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Hemobilia Post Liver Biopsy: Mechanism, Presentation, Complications and Management

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Abstract

Background: Liver biopsy is the gold standard for diagnosing various liver pathology. However, it may be associated with serious complications such as hemobilia, information of which is scarce in the literature.

Objective: This article intends to review various aspects of hemobilia including the mechanism, presentation, diagnosis and management.

Method: Literature review. A systematic review of the literature was performed by searching the PubMed and Medline databases, for all relevant articles in English on hemobilia, published from 1963 to June 2015.

Discussion: The search resulted in retrieval of 56 studies, involving 78 patients with hemobilia. The method of biopsy included percutaneous(51.8%), ultrasound guided percutaneous biopsy(29.6%), transjugular(11.1%), laparoscopic biopsy(3.7%). The predominant symptom of presentation was pain and GI bleed(42.2%), Quincke's triad(39.4%). The mean day of presentation was 5 days. The investigations carried out included angiogram(68%),LFT(47.9%), ultrasound abdomen(45.2%), ERCP(24.6%), endoscopy(16.4%). The vascular anomaly contributing to hemobilia were arteriobiliary fistula(32.6%), arterioportal fistula(36.9%), pseudoaneurysm(21.7%) and arteriovenous biliary fistula(trifistula) (4.3%). Transarterial embolization was carried out in 61.2% of patients with 80% success in arresting bleeding. ERCP with clot extraction was carried out in 20.9%. Surgical intervention included cholecystectomy (23%), CBD exploration and clot extraction (9.23%) and hepatic artery ligation (right or left branch)(9.23%). The complications observed were pancreatitis (41.8%), hemocholecystitis(21.8%), cholangitis(10.9%). Death was seen in 3.6% of patients.

Conclusion: Hemobilia is a rare complication post liver biopsy . Angiogram is both diagnostic and therapeutic. Surgical interventions is limited to those who fail to respond to arterial embolization or develop complications in the gall bladder or CBD.

Keywords: Hemobilia; Liver biopsy; Transarterial; Embolization

Introduction

Hemobilia refers to bleeding into the biliary system. Several reports indicate its occurrence post liver biopsy [1-63]. Hemobilia was first described by Glisson in 1654, in a postmortem diagnosis of a young adult, stabbed by a sword in the liver [46]. Sandblom in 1948 used the term hemobilia to describe hemorrhage into the biliary tree, secondary to trauma [49].It was first reported as a complication of liver biopsy in 1967 [44]. In one of the largest multicenter study, reporting on the complications of liver biopsy, hemobilia was noted in 4 of 68,276 patients (0.006%) [50]. In another report, the incidence of hemobilia, post percutaneous liver biopsy was reported to be 0.023% among 12,750 patients, accounting to 11.5% of all major complications [39]. However, several recent reports indicate the incidence of hemobilia post liver biopsy to be higher at just below 1% [20] and include 0.70% (1/142) [47] and (0.1%) [5, 7]. In this article the literature is reviewed and various factors that influence its cause and its management has been discussed.

Methods

Literature review. A systematic review of the literature was performed on hemobilia, by searching the PubMed and Medline databases for all relevant articles in English, published from 1963 to June 2015. The articles were retrieved using the MeSH(Medical Subject Headings) terms "hemobilia" and "liver biopsy". The data was extracted and studied for demographic details, method of liver biopsy, primary liver disorder warranting a biopsy, clinical presentation, the time of presentation, complications and management including radiological, endoscopic and surgical.

Results

The search resulted in retrieval of 56 studies involving 78 patients and majority (88%) of these studies were case reports; seven of them were case series with 2 or more cases. Unfortunately, some of the studies lacked data regarding various parameters studied and hence the statistics had to be derived from data available (DA). Table 1 and Table 2. There were 21 male and 27 female patients (DA=48 patients) with an average age of 43.9 years (range 1.7-75 years). The biopsy methods included percutaneous biopsy (51.8%), ultrasound guided percutaneous biopsy (29.6%), transjugular biopsy (11.1%), laparoscopic biopsy (3.7%) and laparotomy and biopsy (1.85%). The predominant symptom of presentation was pain and GI bleed (42.2%), Quincke's triad (39.4%), pain and jaundice (5.6%), GI

Table 1: Demographic Details, Presentation, Complications.

	No Of pts	Age- in yrs Sex	Liver Biopsy Technique	Presentation Pain Jaundice GI bleed	Day- of presentation Post procedure	Complications Cholecystitis Cholangitis Pancreatitis
Zhou HB[1] 2014	1	57 F	USbps	P GiBl-mel	7	Cholecystitis Cholangitis Pancreatitis Stress gastric ulcers
Qureshi[2] 2014	1	29 F	Pbps	QT	5	NA
Zaleska-Dorobisz[3] 2014	1	10 M	USbps	P GiBl-Mel/hem	7	Nil
Howlett DC[7] -2013 (UK audit)	2/ 3455bpsy	NA	NA	P GI-Bl Mel =2	NA	NA
Plerhopies TA[4] 2013	1	69 F	TJbps	QT	<1	Cholecystits, gall bladder rupture, Intra-abdominal fluid collection
Marynissen T[5] 2012	6/12 HB	NA	NA	QT-6	6	NA
Gandhi V[6] 2011	1/22(HB)	NA	USbps	NA	6	NA
Kawakubo K[8] 2011	1	67 M	EUS-bps	P J	4	Nil
Egritas O[9] 2010	1	7 F	USbps	P Gibl- Hem& Mel	2	Cholecystitis pancreatitis
Koshy CG[11] 2010	1	36 F	Tjbps	Hypotension-4hr after procedure	<1 4hr	Intra-peritoneal bleeding from subcapsular venous pseudoaneurysm
Hendriks M[10] 2009	1	42 F	USbps	P Gibld-hem	4	Pancreatitis CBD obstruction
Peña LR[12] 2009	1	56 M	Pbps	P J	7	Pancreatitis Reaccumulation of clot after initial extraction. repeat ERCP 3days and stenting
Wood B[13] 2009	1	11 M	USbps	P GiBl- Mel	14	Pancreatitis
Li F[14] 2009	1	51 M	USbps	P GiBl- Mel.	1hr	Pancreatitis
Prata F[15] 2008	2	45&37 F&M	2-USbps	QT-2	5 &4	cholangitis
Rogart JN[16] 2008	1	58 F	Tjbps	P Gi-bl- Mel	2	Pancreatitis
Gurakuqi GC[17] 2008	1	60 M	TJbps (advanced liver disease)	P Gi-Bl-Hem	1	Died- multiorgan failure
Bergmann OM[18] 2007	1	55 F	Tjbps	J Confusion	2	Bilhemia with deteriorating LFT Acute pancreatitis ARDS
Dallal RM[19] 2007	1	34 F	Laparoscbps- during bypass surgery for obesity	P	1	Nil
Edden Y[20] 2006	1	15 M	Pbpsy	P	12	Cholecystitis. Persistent fullness of GB with blood- 14 days
Albuquerque W[21] 2005	1	21 F	NA	QT	1 hr	Pancreatitis, Cholecystitis .
Nowak A[23] 2005	1	55 F	Pbps	P	4	Pancreatitis

Lin CL[24] 2005	1	68 F	USpbs	P	2	Recurrence of bleeding after discharge following ERCP-embolization after 2 days
Kruse-Jarres[22] 2005	1	39 M	Tjbps	P LFT-abnormal	4	nil
Hodgson RS[25] 2004	1	63 F	USbps	NA	4	Pancreatitis
Sharma R[26] 2004	1	55 M	NA	QT	3	Nil
Hashimoto M[48] 2004	3/ (8 cases of HB)	NA	USbps	P Gibl-Mel - 3 Cases	3	Liver infarction post embolisation
Rossi[47] 2002	1/ 142 (usbps)	53 F	USbps	P Gi-Bl- Mel	6	NA
Machicao VI[51] 2002	1	49 M	Pbps	P Gi-bleed	10	Pancreatitis
Sood A.[52] 2002	1	55 M	Pbps	QT	NA	Pancreatitis
Asselah T[27] 2001	1	43 F	Pbps	P Gibl-Mel	4	Pancreatitis
Coelho JC[28] 2001	1	47 M	Pbps	P Gi-bl-Mel	2	Cholecystitis
Gomez-Valero[29] 2001	1	53 F	Pbps	P Gibl-Mel	4	Pancreatitis
Gama-Odrigues J[30] 2001	2	NA	Pbps	P Gibl-2 Cases	5	NA
Moehler M[32] 2000	1	43 F	Mini-laparcBps	P	4	NA
Eurvilaichit C[33] 1999	1	35 F	Pbps	P Gi-bl- mel	3	NA
Jornod P[34] 1999	1	75 F	Pbps	P J	8	Pancreatitis
Lee SL[35] 1999	1	30 F	Pbps	P Gi-bl-Hem&Mel	2	Necrotic GB-cystic duct blocked with clot
Kim HJ[36] 1999	1	NA	NA	NA	NA	Cholecystitis / Pancreatitis
Kwauk ST[37] 1998	1	35 F	Pbps	Gibl-Mel J-2 weeks later after lap cholecystectomy	10	nil Acalculouscholecystitis
Richardson SC[38] 1998	1	49 M	USbps	P GIbl-Mel	9	Pancreatitis
Dousset B[39] 1997	11	NA	Pbps	QT- 7 4=NA	Median-3 (1-25)	Pancreatitis-32%- (4 pt) Cholangitis-37% (4 pt)
Cacho G[45] 1996	1	NA	Pbps	P GI-bld- mel	3	Cholecystitis
Grieco A[53] 1996	1	65 F	Pbps	QT	18hr	Nil
Van Os EC[54] 1996	1	64 M	Pbps	P Gi- bl- hematochezia	24hr	Pancreatitis
Jabbour N[55] 1995	3	26,64,1.7 M=2, F=1	Pbps=1 Laprbps=1 Usbps=1	1 pt-Asymptomatic-detected during routine angiogram post transplant 2nd pt-J+ Gibld 3rdpt= abnormal LFT=hepatic angiogram detected	NA	Multiorgan failure-1 Liver infarction-1
De Ribot X[56] 1995	1	55 F	Pbps	P GIbl-Mel	1	Pancreatitis
Figueras J[57] 1994	1	7 F	Pbps	P Gi-bl-Mel	24hr	Died of massive bleeding despite TAE and before surgical intervention
Merhav[58] 1993	1	41 M	Pbps	P Gi-bl-Mel	1	NA
Manzarbietia[59] 1993	1	51 M	USbps	P Gi-bl-Mel	3	Pancreatitis

Lichtenstein DR 1992[40]	1	39 M	Pbps	P Gi-bl- mel-48 hrs later	4	NA
Okazaki M 1991[60]	1/10 HB	NA	Pbps	P Gi-bl-Mel-Hem	2	NA
Attiyeh FF[41] 1976	1	16 M	Pbps	QT	3	NA
Ball TJ[42] 1975	1		Pbps	QT	2	NA
Levinson JD[43] 1972	1	40 M	Pbps	QT	2	NA
Cox EF[44] 1967	1	27 F	Pbps	QT	NA	NA
	78	M=21 F=27 Age- Avg-43.9 Range-1.7 to 75 **DA=48 cases**	Pbps=28 Usbps-16 Tjbps- 6 Lapcbps=2 Laprbps=1 EUSbps=1 **DA=54 cases**	QT= 25 P+Gibl=30 P+J=4 RAPT=2 Gibl=2 J=1 Hypotension=1 Confusion=1 **DA =71 cases**	Median -4 days **DA=72 cases**	Cholecystitis-12 (21.81%) Pancreatitis-23 (41.81%) Cholangitis- 6 (10.9%) Liver Infarction-2 (3.6%) Mulitiorgan failure-2 (3.6%) Bilhemia-1 (1.81%) Death-2 (3.6%) **DA=55 cases**

HB= haemobilia, USbps= ultrasound guided biopsy, Pbps=percutaneous biopsy, Tjbps= transjugular biopsy, EUS-bps= Endoscopic ultrasound guided biopsy, Lapcbps= laparoscopic biopsy, Laprbps= laparotomy and biopsy, DA= data available, P=pain, J= Jaundice, Gibl=GI bleed, Gibl-Mel= Gi bleed presenting as melena, GIbl-hem= Gi bleed presenting as hematemesis, QT=Quincke's triad, NA= not available, RAPT= routine angiogram post transplant

Table 2: Investigations, Management and Complications.

Series Year	Investigations	Nature of fistula	Management (radiological/ endoscopic)	Surgical Procedure	Discharge Day-Post procedure	Hepatic disorder/ co-morbidities
Zhou HB[1] 2014	LFT US MRCP Endoscope DSA	AVBF	TAE- Rt hepatic artery	Nil	12 days	Abnormal liver function
Qureshi[2] 2014	LFT Angiogram Endoscope	ABF	TAE ERCP- ClExt	Nil	NA	Nil
Zaleska-Dorobisz[3] 2014	LFT US Endoscopy Angiogram	ABF APF	TAE- rt hepatic artery-GianturooWallaoh coil	Nil	4	Chronic hepatitis B
Howlett DC[7] -2013 (UK audit)	NA	NA-2	NA=2	NA=2	NA	NA
Plerhopies TA[4] 2013	LFT CT ERCP	NA	ERCP-ClExt/stenting Perc-chol	Nil	3	Portal hypertension/ deteriorating LFT/ Hemosiderosis/ ESRD
Marynissen T[5] 2012	LFT CT-2 US-4 Angiogram-6	NA-6	TAE-6	NA	NA	NA

Gandhi V[6] 2011	LFT CT Angiogram	NA	NA	NA	NA	NA
Kawakubo K[8] 2011	LFT CT Endoscope	NA	Nasobiliary drainage	Nil	8	Nil
Egritas O[9] 2010	LFT CT Endoscope	NA	Supportive measures-blood products/iv fluids	Nil	10	Mitochondrial disease, familial intrahepatic cholestasis
Koshy CG[11] 2010	Endoscope Hepatic Angiogram Hepatic venogram	APF PsdA	Supportive measures TAE Hepatic vein embolization-platinum coils	Nil	Few days	Cryptogenic liver cirrhosis, portal hypertension, moderate ascites
Hendricks MP[10] 2009	US ERCP-elongated opacities-blood clots	NA	ERCP – sphincterotomy+ stent	Nil	NA	Psoriasis Liver biopsy to rule out methotrexate induced hepatitis
Peña LR[12] 2009	LFT MRCP ERCP	NA	ERCP-spinterotomy+ ClExt-balloon +stenting	Nil	NA	Chronic hepatitis C
Wood B[13] 2009	LFT Endoscopy CT Angiogram	ABF PsdA	NA	NA	NA	NASH
Li F[14] 2009	LFT CT MRCP	NA	Supportive measures only	Nil	2	Alcoholic cirrhosis Post liver / kidney transplant
Prata F[15] 2008	LFT-2 US-1 CT-1 ERCP-2	NA-2	ERCP-sphincterotomy +ClExt -2	Nil	NA	Cirrhosis
Rogart JN[16] 2008	LFT CT Endoscope Angiogram	ABF	TAE	Nil	NA	Hepatitis C infection
Gurakuqi GC[17] 2008	LFT Endoscopy Angiogram	ABF	TAE	Nil	died	Alcoholic cirrhosis Severe coagulopathy
Bergmann OM[18] 2007	LFT US ERCP Angiogram	AVBF (trifistula)	TAE ERCP-ClExt-stenting	Nil	5	ESRD Malignant melanoma
Dallal RM[19] 2007	LFT US HIDA scan ERCP	NA	NA	Lap chol CBD exploration	NA	Hypertension, gastro-oesophageal reflux, polycystic ovarian syndrome
Edden Y[20] 2006	US On table cholangiogram	NA	Supportive measures	Lap chol and on table cholangiogram	2	Persistent elevated liver enzymes/ cryptogenic cirrhosis
Albuquerque W[21] 2005	US-free fluid in peritoneal cavity. GB- echogenic material ERCP+MRCP- edematous pancreatitis/dilated GB,CBD clots Angiogram- no further bleeding seen	NA	ERCP- ClExt -balloon	Lap chol- 5 days after ERCP for recurrent abd pain	NA	Biopsy- preop for renal transplant protocol. Hepatitis C

Kruse-Jarres[22] 2005	US CT	NA	Conservatively with factor V111 replacement only	Nil	4	HIV Hepatitis C Congenital hemophilia
Nowak A[23] 2005	Endoscope ERCP	NA	ERCP ClExt=dormia basket-nasobiliary tube-thrombin infusion	Nil	2	Diabetic Chronic elevation of ALAT- non-alcoholic steatohepatitis
Lin CL[24] 2005	US- Gb-polypoidal mass ERCP-blood in ampulla- clot in CBD	APBF	ERCP-sphincterotomy-CLExt, TAE- with gel foam-segment VII	Nil	7	Chronic C hepatitis
Hodgson RS[25] 2004	US-free fluid around GB Angiogram-pseudoaneurysm/AP biliary fistula	APBF PsdA	TAE- Titanium microcoils	Nil	4	Crohn's disease
Sharma R[26] 2004	LFT- abnormal US- dilated GB, mild IHD dilatation CT-distended GB, IHD dilatation, blood clot in CBD Angiography-filling defect in Rt lobe MRI/MRCP- for follow up	NA	TAE	Nil	NA	Hepatitis B
Hashimoto M[48] 2004	US CT Angiogram	PsdA-2 ABF-1	TAE	Nil	NA	
Rossi[47] 2002	US ERCP-Blood clot in CBD Angiogram	ABF	TAE	Nil	7	Hepatitis C
Machicao VI[51] 2002	LFT CT Angiogram	APF	TAE	Nil	NA	Hepatitis C
Sood A[52]. 2002	LFT CT ERCP	NA	ERCP-sphincterotomy +ClExt	Nil	NA	Hepatitis C
Asselah T[27] 2001	LFT US MRCP- acute pancreatitis/ CBD clot	NA	NA	NA	NA	
Coelho JC[28] 2001	US-thick walled GB-blood clot intraluminal	NA	NA	Lap cholecystectomy		
Gomez-Valero[29] 2001	US Angiogram	APF	TAE	Nil	3	
Gama-Odrigues J[30] 2001	US Angiogram Laparoscopy	ABF=2	Conservative measures=2	Lap cholecystectomy and ligation of hepatic artery- 2 cases	NA	NA
Moehler M[32] 2000	US Angiogram	APF	TAE	Nil	3	Nil
Eurvilaichit C[33] 1999	US Angiogram	ABF	TAE-gelfoam	Nil	3	Nil
Jornod P[34] 1999	LFT US ERCP	NA	ERCP-sphincterotomy-ClExt	Nil	3	Primary biliary cirrhosis

Lee SL[35] 1999	LFT-abnormal Angiogram- no source of bleed seen RBC tagged scan-post cholecystectomy(abnormal LFT/persistent pain)-NAD ERCP- clot in CBD	NAD	ERCP- postop on 5th day –Sphincterotomy-ClExt	Open cholecystectomy-on 3rd day-necrotic GB	NA	Hepatitis C Went home and returned after 72 hrs
Kim HJ[36] 1999	NA	NA	NA	NA	NA	NA
Kwauk ST[37] 1998	CT-hematoma rt lobe of liver ERCP-normal CBD/pancreatic duct LFT- abnormal-2 weeks later Angiogram-24 days after initial presentation and lap chole	PsdA	TAE—coil Percutaneous drainage of gall bladder bed collection	Nil	11	Biliary cirrhosis
Richardson SC[38] 1998	ERCP	APF	NA	NA	NA	Hepatitis C
Dousset B[39] 1997	LFT=11 US=11 Angiogram-11	APF=4 PsdA=2 ABF==3 NAD=1 Vascular flask=1	TAE- successful= 7 Failed =2 technical difficulty Complicated=1 (ischemiccholecystitis		NA	NA
Cacho G[45] 1996	US Endoscopy Angiogram	APF	TAE	Cholecystectomy	NA	nil
Grieco A[53] 1996	US Angiogram-AV fistula- 3rd liver segment ERCP-clot	AVF	TAE- gelfoampledgets	Nil	NA	Polyneuropathy/ endocrinopathy/ monoclonal gammapathy
Van Os EC[54] 1996	Angiogram Endoscopy	PsdA	TAE	Nil	NA	Drug related hepatitis
Jabbour N[55] 1995 (3 cases)	Doppler-2 Angiogram-3 Radionucleide scanning-1 Endoscopy-1	APF-3	Conservative-2 TAE-1	CBD exploration, and 2nd liver transplant for infarction-1 case	NA	Non A/B hepatitis-1 Chronic active hepatititis-1 Cat's eye syndrome-1
deRibot X[56] 1995	ERCP	NA	NA	NA	NA	Chronic elevated liver enzyme
Figueras J[57] 1994	Angiogram	ABF	TAE	Nil	Died	Post liver transplant
Merhav[58] 1993	US Angiogram	PsdA	*Directpercutaneous emoblisation-ultrasound guided.(DPE)* TAE-technically was not possible- tortuous allograft hepatic artery	Nil	NA	Post liver transplant
Manzarbietia[59] 1993	CT MRCP	NA	NA	NA	NA	Post liver transplant
Lichtenstein DR 1992[40]	US Angiogram	ABF	TAE- gelfoam and Gianturco coil	Nil	3	Nil
Okazaki M[60] 1991	US Angiogram	ABF	TAE-gelfoam	NA	NA	Nil
Attiyeh FF[41] 1976	LFT US	NA	Supportive measures only	Cholecystectomy/ CBD exploration/ left hepatic artery ligation		Hodgkins disease

Ball TJ[42] 1975	LFT ERCP Angiogram	NAD	NA	NA	NA	NA
Levinson JD[43] 1972	LFT Angiogram-linear collection of contrast close to biopsy	NAD	ND	T tube decompression of CBD Left hepatic artery branch ligation	NA	Micronodular cirrhosis Granulomatous liver disease, Sarcoidosis
Cox EF[44] 1967	NA	NA	NA	NA	NA	NA
	Angiogram=50(68%) LFT=35 (47.9%) US=33 (45.2%) ERCP=18 (24.6%) Endoscope=12 (16.4%) MRCP=6 (8.21%) Radionucleide scan=3 (4.1%) **DA=73**	ABF=15 (32.6%) APF=16 (16.9%) PsdA=10 (21.7%) AVBF=2 (4.34%) NAD=4 (8.69%) **DA=46**	TAE=38 (61.2%) ERCP+ClExt=13 (20.9%) Supportive measures only=11 (17.7%) DPE=1(1.6%) Percchol=1(1.6%) NBD=1(1.6%) **DA=62**	NPP=30 (46.1%) Chcyst=15 (23.07%) CBDE=4 (6.15%) HAL=6 (9.23%) **DA=65**	Median=6 days	

LFT=liver function test; US= ultrasound; MRCP= magnetic resonance cholangiography; DSA= digital subtraction; CT=computerized tomogram; IHD=intra hepatic duct; DPE=direct percutaneous embolization; NBD= nasobiliary drainage; HAL=hepatic artery ligation=6; Chcyst= cholecystectomy; CBDE= CBD exploration; NPP= no procedures performed; AVF= arteriovenous fistula; ABF=arteriobiliary fistula; APF= arterioportal vein fistula; PsdA= pseudoaneurysm; NA= not available; NAD= no abnormality detected; AVBF= arteriovenous biliary fistula; TAE= transarterial embolization; ClExt= clot extraction; PercChol= percutaneous cholecystectomy; ESRD= end stage renal disease; NASH= non alcoholic steatotic hepatitis

bleed alone (2.8%), and those detected on routine angiogram post liver transplant and liver biopsy (2.8%) and one case each of confusion (1.96%), hypotension and jaundice alone. The mean day of presentation was 5 days. The investigations that facilitated in diagnosis included angiogram (68%), LFT (47.9%), ultrasound (US) abdomen (45.2%), ERCP (24.6%), endoscopy (16.4%), MRCP (8.2%) and radio nucleide scan (4.1%). Angiogram detected arteriobiliary fistula in (32.6%), arterioportal fistula (36.9%), pseudoaneurysm (21.7%), arteriovenous biliary fistula-Trifistula (4.3%) and no abnormality (8.69%), among the 46 patients were data was available. Transarterial embolization was carried out in 61.2% and was successful in 80% of these cases in arresting the bleeding. ERCP with clot extraction was required in 20.9% of patients where CBD clot persisted. In 17.7% of patients no radiological or endoscopic measures were carried out and were managed with supportive therapy only. There was one patient each who underwent percutaneous cholecystostomy, nasobiliary drainage of the biliary tract and ultrasound guided direct percutaneous injection of the vascular fistula, due to technical difficulty in catheterisation and embolization of hepatic artery because of its tortuosity. No additional surgical procedures were carried out in 46.1%; however among the remaining patients, 23% underwent cholecystectomy, 6.15% underwent CBD exploration and clot removal and 9.23% underwent hepatic artery ligation. The complications noted were pancreatitis (41.8%), cholecystitis (21.8%), cholangitis (10.9%), liver infarction in patients with liver transplant (3.6%), multiorgan failure (3.6%), bilhemia (1.8%) among the 55 patients were data was available. Death was noted in 2 patients(3.6%). The median stay of patients was 6 days. However in many of the patients with complications, the data of discharge was not available and the median day of stay of 6 days noted, is likely to represent those without complications.

Mechanism

The term hemobilia relates to bleeding into the biliary system. Majority of the bleeding are post liver biopsy, a reflection of the recentincrease in this invasive procedure, to establish diagnosis of liver pathology [62].They could also be secondary to gallstones, vascular malformations, parasitic infestation, inflammation, tumours, post cholecystectomy [6, 63], acute cholecystitis [64] and trauma [6]. Most of the bleeding is into the intra-hepatic biliary system [1-6, 9-22]. However, bleeding into extrahepatic bile ducts and gall bladder is also reported [8]. The vessels that could be involved include cystic artery, anomalous hepatic artery, portal vein andhepatic artery or its intrahepatic branches [1, 6].Due to the close proximity of the intrahepatic bile duct, hepatic artery and portal vein, a puncture needle during liver biopsy,could easily lead to injuryof all these structures to form arteriovenous bile duct fistula, arterial bile duct fistula and venous bile duct fistula [1]. Bleeding from venous bile duct fistula often stops spontaneously, because of low venous pressure [1]. The bleeding of venous origin could however lead to significant bleeding, if they bleed freely into peritoneal cavity through a subcapsular located bleeding site [11]. An arteriobiliary fistula on the other hand is likely to be symptomatic because of bleeding from a high pressure vascular system into low pressure biliary tract. Hemobilia could also be due to pseudoaneurysm, which was seen in 21% in this review. The pseuodaneurysm formation

may be delayed after a biopsy and are usually a consequence hematoma, progressive compression, and chronic inflammation, all leading to low-grade damage within the liver parenchyma [18,20,55]. This could then predispose to aneurysmal changes in the adjoining hepatic arterial branch, forming a pseudoaneurysm [55]. The risk of vascularbiliary fistula is believed to be increased, when biopsies are carried out in the presence biliary duct obstruction and infection, as the hepatic arterial blood flow increases in such condition [1]. Moreover, hyperplasia and distension of the arterial peribiliary vascular plexus and the feeding hepatic artery branch in periportal area enhances this risk [1]. Fistula involving the hepatic artery, hepatic vein and biliary tree could cause an intrahepatic *trifistula* leading to *bilhemia* and Hemobilia [18]. Bilhemia (bile in vascular system) could causepersistent deterioration of the liver function and confusion post procedure, which can be controlled after treating the fistula [18].The direction of blood flow and development of bilhemia and hemobilia is to a large extent influenced by the intravascular biliary duct pressure gradients. The pressures in healthy subjects are as follows. (1) hepatic artery 100 mmhg, (2) bile duct 10 to 15 mmhg, (3) portal vein 10 mmHg, and (4) hepatic vein 0 to 5 mmHg [18]. The pressure gradient between intrahepatic hollow structures can be affected by pathophysiological changes in various disease states, including cirrhosis and common bile duct obstruction. A supraphysiological biliary-venous pressure gradient(>10mm Hg) is needed to cause clinically significant bilhemia, which may happen in the presence of bile duct obstruction [18]. When pressure is≤10mm Hg, fistulas are likely to close spontaneously. When hepatic artery is involved, the high-pressure system is more prone to persistence of fistula.

Risk of hemobilia in patients with coagulation disorder

Like any other invasive procedure, liver biopsy in patients with coagulation disorders including congenital bleeding disorders is at a risk of bleeding complications [22, 62]. These procedures however can be carried out safely in these patients, if they are under adequate cover of coagulation factors, in the periprocedure period [22]. There are differing opinions as to what constitutes an abnormal coagulation index that would determine a contraindication for liver biopsy. Most centers consider an international normalised ratio (INR)> 1.5 and platelet count of <50,000/mm as strong contraindication [61].

The pathophysiology of Blood clot in Bile duct

The blood does not normally clot within the bile duct because of fibrinolytic activity of bile [65]. However, sometimes the clot if formed, fails to lyse. Sandblom et al reported that when the hemorrhage is severe and rapid, the blood mixes with bile and forms mushy clot [65]. When hemobilia is minor and slow, the mixture does not result, but leads to blood flowing and settling at the bottom, where it forms a solid pure clot that forms cast of the lumen [65]. These pure clots remain stable, whereas mixed clots dissolve rapidly. Hence the fate of clots is related to the bile flow, with the dissolution of clot being rapid when flowing blood is exposed to bile [65, 66]. The difference in surface tension between bile and blood could be another factor that could lead to stasis and clot formation [65].

Presentation

The classical presentation of hemobilia constitutes the Quincke's triad [2, 9] and includes right upper quadrant pain, jaundice and acute gastrointestinal hemorrhage. This is reported in some series to be seen in 50% [38] to 63% of patients [39]; however it constituted 40% of the presentation in this review. The most frequent clinical finding is upper gastrointestinal bleeding (90%); right upper quadrant pain (70%) and jaundice (60%) [9]. The mean interval is reported to be 5 to 6 days following the liver biopsy [2,5, 6, 15, 30, 47]. Hemobilia may present immediately [11, 21, 57] or may be delayed up to a week or as late as 25days [39].The clinical manifestation of hemobilia is determined by the amount and speed of hemorrhage into the biliary tract [1, 6]. Profuse hemobilia often causes severe symptoms with colicky pain and gastrointestinal hemorrhage [65,66]. However, often the bleeding is occult and lacks clinical significance as the blood inconspicuously flows into the intestine [65,66]. Blood clots in the gall bladder can mimic biliary colic or induce hemocholecystitis [20, 21, 45], while the blood clot in CBD may present with obstructive jaundice or complications of pancreatitis [23,25,51,52] and cholangitis, similar to patients with choledocholothiasis [1, 12, 24].

Liver biopsy technique and its influence in causing hemobilia

Liver biopsy is carried out by percutaneous transhepatic approach or by transjugular approach [11, 62]. Transjugualr approach is preferred in patients with severe coagulopathy, ascites, massive obesity or suspected vascular tumours [4, 11,62]. Patients who require simultaneous vascular procedures (such as Venogram or Transjugular Intrahepatic Portosystematicshunt (TIPS) placement or when percutaneous biopsy has failed would be better served by a transjugular approach [62]. The procedure would involve, inserting a catheter into the hepatic vein through the right internal jugular vein, under fluoroscopy guidance. The liver biopsy forceps is then introduced to blindly obtain tissue. The drawback however is that the samples are smaller than those obtained by percutaneous approach [4,62]. It warrants several passes in order to obtain an adequate pathologic specimen with a reported success rate of 97% [4]. The complication rate is around 2.% and comprises mild (abdominal pain, neck hematoma transient Horner's syndrome) or more severe complications (hemobilia, gall bladder puncture, cardiac arrhythmias, pneumothorax, perforation of liver capsule, sampling of adjacent organs) [4]. Although ultra-sound guided biopsies are relatively safer, complications including hemobilia are reported [9, 13, 25, 48]. Complications of percutaneous liver biopsy are fortunately uncommon. Majority (96%) of them appear in the first 24 hours and the remaining 4% usually have their clinical presentation within 10 days [50]. The presence of cirrhosis and neoplasm however increase the risk of complications [20]. In addition to the underlying disease, the risk of complications would also

depend upon the coagulative status, the type and the diameter of biopsy needle used and the number of needle passes, despite being ultrasound guided [6, 9, 62]. US guidance however would reduce the risk of undesired puncture of surrounding organs.Major complications are higher in patients with focal lesion (1.3%) compared to 0.3% in those without a focal lesion [7]. Hemobilia has also been reported following endoscopic ultrasound biopsy of hilar carcinoma through transdudoenal bulb approach [8] and also in those where the biopsy has been carried out laparoscopically [19,32].

Complications of hemobilia

Several complications could occur as a consequence of blood in the biliary system [1].The blood clot could cause obstructive jaundice and may lead to acutecholecystitis [1,4,20,21], cholangitis [1,15] and acute pancreatitis [1, 9, 10, 12-14, 23], intra-abdominal fluid collection [4], persistent distension of gall bladder with gall bladder rupture [4], and acute gastric stress ulcers [1]. Blood clot could raise the intra biliary duct and pancreatic duct pressure leading to acute pancreatitis [1].The clot may disappear in few days time [9, 10] particularly in those who had interventions to drain the biliary system or it may persist longer [20]. In those where the clot in gall bladder persists, have been reported to form gallstones, few months later [35]. Percutaneous cholecystostomy could reduce the GB and biliary tract pressure [4]. Reducing the biliary tract pressure can prevent pancreatitis [1]. Arteriovenous fistula bleeding in the liver often results into an intra-hepatic hematoma and occasionally portal hypertension [1,67]. Lim et al have reported that percutaneous liver biopsy could result in arteriovenous fistula in 38% (8/21) of cases after biopsy [67]. However vascular biliary injury noted in this review included arteriobiliary fistula (32.6%), arterioportal fistula (36.9%), pseudoaneurysm (21.7%) and arterio venous biliary (trifistula) (4.3%). The predominant complications noted in this review included pancreatitis (41.8%), hemocholecystitis (21.8%) and cholangitis (10.9%).

Investigations

The bleeding through the papilla into the duodenum can be established by endoscopy in 33% [39] to 60% of the cases[6,24,68]. Ultrasound doppler could help in diagnosis of a pseudoaneurysm and would appear as a well circumscribed anechoic lesion with a turbulent flow [1, 6, 24, 55]. Contrast enhanced CT scans can demonstrate hematoma, anatomical variations, pseudoaneurysm and cavitating lesions [26, 67]. The appearance on US and CT varies depending on the rapidity and severity of bleeding. US and CT scan may note the hydropic gall bladder and surrounding edema compatible with cholecystitis [9, 22]. Intracholecystic bleeding typically appears as echogenic , non-acoustic polypoidal mass [22, 24]. The echotexture becomesa reticular stranding sludge, as clot lyses [24]. The border of the clot becomes concave and gall bladder appears to have polypoidal mass [24]. MRCP may reveal associated pancreatitis, cholecystolithiasis, cholangiectasis and abnormal signal indicating muddy stone or hematocele in CBD [1]. MRCP shows a negative magnetic signal in the biliary duct and gall bladder, corresponding to the clot in it [21]. If ERCP is performed, it could demonstrate the blood emerging from the papilla figure 1 and the intraluminal blood clot could be documented as filling defect figure 2 [10, 24]. Digital subtraction angiogram (DSA) could detect the site of bleeding and fistula, when the rate of blood loss is> 0.5 ml/min [1]. A strong suspicion of hemobilia warrants an urgent angiography for its diagnostic and therapeutic value. This is in the form of an initial celiac axis angiography, combined with superior mesenteric arteriography, to determine a possible abnormal origin of an anomalous /accessory right hepatic artery from SMA in 20% of the patients [6]. A selective right and left hepatic angiogram are likely to localize the bleeding better, particularly in the presence of pseudoaneurysm [6]. Unfortunately angiogram may appear normal in some patients in the absence of active bleeding or when there is no demonstrable lesion [6, 39]. In the event bleeding continues or recurs, a repeat angiogram is worthwhile and advisable [6].Angiography findings in hemobilia could include arterio-portal fistula, arteriobiliary fistula and pseudoaneurysm [24]. Arterio-portal fistula is reported to occur in 5% of the cases and may remain asymptomatic [24].

Treatment

The main principle in management of hemobilia is resuscitation, control the source of bleeding and maintain the biliary patency [9, 39]. Resuscitation with transfusion is carried out to obtain hemodynamic stabilitywhen hemorrhage is severe and rapid [1, 6, 9, 13, 12]. Any existing coagulopathies are simultaneously dealt with [22]. Nearly 50% of the patients will stop bleeding with the supportive measure of blood products [9, 22, 24, 37, 42, 55]. The remaining patients would require therapeutic interventions, which would involve Transarterial Hepatic Artery Branch Embolization (TAE). TAE is most prudent in patients with pseudoaneurysm, arteriobiliary fistulas, or arterioportal fistula [1,69]. Superselective embolization is safer and more effective treatment for active bleeding. It is carried out using a microcatheter and is desirable as it minimizes spasm and avoids occlusion of the noninvolved arterial branches, particularly in liver transplant patients [69]. Hence, selective embolization as close as possible to the pseudoaneurysm or fistula is opted for,to limit the likelihood of both recurrence and liver necrosis [48,69]. The risk of inadvertent ischemic cholecystitis, hepatic artery main branches embolization, is also avoided [39].

In transplant patients, liver graft dysfunction and biliary ischemia are potential risks.

Embolisation could be carried out using gelatin sponge, autoallergy-sludged blood, spring orb, microcoils, polyvinyl alcohol particles and cyanoacrylate glue [1,6,24]. Coils induce thrombosis and hence for obvious reason may be ineffective in patients with gross coagulopathy [6]. Smaller pseudoaneurysm where coil placement may be difficult, may be effectively treated with cyanoacrylate glue as it conforms to the shape of the pseudoaneurysm,forms a cast instantly and is cheaper than microcolis [6]. Hypophysin is also reported to be commonly

used [1].The success rate of arresting bleeding with TAE intervention is reported to range from 63% [6], 94% (16 out of 17) [6] to 100% [5]. In one of older series involving 11 cases hemobilia,transarterial embolization was successful in 63%, with 18% having technical failure and I case (9%) with ischemic cholecystitis [39]. Recent reports however indicate higher success rate [5, 6]. Failure to arrest bleeding could be due to technical reasons or extensive collaterals [39].In the presence of extensive collaterals,embolization, distal and proximal to the pseudoaneurysm will be required [6]. Alternatively the pseudoaneurysm is occluded with microcoil or glue in addition to proximal occlusion with coils [6].Technical failure could also be due to a tortuous vessel, as in an allograft artery, post transplant [58] or due to intimal injury and spasm of the vessel, during manipulation of the catheter [60]. In very rare cases, it could be due to bleeding into peritoneal cavity of venous origin [11]. In one of the reports, persistent bleeding post TAE was localized to bleeding into the peritoneum from a feeding hepatic vein branch [11]. The bleeding, which was occurring through a subcaspular site, was effectively controlled by transjugular hepatic venogram and embolization [11]. In a post transplant patient where there is difficulty in achieving TAE because of technical difficulty in cannulating a tortuous allograft artery, the bleeding has been successfully dealt with by direct embolization of the aneurysm, under ultrasound guidance [58]. This review noted that TAE was carried out in 63% of the patients with 80% success in arresting the bleeding.

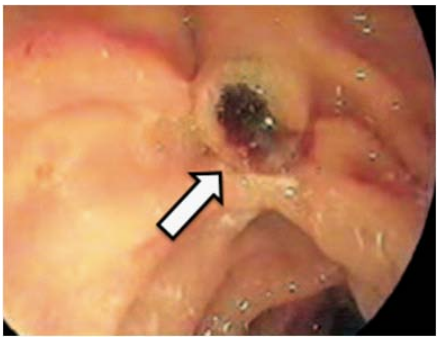

Figure 1: Blood Clot Seen at the Ampulla (arrow) in a Patient with Hemobilia.

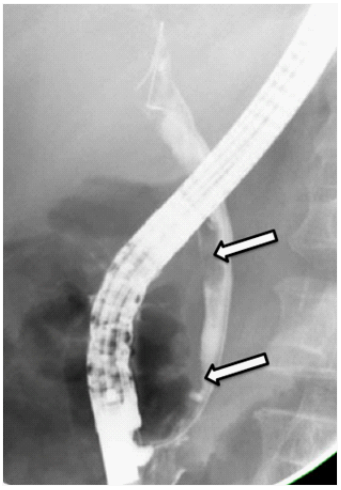

Figure 2: ERCP Revealing Multiple Clots in CBD as Filling Defects (arrows).

Having controlled the bleeding, the attention is then directed to a potential biliary tract obstruction, due to intraluminal clots. If the intraluminal clot does not dissolve and persist beyond 24 to 48 hours leading to progressive deterioration of liver function tests and dilatation of the bile duct (reflected by radiological imaging), then clot extraction and bile duct drainage would be required [4]. Biliary obstruction by clot may require ERCP sphincterotomy and balloon extraction of clots [2, 4, 15, 23]. Recurrent clot formation after an initial successful clot extraction may warrant a repeat of the procedure [12]. Endoscopic nasobiliary drainage has also been used to decompress the biliary tract [8, 23]. In addition, thrombolytic agents have been infused through a nasobiliary catheter to dissolve the biliary clots [70]. Routine placement of biliary stent in the presence of hemobilia is controversial. While some would stent the ampulla to prevent reaccumulation of clot [12], there are others who are concerned of stent forming a nidus which may act as matrix for thrombus attachment and worsening of obstruction [35, 37]. In liver transplant patients who develop hemobilia post liver biopsy, endoscopic approach may not be feasible because of anatomical distortion post bile duct reconstruction. In them, the clots can be dealt by transhepatic approach, to break up the clots progressively and increase its contact surface to flowing bile [71]. In patients with persistent distended gall bladder, a percutaneous transhepatic cholecystostomy could relieve the symptoms, particularly in patients with significant co-morbidities [4].

The role of surgery over the years has declined, after the advent of successful radiological intervention, in arresting bleeding in most of the cases[6, 24, 37].However, surgical intervention will be required when the above measures fail [6, 24].Emergency surgery to control major hemobilia is challenging and hazardous and should be avoided, as the results are poor [6]. Surgical intervention however is unavoidable in the absence of angiographic facility, failure of TAE or in the presence of hepatic sepsis [6]. In the absence of angiographic facility, every attempt should be made to transfer these patients to a center with these facilities. The principle of surgery is to control the bleeding vessels [40, 42], extraction of biliary clots with lavage and biliary tract drainage [39,41]. In the presence of liver necrosis or liver sepsis, a limited liver resection may be warranted. Post ERCP and sphincterotomy, reports suggest the disappearance of clot in GB, within a couple of weeks [24]. However in some cases, despite decompression of the biliary system by ERCP sphincterotomy, the clot in the gall bladder may persist, requiring cholecystectomy. This may deal with symptom related, both to acute cholecystitis or possible dyskinesia [21, 35, 37].The timing of the cholecystectomy could either be immediate [20, 35] or delayed [37], based on the existing symptoms and is carried out preferably laparoscopically.

In addition to performing cholecystectomy, laparoscopic approach has been used to simultaneously carry out ligation of hepatic artery, in patients with persistent bleeding [30].

The reported mortality post iatrogenic hemobilia is around 10 to 12% and is mostly related to those who required surgical intervention [39]. In the recent years the success of angiographic embolization has significantly reduced the need for surgical intervention and hence the mortality. This review noted the mortality in 3.6% of the cases.

Conclusions

Hemobilia is a rare complication of liver biopsy, but is being noted with increasing frequency due its predominant role in establishing diagnosis in various liver pathology. The presentation could be variable but GI bleeding in the presence of jaundice and or pain post liver biopsy, should alert the clinician. Endoscopy and angiogram play a significant role, both as diagnostic and therapeutic tool. Off late, transarterial embolization arrests bleeding in majority of these patients. Role of surgical intervention is limited to those with complications of hemocholecystitis, failure of TAE in arresting bleeding and persisting clot induced obstructive jaundice, despite endoscopic intervention

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