Primary malignant melanoma of the common bile duct: An unexpected finding at pancreaticoduodenectomy: A case report

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Abstract. Bile duct tumours are most commonly primary cholangiocarcinomas, and upfront surgical resection is often undertaken with curative intent, as preoperative histological confirmation is not routinely required. Melanoma, an aggressive malignancy of neural crest origin, can metastasize widely, but involvement of the biliary tract is exceedingly rare. Even rarer is primary melanoma of the bile duct. The present report describes a 44-year-old man presenting with obstructive jaundice and a mass in the common bile duct (CBD) presumed to represent cholangiocarcinoma. The patient underwent pancreaticoduodenectomy, but histopathology unexpectedly revealed malignant melanoma. Comprehensive staging and dermatological assessment excluded a cutaneous, mucosal or ocular primary, supporting the diagnosis of primary CBD melanoma. To the best of our knowledge, this represents the 14th reported case. This case highlights that melanoma, although rare, should be considered in the differential diagnosis of biliary obstruction, especially in younger patients, as it mandates a distinct postoperative oncological management pathway.

Introduction

Malignant melanoma arises from melanocytes derived from multipotent neural crest cells (1). These cells are located in the skin, mucosal membranes, eyes, and neural crest migration sites such as the gastrointestinal tract and brain (1). The metastatic potential of melanoma is wide, with abdominal involvement reported in ~60% of cases (2,3). The biliary tract is rarely involved, with metastasis reported in 15% of gallbladder cases and ~6% of the remaining biliary tree (3,4). Within the biliary tract, the cystic duct and gallbladder are rare metastatic sites, while primary CBD involvement is even less frequent and only sparsely documented (4-6). Primary CBD melanoma is exceptionally rare, and its histopathological definition remains debated, with only 13 cases previously reported (6-9). Prognosis is poor: primary biliary melanoma of the gallbladder has a median survival of 21 months, whereas metastatic melanoma of the gallbladder has a median survival of 8.4 months (6).

Case report

In late October 2024, a 44-year-old male with no significant past medical history and an Eastern Cooperative Oncology Group (ECOG) performance status of 0 presented to King's College Hospital with obstructive jaundice. Computed tomography (CT) revealed a 3.5-cm soft tissue mass within the mid common bile duct (CBD), causing upstream biliary dilatation (Figs. 1 and 2). Liver function tests demonstrated cholestatic derangement, with total bilirubin 153 μmol/l, alanine transferase 638 IU/l, alkaline phosphatase (ALP) 721 IU/l, and gamma-glutamyl transferase (GGT) 832 IU/l. Endoscopic retrograde cholangiopancreatography (ERCP) demonstrated an intraductal mass extending 2 cm into the lower common hepatic duct and involving the cystic duct orifice. A sphincterotomy with plastic biliary stent placement relieved obstruction, resulting in bilirubin normalization to 20 μmol/l within one week. Brush cytology obtained during ERCP was non-diagnostic.

Staging investigations did not reveal any evidence of metastatic disease, thus the patient was counselled for pancreaticoduodenectomy, with intraoperative frozen section of the upper bile duct margin planned to determine the need for additional hepatic resection if positive for malignancy.

At laparotomy, frozen section analysis of the upper CBD margin was negative for malignancy. As the lower CBD was involved by tumour, a pylorus-preserving pancreaticoduodenectomy was performed. The pancreas was soft with a non-dilated duct, and a modified invagination technique was used for the pancreatico-jejunostomy. The patient's initial recovery was uneventful, and he was discharged on postoperative day 8 with no evidence of pancreatic fistula. One week later, however, he was readmitted with abdominal bleeding

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secondary to a gastroduodenal artery pseudoaneurysm. This was successfully managed with embolization and hepatic artery stent placement under angiographic guidance, after which he made a full recovery.

Histopathological examination revealed the CBD lesion to be malignant melanoma. Gross examination of the specimen demonstrated an intraductal polypoid tumour almost completely obliterating the mid CBD and cystic duct, with a dark brown to black solid cut surface containing whitish areas (Fig. 3A). Microscopically, the tumour was composed of epithelioid malignant cells arranged in solid nests and trabeculae, with moderately pleomorphic nuclei and lightly pigmented cytoplasm. Mitotic figures were scattered, and melanin pigment was observed within neoplastic cells and infiltrating macrophages. The stroma was moderately infiltrated by lymphocytes (Fig. 3B). Immunohistochemistry demonstrated diffuse positivity for melanocytic markers (HMB-45, Melan-A, SOX10) and BRAF V600E, while epithelial markers (AE1/AE3, MNF116, CK7) were negative (Fig. 3C-F). The tumour was predominantly intraductal with only focal invasion of the superficial duct wall. A definitive junctional component at the mucosal-submucosal interface was not identified. S-100 immunohistochemistry was not performed, as the diagnosis was supported by diffuse positivity for specific melanocytic markers including HMB-45, Melan-A, and SOX10. All resection margins and regional lymph nodes were free of tumour.

The patient reported a history of nevus excision six years prior, histologically confirmed as a dysplastic nevus without features of melanoma; this lesion was re-examined and again confirmed to be benign. A family history revealed melanoma in a second-degree relative (a cousin), with no additional family history of melanoma or other malignancies. Comprehensive dermatological assessment and full-body skin mapping did not identify any suspicious cutaneous, mucosal, or ocular lesions.

Following multidisciplinary discussion, the patient commenced adjuvant immunotherapy with nivolumab at a standard dose of 480 mg administered intravenously every 4 weeks, for a planned duration of 12 months. This approach was considered appropriate in the context of a BRAF V600E-mutant melanoma, with scheduled interval imaging for surveillance. At the time of last follow-up, the patient remains disease-free 12 months after surgery.

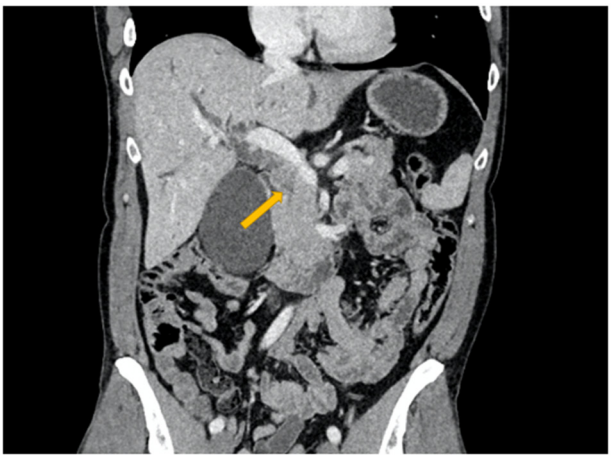

Figure 1. Coronal computed tomography image demonstrating a polypoid intraductal mass within the mid common bile duct (yellow arrow) with associated upstream biliary dilatation.

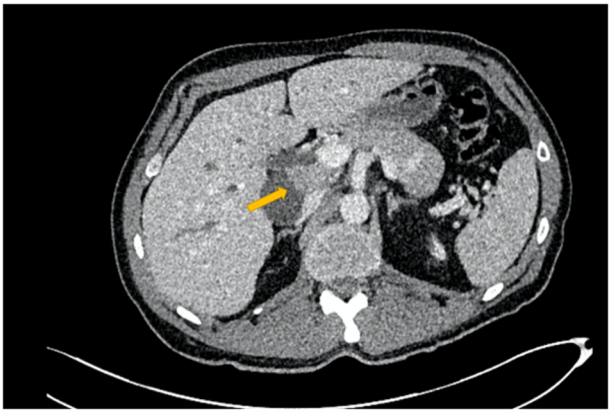

Figure 2. Axial computed tomography image showing a polypoid intraductal mass within the common bile duct (arrow).

Discussion

Painless obstructive jaundice is the most common presentation of pancreatobiliary malignancy. Cholangiocarcinoma typically affects patients in the sixth decade of life, and cases occurring under the age of 50 remain understudied (10). Distal cholangiocarcinoma accounts for 20-30% of all cases (11).

Malignant melanoma has the potential to metastasize to virtually any organ (12). Abdominal involvement is reported in up to 60% of cases with metastatic melanoma (1). The biliary tract is affected in 4-20% of cases, most frequently at the level of the gallbladder (9,13). Cetiner *et al* (12) reported fewer than 20 cases of metastatic melanoma involving the common bile duct (CBD), and to date, no systematic review has been performed.

The clinical spectrum of metastatic disease varies from widespread dissemination with poor prognosis and no curative options (13) to isolated lesions amenable to surgical resection, such as gallbladder metastasis, where cholecystectomy may provide limited disease-free survival (13). Historically, the prognosis of metastatic melanoma was dismal, with 2-year survival rates <2% reported three decades ago (14). However, more recent series demonstrate that resection of isolated intra-abdominal metastatic deposits can yield 5-year survival rates of 12-25% in selected cases (14-16). Complete resection appears to be critical for long-term survival. Wood *et al* (17) reported a 24% 5-year survival among patients undergoing resection of solid organ metastases (adrenalectomy, splenectomy, hepatectomy, pancreatectomy), whereas no long-term survivors were observed following incomplete resection.

Primary melanoma of the CBD is exceedingly rare, and its pathological diagnosis remains controversial due to the absence of specific immunohistochemical features (13). Ricci *et al* (18) proposed diagnostic criteria for primary gallbladder melanoma, which have also been applied to CBD melanoma: absence of prior melanoma, exclusion of other primary sites, solitary polypoid lesion, and presence of a junctional component. Wagner *et al* (19) subsequently emphasized the histological finding of junctional melanocytes

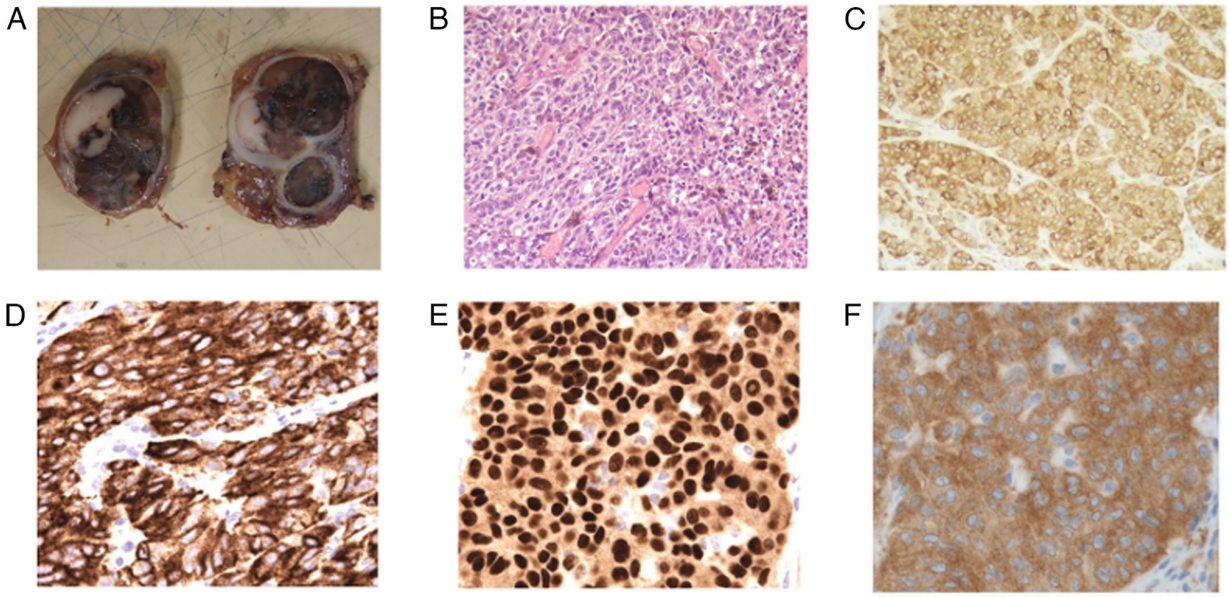

Figure 3. Pathological features of the resected tumor on high-power view microscopy. (A) Gross specimen showing an intraductal polypoid mass with a dark brown cut surface. (B) Histology showing malignant epithelioid cells with melanin pigment (hematoxylin and eosin staining; high-power view; magnification, approximately x400). (C) Immunohistochemistry showing diffuse Melan-A positivity in tumor cells (high-power view; magnification, approximately x400). (D) Immunohistochemistry demonstrating diffuse cytoplasmic positivity for HMB-45 in tumor cells (high-power view; magnification, approximately x400). (E) Immunohistochemistry showing strong nuclear positivity for SOX10 in tumor cells (high-power view; magnification, approximately x400). (F) Immunohistochemistry demonstrating tumor cell positivity for BRAF V600E (high-power view; magnification, approximately x400).

at the mucosal-submucosal interface, confirmed by S-100 immunoreactivity, as the strongest criterion for primary CBD melanoma. However, this feature has not been consistently reported by other authors (6-8).

In the present case, the diagnostic criteria proposed by Ricci *et al* (18) are largely fulfilled, including the absence of a prior melanoma, exclusion of alternative primary sites after comprehensive dermatological and systemic assessment, and the presence of a solitary intraductal polypoid lesion. Although a definitive junctional component, as emphasised by Wagner *et al* (19), was not identified, this feature has not been consistently demonstrated in previously reported cases of primary CBD melanoma. Given the predominantly intraductal growth pattern with only focal superficial invasion and the absence of metastatic disease, a primary biliary origin remains the most plausible diagnosis.

Moreover, although S-100 immunoreactivity and a junctional component have been proposed as diagnostic criteria, these features are not consistently reported in published cases of primary CBD melanoma, and their absence does not preclude the diagnosis when supported by morphology, specific melanocytic markers, and exclusion of alternative primary sites.

To date, only 13 cases of primary CBD melanoma have been described (6-9), with most diagnoses based on exclusion after extensive negative systemic work-up. In both primary and metastatic cases, upfront surgical resection remains the mainstay of treatment (6,17).

Applying the criteria from previous reports, the present case represents the 14th description of primary malignant melanoma of the CBD. While histological confirmation remains debated, the absence of cutaneous, mucosal, or ocular melanoma and the solitary intraductal lesion strongly support this diagnosis.

The identification of a BRAF V600E mutation in the present case is clinically significant and has important therapeutic implications. BRAF mutations are present in approximately 40-50% of cutaneous melanomas and have been associated with responsiveness to targeted therapy using BRAF inhibitors (20,21). Although data on molecular profiling in primary biliary melanoma are extremely limited, the presence of a BRAF V600E mutation provides a rationale for considering targeted therapy in the event of disease recurrence or metastatic progression. This molecular finding further distinguishes the present case from many previously reported cases and highlights the importance of comprehensive immunohistochemical and molecular assessment in rare melanocytic tumours of the biliary tract (20,21).

Although the prognosis of both primary and metastatic biliary melanoma has historically been poor, the present case may represent a more favourable biological and clinical scenario. Young age at presentation, complete (R0) surgical resection, and access to contemporary adjuvant immunotherapy are factors that have been associated with improved outcomes in melanoma more broadly. Nevertheless, given the rarity of primary CBD melanoma and the relatively short duration of follow-up in this case, which represents a limitation of this report, any prognostic inference must be made with caution, and longer-term surveillance remains essential to better define oncological outcomes.

This case underscores the importance of careful evaluation of patient demographics and history, particularly in younger individuals presenting with obstructive jaundice. Although preoperative differentiation from cholangiocarcinoma is difficult, clinicians must be aware of this rare entity. A diagnosis of melanoma after curative-intent pancreaticoduodenectomy represents a major shift in prognosis and postoperative

management, with implications for patients, families, and the multidisciplinary team.

In conclusion, metastatic involvement of the biliary tree occurs in 4-20% of cases of metastatic melanoma. Primary CBD melanoma is exceedingly rare, with only 13 cases previously described. Both entities are associated with poor prognosis, with 5-year survival not exceeding 25% even in resected cases. Nevertheless, complete resection remains the standard of care, offering the best chance for long-term survival.

A comprehensive evaluation of patient history, prior skin lesions, and family history is essential when assessing younger patients with obstructive jaundice. While rare, the possibility of primary or metastatic melanoma should be considered, as unexpected histological findings following major hepatopancreatobiliary surgery can profoundly alter the oncological pathway.

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Availability of data and materials

The data generated in the present study are included in the figures and/or tables of this article.

Authors' contributions

EF conceived and designed the study, collected clinical data, performed analysis, and drafted the manuscript. HA contributed to data collection and clinical management. YZ performed histopathological analysis and interpretation. PS and AP contributed substantially to surgical decision-making and operative management, provided critical clinical input during case review, and contributed to data interpretation. All authors contributed to drafting and revising the manuscript. EF, YZ and PS confirmed the authenticity of all raw data. All authors agree to be accountable for all aspects of the work. All authors have read and approved the final version of the manuscript.

Ethics approval and consent to participate

This case report was conducted in accordance with institutional requirements. The requirement for ethical approval was waived, as this is a single case report not requiring formal review.

Patient consent for publication

Written informed consent was obtained from the patient for publication of this report and accompanying images.

Competing interests

The authors declare that they have no competing interests.

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