



## Research Article

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# Cholangitis after Hemobilia: A Brief Overview

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## Abstract

Hemobilia, defined as the hemorrhage into the biliary tract and blood clots in the bile duct is an uncommon cause of severe cholangitis. The majority of hemobilia are caused by iatrogenic and trauma, gallstones, inflammation, vascular disorders, and malignancy. Hemobilia can cause recurrent obstructive cholangitis and it may bring a fatal patient's condition. The management of major hemobilia consists of hemostasis and reduction of biliary pressure to prevent or cure a cholangitis occurred in succession. Angiography and interventional radiologic intervention is regarded as the gold standard for diagnosis and treatment, respectively. However, the management of the cholangitis after hemobilia was technically challenging requiring multiple therapeutic choices including endoscopic approach. A further research is needed in this area.

## Keywords

Cholangitis, Hemobilia

## Abbreviations

CAH: Cholangitis After Hemobilia; CT: Computed Tomography; CTA: Computed Tomography Angiography; ERCP: Endoscopic Retrograde Cholangiopancreatography; MRCP: Magnetic Resonance Choangiopancreatography; PTC: Percutaneous Transhepatic Cholangiography; PTBD: Percutaneous Transhepatic Biliary Drainage; US: Ultrasonography; PSC: Primary Sclerosing Cholangitis; HCC: Hepatocellular Carcinoma; PTBD: Percutaneous Transhepatic Biliary Drainage; PS: Plastic Stent; ERC: Endoscopic Retrograde Cholangiography; TAE: Transarterial Embolization; MS: Metallic Stent; CBD: Common Bile Duct; EST: Endoscopic Sphincterotomy; SEMS: Self-Expandable Metal Stent; IEBD: Internal-External Biliary Drainage; EUS-HGS: Endoscopic Ultrasound-Hepaticogastrostomy

## Introduction

Hemobilia refers to the fistulous communication between blood vessels and biliary tract. The first report of hemobilia was from Francis Glisson in 1654 [1]. Quincke [2] described the clinical triad of hemobilia consisted of jaundice, upper abdominal pain, and upper gastrointestinal tract bleeding, those are known as Quincke's triad. However, all these three symptoms may be present in only 22 to 35% of patients [3,4]. Hemobilia is an unusual, but blood clots in biliary tract is important cause of bile stasis and jaundice [5,6]. Furthermore, its incidence has gradually increased as hepatopancreatobiliary interventions become more common. Recently, there are many case reports of biliary tract hemorrhage. Although, little attention had been given to the cholangitis after hemobilia (CAH). Therefore, it is important that how to manage the CAH is discussed.

## Literature Search

A PubMed (National Center for Biotechnology Information

at the National Institutes of Health in Bethesda, Maryland, United States) was used for performing search with the key words "hemobilia" and "cholangitis" to extract studies published in recent 5 years. Thirty-eight reports were included in the initial search; thereafter reports that were not describing cholangitis after hemobilia were excluded. Finally, a total of 11 reports and 11 cases matched the definition of CAH were reviewed (Table 1 [7-17]).

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Table 1: Reports of cholangitis after heobilia.

References	Age	Sex	Primary disease	Antiplatelet or anticoagulant medication	Cause of hemobilia	Modality to detect the source of hemobilia	Intervention for hemostasis	Transfusion	Intervention for cholangitis	Recurrence	Death due to hemobilia or cholangitis
Hashioka	54	F	Hereditary hemorrhagic telangiectasia	NS	Hereditary hemorrhagic telangiectasia	CT	None	NS	ERCP, PS	yes	Death due to primary disease
Yilmaz	75	F	Chronic hepatitis B	no	Percutaneous liver biopsy	US	TAE with coil	yes	ERCP, EST, PS	no	Alive
Miyamoto	72	M	PSC, cholangiocarcinoma	NS	Hepatic artery aneurysm(due to PS)	CE-CT	TAE with coil	NS	ERC, EST, SEMS	no	Death due to primary disease
Galambo	49	M	Colorectal cancer	NS	PTBD	angiography	Trans biliary coil embolization	NS	IEBD	no	Death due to primary disease
Nakai	78	F	Cholangiocarcinoma	NS	Tumor involvement to orifice of cystic duct	ERC	None	NS	EUS-HGS	no	Alive
Gollol-Raju	61	M	HCC	yes	Tumor	CTA	ERCP MS	NS	ERCP, EST, MS	no	Alive
Yamauchi	78	F	Benign biliary stenosis	no	PS	CE-CT	TAE with coil	NS	ERCP, PS	no	Alive
Ogura	89	F	HCC	NS	Tumor	CT	ERCP MS(fully covered SEMS)	NS	ERCP MS (fully covered SEMS)	no	Death due to primary disease
An	75	M	Hepatic artery aneurysm	no	Hepatic artery aneurysm	CT	Coil embolization and trans biliary coil embolization	NS	PTBD	no	Alive
Ahmad	25	M	Type I Giant Choledochal Cyst	no	Arteriocholedochal fistulas	CE-CT	Surgery(whipple's pancreaticoduodenectomy)	yes	-	no	Alive
Lynn	65	M	Cholangitis	NS	PTBD	ERC	Surgery(laparoscopic cholecystectomy and CBD exploration)	NS	ERC, PS (failed)	no	Alive

F: Female; M: Male; NS: Not Shown; PSC: Primary Sclerosing Cholangitis; HCC: Hepatocellular Carcinoma; PTBD: Percutaneous Transhepatic Biliary Drainage; PS: Plastic Stent; CT: Computed Tomography; US: Ultrasonography; ERC: Endoscopic Retrograde Cholangiography; CTA: Computed Tomography Angiography; CE-CT: Contrast-Enhanced Computed Tomography; TAE: Transarterial Embolization; ERCP: Endoscopic Retrograde Cholangiopancreatography; MS: Metallic Stent; CBD: Common Bile Duct; EST: Endoscopic Sphincterotomy; SEMS: Self-Expandable Metal Stent; IEBD: Internal-External Biliary Drainage; EUS-HGS: Endoscopic Ultrasound-Hepaticogastrostomy.

## Epidemiology

The etiology of hemobilia is the most commonly indicating iatrogenic injury, accounting for greater than 50% of cases [18-20]. However, the first large reported review of hemobilia by Sandblom in 1973 reported that the majority of cases were accidental trauma, with only 17% found to be iatrogenic in origin [21]. With the increasing use of invasive diagnostic and therapeutic intervention that involves the hepatopancreatobiliary system; iatrogenic trauma has become the predominant cause of hemobilia recently.

Iatrogenic causes include percutaneous transhepatic cholangiography (PTC, percutaneous transhepatic biliary drainage (PTBD, percutaneous and transjugular liver biopsy, transjugular intrahepatic portosystemic shunt, and portal venous interventions. Because of the proximity of the intrahepatic bile duct to the branches of the hepatic vasculature, needle punctures from percutaneous interventions can easily cause fistulous communications leading to hemobilia. And as bile is known to damage blood vessels, simultaneous injury to bile duct and artery can predispose to formation of pseudoaneurysm [22]. The most common cause of endoscopic procedure associated with hemobilia is endoscopic retrograde cholangiopancreatography (ERCP including sphincterotomy [6]. Risk factors for ERCP-related hemobilia have also been reported after endoscopic stent insertion, biliary balloon dilation, intraductal biopsy, vascular anomalies, and trans biliary ductal drainage procedures such as EUS-guided choledochoduodenostomy and hepaticogastrostomy [6,23-25]. Other iatrogenic cause of hemobilia is surgery. Post-cholecystectomy hepatic artery pseudoaneurysm present with hemobilia in approximately 20% of cases [26]; liver transplantation, and pancreaticoduodenectomy are examples of surgeries which can also cause hemobilia [5,26,27]. Non iatrogenic causes of hemobilia have been described blunt liver trauma, stones, inflammatory conditions, parasitic infection, vascular pathology, and neoplasm [27-33]. Furthermore, previous reviews have found that 50% of bleeding into the biliary tree is intrahepatic; the other 50% is mostly from the extrahepatic bile ducts or gallbladder, and rarely the pancreas [34]. When the hemorrhage occurs slowly, blood and bile do not mix owing to their different specific gravities and surface tension. The resultant clots obstruct the bile ducts [35]. Further, major hemorrhage or prolonged clot formation might increase biliary pressure with or without anemia.

## Diagnosis

Hemobilia is frequently accompanied by clot formation within the biliary system. Clot formation within the biliary system may be attributed to differences in specific gravity between blood and bile which prevents the two from mixing. Clots in biliary tract can cause symptomatic jaundice, biliary obstruction, and hepatobiliary inflammation [6]. Then, CAH presents on laboratory data as anemia and hyperbilirubinemia and elevated alkaline phosphatase, aminotransaminases and inflammatory maker. The diagnosis of hemobilia required detects both the location and etiology.

Computed tomography (CT has become a first-choice

examination owing to its non invasive nature, low radiation exposure compared to angiography, rapid results, and diagnostic performance characteristics [34]. CT examination has improved to identify subtle abnormalities [36-38]. CT angiography (CTA is helpful in planning endovascular interventions, and can be particularly useful when dealing with surgically altered anatomy such as transplanted livers [6].

Upper Endoscopy is commonly adopted for patients with upper gastrointestinal bleeding. When blood or clot is seen at the papilla of Vater, hemobilia is likely, and it is encountered sometimes incidentally: Up to 60% of hemobilia cases can be diagnosed by endoscopy [38]. ERCP can be used to visualize the biliary tree or gallbladder and may offer therapeutic options in patients with hemobilia and/or associated biliary obstruction [34].

Angiography is the gold standard for both diagnosis and treatment of hemobilia. It can be expected to detect a vascular abnormality in over 90% of cases of significant haemobilia [39]. As well as detecting active hemorrhage from an arteriobiliary fistula, an arteriportal fistula and pseudoaneurysm may be seen [4].

Other diagnostic methods include fluoroscopy, abdominal ultrasound (US), magnetic resonance choangiopancreatography (MRCP). If an existing biliary drain, fluoroscopy is useful which may show filling defects in the biliary tract. Ultrasonography may show the presence of blood within the biliary tract strongly supports the diagnosis of hemobilia [40]. However, its diagnostic effectiveness is limited due to limited ability and high echogenicity of clots similar to that of the liver itself [4]. Pseudoaneurysms may be recognized as well-circumscribed anechoic lesions with turbulent flow on color Doppler imaging [6]. MRCP shows blood or clots within the biliary system.

## Management

The consensus had defined major hemobilia as “case of hemobilia requiring blood transfusion, if bleeding is prolonged or recurs despite correction of coagulopathy” [4]. Navuluri reported bile stasis due to clots can cause complications such as obstructive jaundice, acute cholangitis, acute cholecystitis, and pancreatitis [6]. Further, “Cholangitis following hemobilia may be severe and, carries a high mortality rate even when treated aggressively with antibiotics and biliary drainage” [4]. Taking these matters into account, the management of major hemobilia was discussed and several reports have described the two main treatment policies: 1) Hemostasis and 2) Biliary decompression [4,6,20,34]. Each of these treatment policies will be described below.

Minor hemobilia may be managed with conservative therapy or minimal interventions, including coagulopathy correction and fluid hydration. If blood-tinged output from an internal-external or external biliary drainage catheter persists, a trial of capping of the drain may also facilitate hemostasis. Other method to manage minor hemobilia include slightly retracting or advancing the tube so that side holes do not engage the injured vessel or upsizing tube to

create a tamponed effect, and it also decompress the biliary obstruction secondary to clots [6]. However, it is important to recognize that if an internal-external drain has been placed, bleeding may continue into the upper GI tract through the transpapillary route [6].

## Hemostasis

The approach of therapy depends on the etiology of the bleeding and degree of hemodynamic instability. Our literature review also showed conservation therapy in 2 patients, TAE and/or coil embolization in 3 patients, transbiliary coil embolization in one patient, and combination of both transartery embolization and transbiliary coil embolization in one patient, covered metal stent in 2 patients, and surgery in 2 patients were reported (Table 1).

**Transcatheter arterial embolization (TAE is the first line of treatment for arterial bleeding):** TAE is effective in significant arterial extravasation, the arterial aneurysms or Pseudoaneurysms, arterio-biliary fistula, and/or intrahepatic or extrahepatic vascular lesions in the patients with hemobilia requiring blood transfusion despite correction of coagulopathy, and in the patients with minor hemobilia causing anemia. Previous reports have shown the success rate of TAE to be 80-100% [41]. Failed treatment is technical or due to inability to identify the bleeding vessel or missed collaterals. TAE is not recommended in the patients as the compromised collateral blood flow predisposes the patient to more extensive ischemic liver damage [42].

Arterial stenting across the site of vascular injury is an alternative to TAE. Placement of a covered stent allows maintaining vessel patency and avoid a liver necrosis complication [43,44]. Further, trans biliary coil embolization is a limited approach when arterial embolization is not feasible due to preclusive anatomic factors and/or a previously inserted coil through the artery [10,15].

Percutaneous thrombin injection (PTI) is an option for hepatic artery pseudoaneurysm with any distal intrahepatic collaterals. Ultrasound-guided or CT-guided PTI into a pseudoaneurysm of the cystic or pancreatic duodenal artery have been reported [27,45,46].

**Management options of endoscopic techniques:** Management options of endoscopic techniques include spraying diluted epinephrine, local epinephrine injection, monopolar or bipolar coagulation, fibrin sealant injection, hemoclipping, balloon tamponading, and stent placement. Linz, et al. reported the use of endobiliary radiofrequency ablation for hemorrhage secondary to malignant hemobilia [47].

**Surgery:** Surgery is rarely necessary and indicated in cases of failed the other modalities, for hemobilia or hepatic sepsis complicated by cholecystitis. Surgical intervention involves ligation of the bleeding vessel or excision of the aneurysm. Partial hepatectomy is another surgical option.

## Biliary decompression

Hemobilia is unusual but important cause of obstructive jaundice. Clot formation can also lead to acute cholangitis,

acute cholecystitis, or even acute pancreatitis [48-50]. If an internal-external or external biliary drainage catheter has been placed, a trial of upsizing of the drain is also helpful in managing worsening biliary obstruction secondary to clots [6].

The ERCP has been accepted as the preferred procedure to treat hemobilia and CAH simultaneously [51-56]. ERCP with biliary sphincterotomy can decompress biliary obstruction. ERCP-guided drainage with sphincterotomy, biliary stenting, and biliary drain placement is reported with over a 95% success rate and an adverse event rate of 5-10% [57]. Also, Endoscopic drainage has similar rates of success and complications to percutaneous drainage [58]. Although endoscopic placement of a plastic biliary stent may become occluded with clot. Therefore, ERCP with sphincterotomy and nasobiliary drainage catheter might be prefer to drainage the clot formation within the biliary system. Alternatively, placement of an additional PTBD can help manage biliary obstruction due to clot [6].

In our review cases, the cases consisted of 6 men and 5 women, aged 25-89 years. The underlying diseases were hepatocellular carcinoma 2 cases, cholangiocarcinoma 2 cases, hereditary hemorrhagic telangiectasia 1 case, Chronic hepatitis B 1 case, colorectal cancer 1 case, Type I Giant Choledochal Cyst 1 case, cholangitis 1 case, idiopathic hepatic artery aneurysm 1 case, and benign biliary tract stricture 1 case. The cause of hemobilia included hepatic artery aneurysm 7 cases, arterio-biliary fistula 3 cases, and telangiectasia 1 case. The modality to detect the source of hemobilia was contrast-enhanced CT 7 cases, ERC 2 cases, angiography 1 case and ultrasonography 1 case. The interventions for hemostasis were transarterial embolization 3 cases, trans biliary embolization 1 case, transarterial and trans biliary embolization 1 case, SEMS insertion 2 cases, surgery 2 cases, and no intervention 2 cases. The intervention for cholangitis were ERCP-guided drainage with plastic stent 3 cases, metallic stent 3 cases, EUS-HGS 1 case, PTBD 1 case, internal and external drainage 1 case, and surgery 2 cases (Table 1).

Among 11 cases, malignant disease most frequently underlies hemobilia. Hepatic artery aneurysm was the most frequent cause of hemobilia. The modality to detect the cause of hemobilia was mostly contrast-enhanced CT as seven cases. The most used treatment was TAE and/or trans biliary embolization with coil. Besides, Placement of SEMS is an alternative option to embolization. Furthermore, ERCP-guided biliary drainage was the most frequent performed for CAH. On the other hand, it was reported that EUS-HGS was performed against CAH. In our reviewed case, recurrences of CAH were confirmed in only 1 patients 9%. Four patients 36% died due to primary disease progression, which is in line with that malignant diseases most frequently underlie CAH.

## Conclusion

CAH may be severe and, remains it is rarely reported. It should be recognized that cholangitis may occur following hemobilia. With the increasing as the arsenal of advanced endoscopic and other minimally invasive hepatopancreatobiliary procedures there has been an increase

in the incidence of iatrogenic haemobilia with cholangitis. Though, TAE still be considered as a first line of treatment for haemobilia. The minute review for hemobilia showed that the management of the CAH was the paradigm is shifting, ERCP including biliary decompression with endoscopic approach are feasible methods for the management of CAH.

## Conflicts of Interest

The authors declare that they have no conflicts of interest.

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