ภาวะเลือดออกจากท่อน้ำดี: วินิจฉัยและรักษา

Hemobilia: Diagnosis and Management

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บทคัดย่อ:
ภาวะเลือดออกจากท่อน้ำดีเป็นสาเหตุที่พบไม่บ่อยของเลือดออกจากทางเดินอาหารและยากต่อการวินิจฉัย อาการแสดงที่พบมักมีอาการเลือดออกจากทางเดินอาหารส่วนต้น ปวดท้อง และเหลือง กลไกการเกิดภาวะเลือดออกจากท่อน้ำดีอาจเกิดจากเนื้องอกของท่อน้ำดี การฉีกขาดหรือเชื่อมต่อระหว่างท่อน้ำดีและหลอดเลือดที่เลี้ยงบริเวณท่อน้ำดี สาเหตุเกิดจากอุบัติเหตุจากการตรวจวินิจฉัยหรือการรักษาทางการแพทย์ อุบัติเหตุทางช่องท้อง นั่นคือการตรวจหรือการรักษา การอักเสบและความผิดปกติของหลอดเลือดบริเวณท่อน้ำดี การตรวจทางสาเหตุเบื้องต้นโดยการส่องกล้อง เอกซเรย์คอมพิวเตอร์หลอดเลือด หรือการตรวจหลอดเลือดโดยการฉีดสี มีความสำคัญต่อการวินิจฉัยที่ถูกต้องและการวางแผนการรักษา หลักการของการรักษาภาวะดังกล่าวคือการช่วยชีวิตเบื้องต้น การหยุดเลือดและการระบายน้ำดีหากเกิดการอุดตัน ซึ่งการรักษาดังกล่าวมีความจำเป็นที่ต้องได้รับความร่วมมือจากหน่วยงานทางการแพทย์ เช่น การรักษาทางยา การส่องกล้อง รังสีร่วมรักษา และการผ่าตัด

คำสำคัญ: การหยุดเลือด, ภาวะเลือดออกจากท่อน้ำดี
Abstract:

Hemobilia is an uncommon cause of gastrointestinal hemorrhage and difficult to diagnosis. Clinical presentations are upper gastrointestinal hemorrhage, abdominal pain and obstructive jaundice. There are various mechanisms of hemobilia such as bleeding tumor of bile duct, ductal tear, a communication or fistula between the biliary tract and vascular system resulting from iatrogenic, trauma, tumor, gallstone, inflammation and vascular disorder. Urgent investigation should be done by endoscopy, computerized angiography and angiography for definite diagnosis and plan of treatment. The principle of therapy are resuscitation, control hemorrhage and restoration bile flow from obstruction. Multi-modality approach is the mainstay of treatment including medical therapy, endoscopy, intervention radiology and surgery.

Keywords: controlling hemorrhage, hemobilia

Introduction

Hemobilia is an uncommon cause of upper gastrointestinal (GI) hemorrhage resulting from various mechanisms such as bleeding tumor of bile duct, ductal tear, abnormal communication or fistula between the biliary tract and vascular system. Hemobilia has been used by Sandblom since the year 19481, he described patients, who had hemorrhage into the biliary tract after blunt abdominal trauma. In 1654, Francis Glisson described mechanisms of the bleeding in post mortem examination, A young noble man presented with massive gastrointestinal bleeding following a deep laceration of the liver. “I believe that if the liver is injured by a contusion, it may lead to blood leaving the body by way of vomit, or the stool for there is no doubt then the bile ducts take unto itself (to the great good of the patient) some of the blood issuing into the liver and leads it down to the intestines, from there it is either impelled upwards through reverse peristalsis, or downwards in the normal way”.2 In 1871, the German surgeon Heinrich Quincke described a case of hemobilia, characterized biliary tract hemorrhage by establishing three clinical features of right upper quadrant pain, obstructive jaundice and upper gastrointestinal hemorrhage. These signs and symptoms are now recognized as classical clinical (Quincke’s) triad.3 In 1972, Sandblom published his extensive review on hemobilia with the largest number of secondary to accidental trauma following with iatrogenic trauma, gallstone, inflammation, vascular disorder and neoplasm.4

Hemobilia has been established in diagnosis not only clinical presentations but also the modern modalities. Therapeutic endoscopy and intervention radiology, are widely available to diagnosis and management. In 1976, Walter was the first person to use angiographic embolization for the treatment of this condition, and this has become the mainstay of treatment in most cases of hemobilia.5 The objective of this article is to up-to-date review in diagnosis and management of hemobilia patients.

In the classic description of the arterial supply to the liver, the celiac trunk trifurcates into left gastric, splenic and common hepatic arteries. The end of common hepatic artery bifurcates into the proper hepatic artery and gastroduodenal artery. The proper hepatic artery trifurcates into the left hepatic, intermediate hepatic and the right hepatic artery, which is originate of cystic artery to supply gallbladder. However, there are numerous variations on this classic pattern. The blood supply of common bile duct divides into two parts, the upper part of the bile duct along with the hepatic ducts receive blood supply from the cystic artery,
and small branches of right hepatic artery, and the lower part bile duct receive by posterior superior pancreatico-duodenal artery (Figure 1).\(^6\,7\)

**Clinical presentation**

Clinical presentations are upper GI hemorrhage, abdominal pain (biliary colic) 70.0% of patients and obstructive jaundice 60.0% of patients. The classic clinical (Quincke’s) triad is presented only 22.0–37.9% of patients.\(^8\) However, the presentation of blood may be seen from percutaneous catheter such as percutaneous transhepatic biliary drainage (PTBD) tube or operative-placed drainage tube. These clinical presentations depend on rate, duration and cause of the bleeding. Clinical significant hemobilia is associated with a 94.0% positive predictive value for concomitant arterial injury found during angiography.\(^9\) Rapid hemobilia is more likely to present with abdominal pain and upper gastrointestinal hemorrhage, with life-threatening possibilities. Slow hemobilia, blood and bile do not mix because of their differences in surface tension and specific gravity, resulting in clot formation and obstruction of the bile duct.\(^8\,10\) Location of blood clot obstruction cause of acute cholangitis, cholecystitis or pancreatitis have been reported.\(^11\)

An arterial source of hemorrhage is usually symptomatic, while venous hemobilia is rare. Pressure gradients in the hepatic venous and portal venous system systems are usually low. The majority of fistula between venous and biliary systems are asymptomatic with the exception in cases of portal hypertension. Venous hemobilia is frequently associated with percutaneous transhepatic biliary drains and can be managed with tamponade effect of upsizing the drainage catheter.\(^12\)

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**Figure 1** Anatomy of the liver and bile duct system\(^6\)
Etiology

The predominant etiology of hemobilia has changed over the time. Historically, hemobilia was associated most commonly with external trauma (both penetrating and blunt). The development of percutaneous interventional techniques, iatrogenic hemobilia is more frequent. Iatrogenic hemobilia currently comprises over 60.0% of all cases followed with non–iatrogenic trauma hemobilia. Other causes of hemobilia are gallstone, inflammation, malignancy and abnormal vascular disorder.4,8,13 Table 1. Identified the etiology of hemobilia in large different case series and periods of time.

Iatrogenic hemobilia

Biliary hemorrhage is reported as a complication of diagnosis and therapeutic procedure on the liver or the bile duct and currently is a majority cause of hemobilia. All kinds of percutaneous liver interventions such as liver biopsy, percutaneous transhepatic cholangiography (PTC), percutaneous biliary therapies (drainage) and percutaneous ethanol injection or radiofrequency ablation procedure are risk for this complication because of a needle leads to incidental trauma of the bile ducts, which are close to branches of hepatic artery and portal vein causing accidental concurrent injury to these structures and fistula formation. Higher incidence of hepatic vascular abnormalities following percutaneous liver interventions 3.8–5.4%.15,16 The incidence of symptomatic hemobilia post percutaneous liver interventions in recent large series are 1.0–2.3%. Percutaneous liver biopsy and PTC have trended to lower rates than indwelling drainage catheter.9,17

Endoscopic retrograde cholangiopancreatography (ERCP) is a procedure of trans–ampulla biliary access and intervention can be a cause of hemobilia, especially in cases of portal bilipathy, indwelling biliary stents (plastic or metal) and intrahepatic vascular anomalies.18,19 Hemobilia occurs following an endoscopic procedure is commonly transient and asymptomatic hemobilia. Post ERC bleeding usually resolves with non–interventional management, however adequate biliary drainage must be confirmed.10

There are numerous case reports of hemobilia from cystic and right hepatic artery pseudoaneurysm as a complications of laparoscopic and open cholecystectomy.20,21 Postoperative bile leakage or infection is thought to be irritating to vessel walls, delaying healing of damaged vessels at surgery and leading to pseudoaneurysm formation. The

Table 1  Etiology of hemobilia from four review of the literature since 1972

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<thead>
<tr>
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<tr>
<td></td>
<td>(n=355) (%)</td>
<td>(n=103) (%)</td>
<td>(n=222) (%)</td>
<td>(n=37) (%)</td>
</tr>
<tr>
<td>Iatrogenic</td>
<td>59 (17.0)</td>
<td>42 (41.0)</td>
<td>148 (67.0)</td>
<td>–</td>
</tr>
<tr>
<td>Accidental trauma</td>
<td>137 (38.0)</td>
<td>20 (19.0)</td>
<td>12 (5.4.0)</td>
<td>–</td>
</tr>
<tr>
<td>Gallstones</td>
<td>53 (15.0)</td>
<td>9 (9.0)</td>
<td>11 (5.0)</td>
<td>–</td>
</tr>
<tr>
<td>Inflammation</td>
<td>46 (13.0)</td>
<td>10 (10.0)</td>
<td>22 (10.0)</td>
<td>8 (21.0)</td>
</tr>
<tr>
<td>Vascular</td>
<td>38 (11.0)</td>
<td>15 (14.0)</td>
<td>20 (9.0)</td>
<td>–</td>
</tr>
<tr>
<td>Neoplasm</td>
<td>22 (6.0)</td>
<td>7 (7.0)</td>
<td>14 (6.3.0)</td>
<td>28 (75.0)</td>
</tr>
<tr>
<td>Others</td>
<td>1 (0.5)</td>
<td>1 (2.7)</td>
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*Study excluded iatrogenic hemobilia
potential risk of hemobilia with any hepatobiliary surgery, which damages to vessels or bile duct may heal with pseudoaneurysm formation causing hemobilia. Liver transplantation and pancreaticoduodenectomy (Whipple operations) have also reported to be complicated by hemobilia.

**Traumatic hemobilia**

The liver is one of the organs most commonly injured by blunt abdominal trauma having been reported in 1.0–8.0% of multiple blunt trauma cases and detected on routine computed tomography (CT scan) approximately 25.0% of cases. Currently, the majority of hemodynamic stable patients with blunt liver trauma are managed with nonsurgical management with clinical success of 50.0–80.0% of patients. Blunt liver injury may result in a shearing injury to the hepatic artery, healing with fibrous formation and form of hepatic artery pseudoaneurysm, which was reported in 1.0–3.0% of blunt abdominal injuries. These pseudoaneurysm may rupture to intra-peritoneal or fistulized to biliary tract manifesting as hemobilia. Penetrating liver injury, are high risk to the liver and vascular injury but lower incidence of hemobilia due to surgeons usually exploring primarily and adequate management during initial operation.

**Cholelithiasis or choledocholithiasis**

Cholelithiasis can cause minor trauma to the mucosa and microscopic bleeding in about 9.0–15.0% of cases. Hemobilia in this setting is more likely to be minor. Cholelithiasis may be a cause of significant hemobilia if the stone erodes through the hepatoduodenal ligament of the cystic artery.

**Inflammatory disorder**

Acalculous inflammation of biliary tract are implicated in 10.0–13.0% of hemobilia cases. Which is a high prevalence in developing countries, where there are more prevalence in parasitic infestation. Some nematodes and trematodes infestation to biliary tract and liver. Including roundworm; *Ascaris lumbricoides*, Liver fluke (*Clonochis sinensis* and *Fasciola hepatica*). They may cause biliary obstruction, ascending cholangitis, acute cholecystitis, pancreatitis, hepatic abscess and hemobilia. Hydatid cysts in the liver caused by Echinococcal infection also leads to perivascular and periportal inflammation causes of pseudoaneurysm formation.

Chronic pancreatitis is a known cause of pseudoaneurysm formation of pancreaticoduodenal, splenic, hepatic and gastroduodenal artery aneurysm. Chronic cholecystitis may be complicated by cystic artery pseudoaneurysm.

**Vascular disorder**

Primary vascular causes of significant hemobilia have been identified in 9.0–14.0% of cases since 1948. True hepatic artery aneurysm are the most common primary vascular disorder to significant hemobilia, but the incidence is diminishing after disappearance of mycotic aneurysm. Primary vasculitis is a cause of aneurysm (polyarteritis nodusa, fibromuscular dysplasia) may be ruptured and fistulized to biliary tract cause hemobilia. Other less common causes include angiodysplasia, arterio-venous malformations and hemangiomas.

Arterial hypertension can result in hemobilia, which usually affects the gallbladder (apoplexy of gallbladder). Portal hypertension is more likely to be a predisposing factor of hemorrhage after iatrogenic or accidental trauma rather than a primary cause. Hemobilia from primary vascular disorders tend to be massive and life-threatening.

**Malignancy**

Primary and secondary hepatobiliary malignancies are common causes of hemobilia in non-iatrogenic, non-traumatic patients, incidence about 6.0–7.0% of previous reported. The number of patients with malignancy
associated hemobilia are rising, predominated in countries, where there are high incidence of hepatocellular carcinoma or cholangiocarcinoma. In recent reports, hepatocellular carcinoma is a cause of hemobilia around 37.8% in non-iatrogenic hemobilia patients. The majority of these patients present in advanced tumor stage and are not candidates for curative treatment.

**Investigation**

The investigation of hemobilia is dependent on the rate of bleeding, as well as the high index of suspicion for hemobilia (underlying diseases, potential risk factors). Hemobilia can occur days to months after injury or procedure. The patients who presented with upper gastrointestinal hemorrhage are consider to esophagogastroduodenoscopy being the first investigation of choice. Side view duodenoscope is useful in making the diagnosis of hemobilia. The yield of endoscopy is dependent on rate and duration of bleeding, all hemobilia patients had lower positive endoscopic findings 12.0–37.5% but in clinical significant hemobilia suggested that the yield was close to 100.0% and further investigation should be undertaken (Figure 2).

**Ultrasound**

Hemobilia may be diagnosed on ultrasound by detection of an echogenic mass (clot formation) within gallbladder. Interpretation of hemobilia by ultrasound has many limitation, fresh blood clot has echogenicity similar to liver parenchyma, few days old clot may be interpreted as a soft tissue mass and later after bile duct contraction and blood clot was conform to tubular structure in the duct may be interpreted as true lumen. These finding is limitation to diagnosis hemobilia. Ultrasound is useful in diagnosis of underlying disease; cholelithiasis, biliary ascariasis, liver mass and pseudoaneurysm of hepatic artery (Doppler ultrasound).

**ERCP**

ERCP should be considered in significant hemobilia or ascending cholangitis patients because it is not only confirmed diagnosis, but also may be potential therapy for clearing all blood clots (bridging therapy). The cholangiography revealed various forms of filling defects in the dilated bile ducts. The most common features are amorphous filling defect, followed by tubular filling defect and cast like filling defect (Figure 3 and 4). Aneurysm or pseudoaneurysm of the hepatic artery may cause indentation of the bile duct or spherical contrast filling defect adjacent to common hepatic duct and disappeared with cessation of contrast injection into the biliary tree. Parasitic infection of the biliary tree may be confirmed with ERCP with cholangiography finding smooth long linear filling defects with tapering ends in dilate bile ducts.

**Computed tomography angiography (CTA)**

In previous reports, conventional CT scan and ultrasound were not helpful for diagnosis of hemobilia because they provide only indirect evidence of hemobilia (gallbladder filled with clot or bile duct dilate). After developed multislice CT angiography, which demon-
Hemobilia

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Figure 4 Endoscopic retrograde cholangiography finding of hemobilia. (A) A large, cast-like filling defect in the dilated common bile duct. (B) A longitudinal, tubular filling defect in the common bile duct. (C) An ill-defined, amorphous filling defect in the proximal common bile duct.

Figure 3 Endoscopic retrograde cholangiography shows multiple large longitudinal and amorphous cast like filling defect in the dilated common bile duct and intrahepatic duct with an oval shaped filling defect in distended gallbladder.

strated a sensitivity of 90.0% and specificity of 99.0% for the detection of massive acute gastrointestinal hemorrhage in arterial phase MDCT. Demonstration of bleeding on MDCT is dependent on the rate of active hemorrhage. CTA can detect contrast extravasation into the parenchyma, clot in gallbladder or biliary system, pseudoaneurysm and primary vascular disorder. The benefit of CTA is to diagnosis, identified etiology and point of the hemorrhage in hemobilia patients. CTA can guide interventional radiologist to selective transcatheter arterial embolization (TAE). This modality is used as a first line investigation in patients of suspected significant hemobilia with or without anomalous origins of hepatic artery (previous surgery or liver transplantation).
Angiography

Diagnosis angiography was first performed to demonstrate gastrointestinal hemorrhage in 1960. The yield of angiography for a vascular abnormality in significant hemobilia was reported to be 88.0–100.0%. Angiography can detect active bleeding from an arterio-biliary fistula, arteriportal fistula and pseudoaneurysm. Angiography is now recognized as the definitive investigation.

Management

The principle of therapy of hemobilia are to resuscitation (Goal directed therapy), controlling hemorrhage and restoring bile flow from obstruction. Multimodality approach is the main stay of treatment including medical therapy, endoscopy, radiologic intervention and surgery.

Controlling hemorrhage

Arterial bleeding is episodic and often does not response to conservative treatment (ongoing transfusion despite correct coagulopathy). Treatment relies almost universally on angiography and percutaneous endovascular techniques. TAE is highly effective in identifying and controlling arterial bleeding in both intrahepatic and extrahepatic hemobilia. The principle of TAE is to decrease pulsatile blood flow to the hemorrhage site and selective embolized with autologous blood, absorbable gelatin sponge, microcoil, polyvinyl alcohol particles, cyanoacrylate or balloons. Successful TAE is to achieve hemostasis at experienced center approaches 75.0–100.0% of patients with significant hemobilia.

Although TAE has a higher success rate in controlling bleeding in both intrahepatic and extrahepatic hemobilia, some etiology of extrahepatic hemobilia may need surgical management such as; bile duct tumor, hemorrhagic cholecystitis. The specific anatomy and etiology should be evaluated in cases of extrahepatic hemobilia or surgical altering anatomy for selective embolization planning.

The liver has a dual blood supply by portal vein and hepatic artery, the goal of embolization is always to preserve as much of the hepatic artery as possible for prevention of hepatic infarction. The complications of arterial access are inguinal hematoma, femoral artery pseudoaneurysm. Complications of the embolization process include hepatic or gallbladder necrosis, gastric ulcer, arterial dissection (intimal tear).

Surgery

The role of surgical management in hemobilia patients is declining, most case of intrahepatic hemobilia are efficacious managed by TAE. Surgery has a high morbidity along with mortality in this setting. The main indication for surgery is failed TAE and etiology of hemobilia is an independent reason for the surgery (cholelithiasis, cholecystitis, extrahepatic bile duct tumor). Surgical control bleeding involves ligation of the bleeding vessel or excision of the aneurysm. If bleeding is uncontrolled, dependent on site of bleeding, intrahepatic site is considered to partial hepatectomy may be required. Hemorrhagic cholecystitis requires urgent cholecystectomy and extrahepatic hemobilia (benign or malignant) consider Roux–en–Y operation.

Restoring bile flow

ERCP

Endoscopic management for biliary decompression is recommended in patients with significant hemobilia concomitant biliary obstruction from intraluminal bleeding and clots. ERCP and biliary sphincterotomy, with or without nasobiliary drainage or biliary stenting is the preferred way to clear the biliary tract (obstructive jaundice, ascending cholangitis or parasitic infection). Patients
with biliary obstruction who are not candidates for endoscopic management require PTBD.\(^{14,40,42}\)

**Conservative treatment**

Spontaneous cessation of bleeding occurs commonly in patients undergoing percutaneous cholangiography or a liver biopsy. The hemobilia usually is minor and should be conservative with expectant management.\(^8,26\) In patients who have hemobilia following PTBD it is recommend that removal of the drain or passing a larger catheter to bile duct for compression\(^44\) but if this method is unsuccessful, TAE will also require.\(^{14,43}\) Pharmacological methods for stopping bleeding is inconclusive, somatostatin has been reported successfully in treatment of hemobilia secondary to pancreatitis.\(^45\)

**Conclusion**

Hemobilia is an uncommon cause of gastrointestinal hemorrhage and biliary obstruction. Successful diagnosis depends on a high index of suspicion. Etiology is changed over the time, iatrogenic source, who have had recent biliary intervention or operative procedure. Urgent investigation should be done, endoscopy or CTA is an initial diagnosis and planning of management. However, TAE is the standard diagnosis as well as the treatment of choice in significant hemobilia patients. Biliary decompression and restoration of bile flow may be necessary in biliary obstruction patients. Multimodality approach is the mainstay management of hemobilia patients and become low morbidity and mortality.

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