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Review Article

Systematic review: Features, diagnosis, management and prognosis of hepatic hematoma, a rare complication of ERCP

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ABSTRACT

Background: Hepatic hematoma (HH) is a rare but severe adverse event following endoscopic retrograde cholangiopancreatography (ERCP).
Aims: To perform a systematic literature review and describe two additional cases, one of which presenting multiple subcapsular/intrahepatic hematomas after ERCP.
Methods: The literature review was performed in PubMed/MEDLINE, EMBASE, and SCOPUS to identify all cases reporting on HH after ERCP.
Results: A total of 48 cases (females 63%, mean age 58.2 ± 20.6 years) were included. The mean symptoms onset time was 46.8 h after ERCP, and the most common symptoms were abdominal pain (91.7%), anaemia (43.8%), hypotension (29.2%) and fever (20.8%). All cases were diagnosed by computed tomography (CT). HH was found mostly in the right hepatic lobe (95.1%) and the mean size was 116 × 93 mm. A conservative management was adopted in 38.3% of cases, while percutaneous drainage, embolization and surgery were needed in 31.9%, 14.9% and 25%. Mortality rate was about 9%. Anaemia (OR 6.9; p = 0.02) and surgery (OR 10.5; p < 0.01) were the only independent factors for unfavorable outcome (death), while abdominal pain (OR 0.1; p = 0.03) and antibiotics administration (OR 0.06; p < 0.001) were associated with better outcome.
Conclusions: HH is a rare but severe complication following ERCP which needs a multidisciplinary approach. Antibiotics administration is the only treatment able to reduce the risk of death.

1. Introduction

Endoscopic retrograde cholangiopancreatography (ERCP) is considered as a standard endoscopic procedure for the management of biliopancreatic diseases. However, in spite of being considered safe, ERCP is associated with high potential for complications [1].

Adverse events occur in about 5%–10% of ERCPs. The most commonly reported complications include post-ERCP pancreatitis, bleeding, perforation, infection (cholangitis), and cardiopulmonary or sedation-related events [2–4]. About this topic, a systematic survey of 21 prospective studies between 1977 to 2006 involving 16.885 subjects reported an overall post-ERCP complication rate of 6.85% with a 0.33% mortality [3].

The development of hepatic hematoma (HH) is a very rare complication of ERCP, reported in the literature for the first time in 2000. From that report, other cases with different characteristics have been described. However, clinical features, diagnostic techniques, management and prognosis of such a complication have never been described.

Here, we report two additional cases of HH, one of which presenting with multiple subcapsular and intrahepatic hematomas, developed after the execution of ERCP; then, we performed a systematic literature review aiming to explore the features, diagnosis, management and prognosis of patients developing post-ERCP HH.

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2. Materials and methods

2.1. Literature search and selection of primary studies

The strategy for building the evidence base for the assessment of the features, diagnosis, management and prognosis of hepatic hematoma onset was performed with a systematic review of the available evidence in the literature, conducted in accordance with the preferred reporting items for systematic reviews and meta-analyses (PRISMA) guidelines [5].

The systematic literature review was performed in PubMed/MEDLINE, EMBASE, and SCOPUS to identify all cases reporting on hepatic hematomas after ERCP from the beginning of indexing for each database till March 2018. Bibliographic review of selected articles was examined as secondary sources for full-length articles of studies. A literature search was performed and verified by 2 independent reviewers (N.I. and G.d.N.) using the following index terms: "hepatic hematoma" OR "subcapsular hematoma" AND "endoscopic retrograde cholangiopancreatography" OR "ERCP".

2.2. Eligibility criteria

Two reviewers (N.I. and G.d.N.) independently evaluated all the studies selected according to the eligibility criteria and any differences between the data sets were resolved by discussion. All the original reports in which the development of HH was documented in patients of any age being treated with ERCP were considered for inclusion. Studies evaluating other diagnostic or operative procedures other than ERCP were excluded. No language restriction was used in the search filter.

2.3. Data extraction and management

Data were extracted independently and entered into standardized Excel spreadsheets (Microsoft Inc., Redmond, Washington, USA). The following data were extracted from each study: first author, year of publication, gender, age, indication for ERCP, type of procedure (i.e. sphincterotomy, biliary stenting, stent exchange, balloon dilation, lithotripsy, stone clearance), type of guide wire, symptom onset, use of anticoagulant drugs, main symptoms, diagnostic technique, liver lobe involved by the HH, lesion size, treatment, antibiotics administration and outcome (death).

2.4. Statistical analysis

Data were analysed using the Statistical Package for Social Sciences (SPSS software v.15.0, Chicago IL, United States) for Windows. The descriptive statistics used included determination of mean values and standard deviation (SD) of the continuous variables, and of percentages and proportions of the categorical variables.

Statistical analysis was performed using chi-square and Mann–Whitney U test, when appropriate. The odd ratio (OR) for quantifying the statistical difference between the dichotomous variables was also calculated.

A p value of less than 0.05 was considered statistically significant.

3. Results

3.1. Case 1

A 75-years-old Caucasian female was referred to our Emergency Room for recurrent episodes of upper abdominal pain and jaundice. Her past medical history revealed only hypertension. Laboratory tests showed mild hypertransaminasemia (aspartate aminotransferase – AST – 2.5 times the upper limits of normal (u.l.n.), alanine aminotransferase – ALT – 3 times the u.l.n.), hyperbilirubinemia (total bilirubin 6.7 mg/dL), increased gamma-glutamyl transpeptidases (4 times the u.l.n.) and alkaline phosphatase (2.8 times the u.l.n.). Abdominal ultrasound revealed a dilated common bile duct with multiple gallstones inside. She was admitted to our Gastroenterology Unit to perform an upper Endoscopic Ultrasound (EUS), which revealed the presence of choledocolithiasis. An ERCP with biliary sphincterotomy was performed by an experienced endoscopist (DGR) using a 0.035 in. diameter, 260 cm length, hydrophilic, straight tip guide wire (Boston Scientific, USA). All common bile duct stones were successfully extracted with a Fogarty balloon.

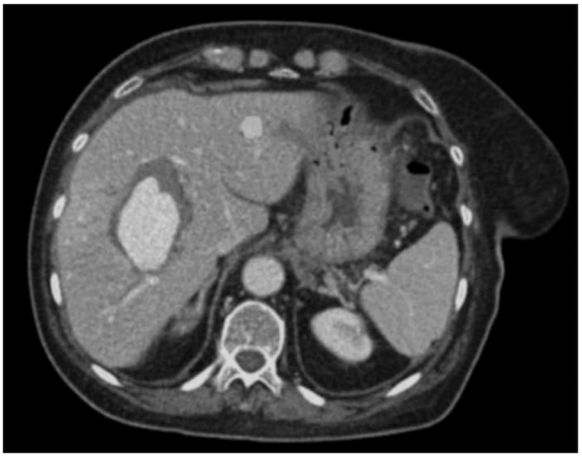

Fig. 1. Abdominal computed tomography showing hepatic hematomas with air inside following endoscopic retrograde cholangiopancreatography (ERCP).

Two days after the endoscopic procedure, the patient experienced an intense abdominal pain in the upper abdominal quadrants. Laboratory exams showed leucocytosis ($2074 \times 1.000/\mu L$), increased C-reactive protein (24 mg/dL with normal values 0–0.5 mg/dL), and the persistence of cholestasis indices. An abdominal computed tomography (CT) revealed a diffuse inflammatory imbibition of the main periportal spaces associated with a peripancreatic and pelvic effusion. Choledochus was dilated up to the papilla (12 mm), while the pancreatic ducts were normal. At the right lobe of the liver, a wide irregular oval cavity was observed, approximately $46 \times 72 \times 91$ mm, with a coarse central bloody air-containing hyperdensity, as a subcapsular hepatic hematoma (Fig. 1). Another similar but smaller intrahepatic hematoma ($10 \times 12 \times 11$ mm) was observed in the left hepatic lobe.

The patient's parameters and hemoglobin level were closely monitored, while broad-spectrum intravenous antibiotics were administered to prevent infections, along with intravenous fluids.

Despite this therapy, abdominal symptoms and laboratory tests did not improved. A new CT was thus performed one day later, showing an unchanged framework.

Despite the absence of any signs of hemodynamic instability, the persistence of symptoms and laboratory irregularities after few days of conservative treatment led the multidisciplinary team (surgeon, endoscopist, radiologist and anaesthesiologist) to decide for a selective angiography with right hepatic artery embolization performed by an interventional radiologist (Fig. 2). The radiological procedure was successful and was followed by a prompt clinical and laboratory improvement over the next three days. The patient was discharged uneventful after 6 days. An abdominal CT, performed 10 days after embolization, revealed a marked reduction of hematoma in the right hepatic lobe and the complete resolu-

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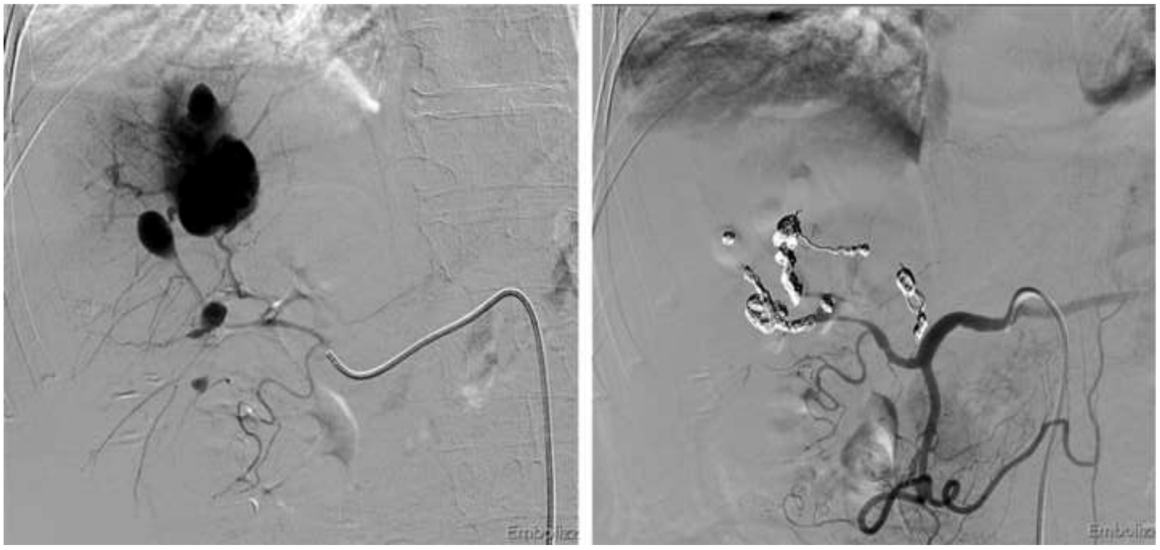

Fig. 2. Arteriography showing vascular embolization.

tion of the left lobe hematoma. After 1 month she was completely asymptomatic.

3.2. Case 2

A 45-years-old Hispanic male was referred to our Gastroenterology Unit for cholestasis due to the recurrence of a benign iatrogenic post-cholecystectomy common bile duct stricture, which had been previously managed with multiple plastic stents. Laboratory exams showed only hyperbilirubinemia (total bilirubin 5.8 mg/dL) and a mild increase in alkaline phosphatase (1.9 times the u.l.n.). A new ERCP was performed by an experienced endoscopist (GM) and a 6 cm fully covered metal stent was placed using a 0.035 in. diameter, 260 cm length, hydrophilic, straight tip guide wire (Boston Scientific, USA). Due to the very tight and stiff stricture, a significant pressure was exerted to advance the stent into the bile duct.

Two hours after the endoscopic procedure, the patient experienced an intense abdominal pain in the upper abdominal quadrants with signs of peritonism. Laboratory exams showed leucocytosis (1526 × 1.000/μL), increased C-reactive protein (18 mg/dL with normal values 0–0.5 mg/dL), and increased alkaline phosphatase (3.4 times the u.l.n.). An abdominal CT revealed a 110 × 80 mm subcapsular hepatic hematoma on the surface of the right lobe of the liver, and the presence of haemoperitoneum.

Since the patient developed hemodynamic instability (hypotension and tachycardia), an urgent laparotomy procedure was performed, finding a rupture of the HH. Damage control and packaging of the patient was successfully performed.

Surgery was followed by a prompt reduction in the abdominal pain and a progressive improvement in laboratory tests. The patient was ordinary discharged after 10 days. After 1 month from surgery, he was completely asymptomatic.

3.3. Systematic review

After literature search and review of titles and abstracts, 41 articles describing 46 cases met our pre-defined inclusion criteria [6–47]. Overall, 48 cases (including also our two cases) had been included in the analysis. Table 1 summarizes findings from all studies reporting the occurrence of post-ERCP hepatic hematoma.

Among 48 patients, 63% were females and the mean age was 58.2 ± 20.6 The most frequent indications for ERCP were choledocolithiasis (64.6%), cholangitis (6.2%), cholangiocarcinoma (4.1%), ampullary adenoma (4.1%) and pancreatic cancer (4.1%), while the remaining cases (17.1%) comprised Wirsung stones, acute pancreatitis, stent exchange, bile duct stricture, gallbladder cancer, bile leak and bile duct adenoma. All patients but 8 (82.9%) underwent sphincterotomy, with a biliary stent placed in 22.9% of cases.

The mean symptom onset time was 46.8 h after ERCP (range 1–360), and the most common symptoms were abdominal pain (91.7%), anaemia – defined as the onset of hemoglobin reduction lower than 12 mg/dL in men and 11.5 mg/dL in women after ERCP – (43.8%), hypotension (29.2%) and fever (20.8%).

All cases were diagnosed by performing an abdominal CT, although abdominal ultrasonography was previously performed in 4 cases.

HH was found mostly in the right hepatic lobe (95.1%) and the mean sizes were 116.2 × 92.9 mm, as measured in the anteroposterior and laterolateral diameters (range for anteroposterior diameter 40–190; range for laterolater diameter 20–190).

After diagnosis, a conservative management was adopted in 38.3% of cases, while percutaneous drainage, embolization and surgery were needed in 31.9%, 14.9%, and 25% of cases, respectively (a combined approach was used in 10.4% of cases).

Intravenous antibiotics were administrated in all but two cases.

Mortality rate was high (about 9%). Death was due to hypovolemic shock in 75% of cases [21,28,35] and sepsis in the remaining ones [30].

When we evaluated the risk factors for death in patients with hepatic hematoma, we found that abdominal pain (OR 0.1; 95%CI 0.02–0.53; $p = 0.03$) and antibiotics administration (OR 0.06; 95%CI 0.006–0.6; $p < 0.001$) were inversely associated with the risk of death, while anaemia (OR 6.9; 95%CI 1.2–67.8; $p = 0.02$) and need for surgery (OR 10.5; 95%CI 1.2–90.2; $p < 0.01$) were the only independent factors for unfavorable outcome (death). Table 2 summarizes these findings.

4. Discussion

The development of hepatic hematoma is a rare but severe adverse event following ERCP. Since the first case has been reported in the literature in 2000 [6], other cases with different characteristics have been described. Presently, no clinical study has evaluated clinical features, diagnostic approach, management and prognosis of such a complication.

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Table 1
Hepatic haematoma post-endoscopic retrograde cholangiopancreatography: literature review.

Study	Gender	Age	Indication for ERCP	Procedure	Type of guide-wire	Symptoms onset	Anticoagulant drugs	First symptom	Diagnosis	Site	Dimension (mm)	Treatment	Antibiotics	Death
Ortega Deballon et al. [6]	M	81	Choledocolithiasis	Sphincterotomy	–	–	No	Abdominal pain	CT scan	–	–	Percutaneous drainage	Yes	No
Horn and Peña [7]	F	88	Pancreatic mass	Sphincterotomy + biliary stent	0.035-in.	48 h	No	Abdominal pain + anaemia	CT scan	Right lobe	–	Conservative	Yes	No
Chi and Waxman [8]	F	43	Pancreatic cancer	Sphincterotomy + biliary stent	0.035 in. straight tip	5 h	No	Abdominal pain	CT scan	Right lobe	80 × 150	Embolization	Yes	No
Ertuğrul et al. [9]	M	41	Cholangiocarcinoma	Biliary stent	–	48 h	No	Abdominal pain + fever	CT scan	Right lobe	78 × 41	Conservative	Yes	No
Priego et al. [10]	F	30	Choledocolithiasis	Sphincterotomy	–	–	No	Abdominal pain + hypotension	CT scan	Right lobe	47 × 110	Surgery	Yes	No
Petit-Laurent et al. [11]	M	98	Choledocolithiasis	Sphincterotomy	–	48 h	Yes	Abdominal pain + fever	US + CT scan	–	–	Percutaneous drainage	–	No
Bhati et al. [12]	F	51	Choledocolithiasis	Sphincterotomy	–	48 h	No	Abdominal pain + hypotension	CT scan	Right lobe	100 × 130	Percutaneous drainage	–	No
Del-Rosi et al. [13]	F	28	Choledocolithiasis	Sphincterotomy + biliary stent	–	48 h	No	Abdominal pain + hypotension	–	–	120 × 60	Conservative	Yes	No
Papachristou and Baron [14]	M	69	Cholangiocarcinoma	Sphincterotomy + biliary stent	0.035 in. soft-tipped hydrophilic	48 h	No	Abdominal pain + anaemia	CT scan	Right lobe	169 × 150	Conservative	–	–
McArthur and Mills [15]	M	71	Choledocolithiasis	Sphincterotomy + biliary stent	0.035 in., 450 cm length straight tip	12 h	No	Abdominal pain	CT scan	Right lobe	50 × 30	Conservative	Yes	No
De La Serna-Higuera et al. [16]	F	71	Choledocolithiasis	Sphincterotomy	0.035 in.	48 h	No	Abdominal pain	US + CT scan	Right lobe	140 × 80	Conservative	Yes	No
Cárdenas et al. [17]	F	54	Bile leak after liver transplantation	Sphincterotomy + biliary stent	–	24 h	No	Abdominal pain + anaemia	CT scan	–	90 × 20	Conservative	Yes	No
De Mayo et al. [18]	M	96	Ampullary adenoma	Sphincterotomy	–	4 h	No	Abdominal pain	–	–	170 × 130	Conservative	Yes	No
Yrribery-Ureña et al. [19]	F	46	Choledocolithiasis	Sphincterotomy	–	48 h	No	Abdominal pain + anaemia	–	–	–	Surgery	–	–
Nari et al. [20]	F	15	Acute biliary pancreatitis	–	–	–	No	Abdominal pain + fever	CT scan	Right lobe	135 × 49	Conservative	Yes	No
Saa et al. [21]	–	92	Choledocolithiasis	Sphincterotomy	–	24 h	No	Anaemia	–	–	–	Percutaneous drainage + surgery	No	Yes
Revuelto Rey et al. [22]	M	41	Choledocolithiasis	Sphincterotomy	–	6 h	No	Abdominal pain + anaemia	CT scan	Right lobe	130 × 110	Conservative	Yes	No
Baudet et al. [23]	F	69	Choledocolithiasis	Sphincterotomy	0.035 in. soft-tipped hydrophilic	4 h	No	Abdominal pain + anaemia + fever	US + CT scan	Right lobe	160 × 65	Embolization + surgery	Yes	No
Pérez-Legaz et al. [24]	F	72	Choledocolithiasis	Sphincterotomy	–	2 h	No	Abdominal pain + anaemia	CT scan	Right lobe	80 × 80	Surgery	–	No
Del Pozo et al. [25]	F	76	Choledocolithiasis	Sphincterotomy	0.035 in.	120 h	Yes	Abdominal pain	CT scan	Right lobe	–	Conservative	Yes	No
Manikam et al. [26]	F	42	Choledocolithiasis	Sphincterotomy + biliary stent	–	40 h	No	Abdominal pain + fever	CT scan	Right lobe	–	Percutaneous drainage	Yes	No
Orellana et al. [27]	M	96	Ampullary adenoma	Biliary stent	–	4 h	No	Abdominal pain	CT scan	Right lobe	170 × 130	Conservative	Yes	No
	M	49	Biliary stent occlusion	Stent exchange	–	2 h	No	Abdominal pain + hypotension	CT scan	Right lobe	–	Embolization	–	No
	F	55	Gallbladder cancer	Stent exchange	–	–	No	Abdominal pain	CT scan	Right lobe	–	Conservative	–	No
Bartolo-Rangel et al. [28]	F	62	Cholangitis	Sphincterotomy	–	–	No	Anaemia + hypotension	CT scan	Right lobe	–	Surgery	–	Yes
Patil et al. [29]	M	50	Cholangitis	Sphincterotomy	–	48 h	No	Abdominal pain	CT scan	Right lobe	50 × 30	Percutaneous drainage	Yes	No
Oliveira Ferreira et al. [30]	M	84	Choledocolithiasis	Sphincterotomy	0.035 in. straight tip	240 h	Yes	Abdominal pain + anaemia	CT scan	Right lobe	90 × 100	Percutaneous drainage	Yes	Yes
Fei and Li [31]	M	56	Choledocolithiasis	Sphincterotomy	0.035 in.	2 h	No	Fever	CT scan	Right lobe	130 × 60	Percutaneous drainage	Yes	No
Klìmovà et al. [32]	M	54	Wirsung stone	Sphincterotomy	0.035 in.	6 h	No	Abdominal pain + anaemia + hypotension	CT scan	Right lobe	190 × 178	Embolization + Percutaneous drainage + surgery	Yes	No

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Table 1 (*Continued*)

Study	Gender	Age	Indication for ERCP	Procedure	Type of guide-wire	Symptoms onset	Anticoagulant drugs	First symptom	Diagnosis	Site	Dimension (mm)	Treatment	Antibiotics	Death
Carrica et al. [33]	F	37	Choledocolithiasis	Sphincterotomy	–	72 h	No	Abdominal pain + anaemia + fever	CT scan	Right lobe	124 × 93	Percutaneous drainage	Yes	No
Yoshii et al. [34]	F	86	Choledocolithiasis	Lithotripsy		30 h	No	Abdominal pain	CT scan	Right lobe	–	Conservative	Yes	No
González-López et al. [35]	F	30	Bile duct stricture	Sphincterotomy + balloon dilation	–	24 h	No	Abdominal pain + anaemia + hypotension	CT scan	Right lobe	–	Surgery	–	Yes
Zizzo et al. [36]	F	52	Choledocolithiasis	Sphincterotomy	0.035 in., 450 cm length straight-tip	24 h	No	Abdominal pain + anaemia + hypotension	CT scan + angiography	Right lobe	150 × 110	Embolization	Yes	No
Servide et al. [37]	M	83	Cholangitis	–	–	360 h	No	Abdominal pain	CT scan	Right lobe	–	Conservative	–	No
Zappa et al. [38]	F	58	Choledocolithiasis	Sphincterotomy	0.035 in.	12 h	No	Abdominal pain + anaemia + hypotension	CT scan	Right lobe	140 × 190	Embolization	–	No
Kilic et al. [39]	F	69	Choledocolithiasis	Sphincterotomy	–	12 h	No	Abdominal pain + hypotension	CT scan	Right lobe	40 × 20	Percutaneous drainage + surgery	Yes	No
Curvale et al. [40]	M	78	Bile duct adenoma	Sphincterotomy + polipectomy	–	1 h	Yes	Abdominal pain + anaemia + hypotension	CT scan	Right lobe	–	Surgery	–	No
Solmaz et al. [41]	M	55	Choledocolithiasis	Sphincterotomy	0.035 in., 450 cm length straight tip	6 h	No	Abdominal pain	CT scan	Right lobe	140 × 67	Conservative	Yes	No
Fiorini et al. [42]	F	47	Choledocolithiasis	Sphincterotomy	–	8 h	No	Abdominal pain + fever	CT scan	Right lobe	45 × 45	Percutaneous drainage	Yes	No
Areopaja Escobar and Pancho Zela [43]	–	47	Choledocolithiasis	Sphincterotomy + biliary stent	–	240 h	No	Abdominal pain	CT scan	Right lobe	–	Percutaneous drainage	Yes	No
Tamez et al. [44]	F	25	Choledocolithiasis	Sphincterotomy	–	12 h	No	Abdominal pain + anaemia + fever	CT scan	Right lobe	152 × 104	Surgery	–	No
Del Moral Martínez et al. [45]	F	37	Choledocolithiasis	Sphincterotomy	–	6 h	No	Abdominal pain + hypotension	CT scan	Left lobe	120 × 107	Conservative	Yes	No
	F	60	Choledocolithiasis	Sphincterotomy	–	168 h	No	Abdominal pain + anaemia + fever	US + CT scan	Left lobe	100 × 60	Percutaneous drainage	Yes	No
Soler Humanes et al. [46]	F	43	Choledocolithiasis	Sphincterotomy	–	–	No	Abdominal pain + anaemia	CT scan + angiography	Right lobe	160 × 160	Percutaneous drainage	–	No
de la Maza Ortiz et al. [47]	F	35	Choledocolithiasis	Sphincterotomy	0.035 in. hydrophilic	12 h	No	Anaemia + hypotension	CT scan	Right lobe	140 × 45	Conservative	Yes	No
	F	54	Choledocolithiasis	Sphincterotomy	0.035 in. hydrophilic	2 h	No	Abdominal pain + anaemia + hypotension	CT scan	Right lobe	120 × 190	Embolization	Yes	No
Present Case 1	F	75	Choledocolithiasis	Sphincterotomy	0.035 in., 260 cm length straight tip	48 h	No	Abdominal pain	CT scan	Right and left lobes	72 × 91 12 × 11	Embolization	Yes	No
Present Case 2	M	45	Biliary stenting after surgical stricture	Sphincterotomy + biliary stent	0.035 in., 260 cm length straight tip	2 h	No	Abdominal pain	CT scan	Right lobe	110 × 80	Surgery	No	No

M, male; F, female; CT, computed tomography; US, ultrasonography; –, data not reported.

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Table 2
Factors associated with unfavourable outcome of hepatic hematoma.

Variables	OR	95%CI	p
Male gender	0.8	0.08–8.5	0.8
Choledocolithiasis	0.5	0.08–3.5	0.6
Late onset (>120 h)	1.1	0.8–1.5	0.4
Abdominal pain	0.1	0.02–0.5	**0.03**
Hypotension	2.2	0.3–14.1	0.5
Anaemia	6.9	1.2–67.8	**0.02**
Fever	1.1	1.0–1.3	0.5
Left lobe	0.9	0.8–1.0	0.6
Anticoagulant treatment	1.1	0.7–1.6	0.5
Conservative management	1.1	1.0–1.3	0.2
Percutaneous drainage	1.9	0.3–12.3	0.6
Embolization	1.1	1.0–1.2	0.3
Surgery	10.5	1.2–90.2	**<0.01**
Antibiotics	0.06	0.006–0.6	**<0.001**

OR, odds ratio; CI, confidence interval. Statistically significant results are expressed in bold.

The real incidence of HH is not known. Orellana et al. [27] found 3 cases of subcapsular HH after ERCP out of 796 ERCP carried out in a 5-year period (incidence rate 0.37%). In our 5-year experience, we found 2 cases of HH out of 1297 ERCPs (0.15%). The real incidence is, however, likely to be underestimated, since asymptomatic clinical course is possible [8]. On the other hand, since the data mainly come from case reports, it could not be excluded that the severity of such a complication has been overestimated.

The pathogenesis of post-ERCP HH is not fully understood and presently it can be only hypothesized according to the few available data.

The most ascribed hypothesis suggests that a too deep insertion of the guide wire would perforate the intrahepatic bile ducts, thus harming the hepatic parenchyma. As a result, small-caliber intrahepatic blood vessels would break and air would enter the hematoma and the bile duct, which would explain the presence of subphrenic air reported in some cases [36,45]. In accordance with this hypothesis, it would be conceivable that using stiffer, thicker and straight tip guide wire could be associated to an increased risk of complication. The available data do not allow us to draw such conclusions (Table 1).

The second hypothesis suggests that the hepatic damage would be secondary to the traction energy applied with the balloon on the bile duct when trying to extract a retained calculus. This force would break bile ductules and vessels, inducing the hepatic bleeding [23]. The two hypotheses do not exclude each other, of course; however, the presence of two HHs in two different hepatic lobes would suggest the second hypothesis as more likely, at least in our first case.

Endoscopist's experience has been advocated as factor correlated with the rate of adverse events during ERCP [1–4]. Although in both our cases ERCPs were performed by experienced endoscopists (who have performed more than one thousand ERCPs) with a dedicated nurse staff, this information is not retrievable from other studies. Nevertheless, it would be possible to speculate that repeated attempts in passing a stenosis with a wire or advancing different catheters within the bile duct system would results in a significant risk of damaging the bile ductules when performed by unexperienced endoscopists or nurses.

Our systematic review revealed that abdominal pain was present in almost all cases (91.7%); moreover, anaemia (43.8%), hypotension (29.2%) and fever (20.8%) were common, and the symptoms onset was mainly after 2 days from endoscopic procedure (46.8 h). However, it is interesting to note that 5 cases of late-onset (>120 h from ERCP) of symptoms have been described [25,30,37,43,45], thus concluding that HH is not only an early complication (within 72 h) of ERCP.

Laboratory exams could arise the suspicion of a post-ERCP complication, as in the cases we described, showing generally leukocytosis, increased cholestasis and, sometimes, reduced hemoglobin levels and hematocrit. However, to confirm the diagnosis, a radiological exam is needed. Ultrasonography, CT and Magnetic Resonance are all useful to characterize the hepatic damage, although CT scan was used to obtain a final diagnosis in all cases included in this review. Specifically, CT is able to accurately define sizes, site and parenchymal features of hematomas. Our review showed HH was found mostly in the right hepatic lobe (95.1%) and the mean sizes were 116 × 93 mm; rarely, HH developed in the left lobe. We have described the first case in literature of multiple HH involving both the hepatic lobes.

Treatment of HH should always be tailored according to the clinical picture and a multidisciplinary team is mandatory. We found that a conservative management was successfully adopted in 38.3% of cases. Conversely, percutaneous drainage, embolization and surgery were needed in 31.9%, 14.9%, and 25% of cases, respectively (a combined approach was used in 10.4% of cases).

On the basis of these results, it is possible to suggest a conservative management in all hemodynamically stable patients, reserving a more invasive approaches (i.e. percutaneous drainage or embolization) in case of instability, in presence of peritoneal irritation or when no improvement is achieved after conservative and antibiotics treatment. However, evidences supporting these conclusions are limited by the study design, the small number of reported cases and the lack of prospective comparative studies, and in general the choice of the treatment should depend also on the local expertise. In our first case availability of an experienced interventional radiology team drove our decision to treat the patient with embolization simply because of lack of clinical and laboratory improvement after few days of conservative treatment and despite the absence of any signs of hemodynamic instability or active bleeding. This choice was also influenced by the local expertise in interventional radiology.

In general, when a non-surgical strategy has been opted, the choice of treating patients with percutaneous drainage rather than embolization or vice versa should be obviously influenced by the local expertise, as in our case. In the present systematic review, we were not able to establish the best indication for percutaneous drainage or vascular embolization (i.e. lesion dimensions or medium of contrast flowing into the HH) because of heterogeneity and limited number of cases and, to date, this choice should depend on the availability of specialized physicians and their own experience.

The most dramatically result found in our review was the high rate of mortality for post-ERCP HH, resulting to be closed to 10%.

We found that anaemia (OR 6.9; $p = 0.02$) and need for surgery (OR 10.5; $p < 0.01$) were the only independent factors for unfavorable outcome (death) in patients with HH. On the other side clinical presentation with abdominal pain and antibiotic administration reduced the risk of death. It is likely that patients who develop anaemia or undergo surgery may have a more severe disease, which could be associated to an increased risk of death; surgery *per se* has an intrinsic risk of unfavorable outcome when performed in patients with hemodynamic instability; it is, however, important to recognize that patients with anaemia had the highest risk of death. This fact would focus on the importance of suspecting the presence of HH as early as possible to start immediately a supportive management. The better outcome of patients presenting with abdominal pain and managed with broad-spectrum intravenous antibiotics further supports this point. These results were in agreement with the fact that death was due to hypovolemic shock in 75% of cases and to sepsis in the remaining ones.

In conclusions, HH is a rare, but severe complication following ERCP, which endoscopists need to be aware, burdened by high rate

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of mortality, especially in patients presenting with anaemia and hemodynamic instability. Broad-spectrum intravenous antibiotics administration is the only treatment able to reduce the risk of death, independently from hemodynamic status of patient. Management should be multidisciplinary, involving gastroenterologist, radiologist and surgeon. Percutaneous drainage or radiologic-guided embolization could be successfully used while the need of surgery seems to be associated with unfavorable outcome.

Conflict of interest

None declared.

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