

SOLITARY METASTASIS TO THE PANCREAS FROM COLON CANCER TREATED WITH RADICAL SURGERY: A CASE REPORT AND LITERATURE REVIEW

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This report describes a rare case of pancreatic metastasis in a 56-year-old woman with a past medical history of malignancy. The patient initially presented with right breast cancer in 2008, which was treated with a modified radical mastectomy followed by adjuvant chemotherapy. Subsequently, she developed right colon cancer and underwent a right hemicolectomy with adjuvant chemotherapy in 2015. In October 2020, during a routine examination, a suspicious lesion was identified in the duodenum and head of the pancreas. A biopsy confirmed the presence of moderately differentiated adenocarcinoma. Following a comprehensive multidisciplinary consultation, the patient was recommended for exploratory surgery to assess the feasibility of a pancreatoduodenectomy (Whipple procedure) with subsequent ileocolic reanastomosis (reconnection of the ileum to the transverse colon), followed by systemic therapy.

Keywords: Metastasis, colon cancer, pancreatoduodenectomy, ileocolic reanastomosis.

I. INTRODUCTION

Pancreatic metastases are uncommon.¹ According to a large autopsy series, the incidence of pancreatic metastasis ranges from 6 to 11%.² Primary lesions often originate from the kidneys, lungs, breasts, and gastrointestinal tract (stomach, small intestine, and colorectum).³ Reports of solitary pancreatic metastasis after resected colorectal cancer are rare.⁴ While many studies have concluded that colorectal cancer with liver metastasis and lung metastasis treated with radical surgery achieved survival benefits, the role of surgery for pancreatic tumors secondary to colon cancer remains controversial.^{4,5}

II. CASE PRESENTATION

The patient was a 56-year-old female

with a past medical history of right breast cancer in 2008 (stage pT1N0M0, histologic type of invasive ductal carcinoma grade 2, treated with modified radical mastectomy and adjuvant chemotherapy) and right colon cancer in 2015 (stage pT4N0M0, histologic type of adenocarcinoma, treated with right hemicolectomy and adjuvant chemotherapy). In October 2020, on her examination, a suspicious lesion in the duodenum and the head of the pancreas was discovered. Upon admission, she weighed 54 kg, had a height of 152 cm, and had an Eastern Cooperative Oncology Group (ECOG) PS 0. She reported no pain or fever; on examination, her abdomen exhibited softness without any reactive responses.

The hemoglobin level was mildly decreased at 96 g/l. The number of white blood cells (4.08 G/l) and platelets (188 G/l) were in normal ranges. The total bilirubin (20.9 μ mol/l), direct bilirubin (8.8 μ mol/l), albumin (34 g/l), and amylase (48 U/l) were also normal. Among the tumor markers, the level of CA 19-9 (59,16 U/

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ml) was elevated, while the levels of CEA (4.53 ng/ml) and CA 15-3 (12.57 U/ml) were within the average limits.

The gastroduodenal endoscopy showed the presence of an ulcerated oozing lesion in the duodenum with a rough surface extending across the entire posterior wall. The lesion was biopsied with pathology result of moderately differentiated adenocarcinoma. When viewed through colonoscopy, the anastomosis was smooth, and no lesions were seen in the remaining colorectal lumen. CT scans showed a hypoattenuating mass in the head of the pancreas, which became hyperdense in contrast scans, invading the duodenum, with the size of 22x23mm, and a 19mm lymph node in the liver hilum. There was also a 15x18mm nodule in the subsegment VII of the liver, with hemangioma characteristics. On PET-CT scans, three tissue-density nodules in the head of the pancreas with increased FDG uptake were found, and no other abnormal lesions were detected. After a thorough

multidisciplinary consultation, exploratory surgery was recommended to assess the possibility of pancreaticoduodenectomy or palliative surgery. The patient agreed to that approach and was scheduled for surgery on October 27, 2020.

The patient underwent a 5-hour surgery, including the removal of the head of the pancreas, duodenum, gallbladder, previous ileocolic anastomosis, lymph nodes dissection, and the establishment of connections between the pancreas and intestines (pancreaticojejunostomy), bile duct and intestines (choledochojejunostomy), stomach and intestines on a jejunal loop (gastrojejunostomy), and the re-connection of the ileum to the transverse colon (ileocolic reanastomosis). This operation was performed by an expert surgeon. There was no need for a blood transfusion during the surgery. After 20 hours in the Intensive Care Department, the patient was transferred to the treatment department in stable condition.



Figure 1. Postoperative specimens

Postoperative pathology results revealed adenocarcinoma of the pancreatic head mass, suspected to be of colon origin, adenocarcinoma

in 3 out of 12 lymph nodes, and no abnormal findings in other specimens.

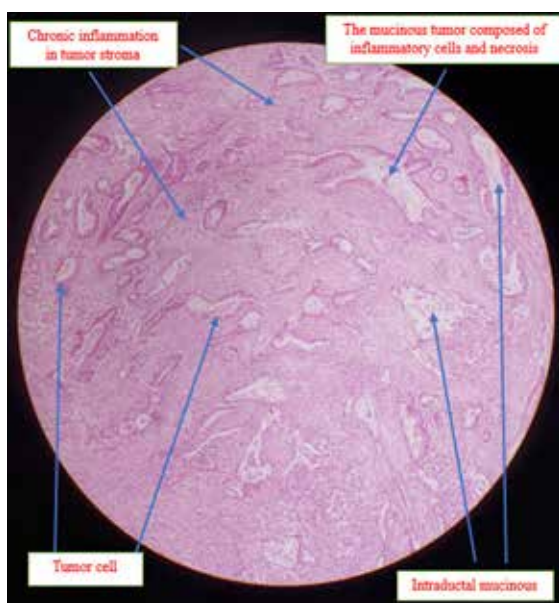


Figure 2. Postoperative pathological image

III. DISCUSSION

1. Overview of pancreatic metastases

Pancreatic metastases are rare, accounting for only 2% of pancreatic malignancies.⁶ According to a large autopsy series, the incidence of pancreatic metastasis was reported to be from 6 to 11%.⁷ People over 60 years old have a higher risk of developing a cancer that metastasizes to the pancreas. However, the two genders have no difference in incidence.⁸ According to many studies in Europe and America, renal cell carcinoma is the most common primary cancer of pancreatic metastasis.^{8,9} However, in Asian countries, lung cancer (microscopic cell lung cancer) is the most prevailing initial lesion that metastasizes to the pancreas, followed by stomach cancer and colon cancer. In contrast, the rate of pancreatic metastases originating from renal cell carcinoma is meager.¹⁰ The high incidence of lung cancer, microscopic cell lung cancer, in Asian countries leads to an increased rate of metastases to other organs, including

pancreatic metastases in this type of cancer. Therefore, the proportion of different cancers in each region may partly affect the rate of primary extrapancreatic cancers that metastasize to the pancreas.

2. Pancreatic metastasis from colon cancer

Sperti and colleagues published many vital reports on pancreatectomy due to cancer from 1980 to 2006. Postoperative pathology results revealed that only 3.3% of lesions were secondary, and 50% of them were metastases from colorectal cancer.⁵ Pancreatic cancer secondary to colon cancer is primarily a solitary tumor. Most cases are metachronous, while synchronous metastases are less common.⁵ Secondary cancers in the pancreas are mainly located in the head and body.¹¹ According to many studies, cases of colon cancer with pancreatic metastasis are often classified as pT3N0/1.^{4,12} Theories suggest that colon cancer frequently metastasizes to the pancreas through the following mechanisms: lymphatic metastasis, blood metastasis, and peritoneal metastasis. No relationship has been demonstrated between the initial stage of primary colon cancer and the means of metastasis to the pancreas. Torres-Villalobos and colleagues hypothesized that cancer cells originating from the cecal tumor with involved lymph nodes might spread through lymphatic vessels along the ileocolic artery.¹² However, some other authors present cases of pancreatic metastases from primary colon cancer without regional lymph node metastases (N0). Similarly, in our case, the pathology results after the colectomy revealed no lymph node metastases (N0).

Recurrence in the pancreas usually occurs between the second year and the third year after primary tumor treatment. This period is considered relatively short compared to renal metastases secondary to colon cancer,

which has been reported to appear 11 years after colon cancer treatment.¹¹ In our case, pancreatic recurrence was detected five years after colectomy.

3. Diagnosis

Previous medical history plays a vital role in diagnosing the disease. Our patient has a history of right breast cancer in 2008 (stage pT1N0M0, histologic type of invasive ductal carcinoma grade 2, treated with modified radical mastectomy and adjuvant chemotherapy) and right colon cancer in 2015 (stage pT4N0M0, histologic type of adenocarcinoma, treated with right hemicolectomy and adjuvant chemotherapy). The detection of lesions in the head of the pancreas in October 2020 raised two questions: is the tumor primary pancreas cancer, or is it a metastasis? If it is secondary, did it originate from breast cancer or colon cancer?

Secondary cancer in the pancreas is often asymptomatic and detected during routine follow-up examinations, but sometimes, jaundice or epigastric pain may be reported.¹³ In our case, the disease was discovered without any clinical symptoms.

Regarding cancer markers, CA 19–9 is not elevated in most cases, while CEA may be slightly elevated.⁴ In our case, no increase in tumor markers was recorded before the pancreatic tumor was detected.

According to the study of Shao. W.S. et al.,¹⁰ ultrasound was performed for 19 patients, and the most familiar images of pancreatic metastasis were homogeneous or heterogeneous hypoechoic masses with clear boundaries and slightly dilated pancreatic ducts.

CT scans cannot distinguish whether pancreas lesions are primary or secondary. In the case of a tumor with central necrosis, central hypoattenuating images can differentiate it

from normal pancreatic parenchyma.⁴ In our case, the mass in the head of the pancreas was hypodense with unclear boundaries and became averagely hyperdense in contrast scans, according to Shao. W.S. CT scans were performed for 18 patients, and most of the lesions in the pancreas showed a reduced density compared to normal pancreatic parenchyma.¹⁰

MRI scans often show images of hypointense or isointense lesions on T1WI and hyperintense on T2WI, and the signals are generally heterogeneous. The pancreatic duct is sometimes slightly dilated, or the tumor invades adjacent vessels.

PET–CT contributes to detecting secondary lesions in and outside the pancreas and can identify primary cancer,¹¹ playing an essential role in choosing appropriate treatment methods. Because our patient had a history of surgery for both breast cancer and colon cancer, a PET–CT scan was especially helpful in diagnosing and detecting secondary lesions. The results revealed three tissue-density nodules in the head of the pancreas with increased FDG uptake, and no abnormal FDG uptake was seen at the surgical sites of the right breast and the ileocolic junction.

Endoscopic ultrasound is beneficial for lesions in the pancreatic head, where it may reveal a hypoechoic mass relative to adjacent pancreatic tissue.¹⁴

Tissue diagnosis can be performed by fine needle aspiration guided by ultrasound, computed tomography, or endoscopic ultrasound. Fine needle aspiration under endoscopic ultrasound is considered a safe, minimally invasive method to diagnose secondary tumors in the duodenum and head of the pancreas.¹⁵ However, tumor biopsy by fine needle aspiration is not recommended

as a routine preoperative test because of the potential risk of peritoneal dissemination.³

In preoperative histopathology reports, adenocarcinoma is usually a tumor with a solid component. In contrast, tumors with a cystic component can be other lesions of the pancreas, such as serous cysts, mucinous adenomas, solid pseudopapillary tumors, or intraductal papillary mucinous tumors of the pancreas. However, the necessity of pre-treatment histopathological diagnosis of pancreatic tumors remains controversial. Some studies suggest that a negative biopsy result will not change the treatment, so all pancreatic lesions that appear after colorectal cancer treatment should be considered metastatic lesions. Meanwhile, some other authors believe that preoperative histopathological diagnosis can prove whether the tumor is malignant or benign, providing evidence to support doctors' treatment decisions. The risk of spreading cancer cells after a preoperative biopsy is minimal. According to the study of Moussa and colleagues,¹⁶ 12 out of 22 cases were diagnosed as secondary pancreatic cancer before treatment was selected. Our patient had a duodenal ulcer, which was biopsied before surgery via gastroduodenal endoscopy, with the result of moderately differentiated adenocarcinoma.

In cases where the pathology results are unclear, immunohistochemistry is often indicated. Secondary pancreatic cancers of colorectal origin often show positivity for CK20 and negativity for CK7, while primary pancreatic carcinomas are frequently positive for CK7. CK7 is positive in 92% of pancreatic carcinomas, compared with 5% of colorectal carcinomas.⁴ CK20 is always present in colorectal cells, while it is found in only 45 to 65% of pancreatic cells.¹⁷ However, immunohistochemistry is only

sometimes accurate, especially in preoperative tumor biopsy, as these specimens contain too few tumor cells or none in case of a wrong location biopsy.¹²

In the study by Sperti et al., one-third of patients had lymph node metastases, including hilar lymph nodes, lymph nodes around the pancreas, and the celiac artery.⁵ During Stoltz's study, no patient had lymph node metastasis.¹⁸ Postoperative pathology results of our patient revealed adenocarcinoma of the pancreatic head mass, suspected to be of colon origin, adenocarcinoma in 3 out of 12 lymph nodes, and no abnormal finding in other specimens, similar to the studies of other authors.¹⁰

4. Treatment

Surgery

Surgical options for patients with secondary pancreatic cancer remain a controversial issue. The fact that these patients are in the late stage with distant metastases raised the question about the role of surgery. Many recent studies have shown that radical surgery in these cases resulted in a longer survival time than other treatment methods, which has changed the perspective of many centers regarding the choice of surgery. However, all the studies were small and single-center, with few unified guidelines for treating secondary pancreatic cancer. A study by Reddy, Wolfgang, and colleagues published in *The Lancet* (2019)⁹ outlined five necessary criteria for selecting appropriate patients with secondary pancreatic cancer for radical surgery. First, primary cancer must have a good prognosis after surgery; second, local lesions of primary cancer must be well-controlled; third, secondary pancreatic tumors need to be proven solitary metastatic lesions; fourth, lesions in the pancreas do not invade adjacent vessels (resectable); and fifth, the patient must be able to tolerate the surgery.

However, invasion of the superior mesenteric vein is not a contraindication for surgery (borderline resection), so surgical options should also be considered for this group of patients in the Shao. W.S. study, all patients who received radical surgery had solitary metastases to the pancreas, with the primary cancer being well-controlled.¹⁰ Subsequent studies have not detected any signs of recurrence, and the patient's survival time is usually perfect. Currently, many studies indicate that radical surgery should be performed for patients with secondary pancreatic cancer.⁶ Regarding surgical methods, some authors have suggested that total pancreatectomy should be performed in these patients because secondary pancreatic lesions may have spread throughout the pancreas without being detected through preoperative workup. Contrary to this, numerous other authors contend that total pancreatectomy not only fails to confer any survival benefit but also elevates the incidence of postoperative complications (particularly postoperative diabetes) and mortality.¹⁹ Therefore, Bassi and colleagues performed partial pancreatectomy for these patients, but the local recurrence rate was high.²⁰ Our patient had lesions in the head of the pancreas and the duodenum. Therefore the multidisciplinary team unified to perform surgery, including the removal of the head of the pancreas, duodenum, gallbladder, lymph nodes, previous ileocolic anastomosis, and the establishment of connections between the pancreas and intestines (pancreaticojejunostomy), bile duct and intestines (choledochojejunostomy), stomach and intestines on a jejunal loop (gastrojejunostomy), and re-connection of transverse colon and intestines (ileocolic reanastomosis).

For cases where pancreatic tumors cannot be removed due to extensive invasion or distant

metastases detected during surgery, palliative surgical methods, including the Roux-en-Y choledochojejunostomy, gastrojejunostomy, and biliary stent placement, will be selected.¹⁰

In cases of secondary pancreatic tumors associated with lesions of other extrapancreatic organs (liver, kidney, stomach, etc.), the indication for radical surgery is still controversial.¹¹ For some authors, these cases are considered to have widespread metastases, preventing the indication of surgery.^{5,12} However, according to some other studies, radical surgery can be performed if all metastatic tumors can be simultaneously removed.¹¹

Common postoperative complications are pancreatic leak and bile leak. Studies have shown no difference in complication rates and mortality rates between radical surgery for multi-organ metastases and isolated pancreatic metastases secondary to colorectal cancer.¹¹

Systemic treatment

Multimodality treatment, including radiotherapy and chemotherapy, is selected for patients with unresectable secondary pancreatic cancer and cases with concurrent distant metastases of other organs.

On the other hand, some authors recommended postoperative adjuvant chemotherapy with the FOLFOX or FOLFIRI regimen even though the efficacy of these treatments is not high. According to Sperti et al.'s study, only one patient among seven who received adjuvant chemotherapy after surgery had good results.⁵ According to the study of Moussa and colleagues,¹⁶ radical surgery was performed in two cases, followed by treatment with postoperative adjuvant chemotherapy, even for cases with peritoneal metastases, in Shao. In W.S.'s study, one patient received chemotherapy alone, and seven received combined chemotherapy and radiotherapy.¹⁰

After surgery, our patient received adjuvant treatment with FOLFIRI and bevacizumab for six cycles.

Survival

Some studies suggested radical surgery increases survival time.²¹ In Shao. W.S.'s study found that the mean overall survival time after radical surgery for pancreatic metastases secondary to colon cancer was 27 months, which was longer compared to that of other primary cancers, such as gastric cancer. In Shao-Wei Song's study, the survival time of the radical surgery group was higher than that of the palliative surgery group. Of the five patients treated with radical surgery, one patient passed away 15 months after surgery, one patient was lost to follow-up, and three patients were living disease-free at the end of the study, with mean survival time of 18 months, while the mean survival time of the palliative surgery group was only 6.8 months.¹⁰

According to Sperti, the mean survival time of secondary pancreatic cancer from colon cancer was 39 months, and early recurrence after surgery often occurred in the liver.¹¹

Our patient is currently healthy, with no evidence of cancer recurrence 36 months after pancreaticoduodenectomy.

IV. CONCLUSION

Any pancreatic lesion that appears after the treatment of early-stage colorectal cancer should be suspected to be secondary. Pretreatment diagnosis is often based on tumor biopsy results through endoscopic ultrasound combined with immunohistochemistry, although the accuracy is not very high. PET-CT allows early detection of systemic metastases and plays an essential role in monitoring the progression of the disease. The choice of treatment depends on each specific patient. Radical surgery confers survival

benefits. Recurrences tend to appear early in many organs, especially the liver. Adjuvant chemotherapy after surgery for metastases has not been proven effective. Our case is isolated, and it requires further research to come up with the right approach, thereby choosing the appropriate treatment for pancreatic metastases secondary to colorectal cancer.

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