Colonic and anal metastases from pancreato-biliary malignancies

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Abstract
Pancreato-biliary malignancies often present with locally advanced or metastatic disease. Surgery is the mainstay of treatment although less than 20% of tumours are suitable for resection at presentation. Common sites for metastases are liver, lungs, lymph nodes and peritoneal cavity. Metastatic disease carries poor prognosis, with median survival of less than 3 mo. We report two cases where metastases from pancreato-biliary cancers were identified in the colon and anal canal. In both cases specific immunohistochemical staining was utilised in the diagnosis. In the first case, the presenting complaint was obstructive jaundice due to an ampullary tumour for which a pancreato-duodenectomy was carried out. However, the patient re-presented 4 wk later with an atypical anal fissure which was found to be metastatic deposit from the primary ampullary adenocarcinoma. In the second case, the patient presented with obstructive jaundice due to a biliary stricture. Subsequent imaging revealed sigmoid thickening, which was confirmed to be a metastatic deposit. Distal colonic and anorectal metastases from pancreato-biliary cancers are rare and can masquerade as primary colorectal tumours. The key to the diagnosis is the specific immunohistochemical profile of the intestinal lesion biopsies.

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Key words: Pancreatobiliary cancer; Rare metastatic sites; Colonic metastasis; Anal metastasis; Immunohistochemistry

Core tip: Pancreato-biliary malignancies often present with locally advanced or metastatic disease. Surgery is the mainstay of treatment although less than 20% are suitable for resection at presentation. Common sites for metastases are liver, lungs, lymph nodes and peritoneal cavity and carry poor prognosis, with median survival of less than 3 mo. Distal colonic and anorectal metastases from pancreato-biliary cancers are rare and can masquerade as primary colorectal tumours. The key to the diagnosis is the specific immunohistochemical profile of the intestinal lesion biopsies.

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INTRODUCTION

Pancreato-biliary malignancies often present with locally advanced or metastatic disease.\(^1\) The commonest tumour type is adenocarcinoma followed by rarer varieties such as neuroendocrine and adeno-squamous cell carcinomas.\(^2\) Surgery is the mainstay of treatment although less than 20% are deemed resectable at the time of presentation.\(^3\) Metastatic disease carries a poor prognosis with median survival of less than 3 months.\(^4\)

The common sites for metastases are the liver, lungs, lymph nodes and peritoneal cavity.\(^5\) Unusual metastatic sites such as kidney,\(^6\) colon,\(^7\) skin,\(^8\) have also been reported. We report two cases where metastases from pancreato-biliary cancers were identified in the colon and anal canal.

CASE REPORT

Case 1
A 79-year-old lady presented with obstructive jaundice. A computed tomography (CT) scan and a subsequent endoscopic ultrasound scan identified a resectable ampullary mass. Staging CT did not reveal any evidence of metastases and the patient underwent a Whipple’s resection following which she made an uncomplicated recovery. The histopathology of the resected specimen confirmed poorly differentiated ampullary adenocarcinoma. The tumour demonstrated a pancreato-biliary immunophenotype being cytokeratin-7/cytokeratin-17/mucin-1 (CK7/CK17/MUC1) positive and cytokeratin-20/homeobox protein CDX2/mucin-2 (CK20/CDX2/MUC2) negative (Figure 1A). Approximately 4 wk after discharge, the patient re-presented with perianal pain exacerbated by defecation. Examination under anaesthesia (EUA) confirmed the presence of an atypical anal fissure, biopsies of which revealed anal mucosa extensively infiltrated by a poorly differentiated carcinoma, demonstrating similar morphological appearance to the original ampullary adenocarcinoma. Subsequent, immunohistochemistry also demonstrated an identical pancreato-biliary phenotype as seen previously (Figure 1B), suggesting that this was a metastatic deposit from the ampullary cancer. The patient underwent two cycles of palliative radiotherapy to the anal canal for control of pain and was discharged with full palliative support. She died approximately 3 wk after discharge.

Case 2
A 63-year-old lady presented with obstructive jaundice due to a biliary stricture involving the hilum of the bile ducts and extending longitudinally into the distal common bile duct. Endoscopic retrograde cholangiopancreato-graphic brushings were inconclusive. She underwent further staging with a CT scan and laparoscopy. The laparoscopy showed no evidence of peritoneal disease, however the CT scan revealed thickening of the sigmoid colon. Colonoscopic biopsies confirmed a submucosal infiltrating moderately differentiated adenocarcinoma with no associated mucosal dysplasia. This was not supportive of a colorectal primary and favoured an extrinsic origin. Subsequent immunohistochemical analysis showed strong staining for CK7, with occasional positive staining for CK20; and negative CDX2, CK17 and Estrogen Receptor (ER) immunoreactivity. This profile, although not specific, was consistent with metastatic deposit from a hilar cholangiocarcinoma. She underwent palliative biliary stenting and was referred for palliative chemotherapy.

DISCUSSION

The colon, rectum and anal canal are rare sites for metastases for any type of malignancy. However, such cases have been reported from primary carcinomas of breast,\(^9\) lung,\(^10\) colon,\(^11,16\) and prostate.\(^17\) Additionally, a small number of such metastases have been reported to occur in relation to cholangiocarcinomas\(^14,15\) and pancreatic adenocarcinomas.\(^13,16,17\) To the best of our knowledge metastasis to the anal canal from pancreato-biliary malignancies has not been reported before in the literature.

The extrinsic nature of these metastatic deposits may not be apparent in superficial mucosal biopsies. Immunohistochemical studies may be warranted in such cases where there is a suspicion of metastases or if there are unusual features such as adenocarcinoma undermining an intact, non-dysplastic mucosal surface. In the two cases that we have presented (Table 1) the immunohistochemical profiles of the tumours were more consistent with pancreato-biliary origin than lower gastrointestinal tract origin although are not definitive and final diagnosis requires correlation with the clinical and radiological parameters. Ampullary adenocarcinomas can demonstrate either an intestinal (CK20/CDX2/MUC2 positive) or pancreatobiliary immunophenotype (CK7/CK17/MUC1 positive), as in case 1. The tumours demonstrating a pancreato-biliary phenotype can also co-express CK20, but this is usually only focal in distribution. On the contrary, the vast majority of colorectal adenocarcinomas demonstrate a typical lower gastrointestinal immunophenotype, being CK20 and CDX2 positive (CDX2 is an intestine-specific nuclear transcription factor, which can be used as a marker for intestinal-type differentiation of colorectal adenocarcinomas).\(^18,19\)

We acknowledge that we do not have direct corroborative histology of the pancreato-biliary primary in the second case. However, unequivocal evidence of a locally advanced malignant pancreatic mass noted on staging CT. Pancreatic biopsy was not attempted due to poor performance status of the patient. In this case there was sufficient radiological and immunohistochemical evidence to support the diagnosis of metastatic deposit in the large
intestine from the primary biliary cancer.

Although pancreato-biliary malignancies commonly lead to metastatic deposits on the peritoneal surfaces, the cases described here did not have any evidence of diffuse peritoneal involvement. There was no evidence of peritoneal nodules, omental infiltration or ascites on any of the CT scans or staging laparoscopy. Therefore we believe that these are focal metastases to the colon and anal canal rather than a part of diffuse peritoneal involvement.

Distal colonic and anorectal metastases are rare. They
may present simultaneously with or in isolation from the primary, with symptoms identical to a primary colo-rectal tumour. The key to diagnosis is a high index of suspicion if the clinical picture is atypical coupled with specific immunohistochemical staining. Atypical immunohistochemical pattern that does not fit with a colorectal primary should raise suspicion regarding metastases from an extrinsic source.

**Table 1  Summarising characteristics of the 2 cases**

| Demographic information | Mode of presentation | Initial investigations and findings | Site of primary lesion | Site of metastases | Histology of metastasis | Outcome |
|-------------------------|----------------------|------------------------------------|-----------------------|-------------------|------------------------|---------|
| 79, female              | Presented with obstructive jaundice | EUS, CT, ERCP, tissue diagnosis obtained after Whipple’s resection Colonoscopy and biopsy, staging CT | Ampullary | Anal canal | Adenocarcinoma, PB type, CK7/CK17/MUC1 positive, (negative for K20/CDX2/MUC2) | Palliation |
| 63, female              | Presented with obstructive jaundice | | Hilum of bile ducts | Sigmoid colon | Microscopy Immunohistochemistry strong CK7 staining, with occasional positive staining for CK20, (negative CDX2, CK17 and ER immunoreactivity) | Palliative percutaneous biliary stenting and chemotherapy |

CT: Computed tomography; EUS: Endoscopic ultrasound scan; ERCP: Endoscopic retrograde cholangiopancreatography.

**Experiences and lessons**

Symptoms from distal colonic and anorectal metastases may be identical to a primary colorectal tumour and the key to diagnosis is a high index of suspicion if the clinical picture is atypical coupled with specific immunohistochemical staining.

**Peer review**

This is a report of two unusual metastases of pancreato-biliary malignancies to the sigmoid colon and anal canal. The cases stress the importance of complete physical examination, including rectodigital examination, and surveillance of the lower gastro-intestinal tract in upper gastro-intestinal and pancreato-biliary malignancies, even though the incidence of such metastasis is rare.

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