

Primary pancreatic neoplasia or metastasis from colon carcinoma ?

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Abstract

Introduction : The pancreas is an unusual but occasionally favored target for metastasis from other primary cancers. Metastases have been described for various non-hematologic neoplasms, such as renal-cell carcinoma, pulmonary small-cell carcinoma, melanoma and gastric carcinoma.

Case report : We report the case of a 77-year old man with a mass in the pancreatic head five years after anterior resection for adenocarcinoma of the colon and three years after resection of a lung metastasis. The patient underwent pylorus-preserving pancreaticoduodenectomy (Longmire-Traverso) and lymph-node dissection of compartment II.

Discussion : It is rare to have solitary metastases to the pancreas which clinically may mimic a primary neoplasm of the pancreas. Clinical features, as well as MRI and PET findings in patients with pancreatic metastasis from colon carcinoma are similar to those of primary pancreatic ductal adenocarcinoma. The diagnosis of metastasis should be considered when patients have a pancreatic mass and a history of non-pancreatic malignant lesions. Radical resection may prolong survival in patients if the pancreas is the only locus for metastasis at the time of diagnosis. (*Acta gastroenterol. belg.*, 2008, 71, 401-408).

Key words : pancreatic metastasis, lung metastasis, colon carcinoma, pylorus-preserving pancreaticoduodenectomy.

Introduction

The pancreas is an uncommon location for metastases from other primary cancers. Metastases have been described for various non-hematologic neoplasms, such as renal-cell carcinoma, pulmonary small-cell carcinoma, melanoma, and gastric carcinoma. Renal-cell carcinoma appears to be the most common primary tumor to yield metastases to the pancreas (1-5). Metastases in the pancreas are difficult to distinguish from primary pancreatic cancers (3) and usually manifest many years after resection of the primary tumor (5-11). We present the case of a 77-year-old man with a mass in the pancreatic head five years after anterior resection for adenocarcinoma of the colon and three years after resection of a lung metastasis.

Case report

A 77-year-old man presented with a history of jaundice, pale stools, dark urine, and pruritus. Abdominal examination was unremarkable, but liver-function tests were elevated. Tumor marker CA 19-9 was moderately elevated (48.6 U/ml, normal 37 U/ml).

Five years before being referred to our institution, the patient had undergone colon resection (anterior resection) for adenocarcinoma of the colon, followed by adjuvant chemotherapy with 5-Fluoruracil (5-FU) and Leucovorin. The tumor was located at the rectosigmoidal region, measuring 5 cm in its largest diameter. Pathologic examination revealed an adenocarcinoma of low differentiation, with infiltration of the muscularis propria (Fig. 1).

Metastases of regional lymph nodes were detected (4/40). The colon carcinoma at stage pT3 pN2 G2 M0 was completely resected (R0).

In the course of regular follow-up, a solitary mass in the lingula of the lung was detected two years later. Video-assisted resection of the metastasis in the lung was performed, followed by adjuvant chemotherapy with Capecitabine and Oxaliplatin. Histopathological examination revealed a metastasis of the primary colon adenocarcinoma (Fig. 2).

CT (Computer tomography) revealed a globular mass, measuring 1.8 cm, in the head of the pancreas (Fig. 3), causing the biliary obstruction.

A temporary plastic stent was inserted. Angio-Magnetic resonance imaging (Angio-MRI) demonstrated a solid inhomogeneous tumor in the head of the pancreas without invasion of the major abdominal vessels, and, therefore, it seemed to be a resectable pancreatic tumor.

ERCP (Endoscopic Retrograde Cholangio-Pancreaticography) showed an irregular stricture of the bile duct suggestive of malignant obstruction.

Positron Emission Tomography (PET) revealed a solitary circumscribed area of pathologically elevated glucose uptake in the head of the pancreas (Fig. 4). No other masses were detected. This lesion showed a maximal SUV_{max} (Standard Uptake Value) of 16.2, which was clearly elevated and, thus, most likely of malignant cause.

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Submission date : 03/03/2008
Revised version : 05/06/2008
Acceptance date : 04/07/2008

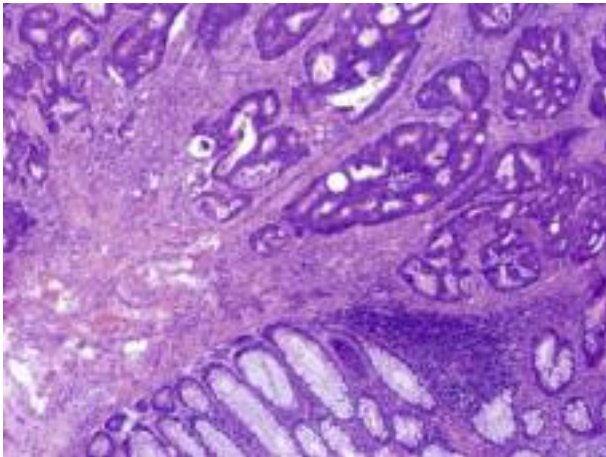


Fig. 1. — Histology.
Histomorphologic appearance of the primary colon carcinoma.

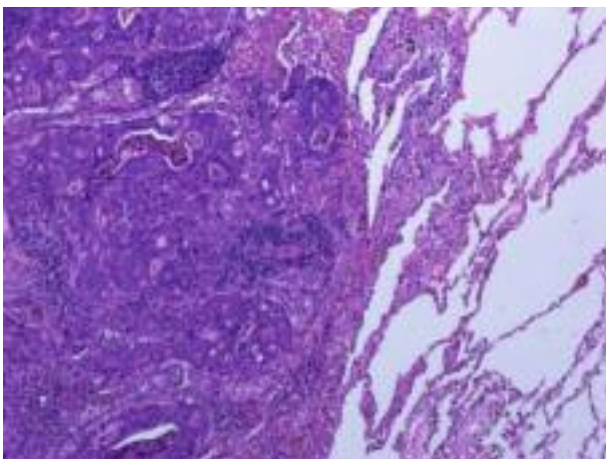


Fig. 2. — Histology.
Histomorphologic appearance of the lung metastasis.

A primary tumor of the pancreas or a metastasis of the colon carcinoma was considered, without any metastasis of the lymph nodes or other organs.

The patient underwent pylorus-preserving pancreaticoduodenectomy (Longmire-Traverso) and lymph-node dissection of compartment II. The postoperative course was uneventful, and the patient was discharged from the hospital without any perioperative morbidity.

Histopathological examination

Grossly, the surgical specimen consisted of the duodenum, measuring 22 cm in length, the common bile duct, measuring 5.5 cm in length, and the head of the pancreas, measuring 5.5 cm in length.

On cut section, the tumor was brown-tan with weakness regions. It was circumscribed; measuring $2.2 \times 2.4 \times 3.0$ cm, and there was no gross evidence of capsule formation. A total of 14 lymph nodes were also removed. Microscopically, the tumor consisted of solid

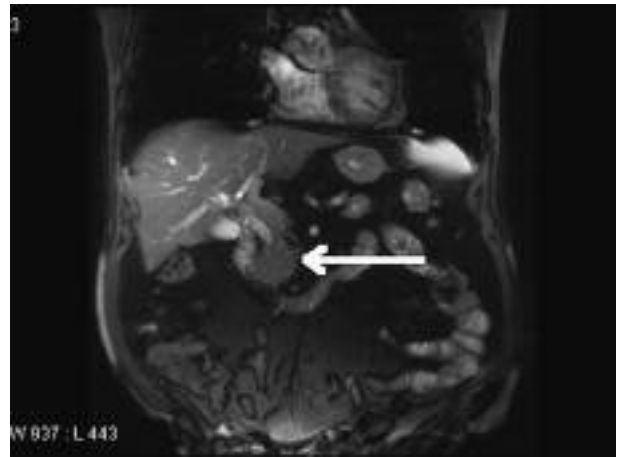


Fig. 3. — Magnetic resonance imaging (MRI).
Angio-Magnetic resonance imaging (Angio-MRI) five years after anterior resection of the colon carcinoma, demonstrated a solid inhomogeneous tumor in the head of pancreas without invasion of the mesenterico-portal vessels.

and glandular formations of atypical epithelial cells and areas of necrosis.

The histomorphological appearance was in good accordance with the primary colon adenocarcinoma or a primary adenocarcinoma of the pancreas (Fig. 5).

Immunohistochemical analysis demonstrated that the tumor stained positively with antibodies towards cytokeratins 19 and 20 (CK 19 and CK20), carcinoembryonic antigen (CEA), CAM 5.2, and CDX2 pathognomic for colon origin.

This marker pattern was considered to be that of a metastasis of the primary colon carcinoma.

Despite complete surgical resection, adjuvant chemotherapy with Capecitabine and Oxaliplatin was implemented to reduce the risk of recurrence.

Discussion

Recurrences of colo-rectal adenocarcinoma can include local, regional, and peripheral lymph nodes as well as metastasis in distant organs, such as the liver and the lung. Solitary metastases to the pancreas are considered to be extremely rare (Table 1a and b). To our knowledge only a few cases have been reported in the literature to date.

Solitary metastases to the pancreas may clinically mimic a primary neoplasm of the pancreas, and it is often difficult to distinguish them by radiological examination.

Only 1-2% of pancreatic cancers can be classified as secondary tumors to the pancreas (12-14). In a study by analyzing 690 autopsy cases with a tumor in the pancreas from another origin, a metastasis to pancreas was diagnosed in 15% of cases (5).

Metastases have been described for various non-hematologic neoplasms (1-6,8-17,31-110), such as renal-cell carcinoma (1-6,8-17,35,37-57,69,74,75,104-110),

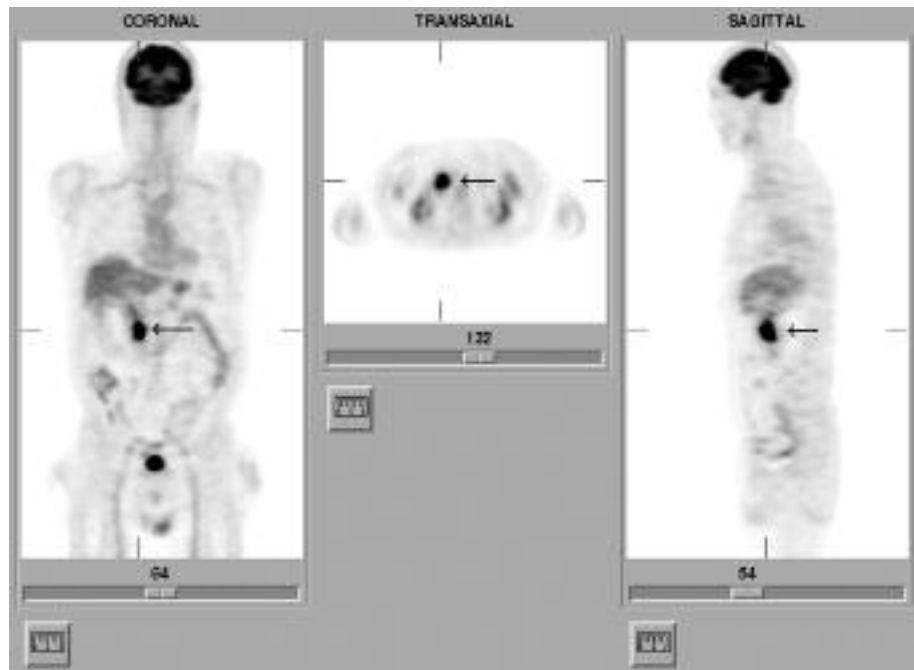


Fig. 4. — Positron Emission Tomography (PET).

Coronally, sagittally, and transaxially reconstructed PET-images on the basis of an iterative reconstruction algorithm using ordered-subset expectation maximization and segmented attenuation correction (final voxel size $4.2 \times 4.2 \times 4.2 \text{ mm}^3$).

Positron Emission Tomography (PET) revealed a solitary circumscribed area of pathologically elevated glucose uptake in the head of pancreas.

This lesion showed a moderate maximal SUV_{max} , being 16.2. No other abnormal sites were detected.

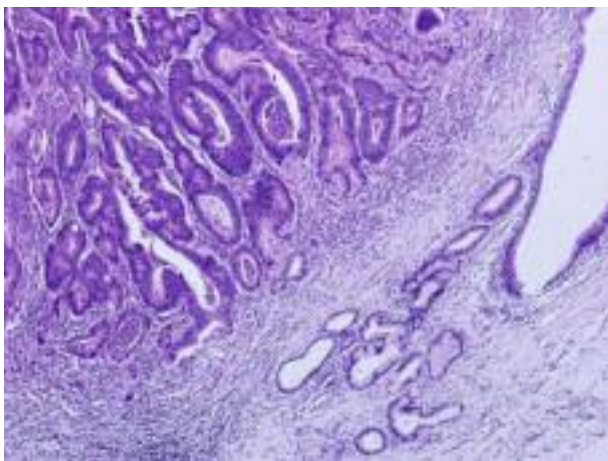


Fig. 5. — Histology.

Histomorphologic appearance of the pancreatic metastasis.

pulmonary small-cell carcinoma (4-6,60,75,85-87,90,91), melanoma (3,17,35,36,75,78,84), sarcoma (3,6,36,94, 96), gastric carcinoma (4,5,7,67,75), and colon carcinoma (4-6,13,15-18) (Table 1 and 2). Renal-cell carcinoma represents the most likely primary cancer for pancreatic metastases (1,2). In a great Japanese study the most primary tumor was gastric carcinoma (20%), followed by lung cancer (18%) and cancers of the extrahepatic bile duct (13%) (5). The range of latency from primary diagnosis and presentation of metastases to the

pancreas is wide. Metastases can occur after the initial tumor more than 20 years (9,10).

Inagaki H. *et al.* described an almost identical case of a 77-year-old man with a mass between the head and body of the pancreas 11 years after anterior resection for adenocarcinoma of the colon sigmoideum (19). The same patient had also metastasis to the lung from the primary colon carcinoma 8 years after initial surgery, for which the patient underwent resection of this metastasis.

In both cases with the sequence of metastasis being primarily to the lung, followed by one to the pancreas years later, it can only be speculated whether the pancreatic metastasis spread from the primary colon cancer or from the lung metastasis.

Metastases to the pancreas often do not cause any symptoms for a long time. Sometimes weight loss, abdominal pain, or jaundice will lead to the diagnosis.

Even it is possible that the symptoms of a pancreatic metastasis are the first sign of an occult primary tumor of another organ (20).

Clinical features, as well as CT-, MRI- and PET-findings in patients with pancreatic metastasis are similar to those of primary pancreatic cancer (21). Often metastases are initially misdiagnosed as primary pancreatic cancers. The diagnosis of metastasis should be considered when patients have a pancreatic mass and a history of non-pancreatic malignant lesions.

EUS with fine-needle aspiration (FNA) of the pancreas has become a useful investigation that allows the

Table 1a. — Pancreatic metastasis from colo-rectal cancer

Reference	Age	Sex	Primary tumor	Latency
Inagaki H., Nakao A., Ando N. <i>et al.</i> A case of solitary metastatic pancreatic cancer from rectal carcinoma : a case report. <i>Hepatogastroenterology</i> , 1998, 45 (24) : 2413-7.	79	male	rectum	131 months
Pereira-Lima J.C., Coral G.P., Bayer L.R. <i>et al.</i> Metastasis from colon carcinoma in the dorsal pancreas of a patient with pancreas divisum : report of a case. <i>Hepatogastroenterology</i> , 2000, 47 (32) : 554-5.	45	female	transverse colon	36 months
Tutton M.G., George M., Hill M.E. <i>et al.</i> Solitary pancreatic metastasis from a primary colonic tumor detected by PET scan : report of a case. <i>Dis. Colon Rectum</i> , 2001, 44 (2) : 288-90.	35	male	transverse colon	14 months
Torres-Villalobos G., Podgaetz E., Anthon F.J. <i>et al.</i> Single pancreatic metastasis from a previously resected carcinoma of the cecum : a case report. <i>Curr. Surg.</i> , 2004, 61(3) : 328-30.	86	female	coecum	8 months
Bachmann J., Michalski C.W., Bergmann F. <i>et al.</i> Metastasis of rectal adenocarcinoma to the pancreas. Two case reports and a review of the literature. <i>JOP</i> , 2007, 8 (2) : 214-22.	61 64	female female	rectum rectum	12 months 18 months

Table 1b. — Case-Series

Reference	Number of cases	Primary Tumors	Colon Carcinoma
Volmar KE, Vollmar RT, Jowell PS <i>et al.</i> Metastases in the pancreas from non-hematologic neoplasms : Report of 20 cases evaluated by fine-needle aspiration. <i>Diagn. Cytopathol.</i> , 2004, 31 : 216-20.	20	9 renal-cell carcinomas 3 melanomas 2 pulmonary small-cell carcinomas 2 breast carcinomas 1 prostate carcinoma 1 pulmonary squamous-cell-carcinoma and 1 GIST	1
Sperti C., Pasquali C., Liessi G. <i>et al.</i> Pancreatic resection for metastatic tumors to the pancreas. <i>J. Surg. Oncol.</i> , 2003, 83 (3) : 161-6.	8	2 renal-cell cancer 1 duodenal leiomyosarcoma 1 malignant fibrous histiocytoma	1
Charnsangavej C., Whitley N.O. Metastases to the pancreas and peripancreatic lymph nodes from carcinoma of the right side of the colon : CT findings in 12 patients. <i>Am. J. Roentgenol.</i> , 1993, 160 (1) : 49-52.	12	3 cecum 5 ascending colon 4 transverse colon	12
Crippa S., Angelini C., Mussi C. <i>et al.</i> Surgical treatment of metastatic tumors to the pancreas : a single experience and review of literature. <i>World J. Surg.</i> , 2006, 30 (8) : 1536-42.	13	5 renal-cell carcinoma 3 breast carcinoma 1 endometrioid carcinoma of the ovary 1 jejunal leiomyosarcoma 1 melanoma and 1 NSCLC	1
Pingpank J.F. Jr., Hoffman J.P., Sigurdson E.R. <i>et al.</i> Pancreatic resection for locally advanced primary and metastatic nonpancreatic neoplasms. <i>Am. Surg.</i> , 2002, 68 (4) : 337-40 ; discussion 340-1.	18	3 biliary carcinoma 3 sarcoma 2 melanoma 1 ovary and 1 unknown primary	8
Eidt S., Jergas M., Schmidt R. <i>et al.</i> Metastasis to the pancreas-an indication for pancreatic resection ? <i>Langenbecks Arch. Surg.</i> , 2007, 392 (5) : 539-42.	12	7 renal-cell carcinoma 4 malignant melanoma	1
DeWitt J., Jowell P., Leblanc J. <i>et al.</i> EUS-guided FNA of pancreatic metastases : a multicenter experience. <i>Gastrointest. Endosc.</i> , 2005, 61 (6) : 689-96.	24	10 renal-cell carcinoma 6 malignomas of the skin 4 lung cancer 1 liver cancer 1 stomach cancer	4

diagnosis of pancreatic masses with high sensitivity and specificity, especially when other modalities have failed (22-27). The diagnostic accuracy by EUS-FNA ranges from 84% to 95 (25). The cytopathological assessment should include cellularity, presence of loosely cohesive aggregates or single tumor cells, quality and quantity of cytoplasm, nuclear polymorphism, chro-

matin patterns, nucleous to cytoplasm ratio, necrosis and special stains (25,27). Histological diagnosis of pancreatic tumors can influence the choice of the best therapeutic approach (22-25,30).

Potential disadvantages could be the need for sedation, complications of the procedure and seeding of needle tract malignant cells.

Table 2. — Different primary non-hematological tumors yield to pancreas metastases

Primary Tumor	References
renal-cell carcinoma	1-6, 8-17, 35, 37-57, 69, 74, 75, 104-110
Gastric carcinoma	4, 5, 7, 67, 75
Esophageal cancer	74, 76
Liver cancer	4, 75, 76
Bile duct cancer	5, 36, 76
GIST	68
Small-lung cancer	4, 5, 6, 60, 75, 85, 86, 87, 90, 91
Squamous non-small-lung cancer	3, 5, 17, 88
Sarcoma	3, 6, 36, 94, 96
Leiomyosarcoma	93, 95
Leiomyosarcoma of the duodenum	15
Leiomyosarcoma of the jejunum	17
Sarcoma of the pulmonary artery	101
Cardic Rhabdomyosarcoma	97
Chondrosarcoma	99
Ewing sarcoma	98
Breast carcinoma	4, 6, 17, 20, 61-63, 74
Malignant phyllodes tumor of the breast	81
Endometrial carcinoma	6
Uterus carcinoma	4
Ovarian carcinoma	4, 36, 74
Endometrial carcinoma of the ovary	17
Ovarian leiomyosarcoma	72
Malignant mixed Mullerian tumor of the ovary	70
Uterine leiomyosarcoma	71
Prostate carcinoma	4
Seminoma	80
Transitional-cell carcinoma of the bladder	3, 5
Intracranial chondrosarcoma	100
Angioblastic Meningeom	79, 92
Melanoma	3, 17, 35, 36, 75, 78, 84
Thyroid	102, 103
Mesotheliomas	4
Malignant fibrous histiocytoma	15, 77
Merkel-cell carcinoma	4, 64-66
Pleuropulmonary blastoma	89
Salivary gland	74

FNA-related complications occurred in 1.1-5% (25,27). Life-threatening complications and minor complications such as self-limited bleeding or abdominal pain have been described (25-27). A bleeding can make a resection later technically more difficult. The risk of bleeding from greater vessels should be limited by using Doppler-technique.

The risks of tumor-cell dissemination is discussed controversially in the literature, peritoneal carcinomatosis or tumor-cell dissemination have been described (29,31). The EUS-FNA through the duodenum is theoretically without any risk of transperitoneal seeding, because the needle tract will be removed with the surgical specimen (27). In patients with resectable lesions of the pancreatic head or tail, the risk/benefit ratio of EUS-FNA should be carefully considered (27). Moreover, there is a lower risk of neoplastic seeding in

patients undergoing EUS-FNA when compared to percutaneous (31).

In our case, we saw no indication for an EUS with or without FNA. The results of these diagnostic tools would have had no influence on the therapeutic approach.

The diagnostic procedure revealed a solitary circumscribed mass in the pancreatic head with a diameter of 1.8 cm without lymph-node invasion or metastasis in other organs. The results of CT and MRT described a typically tumor highly suspicious for malignancy. The high Standard Uptake Value of 16.2 in the PET suggested a malignant lesion. Therefore the indication for a resection of the tumor was indicated in a patient without any other comorbidities and a good health status.

We think that indications for EUS-FNA are given, if

1. all other diagnostic measures for establishing the diagnosis of a tumor of the pancreas have failed (22-24)
2. the pathological examination demonstrates certain markers or gene mutations that are needed for the initiation of special treatments, e.g. EGFR-Cetuximab (22)
3. the results of the biopsies have an influence on the therapy (25,30)
4. the results of the biopsies avoid or minimize surgery (28)
5. it is used in the loco-regional staging of pancreatic tumors (27).

Positron Emission Tomography (PET) detected an unusual side of metastasis from colon carcinoma. The solitary circumscribed area of pathologically elevated glucose uptake had a maximal SUV_{max} (Standard Uptake Value) of 16.2, which was high suspicious for a malignant tumor. We agree to Tutton *et al.* (22), that PET could be an important diagnostic tool in the follow-up of patients with colorectal cancer.

Pancreatic resection for metastases can be performed with low morbidity and mortality rates (22,23), comparable to those of primary pancreatic cancers, especially in high-volume centers. Radical resection may prolong survival in patients if the pancreas is the only locus for metastasis at the time of diagnosis (3,6,15,17).

In prospective series of patients resected for pancreatic metastasis the survival averaged 22-23 months with a range of 14-42 months (6,15). The overall 2- and 5-year survival rates were 62% and 25% (3). In three retrospective analyses the median survival was 26-56 months with a range of 5-105 months (17,25,26).

This interesting case and the review of the literature indicate the necessity of surgical exploration of a pancreatic tumor of unknown origin.

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