Pathophysiology of Jaundice in Amoebic Liver Abscess

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Abstract. Jaundice in patients with amoebic liver abscess is a frequent occurrence. However, the pathophysiology of jaundice in these patients is not fully understood. Hepatic necrosis leads to damage to bile ducts as well as various vascular structures, which in turn leads to biliovascular fistula and jaundice. We studied the mechanism of jaundice in patients with amoebic liver abscess. We prospectively evaluated 12 patients with amoebic liver abscess and jaundice from February 2002 to August 2007. All patients underwent various investigations, including imaging studies. There were 11 males and 1 female patient with a mean age of 41.3 years. Mean duration of illness before presentation was 13.8 days. All patients had fever and jaundice. We detected damaged hepatic veins and bile ducts in all patients with amoebic liver abscess causing biliovascular fistula and hyperbilirubinemia, which reverted to normal after biliary diversion with nasobiliary drainage. Jaundice in patients with amoebic liver abscess is caused by biliovascular fistula resulting from hepatic necrosis leading to damage to bile ducts and hepatic veins.

INTRODUCTION

The incidence of jaundice in patients with amoebic liver abscess varies between 6% and 29%.1–7 The mechanism of jaundice in these patients is still controversial. Various explanations of jaundice in these patients have included pressure of an abscess on hepatic ducts7–10 or that it is parenchymal or cholestatic in nature.3,6,11 Amoebic liver abscess is a well-circumscribed region of dead hepatocytes, liquefied cells, and cellular debris.12 Varying degrees of biliary damage have also been reported in patients with amoebic liver abscess.5 Similarly, vascular injury caused by hepatic necrosis is expected in these patients to result in biliovascular fistula. As a result, a mixture of bile and blood may accumulate in the damaged area of the liver and be diverted toward low-pressure areas. If the damaged vessel is the hepatic or portal vein, the mixture flows toward the hepatic or portal vein side and leads to a rapid rise of bilirubin. Therefore, we prospectively studied the mechanism of jaundice with amoebic liver abscess.

MATERIALS AND METHODS

Twelve patients with a solitary amoebic liver abscess and jaundice were included in this study between February 2002 and August 2007. A diagnosis of amoebic liver abscess was based on ultrasonogram as well as positive amoebic serology.13 Jaundice was diagnosed only when the serum bilirubin was above 2 mg/dL. All patients underwent routine laboratory investigations along with imaging and serology. Endoscopic retrograde cholangiopancreatography (ERCP) and nasobiliary drainage and percutaneous catheter drainage were done in all patients along with anti-protozoal and antibiotic treatment. Written informed consent was obtained from all patients, and the board of Institute doctors reviewed and approved the study.

RESULTS

A total of 12 patients were included in this study (11 males, 1 female), with a mean age of 41.3 ± 9.2 years (range, 30–65 years). All patients had jaundice and fever. Clinical findings and investigations are shown in Table 1. All patients were positive for amoebic serology. Ultrasonogram and computed tomography revealed solitary abscess in the right (11 patients) or left (1 patient) lobe with damaged right or left hepatic vein in all patients (Figures 1 and 2). ERCP in all patients showed biliary communication with abscess cavity (Figure 3). In 8 patients, contrast media extravasation was also seen in the hepatic veins after the biliary leak was observed draining into the abscess cavity (Figure 4). All patients underwent 7F nasobiliary drain placement. All patients also underwent percutaneous catheter drainage for a mean period of 15.2 days (range 7–21 days). All patients were also treated with metronidazole, 800 mg, 3 times a day with ciprofloxacin for 10 days. Bilirubin returned to normal and the leak subsided with nasobiliary drainage for a mean period of 12.1 days (range 7–21 days) (Figure 5). There were no procedure-related complications.

DISCUSSION

Hyperbilirubinemia in amoebic liver abscess has been seen with varying frequency and depth.1–7 The level of serum bilirubin in our patients varied from 4.2 to 21.3 mg/dL. Jaundice in patients with amoebic liver abscess has been explained by

| Table 1
<table>
<thead>
<tr>
<th>Parameter</th>
<th>Number (N = 12)</th>
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<tr>
<td>Clinical features</td>
<td></td>
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<tr>
<td>Age (years)</td>
<td>41.3 ± 9.2</td>
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<tr>
<td>Sex (male/female)</td>
<td>11:1</td>
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<tr>
<td>Duration of illness (days)</td>
<td>13.8 ± 6.57</td>
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<tr>
<td>Abdominal pain</td>
<td>9 (75)</td>
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<tr>
<td>Fever</td>
<td>12 (100)</td>
</tr>
<tr>
<td>Jaundice</td>
<td>12 (100)</td>
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<tr>
<td>Anorexia</td>
<td>6 (50)</td>
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<tr>
<td>Investigations</td>
<td></td>
</tr>
<tr>
<td>Total leukocyte count (cells/mm³)</td>
<td>13608 ± 4931</td>
</tr>
<tr>
<td>Serum bilirubin (mg/dL)</td>
<td>8.7 ± 5.1</td>
</tr>
<tr>
<td>Serum glutamic oxaloacetic transaminase (U/L)</td>
<td>43.0 ± 25.7</td>
</tr>
<tr>
<td>Serum glutamate pyruvate transaminase (U/L)</td>
<td>38.7 ± 16.6</td>
</tr>
<tr>
<td>Alkaline phosphatase (KA units)</td>
<td>35.6 ± 18.3</td>
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<tr>
<td>Size of abscess (cm)</td>
<td>11.0 ± 1.8</td>
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* Data are mean ± SD; figures in parentheses are percentages.
various mechanisms, such as pressure on biliary ducts\textsuperscript{7,10} or as being cholestatic or parenchymal in nature.\textsuperscript{3,6,11} The mechanism of hyperbilirubinemia in amoebic liver abscess was studied previously.\textsuperscript{5,8} In these studies, in patients with amoebic liver abscess, the transport maximum, which represents the rate of bromosulfophthalein (BSP) excretion by hepatic parenchymal cells, was significantly reduced. However, storage capacity was well preserved. In another study, authors also demonstrated significantly reduced BSP excretion in patients with amoebic liver abscess with jaundice.\textsuperscript{7} We demonstrated damaged biliary ducts and hepatic veins in amoebic liver abscesses resulting in biliovascular fistula. Earlier authors also demonstrated no obstruction to the main left or right hepatic duct but did report definite compression and even destruction of some of the tributaries of the involved lobe bile duct.\textsuperscript{5} Delayed BSP excretion in patients with amoebic liver abscess with jaundice, as seen in earlier studies,\textsuperscript{7,8} also supports biliary–vascular fistula, as demonstrated in our study. Clinical manifestations of biliary–vascular fistulas depend on the pressure gradients between the vascular system and the biliary tract. In a normal subject, the mean hepatic artery pressure is 100 mmHg and the hepatic vein pressure is 0–5 mmHg. Therefore, when a biliary–vascular fistula involves an artery, the pressure gradient causes the flow of blood into the

\begin{figure}[h]
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\includegraphics[width=\textwidth]{figure1.png}
\caption{Ultrasonogram showing abscess in right lobe with damaged right hepatic vein.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure2.png}
\caption{Computed tomography showing abscess in right lobe with damaged right hepatic vein.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure3.png}
\caption{ERCP showing biliary communication with abscess cavity.}
\end{figure}

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{figure4.png}
\caption{Cholangiogram showing nasobiliary drain with contrast media extravasation into the hepatic vein (arrow) after visualizing biliary leak into abscess cavity.}
\end{figure}
bile duct, termed hemobilia. When a biliary–vascular fistula involves a venous system (portal or hepatic), the pressure gradient directs the bile and blood mixture toward the right side of heart—termed bilhemia—leading to a rapid rise of bilirubin without much enzyme increase. Bilhemia is a frequent occurrence after traumatic injury to the liver.

There are no reports of bilhemia in patients with amoebic liver abscess. All of our patients with amoebic liver abscess with jaundice had bilhemia. Various treatment modalities have been used for patients with bilhemia, including surgery, biliary drainage by sphincterotomy, stenting, nasobiliary drain, continuous T-tube suction, balloon occlusion of fistula, and covered stent placement. The principle of therapy of biliovascular fistula is to decrease the pressure gradient across the Oddi sphincter, thereby causing reversal of bile flow. Reversal of bile flow helps in closure of the biliovenous fistula by preventing entry of bile into the abscess cavity and hence into the hepatic vein. Various methods, such as long or short stents and nasobiliary drain with or without sphincterotomy, have been used to facilitate biliary drainage and leak closure in patients with post-cholecystectomy biliary leaks by decreasing the pressure gradient across the sphincter. Endoscopic sphincterotomy carries a risk of complications, and a repeat endoscopy is required to remove stent; hence, we managed all of our patients with nasobiliary drainage. Normalization of bilirubin and leak closure with biliary drainage support biliovascular fistula as the cause of jaundice in patients with amoebic liver abscess.

In conclusion, jaundice in patients with amoebic liver abscess is caused by biliovascular fistula. Nasobiliary drainage without sphincterotomy is an effective method of treatment of such patients.

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