The nodularity associated with cirrhosis is typically relatively fine and diffuse rather than coarse and lobulated [2]. However, non-cirrhotic causes of fine, diffuse nodularity are occasionally encountered and include pseudocirrhosis of treated breast cancer metastases to the liver, fulminant hepatic failure, miliary metastases, sarcoidosis [3–6].

Pseudocirrhosis of Treated Breast Cancer Metastases to the Liver

A variety of hepatic contour changes can occur in breast cancer patients with metastases to the liver after chemotherapy including fine, diffuse nodularity that resembles cirrhosis (Fig. 1), which is commonly referred to as “pseudocirrhosis” [3]. Multifocal retraction of the liver capsule and enlargement of the caudate lobe also can be seen in this setting. The hepatic contour changes due to these conditions usually are easily distinguishable from cirrhosis because of characteristic features. The nodularity associated with cirrhosis is typically relatively fine and diffuse rather than coarse and lobulated [2]. However, non-cirrhotic causes of fine, diffuse nodularity are occasionally encountered and include pseudocirrhosis of treated breast cancer metastases to the liver, fulminant hepatic failure, miliary metastases, and nodular regenerative hyperplasia.

C T of patients with established cirrhosis shows diffuse surface nodularity of the liver and also may show decreased liver volume with relative hypertrophy of the left and caudate lobes or signs of portal hypertension. When seen at imaging, diffuse hepatic surface nodularity or signs of portal hypertension (i.e., splenomegaly, ascites, or portosystemic varices) are usually due to cirrhosis, but other conditions can also cause these findings. Knowledge of radiologic mimics of cirrhosis is increasingly important because some have been described only recently and because an erroneous diagnosis of cirrhosis in some settings could adversely impact contemporary treatment options. For example, underlying cirrhosis lowers the transplantation status of patients with acute hepatic failure. This article aims to provide a practical and current review of the conditions other than cirrhosis that can result in diffuse hepatic surface nodularity or signs of portal hypertension.

Noncirrhotic Causes of Diffuse Hepatic Surface Nodularity

General Comments

Diffuse irregularity of the hepatic contour may be fine or coarse (Appendix 1). Causes of coarse lobulation include chronic Budd-Chiari syndrome, chronic portal vein thrombosis, and pseudomyxoma peritonei [1]. The hepatic contour changes due to these conditions usually are easily distinguishable from cirrhosis because of characteristic features.
hepatic failure developing in the setting of cirrhosis. The distinction of acute from acute-on-chronic hepatic failure may be clinically difficult and hepatic surface nodularity might be considered indicative of underlying cirrhosis, adversely impacting transplantation status. Recently, fulminant hepatic failure alone was shown to result in diffuse surface nodularity because of a combination of alternating foci of confluent regenerative nodules and necrosis rather than cirrhosis [8] (Figs. 4 and 5).

**Miliary Metastases**

Diffuse surface nodularity due to miliary metastases is rare (Figs. 6 and 7) and is unlikely to mimic cirrhosis. In a large ultrasound study [4] of hepatic metastases (n = 225), surface irregularity was observed in 16 patients (7%); in only two patients, one with squamous cell carcinoma of the tonsil and one with ovarian carcinoma, was surface nodularity the only sign of metastatic disease [4].

**Sarcoidosis**

Sarcoidosis of the liver is common pathologically but is rarely visible at imaging because the noncaseating granulomas are usually microscopic. Occasionally, hepatic sarcoidosis can be visible as diffuse granular heterogeneity with or without fine nodularity of the hepatic surface [5] (Figs. 8 and 9).

**Noncirrhotic Causes of Portal Hypertension**

**General Comments**

Noncirrhotic causes of portal hypertension (Appendix 2) include chronic Budd-Chiari syndrome, chronic portal vein thrombosis, sarcoidosis, schistosomiasis, nodular regenerative hyperplasia, congenital hepatic fibrosis, idiopathic portal hypertension, and early primary biliary cirrhosis [9].

**Nodular Regenerative Hyperplasia**

Nodular regenerative hyperplasia is a rare but increasing recognized condition characterized by widespread transformation of normal liver parenchyma into hyperplastic regenerative nodules that vary in size from microscopic to large and masslike [10]; the absence of fibrosis distinguishes nodular regenerative hyperplasia from cirrhosis. From a radiologic perspective, there appear to be two forms of the condition: a diffuse form in which the nodules are small and a widespread and a focal form in which the nodules are few in number, are scattered throughout the liver, and measure up to a few centimeters.

The pathogenesis of diffuse nodular regenerative hyperplasia is unknown, but there are well-recognized associations (Appendix 3) with systemic cardiovascular, myeloproliferative, and autoimmune diseases, particularly systemic lupus erythematosus; the administration of certain drugs including chemotherapy; solid organ and bone marrow transplantation; and HIV infection [10]. Focal nodular regenerative hyperplasia has been primarily reported in long-standing Budd-Chiari syndrome, although similar masses have also been reported in autoimmune hepatitis [11, 12]. Diffuse nodular regenerative hyperplasia frequently results in noncirrhotic portal hypertension [10], and affected patients may present with variceal bleeding or hypersplenism.

Imaging findings in patients with nodular hyperplasia can be subtle across all techniques, although parenchymal findings may be more obvious on ultrasound than on CT or MRI [13]. At ultrasound, widespread nodularity suggestive of cirrhosis or multiple masses may be seen (Fig. 10). At CT, the nodules may be hypodense with little enhancement. At MRI, diffuse nodular regenerative hyperplasia is usually of similar signal intensity to the liver on T1, T2, and gadolinium-enhanced sequences. Surface nodularity and features of portal hypertension may be seen across all techniques (Fig. 11). In focal nodular regenerative hyperplasia, CT or MRI typically shows multiple hypervascular masses in a patient with long-standing Budd-Chiari syndrome or autoimmune hepatitis. These masses may suggest metastases or hepatocellular carcinoma, although stability on follow-up studies or biopsy should help in making the correct diagnosis.

**Early Primary Biliary Cirrhosis**

Investigators recently found that portal hypertension can develop early in primary biliary cirrhosis—even before the onset of cirrhosis [14]—possibly resulting from compression of the portal venous branches by granulomatous inflammation causing presinusoidal fibrosis and portal hypertension [14]. This condition has been described as the portal hypertensive variant of primary biliary cirrhosis and appears to carry a higher risk of hepatocellular carcinoma than the other variants of primary biliary cirrhosis.

**Congenital Hepatic Fibrosis**

Hepatic involvement in this multisystem autosomal recessive disorder consists of widespread periportal fibrosis leading to portal hypertension [15]. Portal vein thrombosis is common, and segmental biliary dilatation may also be observed (Fig. 12).

**Idiopathic Portal Hypertension**

Idiopathic portal hypertension is characterized by long-standing presinusoidal portal hypertension of unknown cause in adults and may reflect damage to the intrahepatic small portal veins or portal tracts by an immunologic disturbance, thrombembolism, or an infection. Imaging findings (Fig. 13) include subcapsular parenchymal atrophy, portal and parenchymal fibrosis, and portal venous thrombosis. Interestingly, cirrhosis does not develop even in the advanced stages of the disease [16].

**Conclusion**

Diffuse surface nodularity of the liver or signs of portal hypertension usually reflect underlying cirrhosis, but noncirrhotic causes of these imaging findings include pseudocirrhosis of treated breast cancer metastases to the liver, fulminant hepatic failure, miliary metastases, sarcoidosis, schistosomiasis, congenital hepatic fibrosis, idiopathic portal hypertension, early primary biliary cirrhosis, chronic Budd-Chiari syndrome, chronic portal vein thrombosis, and nodular regenerative hyperplasia.

Pseudocirrhosis of treated breast cancer metastases can be easily identified by reviewing the patient’s medical history and prior imaging examinations. Pseudocirrhosis of fulminant hepatic failure should be considered in previously healthy patients with acute liver decompensation. Miliary metastases should be considered when fine hepatic surface nodularity is seen in a patient with a known primary malignancy and no signs of portal hypertension. A raised serum angiotensin-converting enzyme level or mediastinal adenopathy suggests sarcoidosis. Congenital hepatic fibrosis should be considered in children with findings of portal hypertension, particularly if there are cysts in the kidneys. A smooth liver of normal size with features of portal hypertension should raise suspicion for idiopathic portal hypertension, but biopsy may be required because this diagnosis is one of exclusion. Diffuse nodular regenerative hyperplasia should be considered when multiple small masses are seen in the liver of a patient with known risk factors, particularly if the clinical picture does not favor malignancy and if the lesions are more prominent at ultrasound than on other techniques. Focal nodular regenerative hyperplasia should be considered when multiple hypervascular hepatic masses are seen in a patient with long-standing Budd-Chiari syndrome or autoimmune hepatitis.
Although these distinguishing features may be helpful, histologic correlation will be required to diagnose some cases. Careful radiologic analysis and clinical correlation may be required to prevent an erroneous diagnosis that could potentially adversely impact management.

References


APPENDIX 1: Noncirrhotic Causes of Diffuse Hepatic Contour Irregularity

Coarse lobulation
Chronic Budd-Chiari syndrome
Chronic portal vein thrombosis
Pseudomyxoma peritonei
Fine nodularity
Pseudocirrhosis of treated breast cancer metastases to the liver
Fulminant hepatic failure
Miliary metastases
Sarcoidosis

APPENDIX 2: Noncirrhotic Causes of Portal Hypertension

1. Chronic Budd-Chiari syndrome
2. Chronic portal vein thrombosis
3. Sarcoidosis
4. Schistosomiasis
5. Nodular regenerative hyperplasia
6. Congenital hepatic fibrosis
7. Idiopathic portal hypertension
8. Early primary biliary cirrhosis

APPENDIX 3: Associations of Diffuse and Focal Forms of Nodular Regenerative Hyperplasia

Diffuse form
- Cardiovascular diseases
- Myeloproliferative diseases
- Autoimmune diseases, particularly systemic lupus erythematosus
- Certain drugs including chemotherapy
- Solid organ and bone marrow transplantation
- HIV infection

Focal form
- Chronic Budd-Chiari syndrome
- Autoimmune hepatitis
Fig. 1—62-year-old woman with breast cancer treated with chemotherapy.  
A, Axial contrast-enhanced CT image obtained after patient had received chemotherapy treatment shows diffuse surface nodularity in liver and recanalized umbilical vein (arrow); these findings are suggestive of cirrhosis.  
B, Axial contrast-enhanced CT image obtained 6 months before A, which was before patient started chemotherapy, shows multiple hepatic metastases. Liver is otherwise normal. Setting of breast cancer metastases treated with chemotherapy indicates rapid development of diffuse changes seen in A likely represents pseudocirrhosis of treated breast cancer.

Fig. 2—59-year-old woman with multiple hypodense biopsy-proven hepatic metastases from invasive ductal carcinoma of breast.  
A, Axial contrast-enhanced CT image obtained before patient started chemotherapy.  
B, Axial contrast-enhanced CT image obtained 6 months after A—that is, after patient had started chemotherapy—shows diffuse hepatic nodularity, bland ascites (asterisk), esophageal varices (arrow), and partial regression of hepatic metastases. Findings are of pseudocirrhosis of treated breast cancer metastases; however, without prior studies and clinical history, these findings could suggest diagnosis of cirrhosis.
Fig. 3—68-year-old woman who presented for imaging after receiving two cycles of chemotherapy for hepatic metastases thought to be from primary pancreatic carcinoma. 
A, Axial contrast-enhanced CT image shows liver surface is coarsely lobulated with several irregular hypodense parenchymal lesions. Appearance was considered suggestive of pseudocirrhosis, casting doubt on diagnosis of pancreatic cancer. 
B, Axial contrast-enhanced image obtained at more superior level than A shows small hypervascular lesion (arrow) in right breast. Further workup including resection of breast mass confirmed diagnosis of metastatic breast cancer.

Fig. 4—61-year-old man with fulminant hepatic failure and history of chronic hepatitis B infection. 
A, Contrast-enhanced CT image shows nodularity (arrow) of liver surface outlined by ascites; these findings are suggestive of cirrhosis. Histopathologic examination of explanted liver 5 days later showed confluent regenerative nodules surrounded by large areas of necrosis, but no cirrhosis. Hepatic surface nodularity is not a reliable sign of underlying cirrhosis in fulminant hepatic failure and should not be used to diagnose cirrhosis in this setting. 
B, Photomicrograph of explanted hepatic surface from transplant surgery performed 5 days after A shows that irregularity of liver surface reflects combination of confluent regenerative nodules (R) and alternating bands of necrosis (N). (H and E, ×200)

Fig. 5—67-year-old woman with fulminant hepatic failure that developed 6 weeks after commencement of methyldopa therapy for hypertension. Sagittal ultrasound image of right hepatic lobe shows nodularity (arrow) of liver surface outlined by ascites; these findings are suggestive of cirrhosis. Histopathologic examination of explanted liver 3 days later showed confluent regenerative nodules surrounded by large areas of subacute necrosis but no cirrhosis.
Fig. 6—64-year-old woman with metastatic lobular breast cancer. Axial contrast-enhanced CT image shows fine nodularity of hepatic surface. Liver biopsy revealed metastatic breast cancer without cirrhosis.

Fig. 7—58-year-old woman with bilateral lobular breast cancer. Axial contrast-enhanced CT image shows widespread diffuse parenchymal and surface hepatic nodularity. Biopsy revealed metastatic disease without cirrhosis.

Fig. 8—32-year-old man with sarcoidosis. Axial contrast-enhanced CT image shows widespread diffuse parenchymal and surface hepatic nodularity (arrow). Appearance of liver on CT alone could be interpreted as cirrhosis, but note multiple hypodense nodules in spleen. Retroperitoneal adenopathy (not shown) was also present. Nodal biopsy confirmed diagnosis of sarcoidosis.

Fig. 9—44-year-old man with sarcoidosis. Axial unenhanced CT image shows splenomegaly (asterisk) and recanalized umbilical vein (arrow) arising from somewhat shrunken and irregular liver. Liver biopsy revealed sarcoidosis without cirrhosis. Sarcoidosis is one cause of noncirrhotic portal hypertension.
Radiologic Mimics of Cirrhosis

Fig. 10—58-year-old man with history of renal transplantation for HIV nephropathy who presented with sepsis 1 day after right hemicolectomy for colonic volvulus. 

A, Sagittal ultrasound image of right hepatic lobe shows subtle echogenic nodularity of liver that could be considered suggestive of cirrhosis. Representative nodule (arrow) is visible anteriorly.

B, Axial contrast-enhanced CT image shows subtle parenchymal heterogeneity consisting of small hypodense nodules. Representative nodule (arrow) is visible posteriorly. Subsequent liver biopsy confirmed diagnosis of nodular regenerative hyperplasia.

Fig. 11—60-year-old man with portal hypertension leading to gastrointestinal bleeding, ascites, and thrombocytopenia due to biopsy-proven nodular regenerative hyperplasia in liver transplant; transplantation was performed 18 years earlier for primary sclerosing cholangitis. Axial contrast-enhanced CT image shows liver surface (arrow) is irregular and shows relative hypertrophy of left hepatic lobe (asterisk). These findings mimic those of cirrhosis.

Fig. 12—11-year-old girl with renal failure due to autosomal recessive polycystic kidney disease. Coronal T2-weighted MR image shows kidneys (K) are replaced by innumerable relatively small cysts. Focal segmental biliary dilatation (arrow) in liver reflects coexistent congenital hepatic fibrosis, which can occur in association with autosomal recessive polycystic kidney disease and is cause of noncirrhotic portal hypertension. Note spleen (asterisk) is enlarged.

Fig. 13—68-year-old man with idiopathic portal hypertension. Axial contrast-enhanced CT image shows splenomegaly (S), gastroesophageal varices (white arrow), and ascites (black arrow), but liver appears normal in size and contour. Liver biopsy confirmed absence of cirrhosis; final diagnosis was idiopathic portal hypertension.

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