Successful endoscopic management of a persistent bronchobiliary fistula with Histoacryl®/Lipiodol® mixture

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ABSTRACT

INTRODUCTION A bronchobiliary fistula (BBF) following liver directed therapy (resection/ablation) is a rare complication in which an abnormal communication between the biliary tract and bronchial tree is formed. This case report describes the successful management of a persistent BBF following multiple liver wedge resections and microwave ablation in a patient with a metastatic neuroendocrine tumour of the terminal ileum.

CASE HISTORY A 69-year-old man presented with unexplained weight loss and was subsequently diagnosed with a neuroendocrine tumour of the terminal ileum and liver metastasis. Following elective right hemicolectomy and multiple bilobar liver wedge resections combined with liver microwave ablation, he developed an early bile leak. A month later, a right subphrenic collection was identified and four months following surgery, biloptysis was noted. Numerous attempts with endoscopic retrograde biliary drainage (ERBD) failed to achieve sufficient drainage. The patient was treated successfully with endoscopic injection of a mixture of Histoacryl® glue (B Braun, Sheffield, UK) and Lipiodol® (Guerbet, Solihull, UK). There was no evidence of the BBF one year following intervention.

CONCLUSIONS This novel approach for persistent BBF management using endoscopic Histoacryl® glue embolisation of the fistula tract should be considered either as an adjunct to ERBD or when biliary tract decompression by drainage and/or sphincterotomy fails, prior to proceeding with surgical interventions.

KEYWORDS

Liver – Bronchobiliary fistula – Histoacryl® – Biloptysis – Endoscopic retrograde drainage

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BBF is defined as an abnormal communication between the biliary system and bronchial tree,¹ and is notoriously difficult to manage. Literature regarding best management of these patients is sparse and guidelines are notably absent. Cases of BBF have been documented as emerging following hepatic malignancies, hepatic infections, trauma and also procedural, radiological or surgical interventions.² There is no consensus on the best approach for this complication, whether it be via biliary drainage, endoscopic^{3,4} or bronchoscopic^{5,6} application of glue, or surgical repair of the diaphragmatic defect and excision of the fistula.^{2,7} We report a case of BBF after microwave ablation and resection of neuroendocrine tumour liver metastases, treated endoscopically with a mixture of Histoacryl® (*n*-butyl-2-cyanoacrylate; B Braun, Sheffield, UK) and Lipiodol® (ethiodised oil; Guerbet, Solihull, UK).

Case history

A 69-year-old man presented at a peripheral hospital with unexplained weight loss in October 2014. Past medical history included Parkinson's disease and bilateral femoral deep vein thrombosis treated with long-term low molecular weight heparin. He had a complete workup including computed tomography (CT), which demonstrated a number of suspicious nodules in segments VI and VII of the liver as well as thickening of the ileocaecal valve. At colonoscopy, a polypoid lesion biopsy showed a well differentiated neuroendocrine tumour. The patient was referred to our hospital in January 2015 and octreotide functional imaging confirmed these lesions in the liver to be octreotide positive. A long acting somatostatin analogue was commenced.

In May 2015 the patient underwent an elective right hemicolectomy and multiple bilobar liver wedge resections combined with liver microwave ablation. Intravenous octreotide infusion (50µg/hour) was given perioperatively for 72 hours as per our protocol. Intraoperative ultrasonography was performed, which identified more than ten liver lesions. Some of the metastases had smaller satellite lesions close by. All the peripheral liver metastases were removed using CUSA® (Cavitron Ultrasonic Surgical Aspirator) Excel (Integra, Plainsboro, NJ, US; 23kHz) and argon. Three metastases located deep within segments V, VI and VII (measuring 1.38–2.00cm) were subjected to microwave ablation (Acculis® Microwave Tissue Ablation System; AngioDynamics, Latham, NY, US; 2.45GHz) (Fig 1). Ablation was performed using a 140W microwave generator with a 14cm long antenna for four minutes for each lesion. Owing to the proximity of a lesion in segment IVb to the gallbladder, a cholecystectomy was also performed.

Histological examination of the resected liver metastases indicated a disseminated liver disease with 24 tumour deposits (Table 1). The histological pattern of the lesions showed identical organoid growth pattern with nests of acinar differentiation formed by monotonous epithelial tumour

cells, with scant cytoplasm and rounded nuclei, giving a ‘salt and pepper’ appearance. Ki-67 immunostaining was very low (<1%) with no mitosis (grade 1). Immunohistochemistry was strongly positive for chromogranin A and synaptophysin.

After surgery, the patient developed an early bile leak. On the second postoperative day, endoscopic retrograde cholangiopancreatography (ERCP) revealed a leak from a branch of the right anterior hepatic duct (Fig 2), which was treated successfully with a large sphincterotomy and placement of a 7Fr plastic stent (13cm long) in the right hepatic duct. The abdominal drain was removed on the seventh postoperative day and the patient was discharged on day 9 in good general condition with a long acting somatostatin analogue (lanreotide 90mg).

A month following surgery, the patient was readmitted with right upper quadrant abdominal pain, and CT revealed a right subphrenic collection with ipsilateral pleural effusion and lobar atelectasis. The perihepatic collection was drained under ultrasonography guidance, revealing a thick red-brown aspirate. The patient was subsequently monitored by CT (Fig 3). An incidental finding of a hepatic artery pseudoaneurysm was also noted, which required selective embolisation of a branch of the right posterior hepatic artery.

Four months postoperatively and after a brief improvement clinically, the patient re-presented with a productive, bile stained cough and shortness of breath. Magnetic resonance imaging and CT confirmed a BBF. During a period of six months, the patient had three admissions with clinically active BBF. Our initial approach was to treat the BBF endoscopically with ERCP and stenting. Overall, there were four unsuccessful attempts of endoscopic retrograde biliary drainage (ERBD), employing a number of methods including larger diameter plastic stents (10Fr) and a covered self-

Figure 1 Magnetic resonance imaging of the liver showing a lesion in segment V measuring 13.8mm (arrow) that was treated with microwave ablation

Table 1 Histological results of wedge liver resections			
Resected liver segment	Number of deposits	Size	Grade
II	1	18mm	G1
III	4	3–6mm	G1
IVb	6	5–17mm	G1
V	4	4–13mm	G1
VI	8	0–14mm	G1
VII	1	15mm	G1

Figure 2 Endoscopic retrograde cholangiopancreatography showing contrast leakage from right-sided bile duct

expanding metal stent (8cm). Hepatobiliary iminodiacetic acid (HIDA) imaging excluded a disconnected bile duct (Fig 4).

Bilioptysis persisted for seven months following the initial surgery. Further ERCP was therefore attempted with the aim of using glue to seal the fistula site. This ERCP demonstrated a leak into the pleural cavity from a branch of the right hepatic duct (Fig 5). A soft wire was manipulated down to the peripheral right duct and a cannula advanced into the fistula tract. The fistula tract was injected with a 2ml mixture of

Histoacryl® glue and Lipiodol® (1:2 mix), and occluded cholangiography confirmed that the fistula site had been sealed. Prior to discharge, repeat HIDA imaging and ERCP (Fig 6) revealed no evidence of a bile leak and resolution of the fistula.

Four months after the glue procedure, the patient was readmitted with pneumonia in the right lower lobe (without bilioptysis) and treated conservatively with intravenous antibiotics. Repeated ERCP confirmed the absence of a bile leak (Fig 7). The blocked metal stent was removed, leaving a

Figure 3 Computed tomography showing moderate subcapsular hepatic collection with drain in dependent position (arrow) complicated by right subdiaphragmatic fluid collection. A comparison with previous imaging showed that this collection had reduced in size. The internal biliary stent and several bilobar metastases are also visible

Figure 4 Hepatobiliary iminodiacetic acid imaging showing a subphrenic collection communicating with the right lower lobe forming a fistula (arrow)

Figure 5 Endoscopic retrograde cholangiopancreatography showing fistula tract communicating with the pleural cavity originating from the right duct marked by two surgical clips (arrow)

Figure 6 Endoscopic retrograde cholangiopancreatography at two weeks following glue injection showing resolution of previous bile leak

Figure 7 Endoscopic retrograde cholangiopancreatography at four months following glue injection showing resolution of previous bile leak

patent sphincterotomy. At routine follow-up one year after surgery, the patient had no clinical or radiological evidence of a BBF and no measurable disease.

Discussion

Classically, hydatid disease was the leading cause of an acquired BBF. However, since the advent of extensive invasive procedures and surgical interventions for liver pathologies, a number of other causative factors have been documented.⁸ In the current case, the use of microwave ablation resulted in the injury of the right hepatic duct and a delayed BBF. A high index of suspicion and early diagnosis of bile leak are key factors for the prevention of BBF.⁹

Definitive management options for patients with a BBF include different interventional and surgical approaches. The main objective is to either repair the fistula tract or decompress the bile duct system. Before the development of invasive radiology, BBF treatment was surgical (including laparotomy with fistulectomy and primary repair of the bile duct or hepaticojejunostomy).^{2,10} A thoracic approach with fistulectomy and soft tissue reconstruction has also been described.^{10,11} Delay in the management of BBF may result

Table 2 Case reports documenting the use of glue for BBF

Case report	Age / sex	Primary disease	Treatment of primary disease	Therapeutic approach	Prior interventions	Intervention	Follow-up
Herold, 1995 ¹⁵	F	Liver abscess	Drainage	Endoscopic	–	Repeated fibrin and NBCA sealing	–
Memis, 2000 ¹⁶	40 M	Hydatid cyst	Right hepatectomy	Percutaneous	Internal-external biliary drainage, balloon dilation	2ml NBCA / ethiodised oil (1:1 ratio), covered self-expanding nitinol stent	Asymptomatic, 9 mths
Goldman, 2007 ⁵	49 F	Colorectal liver metastasis	Hepatic wedge resection	Bronchoscopic	ERBD	Several microcoils and 3ml NBCA / ethiodised oil (60: 40 ratio)	Asymptomatic, 3 mths, cancer related death
Kim, 2008 ⁶	56 F	Hepatocellular carcinoma	Right hepatectomy, TACE, RFA	Bronchoscopic	ERBD, PTBD	Mixture (1ml NBCA / 2ml ethiodised oil)	Asymptomatic, 3 mths, death due to hepatic failure
Mukkada, 2014 ⁴	29 M	Abdominal trauma	Laparotomy	Endoscopic	ERBD, non-anatomical left lateral segmentectomy, disconnection of BBF	3 microcoils and 0.5ml NBCA, repeated after 4 days with 2 microcoils and 0.5ml	Asymptomatic, 9 mths
Jiang, 2014 ¹⁷	47 F	Cholangiocarcinoma	RFA	Percutaneous	–	Pleurocentesis: 1.8ml NBCA via chest drainage tube	Asymptomatic, 10 mths

BBF = bronchobiliary fistula; ERBD = endoscopic retrograde biliary drainage; HCC = hepatocellular carcinoma; NBCA = *n*-butyl-2-cyanoacrylate; PTBD = percutaneous transhepatic biliary drainage; RFA = radiofrequency ablation; TACE = transarterial chemoembolisation

in further damage to the lung and the need for a pulmonary lobectomy.

Nowadays, less invasive techniques are preferred. The initial approach for BBF is mainly interventional, including ERBD⁵ or percutaneous transhepatic biliary drainage.¹⁰ Decreasing the pressure gradient between the common bile duct and the duodenum leading to preferential drainage of bile through the stent produces consistently good outcomes. Drainage via a lower pressure system allows a reduction in fistula output and subsequent healing. In some patients, this can be a lengthy process and the fistulous tract may never heal. A review study of 68 BBF cases found ERBD to be the preferred method (used in 24 patients), with a recovery rate of 95.8% compared with 76.9% for traditional surgery.¹⁰ There was no information regarding recurrence in these two groups.

During the last decade, successful use of Histoacryl® glue under bronchoscopic guidance^{5,6} has also been reported. The active ingredient in Histoacryl® glue is monomeric *n*-butyl-2-cyanoacrylate, and its use as a tissue adhesive has been widely accepted for oesophageal varices,¹² wound closure¹³ and anal fistulas.¹⁴ To our knowledge, only two case reports have documented the use of glue via an endoscopic approach for the management of a persistent BBF.^{4,15} Simultaneous biliary drainage and injection of glue has been shown to result in rapid resolution of biliptysis, both in the literature and in our patient. Our patient sustained immediate symptomatic relief whereas repeated ERBD and sphincterotomy failed to produce comparable results. Other case reports documenting the use of glue have noted similarly favourable outcomes (Table 2).^{4-6,15-17}

Conclusions

This novel approach for the management of persistent BBF using endoscopic Histoacryl® glue embolisation of the fistula tract should be considered either as an adjunct to ERBD or when biliary tract decompression by drainage and/or sphincterotomy fails, prior to proceeding with surgical interventions.

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