Case Series

Beware the pancreatic incidentaloma in colorectal tumours: pancreatic adenocarcinoma with metastases to the colon and rectum

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Abstract
Colorectal cancer (CRC) is the third most diagnosed malignancy in the Western world. Routine staging of CRC often identifies incidental lesions on cross-sectional imaging. Appropriate treatment is dependent on a correct histological diagnosis. Pancreatic Ductal Adenocarcinoma (PDAC) is a rarer and often devastating diagnosis for which the treatment pathway differs significantly to CRC. We report two rare cases: the first recorded case of PDAC with synchronous rectal metastasis and a case of an acute presentation with large bowel obstruction from synchronous colonic metastasis. Both cases presented a significant diagnostic challenge. The management of both cases would have been altered had the histological diagnosis been known prior to surgery. Clinicians treating CRC should be wary of incidental lesions on staging investigations as they rarely represent an occult extra-intestinal primary malignancy. Immunohistochemistry plays an important role in ascertaining the origin of gastrointestinal malignancy.

Introduction
Colorectal tumours are common and usually due to neoplastic transformation at various stages of the adenoma-carcinoma pathway [1]. Colorectal cancer (CRC) is the third most diagnosed malignancy in the Western world, with an estimated incidence of 38.7 per 100 000 persons per year [2]. Rectal adenocarcinoma accounts for almost one-third of all CRC [2]. Standard of care for rectal cancer includes neoadjuvant radiotherapy for locally advanced tumours (clinically T3 or above or lymph node positive). Histological confirmation of adenocarcinoma is recommended prior to treatment of CRC, but is particularly important when considering neoadjuvant therapy for rectal cancer [3]. Pancreatic ductal adenocarcinoma (PDAC) is a rarer but often devastating diagnosis; <20% of patients have surgically resectable disease at presentation and overall 5-year survival is ~5% [4]. Metastases to liver and lung are common and account for 90% of PDAC-associated deaths [5]. Metastatic disease to the gastrointestinal tract from PDAC is rare [6]. We report two cases of PDAC with synchronous colorectal metastases, each presenting a significant diagnostic challenge.
Case Series

Case A

An 82-year-old man with no significant medical history presented with progressive change in bowel habit and abdominal pain for 2 months. Colonoscopy 1 year prior had only revealed diverticulosis but on rectal examination at re-presentation a firm mass was palpable within the rectum. Colonoscopy was repeated and revealed an ulcerated non-obstructing low-rectal mass 3 cm in size (Fig. 1). Biopsies reported adenomatous change with at least high-grade dysplasia and a focus suspicious for invasive adenocarcinoma.

Routine staging for rectal cancer was performed. Magnetic resonance imaging (MRI) of the pelvis revealed an anterior rectal mass 7–8 cm from the anal verge with invasion into the seminal vesicles and at least three lymph nodes suspicious for metastases (cT4aN2). Computed tomography (CT) chest, abdomen and pelvis revealed enlarged nodes along the inferior mesenteric artery chain, but no definite metastatic disease was reported (Fig. 2). A 1.4 cm low attenuation hypo-enhancing mass in the distal pancreas occluding the splenic vein was reported as an incidental finding. Serum carcinoembryonic antigen (CEA) was 1.71ug/L and serum carbohydrate antigen 19-9 (Ca 19-9) was mildly elevated at 78u/ml.

Multidisciplinary team (MDT) discussion involving a pancreatic surgeon deemed a primary rectal adenocarcinoma with either incidental primary malignant or metastatic lesion in the distal pancreas as the likely diagnoses. Treatment recommended was neoadjuvant long-course chemoradiotherapy for the rectal tumour followed by rectal resection and distal pancreatectomy.

Following neoadjuvant therapy restaging showed a slight reduction in size of pancreatic tumour from 14 to 12.6 mm and was again reported as consistent with a metastasis from a primary rectal malignancy. A laparoscopic ultra-low Hartmann’s procedure (gastrointestinal continuity not restored due to functional status preoperatively) combined with distal pancreatectomy and splenectomy was performed.

Histopathology revealed a well to moderately differentiated, 18 mm PDAC in the pancreatic tail with microscopically demonstrated grossly intact colorectal mucosa with extensive infiltration by adenocarcinoma from the sub-serosal aspect. The tumour in the submucosa and underlying structures of rectum showed immunoreactivity for CK7 while CK20 and CDX2 were negative; however, the overlying rectal mucosa showed reactivity to CK20 and CDX2 but was negative for CK7 (Fig. 3).

Case B

A 71-year-old man with a background of cardiac disease and obstructive sleep apnoea presented to the emergency department with symptoms of large bowel obstruction. Urgent CT abdomen and pelvis revealed short segment hepatic flexure thickening and stranding with evidence of obstruction at this point. An additional soft tissue mass in the tail of the pancreas encasing the splenic vasculature was reported as suspicious for metastatic disease from a primary colonic malignancy or a synchronous primary pancreatic malignancy (Fig. 4). Serum CEA was 5.32ug/L and serum Ca 19-9 was significantly elevated at 1180u/ml.

Due to the presence of large bowel obstruction, the patient proceeded to an urgent laparotomy. Operative findings were of a hard sclerotic mass within the pancreatic tail involving the splenic hilum. A further cicatrizing tumour was identified at the hepatic flexure with obstruction of the ascending colon. A right hemicolectomy and distal pancreatectomy with en-bloc splenectomy was performed.
Histopathology of the pancreatic resection revealed a 45 mm moderately differentiated PDAC with lymphovascular and perineural invasion. The colonic specimen revealed infiltration of metastatic PDAC from the serosal aspect into the muscularis and submucosa with focal areas infiltrating into mucosa. One of 18 mesocolic lymph nodes resected contained PDAC. Immunostaining of both tumours was positive for CK7 and negative for CK20.

DISCUSSION

We report two cases of PDAC with synchronous colorectal metastases from the same institution within a 4-month period. In both instances a presumptive diagnosis of CRC with either distant metastasis to the pancreas or incidental pancreatic tumour was made, and treatment proceeded according to that recommended for CRC. If the true diagnosis was known the management of both cases could have differed significantly.

CRC is common and in a patient with lower gastrointestinal symptoms, imaging and/or histology suggestive of a primary CRC this is likely to be the presumed diagnosis, even in an MDT setting with numerous CRC specialists and a pancreatic surgeon. Pancreatic lesions are metastases in only 0.5–3% of cases [7] and pancreatic metastases from a colorectal primary are rare with only isolated case reports in the literature [8–10]. When distant CRC metastases are present, modern management tends to support multi-visceral resection if complete cytoreduction is possible [11], hence aggressive surgical treatment was pursued in both cases. The worldwide incidence of PDAC has more than doubled in the past 20 years [4] and will likely continue to grow with our ageing population. PDAC carries a poor prognosis and metastasis is a contra-indication to attempting curative resection. However, pancreatic acinar cell cancer (PACC) metastases to the colorectum have been documented in four previous reports [12–15]. The mechanism is suggested to be as a result of increased production of digestive enzymes and in particular cytochrome C, a mitochondrial filament protein, in the tumour tissue.

In conclusion, we report two rare cases of synchronous colorectal metastasis from PDAC in which the diagnosis was not known until after combined colorectal and pancreatic resection. The management of both cases, but case A (rectal metastasis) in particular, would have been significantly altered had the histological diagnosis been known prior to treatment. Immunohistochemistry is an important tool in determining the tumour tissue origin in both cases.

REFERENCES

1. Fearon ER, Vogelstein B. A genetic model for colorectal tumorigenesis. Cell 1990;61:759–67.
2. Siegel R, Miller K, Goding Sauer A, Fedewa S, Buttery L, Anderson J, et al. Colorectal cancer statistics, 2020. CA Cancer J Clin 2020;70:145–64.
3. Hughet F, Muckerjee F, Javle M. Locally advanced pancreatic cancer: the role of definitive chemoradiotherapy. Clin Oncol 2014;26:560–8.
4. Pourshams A, Sepanlou S, Ikuta K, Bisignano C, Safiri S, Roshandel G, et al. The global, regional, and national burden of pancreatic cancer and its attributable risk factors in 195 countries and territories, 1990–2017: a systematic analysis for the global burden of disease study 2017. Lancet Gastroenterol Hepatol 2018;4:934–47.
5. Das S, Batra S. Pancreatic cancer metastasis: are we being pre-EMTed? Curr Pharm Des 2015;21:1249–55.
6. Cannistrà M, Ruggiero M, Zullo A, Serafini S, Grande R, Nardo B. Metastases of pancreatic adenocarcinoma: a systematic review of literature and a new functional concept. Int J Surg 2015;21:S15–S21.
7. Lasithiotakis K, Petrakis I, Georgiadis G, Paraskakis S, Chalkiadakis G, Chrysos E. Pancreatic resection for metastasis to the pancreas from colon and lung cancer, and osteosarcoma. JOP 2010;11:593–6.
8. Lee CW, Wu RC, Hsu JT, Yeh CN, Yeh TS, Hwang TL, et al. Isolated pancreatic metastasis from rectal cancer: a case report and review of literature. World J Surg Oncol 2010;8:26.
9. Tani R, Hori T, Yamada M, Yamamoto H, Harada H, Yamamoto M, et al. Metachronous pancreatic metastasis from rectal cancer that masqueraded as a primary pancreatic cancer: a rare and difficult-to-diagnose metastatic tumor in the pancreas. Am J Case Rep 2019;20:1781–7.
10. Su L, Wernberg J. Synchronous distal pancreatic metastatic lesion arising from colonic adenocarcinoma: case report and literature review. Clin Med Res 2014;12:166–70.
11. Stewart C, Warner S, Ito K, Raof M, Wu G, Kessler J, et al. Cytoreduction for colorectal metastases: liver, lung, peritoneum, lymph nodes, bone, brain. When does it palliate, prolong survival, and potentially cure? Curr Probl Surg 2018;55:330–79.
12. Sun J, Zhang X, Huang H, Zhang Y, Wang K, Cui S. Rectal metastasis from a previously resected carcinoma of the pancreas: a case report. Transl Cancer Res 2020;9:3018–23.
13. Yewale R, Ramakrishna B, Vijaykumar K, Balasundaram P, Arulprakash S, Radhakrishna P, et al. Pancreatic adenocarcinoma with synchronous colonic metastases. ACG Case Reports Journal 2020;7:e00299.
14. Bellows C, Gage T, Stark M, McCarty C, Haque S. Metastatic pancreatic carcinoma presenting as colon carcinoma. South Med J 2009;102:748–50.
15. Kahl R, George K, Patel K, Stawick L. Pancreatic adenocarcinoma with rare sigmoid colon metastasis. ACG Case Reports Journal 2019;6:e00132.
16. Nogueira S, Pinto B, Silva E, Garcia H, Carneiro F. Pancreatic cancer presenting as colonic disease. A rare case report. Int J Surg Case Rep 2018;44:4–7.
17. Vrakas S, Kourkoulis P, Koutoufaris G, Manoloudaki K,ourgias V. An unusual case of colonic mass. Clin Case Rep 2021;9:e04848.
18. DY -Jung P, Krishnamurthi S, Chahal P, Downs-Kelly E, Morris-Stiff G. Pancreatic metastases to the colon: an unusual cause of colonic obstruction. BMJ Case Rep 2019;12:e228578.
19. Inada K. Metachronous colonic metastasis from pancreatic cancer seven years post-pancreatoduodenectomy. World J Gastroenterol 2013;19:1665.
20. Kim W, Lee Y. Metachronous colonic metastasis from pancreatic cancer presenting as mechanical obstruction: a case report. Clin Imaging 2015;39:699–701.
21. Ohara Y, Oda T, Enomoto T, Hisakura K, Akashi Y, Ogawa K, et al. Surgical resection of hepatic and rectal metastases of pancreatic acinar cell carcinoma (PACC): a case report. World J Surg Oncol 2018;16:158.
22. Barak V, Goike H, Panaretakis K, Einarsson R. Clinical utility of cytokeratins as tumor markers. Clin Biochem 2004;37:529–40.