from portal hypertension, and cirrhosis accounts for up to 80% of cases of ascites.[11]

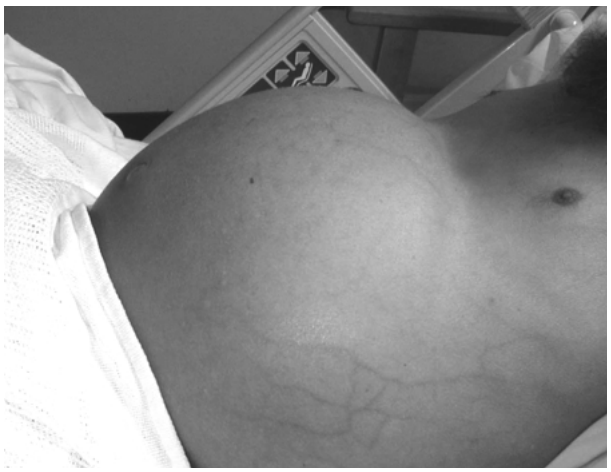

Figure 4. Tense ascites.

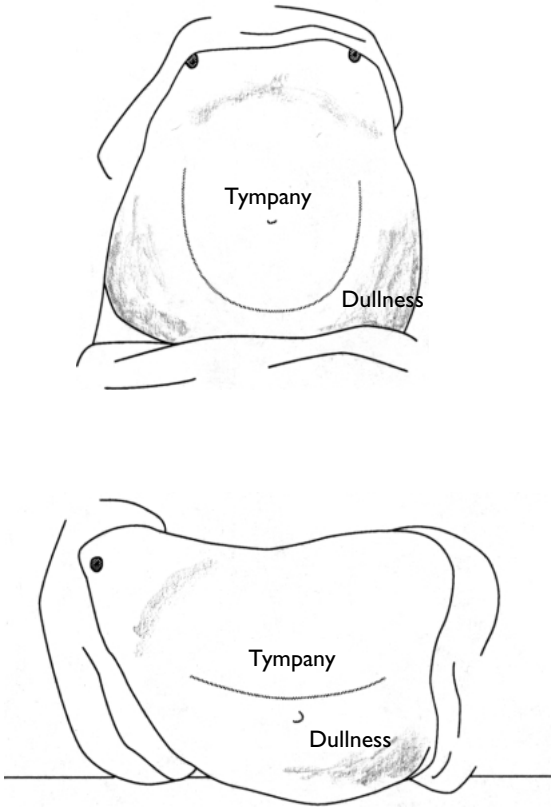

Figure 5. Elicitation of shifting dullness. (*top*) Supine position. (*bottom*) Lateral decubitus position.

Ascites is not specific to liver disease; other causes of ascites include cancer, heart failure, and the nephrotic syndrome. Severe, or tense, ascites is shown in **Figure 4**.

The physical examination maneuvers used to detect ascites include assessing for bulging flanks, flank dullness, shifting dullness, a fluid wave, and a puddle sign. All of these maneuvers are performed with the patient in a supine position, with the exception of the puddle sign. Bulging flanks and flank dullness are considered present only if bulging and dullness to percussion are bilateral. To test for shifting dullness, the patient should be instructed to roll from the supine position to the lateral decubitus position on both the left and the right sides (**Figure 5**). Percussion of the abdomen is performed in both positions. In the supine position, tympany is noted in the periumbilical region as the accumulated fluid is displaced to the flanks, where dullness to percussion is noted. With the patient in the lateral decubitus position, the area of tympany shifts upward, hence the term *shifting dullness.*

A fluid wave can be demonstrated by percussing on one side of the abdomen while palpating the other side of the abdomen with the palm of the opposite hand. The puddle sign is elicited by asking the patient to assume a position on the knees and elbows. The umbilical area is percussed for dullness, which is a sign of fluid pooling. The sensitivity and specificity of each of these physical examination maneuvers are presented in **Table 1**. Although flank dullness is the most sensitive maneuver in detecting ascites, it is not very specific. The detection of a fluid wave is the most specific maneuver.

Table 1. Physical Examination Findings to Detect Ascites

Finding	Sensitivity	Specificity
Bulging flanks	0.78	0.44
Flank dullness	0.94	0.56
Shifting dullness	0.83	0.56
Fluid wave	0.50	0.82
Puddle sign	0.51	0.51

Reprinted from Cattau EL Jr, Benjamin SB, Knuff TE, Castell DO. The accuracy of the physical examination in the diagnosis of suspected ascites. JAMA 1982;247:1165.

ENCEPHALOPATHY

Hepatic encephalopathy is a neuropsychiatric complication of chronic liver disease. It is defined as a disturbance in central nervous function due to hepatic insufficiency and is characterized by a change in personality, impaired intellect, and a depressed level of consciousness.[12] Hyperammonemia is common in chronic liver disease and may have a role in the development of hepatic encephalopathy. Ammonia is a degradation product of intestinal flora and has neurotoxic effects.

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Plasma ammonia levels are usually elevated in patients with hepatic encephalopathy, although levels may be normal in up to 10% of patients with hepatic encephalopathy.[13] The grading of hepatic encephalopathy is shown in **Table 2**.

Table 2. Grading of Hepatic Encephalopathy

Grade	Description
0	Normal mental status. Asterixis absent.
1	Mild confusion. Asterixis can be detected.
2	Lethargy with inappropriate behavior. Obvious asterixis.
3	Somnolent with incomprehensible speech and marked confusion
4	Coma

Adapted with permission from Blei AT, Cordoba J. Hepatic encephalopathy. Practice Parameters of the American College of Gastroenterology. Am J Gastroenterol 2001;96:1969.

ASTERIXIS

Asterixis (flapping tremor) is described as a jerky rhythmical tremor. It is a negative myoclonus caused by brief pauses in muscle activity. Asterixis is best demonstrated by having the patient extend the arms and dorsiflex the hands. Asterixis is not specific to chronic liver disease and can be seen in other metabolic disorders, such as renal failure, hyponatremia, hypoglycemia and nonketotic hyperglycemia.[14] The relationship between asterixis and hyperammonemia has been established.

CONCLUSION

Many signs of chronic liver disease can be detected by simple observation. Although many of these signs are not specific for liver disease, their presence, particularly in patients with risk factors or other indicators of liver disease, often warrants a work-up that includes hepatic studies. **HP**

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