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Case report

# Cutaneous metastases from cholangiocarcinoma following percutaneous transhepatic biliary drainage: Case report and literature review

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ABSTRACT

Percutaneous transhepatic biliary drainage (PTBD) is commonly used in the management of cholangiocarcioma. Major and minor complications of PTBD such as cholangitis, haemorrhage and catheter dislocation are well documented. A lesser reported complication are cutaneous metastases following PTBD for cholangiocarcinoma.

We report a case of a 79 year old man who presented with right upper quadrant pain, jaundice and weight loss, with dilated intra-hepatic bile ducts on imaging. The cytology results from a sample taken during endoscopic retrograde cholangiopancreatography were highly suspicious of cholangiocarcioma. A PTBD was subsequently performed and bilateral metal biliary stents were placed without external drainage. Five months after the PTBD he was found to have a hard nodule under the PTBD puncture site. The nodule was excised and the histology confirmed a cholangiocarcinoma metastasis.

A review of the literature identified twelve cases of cutaneous metastases from cholangiocarcinoma, following PTBD. In addition, tumour seeding along the catheter tract following PTBD, with metastatic deposits on the abdominal wall, peritoneoum, chest wall, pleural space, and liver parenchyma have also been reported.

Health care professionals should be aware of this rare complication and offer appropriate management options to patients.



## 1. Introduction

Cholangiocarcinomas are rare and account for 3% of all gastrointestinal tumours.[1] They are malignant neoplasms which arise from the biliary ductular epithelium. Cholangiocarcinomas typically present late, with signs of obstructive jaundice. In such setting, liver failure and recurrent sepsis from cholangitis partly account for the high morbidity and mortality rate associated with this malignancy. Complete surgical resection offers the only chance for cure. However, due to the late presentation of the disease, the majority of patients have unresectable disease at the time of presentation.[1] Thus, palliative care is the mainstay of treatment for many patients.

Percutaneous transhepatic biliary drainage (PTBD) has become established practice in the management of cholangiocarcinomas. Major complications of percutaneous transhepatic cholangiography (PTC) and PTBD have been reported to occur in fewer than 4%[2] and 7–10%[3] of patients respectively. Major complications include cholangitis, haemorrhage, bile leakage and peritonitis.[3–5] Minor complications, such as catheter dislocation and blockage, local infections and granulomas at the catheter entry site have been reported to occur in 20% of cases.[3]

Cutaneous metastases from seeding along the catheter tract following PTBD for cholangiocarcinoma have been reported sporadically in the literature[4,6–12] and the incidence has been reported to range between 0.6% and 6%.[10]

This case report describes a rare case of cutaneous metastasis at the PTBD site in a patient with cholangiocarcinoma. In addition, we conducted a literature review of all documented cases of cutaneous metastases secondary to cholangiocarcinoma following PTBD.

## 2. Case report

A 79 year old man presented to his General Practitioner (GP) with a 2 week history of intermittent right upper quadrant pain, jaundice, pruritus and weight loss. He was found to have deranged liver function tests with a bilirubin of 184 μmol/l, alkaline phosphatase of 646 U/L, alanine transferase of 223 U/L and a CA 19.9 of 83 U/ml. The patient was referred to the fast track jaundice service and underwent a liver ultrasound scan which showed dilated intra-hepatic bile ducts.

A triple phase abdominal computer tomography (CT) scan demonstrated moderate to severe intrahepatic duct dilatation and

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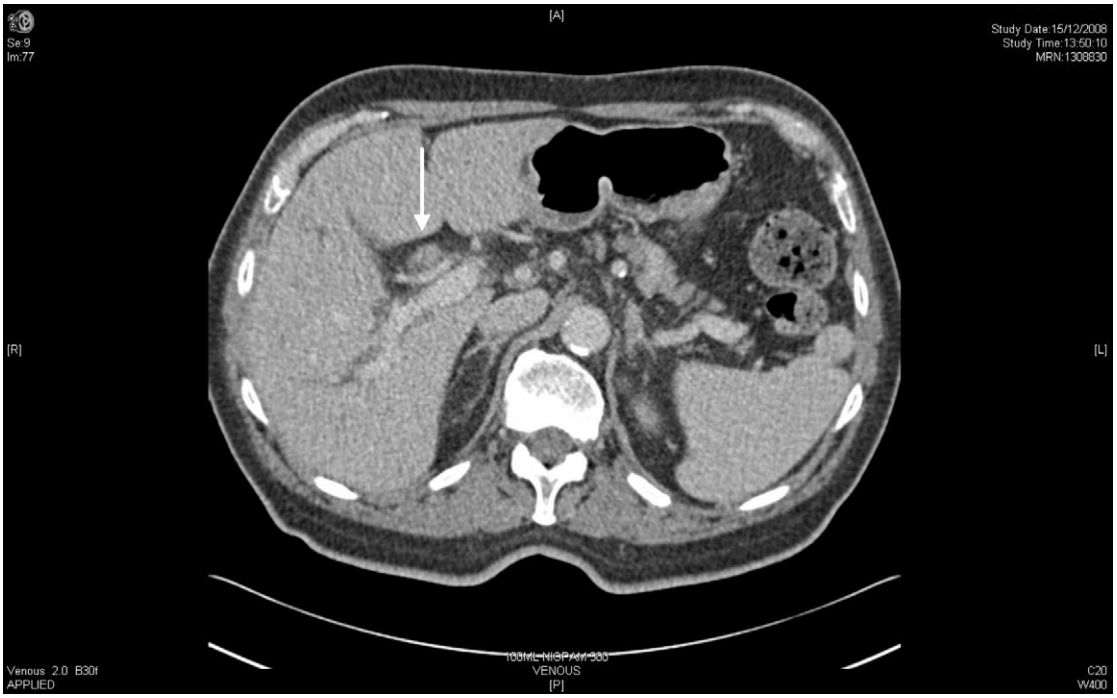


**Fig. 1.** Abdominal computed tomography showing intrahepatic duct dilatation to the hilum and an area of abnormal soft tissue seen anterior to the portal vein and hepatic artery.

an area of abnormal soft tissue (Fig. 1). The appearances were suggestive of a hilar cholangiocarcinoma, with no evidence of metastatic disease.

Two days later, the patient was admitted with worsening symptoms and an endoscopic retrograde cholangiopancreatography (ERCP) was performed. Appearances were suggestive of Bismuth IV hilar cholangiocarcinoma. The left intra-hepatic ducts were grossly dilated and an 11 cm plastic stent was placed with good effect. The right system was completely occluded and it was not possible to stent it. Cytology brushings taken at ERCP demonstrated epithelial groups with nuclear enlargement, flat nuclei, loss of polarity and hyperchromatism. The features were highly suspicious of adenocarcinoma of biliary epithelium.

The patient was discussed at the regional specialist hepatopancreaticobiliary multidisciplinary meeting. As standard, the surgical management option would have entailed a right portal vein embolisation to allow compensatory hypertrophy of the relatively small left lobe followed by an extended right hepatectomy. In view of the patients' numerous and very significant co-morbidities, including previous cerebrovascular event, ischaemic heart disease, hypertension, hypercholesterolaemia and aortic sclerosis palliative management was recommended.

The patient underwent a further ERCP to remove the left sided plastic stent. A PTBD was subsequently performed (Fig. 2) and bilateral parallel metal biliary stents were placed successfully as

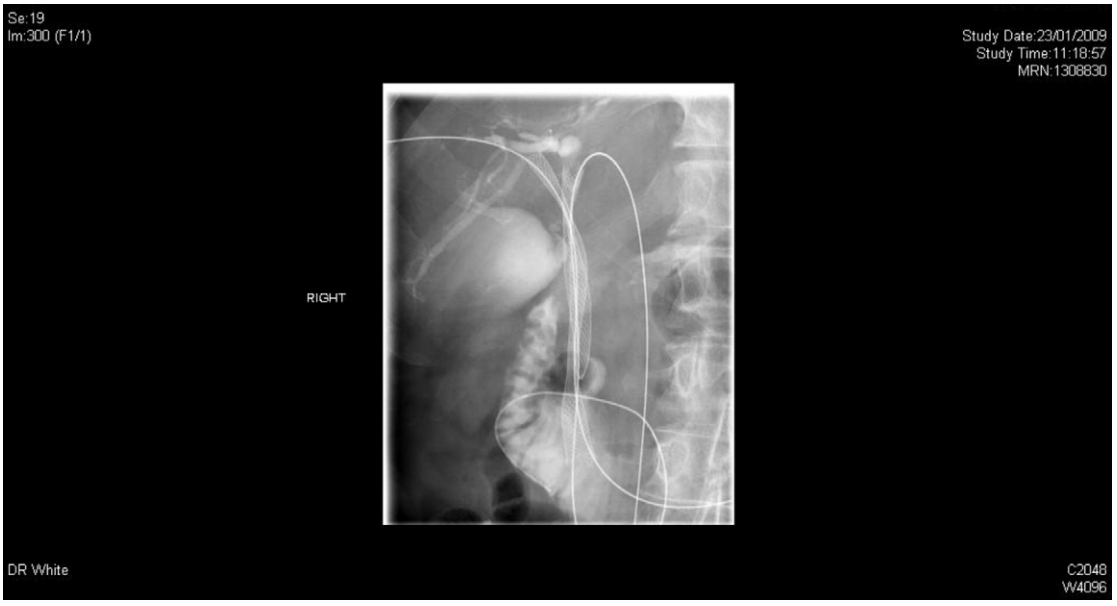


**Fig. 2.** A percutaneous catheter cholangiogram demonstrating bilateral biliary stents in situ.

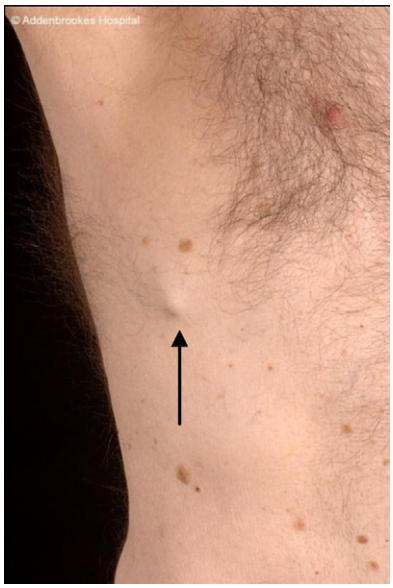


**Fig. 3.** Palpable nodule at the site of previous PTBD.

a primary procedure. No external drain was left in situ and there were no immediate complications.

Five months after the PTBD, the patient developed a prominent hard, non-tender, mobile nodule, measuring approximately 1.5 cm in diameter adjacent to a smaller mass on his lower right chest wall, immediately under the puncture site from his previous PTBD (Fig. 3).

It caused the patient significant discomfort when lying on his right side. An ultrasound examination demonstrated two separate heterogenous subcutaneous lesions on the right chest wall, one lesion measured 0.8 cm in diameter and the other was 2 cm × 5 cm.

The lesions were removed under local anaesthetic, aiming to improve pain control. The microscopic findings of the histology showed moderately differentiated adenocarcinoma with luminal necroinflammatory debris and an associated dense fibrous sclerotic stroma, suggesting it was a subcutaneous deposit of metastatic adenocarcinoma. Immunohistochemistry showed the tumour to be strongly CK7 positive, with patchy co-expression of CK20. TTF-1, CA125 and PSA were all negative. This immunoprofile, in the context of the tumour morphology, suggested the primary was a cholangiocarcinoma. The patient died in his own home 3 months later.

## 3. Discussion

During a five year period in our institution, fifty-nine patients were diagnosed with cholangiocarcinoma. Twenty-nine (49%) of these patients underwent PTC or PTBD and one (3.4%) of twenty-nine patients developed cutaneous metastases following the procedure.

Twelve cases of cutaneous metastases from cholangiocarcinoma, following PTBD, were identified in the literature[6,11–17] (Table 1). The average age of the patients was 68.1 (range 59–79). Six of these patients were male (50%), three patients were female (25%) and three were not specified (25%).

The mean time elapsed from PTBD and detection of cutaneous metastasis was 9 months (range = 3–20 months). The mean length of survival after the detection of cutaneous metastases was 9 months (range = 10 weeks to 20 months). Six patients died as a consequence of their cholangiocarcinoma (one of these six patients had surgical excision of their cutaneous metastases). The outcome after the detection of metastases was not documented in three cases. Three patients were well on follow-up at 8, 12 and 18 months and they had all underwent surgical resection of the cutaneous metastasis.

The incidence of cholangiocarcinoma remains low, as such clinical decisions are often based on retrospective studies. PTC and PTBD has been used in the management of malignant obstructive jaundice for precise delineation of intrahepatic ductal anatomy, as palliative treatment in unresectable patients and as a way in which to reduce serum bilirubin preoperatively in resectable patients. However, there has been much debate about the benefits of preoperative PTBD. A number of studies have evaluated the morbidity and mortality associated with pre-operative PTBD. Several nonrandomized studies favoured the use of pre-operative PTBD for patients with pre-operative hyperbilirubinaemia.[13,14] However, three prospective, randomized studies analysing pre-operative PTBD demonstrated no advantage for preoperative drainage.[15–17] In fact, McPherson et al. suggested higher mortality in the PTBD group than the non-PTBD group. Currently, PTC and PTBD are commonly used as palliative treatment in unresectable patients.

PTBD is associated with both major and minor complications. A lesser documented complication is metastatic tumour seeding along the catheter tract following PTBD, which has been reported sporadically in the literature. In 1980, Oleaga reported the first case of extension of a cholangiocarcinoma into the drainage catheter site following PTBD. A retrospective analysis of 67 patients who underwent PTBD for extrahepatic cholangiocarcinoma found three

**Table 1**
Patients with cholangiocarcinoma who developed cutaneous metastases following percutaneous transhepatic biliary drainage.

| Author | Sex | Age | Histology of primary | Histology of metastases | Detection of metastases after PTBD | Time catheter was in place | Management of metastases | Outcome after detection of metastases |
|---|---|---|---|---|---|---|---|---|
| Oleaga | M | 60 | No biopsy | Adeno | 16 m | 3 m | RTx & ICNB | ND |
| Shorvon | M | 73 | Adeno | Adeno | 3 m | 7 d | ND | DOD: (5 m) |
| Demas | ND | ND | Adeno | ND | ND | ND | ND | ND |
| Tersigni | M | 66 | G1 adeno | ND | 13 m | 16 d | RTx & CTx | DOD: (4 m) |
| Tersigni | F | 79 | ND | ND | 4 m | 4 d | ND | ND |
| Loew | M | 67 | G2 adeno | Adeno | 7 m | 2 m | ND | DOD: (2.5 m) |
| Sakata | F | 63 | G1 adeno | ND | 14 m | ND | RTx | DOD: (20 m) |
| Sakata | M | 70 | G2 adeno | ND | 20 m | ND | ECT | DOD: (9 m) |
| Sakata | M | 76 | G3 adeno | ND | 7 m | ND | BSM | DOD: (3 m) |
| Balzani | F | 59 | Cholangio | Adeno | 3 m | ND | ECT | NED: (12 m) |
| Mizuno | ND | ND | Cholangio | Adeno | 'several m' | ND | AWR | NED: (18 m) |
| Mizuno | ND | ND | Cholangio | Adeno | 'several m' | ND | AWR | NED: (8 m) |

Adeno = adenocarcinoma, m = months, RTx = radiotherapy, ICNB = intercostal nerve block, ND = not documented, d = days, DOD = died of disease, G1 = well differentiated, CTx = chemotherapy, G2 = moderately differentiated, ECT = excision of catheter tract, G3 = poorly differentiated, BSM = best supportive management, cholangio = cholangiocarcinoma, NED = no evidence of disease, AWR = abdominal wall resection & reconstruction.

patients with catheter tract implantation metastases (Table 1), which presented as subcutaneous nodules.[10]

In addition, there have been reports of metastatic seeding at the abdominal wall and peritoneum, chest wall and pleural space and liver parenchyma following PTBD.[5,18,19] Sakamoto conducted a prospective study over a 22 year period, in which 7 of 206 (3.4%) patients who underwent PTBD developed tumour seeding in the PTBD sinus tract as a late complication. These findings would suggest that the incidence of metastatic tumour seeding along the biliary catheter tract is not as low as initially suspected. However, the development of cutaneous metastases following PTBD appears to be rarer.

The precise mechanism in which these implantation metastases occur remains uncertain. It has been suggested that catheters which are left in situ longer and catheters which are manipulated and exchanged more frequently increase the risk of metastatic seeding.[20] Tanaka reported that patients who had bile positive for tumour cells preoperatively were at higher risk of developing peritoneal metastases and a study by Mizuno showed that approximately 30–47% of patients with malignant tumours had tumour cells within the bile. It therefore seems plausible that the malignant cells in bile may adhere to the biliary catheters during PTBD, depositing tumour cells on exiting the skin, and hence promoting the development of cutaneous metastases. The theory of dissemination of malignant cells during guidewire or catheter exchange may have accounted for the development of cutaneous metastases in our patient in whom primary stenting was performed with no external drains in place.

The optimum management for cutaneous metastases from cholangiocarcinoma, following PTBD, remains uncertain. Several authors have suggested aggressive surgical resection of the metastatic deposits to improve morbidity and mortality[10,18] particularly in patients with 'curative disease'. As implantation metastases are a form of local recurrence rather than systemic dissemination[12] achieving negative margins could potentially lead to long-term survival. Mizuno reported two cases in which survival at 8 and 18 months was achieved following surgical resection of the metastatic tumour.

In conclusion, health care professionals should be aware of this form of complication in order to offer appropriate support and management options.

## Conflicts of interest statement

None.

## Funding

None.

## Ethical approval

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request".

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