

CASE REPORT

Metastasis of Rectal Adenocarcinoma to the Pancreas. Two Case Reports and a Review of the Literature

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ABSTRACT

Context The vast majority of pancreatic tumors are of pancreatic origin. Nonetheless, a variety of extrapancreatic tumors can involve the pancreas and may manifest with different clinicopathological characteristics.

Case report We report on two patients with a history of rectal cancer who were referred to our department with a pancreatic mass: one patient 2 years after a low anterior resection (TNM stage: pT3 pN0 pM0), the other patient 2.5 years after an abdominoperineal resection (TNM stage: pT3 pN1 pM0). In the first case, computed tomography showed a cystic mass in the pancreas but fine-needle biopsy followed by cytopathological analysis revealed only necrotic tissue. In the other patient, magnetic resonance tomography showed a hypodense structure in the pancreatic body/tail. Suspecting pancreatic tumors, distal pancreatectomies were carried out. Subsequent histological examination revealed metastases of rectal cancer in both cases.

Conclusion In patients with a history of a malignant tumor, a newly diagnosed mass in the pancreas - although rare - should raise the suspicion of metastatic disease. Surgical resection may be an option for a curative approach which can be offered to otherwise healthy patients if there is no evidence of other metastases.

CASE PRESENTATIONS

Two patients were referred for explorative laparotomy and resection of the tumors in the pancreas.

Case 1

A 61-year-old woman in good general condition presented to our department complaining of abdominal pain in the left upper quadrant. She had had the pain for at least one year. Past medical history revealed that a low anterior resection for a poorly differentiated (G3) rectal adenocarcinoma had been performed 2 years before presentation (TNM stage: pT3 pN0 pM0); neoadjuvant radiation therapy had been administered before that surgery and no adjuvant treatment had been given. Computed tomography of the abdomen showed a cystic structure in the pancreatic tail (Figure 1a,b); upon fine needle biopsy and cytopathological analysis, only necrotic tissue was detectable. Neither colonoscopy nor chest X-ray showed any signs of local recurrence or metastases of the rectal cancer. Routine laboratory testing, including blood count, levels of serum electrolytes as well as renal and liver function tests, did not show any significant changes. However, tumor markers CA 19-9 and CEA were elevated: CA 19-9: 541 U/mL (reference range: 0-37 U/mL), CEA: 128 µg/L (reference range: 0-2.5 µg/L).

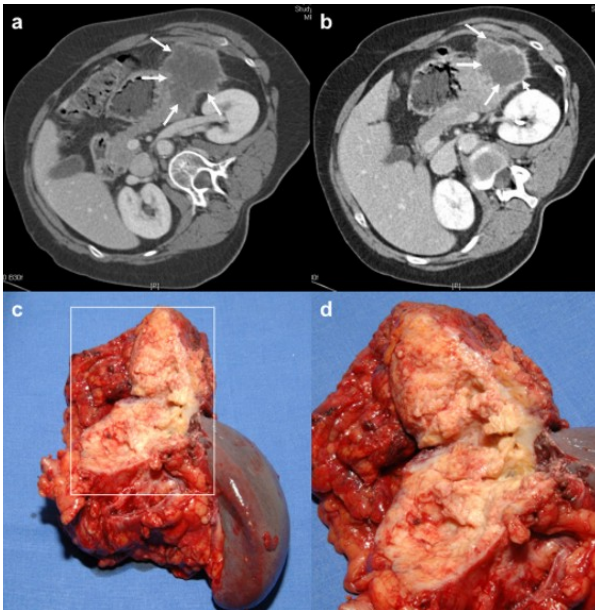


Figure 1. Abdominal CT scan of case 1 which shows the tumor mass (5.9x6.3 cm) in the tail of the pancreas (arrows; **a. b.**). Resected specimen with pancreatic tail and spleen (**c.**) and a closer view of the tumor in the pancreatic tail (**d.**).

Case 2

The second patient was a 64-year-old woman in good general condition who was referred to our department 2.5 years after surgery for rectal cancer performed in March 2003 and subsequent adjuvant radiochemotherapy. Histological examination at that time had shown a moderately differentiated (G2) adenocarcinoma with TNM stage pT3 pN1 pM0. At the end of 2004, the patient presented with metastases to the lungs, which were resected by a partial left lobectomy. In 2005, the patient presented with elevated tumor markers (CEA 24.4 µg/L; reference range: 0-2.5 µg/L). Magnetic resonance tomography showed hypodense structures in the pancreatic body/tail, suspicious for metastases of rectal cancer (Figure 2a,b).

OPERATIVE DETAILS

Case 1

In the first patient, surgical exploration revealed a large mass with a diameter of 6 centimeters in the tail of the pancreas, in close proximity to the spleen and stomach. As there was no evidence of any metastatic disease to the liver or peritoneal cavity, a careful

mobilization was carried out, followed by a distal pancreatectomy. In addition, a splenectomy and a wedge resection of the stomach were performed. Figure 1c,d shows the specimen and a closer view of the metastasis to the pancreas.

Case 2

The surgical exploration of the second patient revealed no evidence of any metastases to the peritoneal cavity, the liver or the pancreatic head. A tumor of approximately 5 cm was found in the body/tail of the pancreas, in close proximity to the splenic artery. Thus, a distal pancreatectomy with splenectomy was performed.

PATHOLOGIC EXAMINATION

Case 1

Pathologic examination of the operation specimen revealed a firm, solid mass in the pancreatic tail, measuring 6 cm at its largest

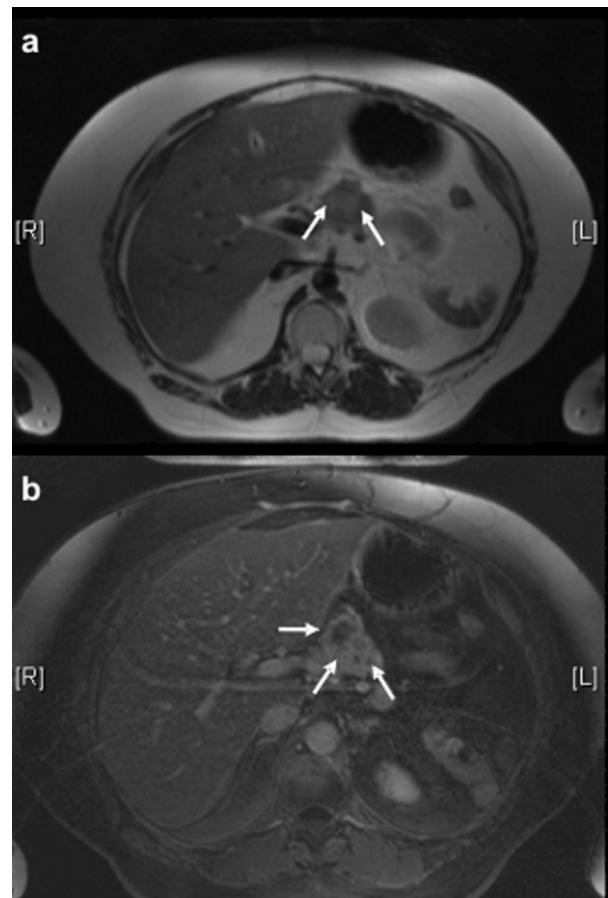


Figure 2. Abdominal MRI scan of case 2: A 4x4 cm hypointense mass in the pancreatic tail (arrows).

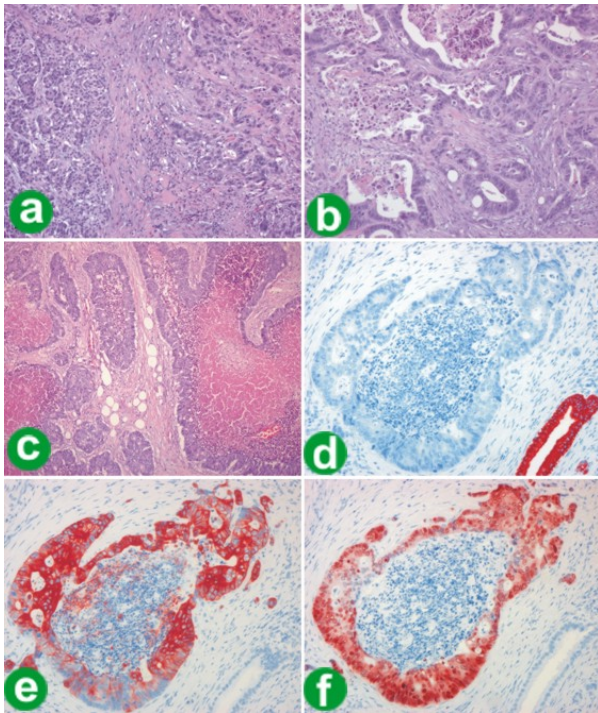


Figure 3. Histomorphological and immunohistochemical findings in the pancreatic masses of case 1 (a. b.) and case 2 (c. d. e. f.): Both tumors displayed irregular glandular formations of pleomorphic epithelial cells with basophilic cytoplasm and prominent nucleoli. There was mild to moderate desmoplastic stromal reaction (a. b.) and marked necrosis (c.). The tumor margins towards the pancreatic tissue (a. pancreatic tissue depicted on the left) and towards the peripancreatic fatty tissue were not well-defined. Immunohistochemically, the tumor lacked expression of cytokeratin 7 (d.). On the other hand, the tumor cells showed expression of the intestinal markers cytokeratin 20 (e.) and CDX2 (f.).

diameter. The cut surface was white and contained multifocal foci of necrosis. The tumor showed invasion of the peripancreatic fatty tissue without well-defined margins. Furthermore, an intrapancreatic accessory spleen of 1.3 cm was found in the pancreatic tail. Microscopically, the tumor consisted of solid and sheet-like formations as well as irregular and distorted glandular formations of atypical epithelial cells (Figure 3ab). The tumor displayed marked necrosis. Immunohistochemically, the tumor cells showed expression of cytokeratin 20 and CDX2, while cytokeratin 7 did not stain the tumor cells. The tumor invaded the peripancreatic fatty tissue. Lymph node metastases were detected in 4 of 18 peripancreatic lymph nodes. The resection margins were free of

tumor. The diagnosis was pancreatic metastasis of a poorly differentiated adenocarcinoma of intestinal differentiation (well compatible with a metastasis of the known rectal adenocarcinoma).

Case 2

At gross pathologic examination of case 2, a 5 cm solid, firm mass having a white to greyish cut surface was found in the pancreatic tail, infiltrating the peripancreatic fatty tissue, the spleen, and the wall of an adjacent gastric wedge resection specimen. Necroses were seen in the peritumoral soft tissue. Microscopically, the tumor displayed irregular glandular formations of atypical epithelial cells, containing abundant and frequently comedo-like necrosis (Figure 3c). Immunohistochemically, the tumor cells were negative for cytokeratin 7 (Figure 3d) but positive for cytokeratin 20 (Figure 3e) and CDX2 (Figure 3f). The tumor invaded the peripancreatic fatty tissue, the spleen, the adjacent gastric wall and two of nine peripancreatic lymph nodes. Acute inflammation and plurifocal necroses were seen in the pancreatic and fatty tissue surrounding the tumor. The resection margins were free of tumor. The diagnosis was pancreatic metastasis of a moderately differentiated adenocarcinoma of intestinal differentiation (well compatible with a metastasis of the known rectal adenocarcinoma).

CLINICAL COURSE

Case 1

The patient recovered postoperatively without any complications. The routinely placed drains were removed on the first postoperative day. The patient was discharged eight days after surgery. Adjuvant chemotherapy was refused by the patient. Six weeks later, the patient presented again with a palpable tumor in the skin of the chest wall which was also resected. Histopathology revealed a lesion which was also compatible with a metastasis of the rectal cancer.

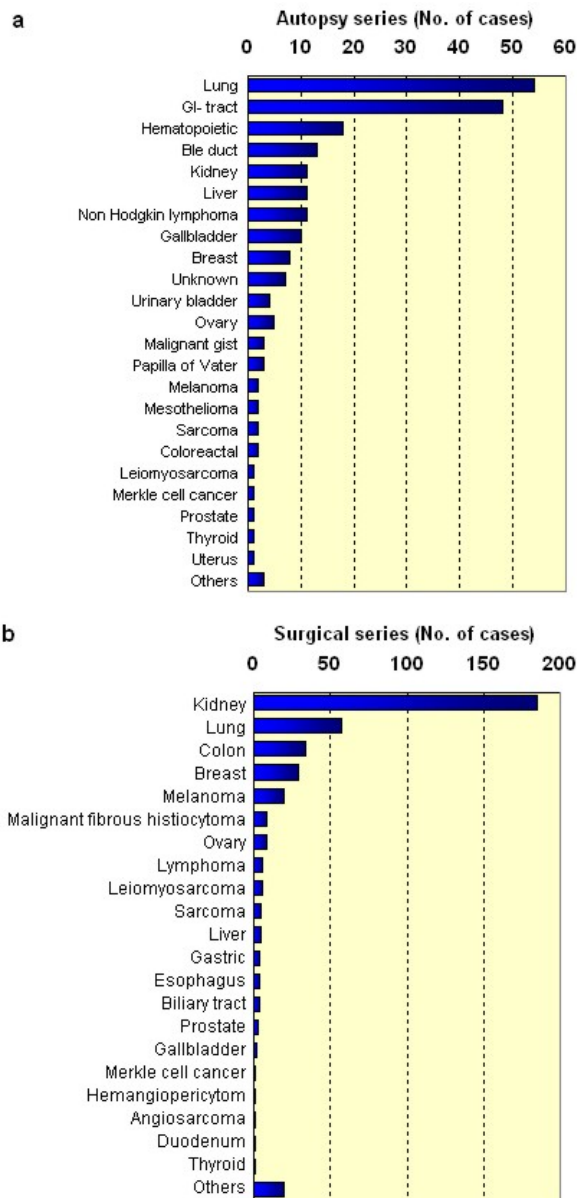


Figure 4. Number of cases of metastasis to the pancreas in autopsy series (a.) [1, 3] and surgical series (b.) [2, 3, 8, 9, 10, 11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22, 23, 34, 25, 26, 27, 28, 29, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 41, 42, 43, 44, 45, 46, 47, 48, 49, 50, 51, 52, 53, 54, 55, 56, 57, 58, 59, 60, 61, 62, 63, 64, 65, 66, 67, 68, 69, 70, 71, 72, 73, 74, 75, 76, 77, 78, 79, 80, 81, 82, 83, 84, 85, 86, 87, 88, 89, 90, 91, 92, 93, 94, 95, 96, 97, 98, 99, 100, 101, 102, 103].

Case 2

The second patient also had a smooth postoperative course without any complications. The routinely placed drains were removed on the first postoperative day. The patient was discharged twelve days after surgery. Six months later, the patient

presented with a metastasis to the liver which was resected. Thereafter, the patient was treated with 5-fluorouracil/folinic acid (5-FU/FA) and oxaliplatin (FOLFOX) for four months and, subsequently, with capecitabin (Xeloda®) and oxaliplatin.

REVIEW OF THE LITERATURE ON METASTASES TO THE PANCREAS

The majority of pancreatic tumors are primary [1, 2], and metastases to the pancreas are rare. A variety of extrapancreatic tumors can involve the pancreas secondarily and may manifest with different clinicopathological characteristics. The final diagnosis of metastatic disease to the pancreas can be confirmed either by operative resection and subsequent histopathological examination of the resected specimen or by fine needle aspiration.

In 4,955 adult autopsies and 973 pancreatic surgical specimens, the prevalence of different metastatic tumors in the pancreas was 1.6% of all examined autopsy cases and 3.9% of patients with pancreatic resections [1]. These tumors had various origins, including the lung, gastrointestinal tract, kidney, breast, liver, ovary, and urinary bladder [1]. In 690 autopsies of patients with a malignant primary tumor other than pancreatic cancer, a metastasis to the pancreas was diagnosed in 15% of cases [3]. This study indicates that, in about one out of six autopsy cases of patients with malignant tumors, metastases to the pancreas can be found. In a Japanese study, the most common origin of the primary malignancy was the stomach, followed by the lung in 17% of cases and the extrahepatic bile duct in 13%; in this series, 18% of the secondary tumors in the pancreas were due to direct invasion by the primary tumor, including malignant stomach tumors (19%) and extrahepatic bile duct cancer (54%) [3]. In Figure 4, the different primary tumors found in patients with metastases to the pancreas are shown, broken down by autopsy series and resection. The publications included are case reports and retrospective analyses.

DISCUSSION

Although metastases to the pancreas are rare, in patients with a pancreatic mass, metastatic disease may be considered, especially if the patient has a history of malignant disease. The most common sources of primary tumors generating such metastases are the kidney and the lungs; in a few cases, colorectal and breast cancer as well as melanomas are possible primaries. The published data show that, especially for metastases from kidney cancer, there may be a long time between resection of the primary tumor and the appearance of the metastases. In a series of 4,955 autopsy cases, 42% of the tumors in the pancreas were metastases from other organs [1] and, in a study of 690 autopsy cases in patients with malignant tumors, a metastasis to the pancreas was diagnosed in 15% of the cases [3]. Metastases to the pancreas have various manifestations; they can present as solid tumors, cystic structures, and hypodense or hyperdense structures on computed tomography imaging [4, 5]. If there is doubt, an explorative laparotomy should be performed to confirm the diagnosis and to resect the tumor.

Immunohistochemical examinations may be helpful in establishing the diagnosis if clinical or histomorphological features indicate the possibility of a metastasis to the pancreas. Whereas only a few cases of colorectal adenocarcinoma show expression of cytokeratin 7, most of these tumors express cytokeratin 20 [6]. An opposite staining pattern is found in pancreatic ductal adenocarcinoma [6]. Furthermore, CDX2 is frequently expressed in colorectal carcinoma whereas it is only rarely expressed in pancreatic ductal adenocarcinoma [7]. In cases such as the ones presented, the application of a combination of several antibodies may be especially helpful for diagnosis, although the expression of the detected proteins is not exclusively confined to one tumor entity or the other.

As shown in prospective analyses of patients resected for metastases of the pancreas, a median survival of up to 22 months and 5-

year survival rates of 25% after resection of the metastatic disease are reported [8, 9]. Surgical resection may be offered to patients with metastatic disease to the pancreas, and they should be referred to centers with experience in pancreatic surgery.

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