

# Imaging of Biliary Infections

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## Abstract

### Keywords

- ▶ biliary infections
- ▶ cholangitides
- ▶ parasites
- ▶ immunocompromised
- ▶ echinococcal

Biliary tract infections cover a wide spectrum of etiologies and clinical presentations. Imaging plays an important role in understanding the etiology and as well as the extent of disease. Imaging also plays a vital role in assessing treatment response once a diagnosis is established. This article will review the imaging findings of commonly encountered biliary tract infectious diseases.

Infections of the biliary tree can have a myriad of clinical and imaging manifestations depending on the infectious etiology, underlying immune status of the patient and extent of involvement.<sup>1,2</sup> Bacterial infections account for the vast majority of infectious cholangitides though parasitic, fungal, and viral infections can also affect the biliary system. Clinically, the range of clinical manifestations of bacterial infections extends from an acute medical emergency with clinical symptoms of right upper quadrant (RUQ) pain, fever, and jaundice to indolent and chronic, low-level infections.

## Bacterial Cholangitides

Bacterial cholangitis is a clinical syndrome that arises when infected bile enters the circulatory system.<sup>3–5</sup> Cholangitis typically manifests as fever, jaundice, and RUQ pain (Charcot's triad) and may or may not result in biliary sepsis. Reynolds pentad describes the combination of fever, jaundice, and RUQ pain with hypotension and confusion/lethargy. Commonly encountered microorganisms include *Escherichia coli*, *Enterococcus*, *Klebsiella*, and *Pseudomonas*, as well as anaerobes.<sup>4,6</sup> The combination of microbiological contamination of bile in the setting of increased biliary pressure can lead to the clinical manifestation of acute cholangitis.<sup>5,7</sup> Elevated biliary pressures directly impact the severity and mortality of acute cholangitis.<sup>8</sup> Interruption of normal flow of bile into the

duodenum can lead to a cascade of changes to the host immune defense mechanisms of chemotaxis and phagocytosis.<sup>7</sup> The resultant lack of bile and secretory immunoglobulin A from the gastrointestinal tract lead to changes of the normal bacterial flora, disrupted mucosal integrity, and diminished inactivation of endotoxins resulting in sepsis.

## Imaging Features of Acute Cholangitis

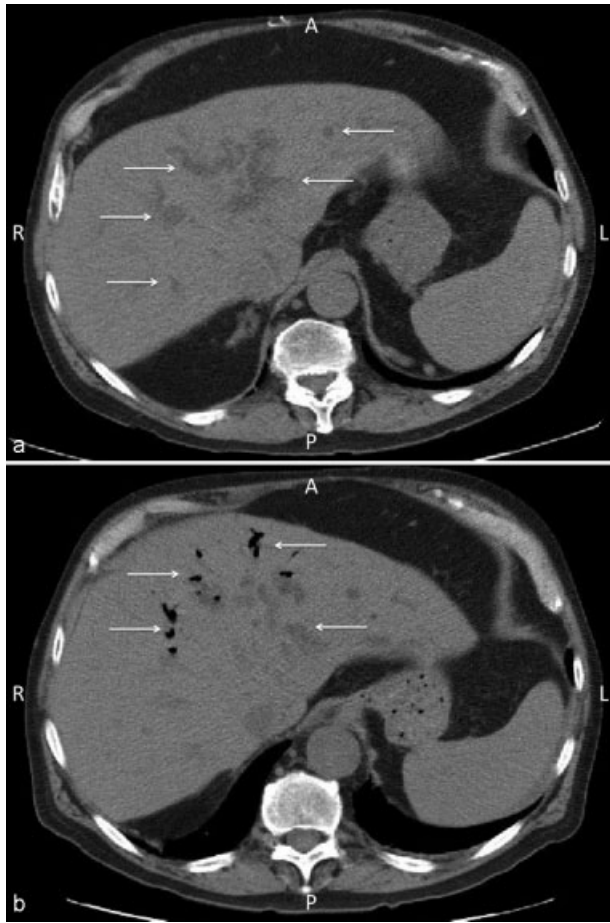
Diagnostic cross-sectional imaging of the liver and biliary tree is necessary for evaluation of the patient with clinical features of cholangitis.<sup>9–11</sup> Ultrasound (US) is a valuable diagnostic tool for the evaluation of the liver and bile ducts and is associated with high sensitivities and specificities for evaluation of biliary obstruction.<sup>10</sup> Although it is widely available, noninvasive, and cost-effective, it has limited evaluation of the distal common bile duct, a common site for stones. Computed tomography (CT) and magnetic resonance imaging (MRI) offer improved anatomic resolution and assessment of extrahepatic structures than US and therefore are more frequently utilized to assess biliary obstruction and its potential causes (▶**Fig. 1**).<sup>12–16</sup> Biliary obstruction can be diffuse or only involve segmental or centrally located ducts and is frequently associated with enhancement of the bile duct wall.<sup>9</sup> CT offers the ability to assess the extent of obstruction and parenchymal changes that may be associated with cholangitis.<sup>17</sup> Arai et al

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**Fig. 1** (a) Axial unenhanced CT scan of the liver in a patient who is s/p liver transplant with fever and sepsis. White arrows point to intrahepatic biliary ductal dilatation. (b) Axial unenhanced CT scan of the liver in a patient who is status post liver transplant with fever and sepsis taken 12 hours after scan obtained in (a). White arrows indicated new pneumobilia within dilated intrahepatic bile ducts, consistent with ascending cholangitis. CT, computed tomography.

compared hepatic parenchymal patterns on dynamic CT of patients with cholangitis to those without and found that inhomogeneous enhancement was significantly higher in patients with cholangitis and that this finding resolved following treatment.<sup>11</sup>

### Parasitic Infections

Parasitic infections have a spectrum of clinical manifestations depending on their underlying etiology. When combined with bacterial infections, there is much overlap with bacterial cholangitis. Eosinophilia is a common clinical manifestation of parasitic infections and can be helpful in the diagnostic evaluation of suspected biliary inflammation.

#### Fascioliasis

*Fasciola hepatica* is the causative parasite responsible for fascioliasis. *Fasciola hepatica* is a liver fluke that is commonly encountered in underdeveloped countries. The pathway to human infection is somewhat circuitous that results from accidental ingestion of vegetables or water sources that are



**Fig. 2** Contrast material-enhanced axial CT scan of the liver that demonstrates segmental biliary duct dilatation (white arrows) in the periphery of the liver. CT, computed tomography.

infected with metacercariae. Once ingested, the metacercariae penetrate the upper gastrointestinal tract and eventually migrate into the peritoneal cavity. From the peritoneal cavity, they penetrate the liver capsule and infect the liver where they can remain for extended periods of time. CT imaging during the hepatic phase shows irregular areas of hypoattenuation, often in the periphery of the liver (→ **Fig. 2**). Eventually, the flukes enter the biliary tree where they cause inflammation, ductal thickening, and localized obstruction.<sup>18</sup>

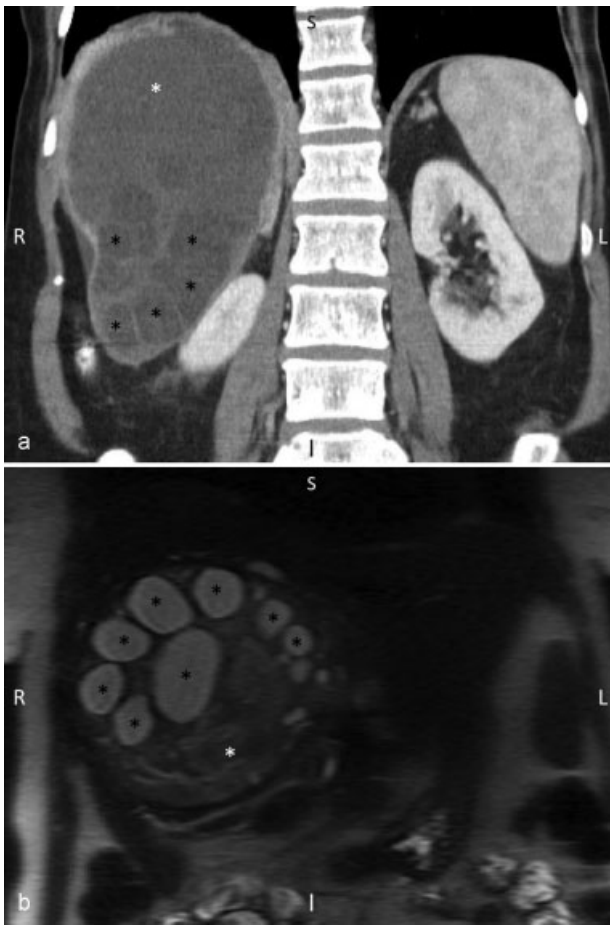
### Echinococcal Infections

Echinococcosis results from *Echinococcus multilocularis* and *Echinococcus granulosus* infestation. Both parasites are cestodes in which foxes and dogs act as definitive hosts. Human infection arises from ingestion of vegetables contaminated with parasitic eggs. After ingestion, embryos release eggs into the intestine, which then penetrate the bowel wall and are delivered to the liver via the portal venous system where they encyst within the hepatic parenchyma.<sup>19</sup> Imaging findings of *E. granulosus* hepatic infections depend on the different growth stages of the hepatic cyst. Early infections are characterized by a simple cyst on CT or MRI.<sup>20,21</sup> The development of daughter cysts within the primary cyst gives a characteristic spoke wheel pattern (→ **Fig. 3**). Without therapy, the echinococcal cysts can enlarge and extend into the biliary tree leading to filling defects and obstruction.<sup>22–25</sup>

Imaging features of *E. multilocularis* differ from *E. granulosus*. *Echinococcus multilocularis* hepatic infection manifests as a multilocular cystic structure that induces intense fibrosis and that can extend out of the liver into surrounding structures, including the biliary tree and hepatic vessels.<sup>20,21,26</sup>

#### Schistosomiasis

The trematodes *Schistosoma mansoni* and *Schistosoma japonicum* are venoinvasive parasites that infect humans through contact with contaminated water. The parasites are capable of cutaneous penetration after which they migrate to pulmonary parenchyma and eventually invade branches of



**Fig. 3** (a) Coronal contrast material-enhanced CT scan of the liver demonstrates multiple daughter cysts (black asterisks) within the primary *Echinococcus* liver cyst (white asterisk). (b) Coronal T2WI of the liver demonstrates multiple daughter cysts (black asterisks) within the primary *Echinococcus* liver cyst (white asterisk). CT, computed tomography; T2WI, T2-weighted imaging.

the portal venous system via branches of the superior and inferior mesenteric veins.<sup>27</sup> Although in the portal veins, the eggs grow to sexual maturity where male and female worms mate before migrating to the bowel wall. Some eventually infect the liver via the portal vein and once deposited within the liver, the eggs activate an immunologic response that stimulate granulomatous response and eosinophilia that ultimately leads to liver fibrosis.<sup>28–30</sup> Periportal fibrosis can lead to changes of the biliary tree that manifests as obstruction (rarely) or pruning of distal biliary branches and bile duct proliferation.<sup>30,31</sup>

### Ascariasis

Ascariasis is a parasitic infection that is caused by the helminth *Ascariasis lumbricoides*, which is a type of roundworm that afflicts approximately 1 billion people worldwide.<sup>32</sup> Humans become infected when they ingest water or vegetables contaminated by eggs. The ingested eggs subsequently hatch in the small intestine. *Ascariasis lumbricoides* larvae penetrate the bowel wall and are carried into the liver (and lungs)

through the portal vein where they can eventually invade the biliary tree, especially the common bile duct.<sup>33–37</sup> Stone formation can occur due to dead parasites within the biliary tree and hepatic abscesses can develop.<sup>35,38,39</sup>

Clinically, abdominal symptoms include abdominal distention, biliary colic, nausea, and anorexia. US imaging is considered the first-line imaging modality when the clinical suspicion is high. Typical sonographic features include linear echogenic structures within the common bile duct or gallbladder.<sup>40–42</sup> Posterior acoustic shadowing is not a typical sonographic feature. Although endoscopic retrograde cholangiopancreatography is the diagnostic gold standard, cross-sectional imaging with CT or MRI/magnetic resonance cholangiopancreatography (MRCP) is useful adjuncts to US. CT shows hyperattenuating linear structures within the common bile duct or gallbladder.<sup>37</sup> MRCP findings include low signal intensity on T2-weighted imaging.<sup>43–45</sup>

### Biliary Infections in the Immunocompromised

Immunocompromised patients are at risk of hepatobiliary tract infections.<sup>46,47</sup> The human immunodeficiency virus can involve the hepatobiliary tree, especially in individuals with severe immunosuppression (CD4 counts < 100/mm<sup>3</sup>).<sup>48,49</sup> A wide variety of causative organisms have been associated with acquired immune deficiency syndrome (AIDS)-related cholangiopathy, including *Cryptosporidium*, *Cryptococcus*, cytomegalovirus (CMV), *Mycobacterium*, and histoplasmosis.<sup>49–53</sup> Clinically, AIDS-related cholangiopathy presents as RUQ pain, usually in the setting of serologic manifestations of liver function abnormalities. Imaging features of AIDS-related cholangiopathy resembles findings of sclerosing cholangitis.<sup>54</sup> Cholangiographic abnormalities often demonstrate a beaded appearance of the bile ducts with segmental strictures.<sup>55</sup> MRCP shows characteristic ductal abnormalities such as papillary stenosis, intraductal strictures, and extrahepatic long-segmental strictures or a calculous cholecystitis.<sup>56–61</sup>

Patients who have undergone liver transplant represent another group at risk of biliary infections. Cholestatic liver disease is the most commonly encountered problem following orthotopic liver transplant (OLT) and can result from several causes. Viral infection, rejection, or ischemic injury to the bile ducts have been reported in OLT patients.<sup>62–65</sup> Percutaneous biopsy is often necessary to elucidate the etiology of cholestasis, especially when ischemic, rejection, or drug effects are suspected.<sup>66</sup> However, there can be significant overlap with obstructive and nonobstructive causes of cholestatic liver injury OLT patients such that an accurate diagnosis often requires cross-sectional imaging. MRCP and transhepatic cholangiography are more sensitive than US for the assessment of biliary stasis in OLT patients.<sup>67,68</sup> Liver transplant recipients are also prone to opportunistic viral infections, of which CMV is most common.<sup>69</sup> CMV-infected immunocompetent individuals are usually asymptomatic. In the immunosuppressed liver transplant recipient, however, CMV infection can present with

severe clinical symptoms including fever, mononucleosis, gastritis, colitis, abdominal pain, and diarrhea. Liver involvement of CMV includes hepatitis with a cholestatic presentation based on liver function abnormalities.<sup>70</sup> Biopsy is often necessary to excluded tissue rejection. In addition, biologic markers of CMV pp65 or CMV DNA by polymerase chain reaction are detectable at very early stages of infection.<sup>70,71</sup> To combat the effects of CMV infection, aggressive antiviral prophylaxis with valganciclovir or ganciclovir for up to 3 months following liver transplant is often employed. This approach, however, may result in delayed onset CMV disease once antivirals are discontinued.<sup>72</sup> Another approach is to carefully monitor serologic CMV viral loads or pp65 antigenemia for signs of infection and initiate antiviral therapy once infection is detected. This strategy allows very short-term low level of CMV infection, which may act to prime the hosts' immune system to develop CMV immunity. Fortunately, ganciclovir is a highly effective antiviral for CMV infections and most liver transplant recipients show good treatment response after initiation of therapy.

## Conclusion

Infections of the biliary tree comprise a wide range of etiologies and clinical manifestations. The role of diagnostic imaging is critical to help identify its causes, to determine the extent of disease, and to assess for infection-related complications.

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