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ORIGINAL ARTICLE

Surgical resection of metastasis to the pancreas

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Purpose: Metastasis to the pancreas is rare, and the benefit of resection for pancreatic metastasis is poorly defined. The aim of this study was to review our experiences of the operative management of metastasis to the pancreas. **Methods:** Between 1995 and 2009, 11 patients (8 men and 3 women; median age, 54 years) were admitted to our institution with a metachronously metastatic lesion to the pancreas and later underwent pancreatic resection. The clinical features and outcomes of treatments were examined. **Results:** The primary cancers were renal cell carcinoma (RCC, n = 7), carcinoid tumor (n = 2), rectal cancer and leiomyosarcoma. Six patients underwent distal pancreatectosplenectomy, 3 pancreaticoduodenectomy and 2 patients underwent enucleation for small RCC. One patient died of metastatic RCC at 53 months after surgery and ten patients remain alive; four patients without disease at 7 to 69 months postoperatively, and the other six with disease at 11 to 68 months. Median postoperative survival of all patients was 34 months. **Conclusion:** Patients with a low surgical risk should be considered for pancreatic metastasectomy if curative resection is possible. Primary cancer type, which is associated with survival benefit, would be the best candidate for surgical resection of metastases to the pancreas.

Key Words: Pancreatic metastasis, Pancreatic metastasectomy, Metastatic pancreatic cancer

INTRODUCTION

The vast majority of pancreatic tumors are primary, and metastatic tumors of the pancreas are rare, although direct invasion from advanced cancers in neighboring organs is sometimes observed. Metastatic tumors in autopsy series have been reported in from 3% to 11% [1,2]. Furthermore, the majority of patients with pancreatic metastasis have widespread disease [3]. Metastatic disease to the pancreas has been only infrequently diagnosed in living patients. Furthermore, although surgical resection of metastatic lesions to the liver, lungs, and brain have been shown to improve survival and quality of life, the optimal management of pancreatic metastasis has not been clearly delineated. However, over the past few years, morbidity and mortality improvements after surgical resection of the pancreas have enabled patients with metastatic disease to be treated with radical intent [4,5]. Here, we report our experiences of eleven patients who underwent pancreatic resection for metastasis to the pancreas.

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METHODS

Between January 1995 and March 2009, 11 patients underwent pancreatic resection for a metastatic tumor to the pancreas at the Samsung Medical Center, Sungkyunkwan University School of Medicine. During the same period, 1,181 pancreaticoduodenectomies, 73 total pancreatectomies and 317 distal pancreatectomies, were performed for various pancreatic diseases. We excluded patients who underwent pancreatic resection because of direct involvement of the gland by other abdominal tumors. All patients had a metachronous lesion and the pancreas was a site of metastasis at the time of resection. Primary tumors were reviewed to confirm diagnoses and to identify possible correlations with cancer type. Standard operative procedures were adopted for resectable tumors: pylorus-preserving pancreaticoduodenectomy for tumors in the head, and distal pancreatosplenectomy for tumors in the body or tail. Primary tumor histologies and treatments, times between primary operations and metastasis diagnoses, presenting symptoms, diagnostic tools, surgical treatments, and perioperative morbidities and mortalities were evaluated, by conducting a retrospective review of medical records and by contacting patients directly.

RESULTS

Median patient age was 54 years (range, 35 to 75 years), and 8 men and 3 women were included in the study. Of these 11 patients, 7 patients had been previously treated for renal cell carcinoma (RCC), 2 for a carcinoid tumor, 1 for rectal adenocarcinoma, and 1 for leiomyosarcoma of the lower extremity. Details of clinical findings are summarized in Table 1.

The median time between primary surgery and a diagnosis of pancreatic metastasis was 51 months (range, 14 to 180 months). Nine patients were asymptomatic and metastatic lesions were discovered during follow-up. The symptomatic 2 patients experienced neck mass and dizziness 180, 118 months after nephrectomy for RCC, respectively. The patient with neck mass had 4.8 cm enhancing mass and the other patient had a 5.3 cm heterogeneously enhancing mass with an internal ill-defined low-density area in the pancreatic tail by computed tomography (CT). Of all patients, CT scans revealed a heterogeneously enhancing pancreatic mass in 9 patients (7 RCC and 2 carcinoid metastases) and a low density lesion in the remaining patients (rectal cancer and metastasis from leiomyosarcoma, respectively).

Two patients with carcinoid metastasis underwent 18-fluorodeoxyglucose positron emission tomography (FDG PET) and achieved a positive finding. One patient showed another region of increased focal uptakes by 18-FDG in the pancreatic head and uncinate process, which were not detected by CT, but which were confirmed by endoscopic ultrasonography.

Three patients showed evidence of concurrent ex-

Table 1. Clinical findings of eleven patients with metastasis to the pancreas

Patients	Age (yr)	Sex	Diagnosis	Primary treatment	Intervals between primary tumor and metastases (mo)	Symptoms	Site	No. of tumors	Extrapancreatic disease
1	59	M	Renal cell carcinoma	Nephrectomy	180	Neck mass	Tail	Multiple	Thyroid
2	75	M	Renal cell carcinoma	Nephrectomy	118	Dizziness	Tail	Solitary	–
3	66	M	Renal cell carcinoma	Nephrectomy	99	Asymptomatic	Head	Solitary	–
4	56	M	Renal cell carcinoma	Partial nephrectomy	64	Asymptomatic	Body	Multiple	Local recur
5	66	F	Renal cell carcinoma	Nephrectomy	14	Asymptomatic	Tail	Solitary	–
6	54	M	Renal cell carcinoma	Nephrectomy	31	Asymptomatic	Body	Solitary	–
7	51	M	Renal cell carcinoma	Nephrectomy	46	Asymptomatic	Head, body	Solitary	–
8	35	M	Carcinoid tumor	Thymectomy	108	Asymptomatic	Head, body	Multiple	Mediastinum
9	48	F	Carcinoid tumor	Right hemihepatectomy	51	Asymptomatic	Body	Solitary	–
10	41	M	Rectal cancer	Low anterior resection	14	Asymptomatic	Tail	Solitary	–
11	49	F	Leiomyosarcoma	Wide excision	50	Asymptomatic	Head	Solitary	–

trapancreatic disease (2 RCC and 1 carcinoid). The patient with carcinoid tumor had a mass about 10 × 6 cm in the anterior mediastinum. Percutaneous fine needle biopsies of the mediastinal and pancreatic masses were performed and returned a diagnosis of metastatic carcinoid. The one patient with RCC, who had previously undergone partial nephrectomy for right RCC, had 2 metastatic lesions, in the posterior of pancreatic body and in the tail of the pancreas, respectively, according preoperative imaging studies. After exploration, however, the mass in the posterior of pancreatic body was found to be extrapancreatic. The other patient with RCC visited other hospital due to neck mass and underwent unilateral thyroidectomy, which pathologic diagnosis was clear cell carcinoma from RCC. After referral to our institution and work up for systemic spread of RCC, another lesion was detected in the tail of the pancreas by CT. These 3 patients underwent surgical resection for multiple metastases due to the treatment principle of the primary tumor with metastatic lesion.

Before surgery, 8 of the 11 patients had a high clinical suspicion of a metastatic lesion. In the other three patients with RCC, rectal cancer, and leiomyosarcoma, metastatic tumors were initially misdiagnosed as pancreatic endocrine tumor, primary pancreatic carcinoma and cystic tumor, respectively. One patient with rectal cancer received concurrent chemoradiotherapy after primary surgery, and one patient with leiomyosarcoma in the right inguinal area underwent radiotherapy due to a positive resection margin after wide excision.

In 9 patients, tumors were resected with curative intent and enucleation was performed in 2 patients because metastatic tumor was small and exophytic. Pancreaticoduodenectomy was performed in three patients including total pancreatectomy, and distal pancreatosplenectomy was performed in the other 6. In the patient with a mediastinal mass, wide excision of the tumor was combined with pancreatic resection. There was no perioperative death. Postoperative complications occurred in 3 patients: two experienced a postoperative pancreatic fistula (POPF) of grade A and B, as defined by the International Study Group of Pancreatic Surgery, and the other POPF of grade B and an intra-abdominal abscess. The former resolved with conservative treatment and the latter was treated with percutaneous drainage. In all 11 cases, pancreatic metastases had the same histopathologic features as primary tumors; median tumor size was 3.2 cm (range, 0.9 to 8.5 cm).

One patient died of metastatic RCC at 53 months postoperatively. Ten patients remain alive: four patients with a disease-free status at 7 to 69 months postoperatively, and the other six with disease at 11 to 68 months (Table 2). Median postoperative survival of 11 patients who all underwent surgery for metastatic pancreatic lesions was 34 months (range, 7 to 69 months).

Table 2. Surgical treatment and follow-up survivals

Patients	Preoperative diagnosis	Operation	Associated procedure	Tumor size (cm)	Adjuvant therapy	Follow-up	Status	Survival (mo)
1	Metastasis	Distal pancreatectomy	Thyroidectomy	4.8	Immunotherapy	Brain metastasis	Alive	68
2	Pancreatic endocrine tumor	Distal pancreatectomy	–	5.0	–	Lung metastasis	Dead	53
3	Metastasis	PPPD	–	3.2	–	Liver, lung metastasis	Alive	12
4	Metastasis	Distal pancreatectomy	Wide excision	3.0	–	Right adrenal, lung metastasis	Alive	32
5	Metastasis	Distal pancreatectomy	–	4.0	Immunotherapy	Lung metastasis	Alive	34
6	Metastasis	Enucleation	–	0.9	Chemotherapy	Disease free	Alive	7
7	Metastasis	Enucleation	–	1.3	Immunotherapy	Disease free	Alive	69
8	Metastasis	Total pancreatectomy	Mediastinal mass excision	8.5	–	Local recurrence	Alive	11
9	Metastasis	Distal pancreatectomy	–	1.5	–	Disease free	Alive	12
10	Pancreatic cancer	Distal pancreatectomy	–	2.2	–	Disease free	Alive	30
11	Cystic tumor	PPPD	–	4.0	Radiotherapy	Lung metastasis	Alive	21

PPPD, pylorus-preserving pancreaticoduodenectomy.

DISCUSSION

Metastatic lesions to the pancreas are uncommon, and account for less than 2% of all pancreatic malignancies. The tumors that metastasize most frequently to the pancreas are renal cell carcinoma, melanomas, sarcoma, and colon, lung, and breast cancer [1,2,6]. Although pancreatic metastasis is rare, high volume centers will encounter patients with resectable metastatic disease. Reddy et al. [7] reported on 49 patients that underwent pancreatic resection for metastases from 1970 to 2007, which is the largest single institutional series on pancreatic resection for metastatic nonpancreatic cancers. At our center, 11 (0.7%) of 1,571 pancreatic resections were performed for metastatic tumors of the pancreas, which appears to be low compared with other series [1,2,5,8]. The symptoms of pancreatic metastases are frequently non-specific and subtle, therefore pancreatic metastases are often found during regular surveillance imaging for primary cancers. Reddy et al. [7] reported that 45 of 49 patients (92%) had symptoms of abdominal pain, jaundice, weight loss, whereas another study reported that 6 of 13 patients (46%) were asymptomatic [2]. In our series, 9 of 11 patients (82%) were asymptomatic.

The preoperative differential diagnosis between a primary pancreatic neoplasm and a metastatic tumor may be problematic. Palmowski et al. [9] showed that unlike pancreatic adenocarcinoma, secondary pancreatic cancers usually show arterial phase enhancement on contrast- enhanced CT scans. Furthermore, unlike pancreatic adenocarcinoma, metastatic pancreatic lesions from RCC, colorectal cancer, and breast cancer tend to be rim-enhanced. In the present study, 9 metastatic lesions from 7 RCC and 2 carcinoid tumor were rim-enhanced or heterogeneously enhanced, whereas the other 2 lesions from rectal cancer and leiomyosarcoma were not. Furthermore, in order to avoid major surgery, accurate preoperative staging must be done in patients with widespread disease [3,4,10,11], and 18-FDG-PET has proven to be useful in this context [5,12]. Our patient with a metastatic carcinoid tumor in the mediastinum and pancreas was found to have two other lesions by 18-FDG-PET, which were not detected by CT, but which were finally confirmed by endoscopic ultrasonography. Percutaneous and endoscopic fine-needle biopsies may help establish a pathological diagnosis when a metastatic tumor is not amenable to surgery, but may be treated with chemotherapy.

The time between diagnosis of primary cancer and the detection of pancreatic metastasis varies widely, and in particular, renal cell cancers are associated with a prolonged disease-free interval [4,6,13]. In the present study, the median time between primary disease and metastasis diagnoses for the renal cell cancer patients was 64 months (range, 14 to 180 months), and for the other patients was 50.5 months (range, 14 to 180 months).

Surgical resection of metastatic tumors to the pancreas should be approached by carefully applying appropriate selection criteria, because of the substantial morbidity associated with pancreatic resection and the questionable benefit of resection for pancreatic metastasis. Reddy and Wolfgang [14] in a systemic review of the literature, evaluated 243 patients who had undergone radical pancreatic resection for metastatic disease, and concluded that the effectiveness of pancreatic resection for metastatic tumor is dependent on the tumor biology of the primary cancer. RCC was found to be associated with best outcome, whereas lung cancer predicted the worst. Of their 243 patients, 193 (80%) had RCC, 19 colon cancer, 12 melanoma, and 12 sarcoma: median survivals and 5-year survival rates of patients with metastatic RCC were 8.75 years and 66%; those of patients with metastatic colorectal cancer were 54 months and 27%; those of patients with metastatic sarcoma 40 months and 14% and median survival of patients with metastatic melanoma 14 months. We could not estimate 5-year survival in our cohort because there were only 11 patients. Reddy and Wolfgang [14] also suggested criteria for patient selection, namely, a primary cancer type associated with a good outcome, control at the primary cancer site, isolated metastases, resectability of metastasis, and the patient's ability to tolerate pancreatic resection. Though 2 patients with RCC and one patient with carcinoid had a extrapancreatic disease in the present study, metastasectomy was performed and these 3 patients were alive at the end of the study. It is difficult to conclude that surgical resection of multiple metastasis will provide survival benefit. It may be reasonable to follow the treatment

principle of the primary tumor when multiple metastasis was recognized.

Originally, radical nephrectomy was the gold standard for RCC without metastasis. However, the increase in small renal tumors incidentally found at earlier stages has lead to organ preserving surgery which been more frequently preferred to radical nephrectomy for tumors less than 4 cm in diameter and limited to the kidney. For smaller tumors (< 2 cm in diameter), simple enucleation, dissecting around the pseudocapsule of the tumor, can be applied [15]. Similarly, we assumed that the biology of primary tumor would be same as if metastasis is solitary and the size is small. Therefore, metastatic RCC to the pancreas less than 2 cm in diameter that was not close to a main pancreatic duct can be a good indication for organ preserving pancreatectomy such as enucleation. In our series, 2 patients with metastatic RCC smaller than 2 cm underwent enucleation and has been disease-free status at 7, 69 months postoperatively. However, further studies in organ preserving pancreatectomy for small metastatic RCC are necessary.

Since our study has the limitation of small sample size, heterogeneity of the primary tumor, some combination of adjuvant therapy and retrospective design, it might be difficult that surgical resection of pancreatic metastases would provide survival benefit. Additional follow up of our cohort and more experience of surgical resection for pancreatic metastasis would clarify these limits.

In conclusion, patients with a low surgical risk should be considered for pancreatic metastasectomy if curative resection is possible. Careful selection of patients undergoing pancreatic resection for metastatic disease should be based on the primary cancer type which is associated with survival benefit after metastasectomy.

CONFLICTS OF INTEREST

No potential conflict of interest relevant to this article was reported.

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