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Review

Massive Hemobilia in Childhood

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Abstract

Hemobilia is very rare in the pediatric population, and so it continues to be a diagnostic challenge. Hemobilia is an abnormal communication between a vessel of the splanchnic circulation and the biliary system. Treatment planning for hemobilia in children should be performed; therefore, the differential diagnosis is very important in order to find the cause of the upper gastrointestinal bleeding. Awareness of potential causes and the management of upper gastrointestinal bleeding and hemobilia should enable physicians to treat their patients more effectively.

This study is a review of potential etiologies of hemobilia and the challenges involved in the diagnosis and surgical management of massive hemobilia, especially in children.

Keywords: Biliary computed tomography angiography; endoscopic retrograde cholangiopancreatography; endoscopy; hemobilia; magnetic resonance cholangiopancreatography; obstructive jaundice.

Hemobilia is blood loss into the bile ducts; it is a very rare cause of upper gastrointestinal bleeding, which may be caused as a result of traumatic or nontraumatic reasons [1,2].

Hemobilia usually occurs secondary to accidental or iatrogenic hepatobiliary trauma, such as a liver puncture performed in the diagnosis and/or therapy of hepatobiliary disease, or hepatobiliary system intervention [3,4]. It has been reported that patients who had undergone percutaneous transhepatic biliary drainage had a higher risk of arterial injury than patients who had undergone percutaneous transhepatic cholangiography (2.6% vs 0.7%). Ongoing hemobilia was seen in 87% of the patients, and was the most common sign of arterial injury [5]. Rarely, hemobilia has been an indicator of cystic artery pseudoaneurysm after a trauma [6].

Nontraumatic hemobilia is another rare cause of upper gastrointestinal hemorrhage in children. The most common causes of nontraumatic hemobilia in children are infections, such as a liver abscess; multiple aneurysms due to parasitic infestation; vascular malformations; anatomical abnormalities, like gastric ectopia and duplication; biliary pathology, such as papillomatosis and polyps of the gallbladder; and bleeding disorders, like von Willebrand disease [7-13]. Other documented nontraumatic causes that have been described in adults include malignant or benign tumors, systemic lupus erythematosus, sarcoidosis, cholelithiasis, cholecystitis, choledochal cyst, gallbladder ulcer, pancreatitis, and warfarin therapy [14-20]. Nontraumatic hemobilia associated with cholecystitis is very rare. However, acute hemorrhagic cholecystitis, rupture of an arterial pseudoaneurysm, a fistula between the cystic/hepatic ar-

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tery and the gallbladder or biliary system, worm infestation of the biliary tract, vasulitic syndromes, and anticoagulant drug overdose and lysosomal disorders, such as metachromatic leukodystrophy, have been some of the reported causes [12,21-24].

Spontaneous fistulous communication between the cystic artery and the gallbladder is rare without prior trauma or intervention. The erosion of a gallbladder ulcer into the cystic artery due to ectopic gastric tissue was reported to be the cause of non-aneurysmal spontaneous cystic artery bleed; however, no definite ulcer was found [20]. Excessive acid secretion in the biliary tract caused by ectopic gastric mucosa may result in inflammation of the perivascular tissue and weakening of the vessel walls. The subsequent ulcer formation from ectopic gastric mucosa may rupture into the biliary tree and result in hemobilia. Ectopic gastric tissue has been thought to occur as a result of inflammatory processes in the vicinity of the vessel and may rupture into the gallbladder, cystic duct, or the bile duct, with resultant hemobilia, or rarely, may rupture into the peritoneal cavity [20,25,26]. Due to the close proximity of embryonic endodermal cells that give rise to the stomach and gallbladder mucosae, congenital displacement of gastric precursor cells to the gallbladder could result in gastric heterotopia [27,28]. The relative infrequency of mucosal ulceration from heterotopic gastric mucosae in the biliary tree has been attributed to the presence of alkaline bile [28].

Hemobilia from a primary or secondary liver tumor has occasionally been reported in the literature. Hemobilia in this setting is usually observed in association with an obvious liver mass or abnormal liver function tests. However, biliary tract hemorrhage has been reported as the primary presentation of cystadenocarcinoma of the liver in the absence of a significant mass or abnormal liver function tests [29]. The first report of histopathology results in heterotopic gastric mucosae of the gallbladder was presented in 2001 as pyloric gland type and intestinal metaplasia with dysplastic changes [30]. Since heterotopic tissues may promote carcinogenesis of the gallbladder, close attention should be paid to any occurrence of such lesions in the biliary tract [31-33]. Some cases of heterotopic gastric mucosa in the gallbladder have been presented with metaplasia. Adenocarcinoma with eosinophilic cells and non-overlapping low-grade nuclei arising from heterotopic gastric mucosa in the duodenal bulb has been reported as a new tumor entity [34]. The first gastrointestinal cyst choristoma with endocrine cells in the cystic duct and gallbladder was reported in 2008 [35].

Clinical Presentation

Gallbladder abnormalities may cause abdominal pain in children and should be included in the differential diagnosis. They are an uncommon condition associated with chronic abdominal pain, but should be considered in a child with a mass in the portal triad and biliary obstruction. The classic combination of right upper abdominal pain, jaundice, and gastrointestinal bleeding is pathognomonic of hemobilia; however, it has been reported in only 22% of adult patients [1-4,7-20]. Nontraumatic hemobilia is rare in children, and many patients do not present with the classic triad symptoms of biliary colic, obstructive jaundice, and intestinal bleeding [3,6]. It has been suggested that clots have the potential to cause late stone formation as a result of pigment deposition, encrustation, or calcification.

Patients may present with symptoms of upper gastrointestinal bleeding in a chronic or acute manner. The history of melena may be profuse or minimal, intermittent, or continuous, and stool color may be especially confusing in a child using oral iron. Massive hemobilia may present as an acute, life-threatening hemorrhage, even in the subset of nontraumatic hemobilia. It has been suggested that hemobilia should be part of the differential diagnosis for patients with other hepatobiliary diseases who present with a gastrointestinal bleed [2,7,18]. When hemobilia is suspected in a child, a complete parasitic screen should be performed. The presence of jaundice in such patients should raise the suspicion of hemobilia [9,13]. Heterotopic gastric mucosa in the biliary tract is often discovered incidentally, but it may cause symptoms from gallbladder obstruction to inflammation or perforation [36-38]. It may also be detected incidentally in radiological imaging studies. Although heterotopic gastric tissue has previously been found in the gallbladder in young males, none has been reported in the extrahepatic bile ducts. Furthermore, hemorrhage has never been described as a complication of gastric heterotopia of the gallbladder. Gastric heterotopia associated with gastrointestinal bleeding has been most extensively documented as originating from other locations, such as the Meckel's diverticulum, intestinal duplication, the small bowel and the rectum [9]. Clinical presentation was that of typical peptic ulceration involving hematemesis and melena [39].

Diagnosis

A high index of suspicion and the use of the appropriate diagnostic tools can help diagnose and treat gastric heterotopia as a rare cause of hemobilia. Slow bleeding has been more likely to be associated with the formation of durable clots and biliary obstruction [40]. A clot in the lu-

men of the gallbladder can mimic a mass, stone, or sludge. Ultrasound (US) may reveal mobile or hypoechoic masses, as well as nonshadowing filling defects [40,41]. Doppler US can aid in the distinction of a clot from a mass by demonstrating flow in the gallbladder lumen, but cannot differentiate conclusively between hemobilia and echogenic bile sludge [40,41]. Computed tomography (CT) has emerged as a useful tool in the screening of hemobilia [40,41]. CT should be performed after fasting. Pre- and postcontrast scans should be obtained for the best demonstration of blood in the gallbladder. CT and biliary CT angiography are helpful in suggesting a diagnosis, detecting other abnormalities, and localizing the cause of the bleeding as well as assisting in planning the management of these patients. CT angiography is also useful in the definitive diagnosis and treatment [41]. Selective arterial angiography is helpful in identifying the source of gastrointestinal hemorrhage; it may provide detailed information of the bleeding, but is less appropriate as an initial screening method. Angiographic video seen in hemobilia cases is a classic depiction of a fistulous communication between the cystic artery and the gallbladder/common bile duct lumen [42-45]. Magnetic resonance imaging (MRI) is the first choice in suspected cases of hemobilia, especially in childhood. Magnetic resonance cholangiopancreatography (MRCP) findings demonstrate gallbladder hemobilia as a mixed signal intensity that is consistent with blood products in various stages of breakdown [42-46]. A radionuclide "tagged" red cell scan will be positive for a biliary source if the hemorrhage is brisk. [46] However, bleeding scans typically entail a delay of several hours, which is problematic when the patient is unstable.

Endoscopy is the initial choice for the method of investigation in the evaluation of upper gastrointestinal hemorrhage in adults [46]. Direct visualization of the duodenal papilla may reveal blood and/or a clot exiting into the duodenum, which confirms the diagnosis of hemobilia. When the patient is hemodynamically stable, an upper endoscopy is necessary to identify blood at the ampulla of Vater to confirm a diagnosis of hemobilia and to exclude more common causes of upper gastrointestinal bleeding. The classic endoscopic observation is blood coming from the duodenal papillae; this finding is a diagnostic tool in hemobilia [43,45]. Endoscopy may also demonstrate a duodenal ulcer with a blood clot. Similar observations have been reported in the literature: a cholecystoenteric fistula site was confused with a duodenal ulcer. Filling defects seen on cholangiograms could well be blood clots rather than stones, especially if they are floating. Endoscopic retrograde cholangiopancreatography (ERCP) is rarely helpful in localizing the source of the bleeding, although biliary sphincterotomy with clearance of the clot using basket catheter sweeps may be helpful if the patient has a biliary obstruction. A biliary stent is generally not helpful, as the stent will quickly become occluded by the clot. Several investigators have reported success with direct (peroral endoscopic) cholangioscopy in diagnosing hemobilia [43,45].

Treatment Modalities

AThe aim of treatment in cases of hemobilia is to stop the bleeding and to restore bile flow past the clots. Treatment modalities used to stop bleeding include angiography with embolization, surgical intervention, observation, and electrocoagulation or photocoagulation. For anatomical reasons, most authors have advocated surgical therapy for extrahepatic hemobilia. Angiography is clearly the most effective method to control intrahepatic bleeding sources, with success rates above 95% [42,43,45-48]. More recently, angiographic embolization has been shown to be useful to control extrahepatic bleeding, even after surgical failure. Some causes of extrahepatic bleeding may lend themselves to surgical correction, such as bleeding from the bile duct or gallbladder mucosa. Thus, the specific anatomy should be carefully evaluated in cases of hemobilia from extrahepatic sites and embolization should be considered when it appears to be the safest method and is technically possible. There have been no significant side effects or complications clinically associated with transcatheter arterial embolization, except one gallbladder infarction, which was noted in surgery, and cholecystectomy was performed with excision of the hepatic artery aneurysm [49-51]. However, technical features of cases, such as scarring from a previous operation, may limit surgical effectiveness. Hepatobiliary necrosis (6%), abscess formation (9%), bleeding (6%), and gallbladder fibrosis (2%) have occurred following arterial embolization [47-51]. Though such a picture is rare, it has been mistaken for a pseudoaneurysm of the cystic artery. A subsequent intraoperative review of the findings voided the final diagnosis when the gallbladder was filled with blood clots and there was no detectable pseudoaneurysm in the vicinity. Before the advent of angiographic localization and embolization in resectional surgeries of the gastrointestinal tract, gastrectomy, cholecystectomy, colectomy, and hepatic resections were performed in a last resort in order to control bleeding in cases of hemobilia, but were largely unsuccessful [4].

Most authors have pursued proximal hepatic exploration and ligation of the cystic artery along with early cholecystectomy in the management of hemobilia due to ectopic

gastric tissue [40-46]. However, in the face of uncontrolled bleeding, a reasonable approach would be to perform a diagnostic angiography and a simultaneous intervention for accurate localization of the source of the bleed and immediate control, which can be followed by an urgent cholecystectomy [49-51]. In recent years, with the advent of minimally invasive procedures, accurate diagnosis and treatment can be rendered using these techniques with less morbidity. Endoscopy and ERCP or selective arterial angiography can be very difficult to perform, especially in a small child who is hemodynamically unstable. CT and CT angiography, MRCP, or diagnostic endoscopy is typically not attempted in small children as a first option with an unstable hemodynamic condition. It has been reported that unstable hemodynamics led to continued massive bleeding and a decision to perform emergency surgical exploration to control the hemorrhage as well as for definitive therapy due to the failure of medical treatment [40-51]. Surgery is also used as a salvage option for failed minimally invasive procedures or when there are complications. Sometimes, open surgery has been one of the first methods in management of the massive hemobilia, especially in small children. Early surgical exploration and emergency laparotomy is attempted as a result of an unstable hemodynamic state, though massive blood transfusions may be required in these patients.

Conclusion

Management of hemobilia is aimed at stopping the bleeding, maintaining a continuous flow of the biliary system, and curing the underlying etiology. The advent of interventional radiology has contributed to the nonsurgical management of many of these cases, but in small children, the size of the vasculature and hemodynamic instability may limit the options for cannulation and/or subsequent interventions. Surgery has a definitive role in patients with hemodynamic instability, after failed embolization, and/or in patients requiring laparotomy for other reasons, and especially in small children. If the patient has massive hemobilia and acute, obstructive jaundice, emergency surgical exploration might be a diagnostic and therapeutic and lifesaving tool.

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