Successful Retreatment With Chemoradiotherapy for Local Recurrence of Pancreatic Adenocarcinoma After Neoadjuvant Therapy and Pancreaticoduodenectomy

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CASE REPORT
A 68-year-old man with a history of diabetes and alcohol abuse presented with constitutional symptoms and obstructive jaundice in April 2009. Endoscopic ultrasound (EUS) demonstrated a 3.2 × 2-cm mass in the head of the pancreas, abutting the portal vein and encasing the common bile duct. A biopsy was positive for adenocarcinoma, and the tumor was judged to be borderline resectable. The patient was treated with neoadjuvant docetaxel and gemcitabine for 3 cycles, followed by twice-weekly gemcitabine 50 mg/m² and external beam radiotherapy (total dose, 54 Gy by intensity-modulated radiation therapy [IMRT], per Pipas et al.¹ Treatment induced a −25% reduction in tumor size at restaging, despite an initial delay and dose reductions related to prolonged elevation in results of liver function studies after biliary stenting. In November 2009, the patient underwent pancreaticoduodenectomy. Pathology revealed an invasive, poorly differentiated pancreatic adenocarcinoma with treatment-related change. Surgical margins and 22 lymph nodes were negative for tumor. The postoperative course was complicated by a 6-week hospital stay for ascites and poor wound healing, due to previously unrecognized alcoholic cirrhosis. The patient eventually made a full recovery and returned to work, but in June 2010, he presented for a surveillance abdominal computed tomographic (CT) scan that showed an irregularity in the pancreatic remnant (Figure 1). A repeat EUS demonstrated a 3-cm pancreatic tail mass that encased splenic vessels, and adenocarcinoma was confirmed by biopsy. Comparison with the prior tumor by light microscopy and immunohistochemistry revealed the specimens to be identical. In addition, massively parallel sequencing of a 50-gene cancer hotspot panel in DNA extracted from both tumors revealed a single PIK3CA polymorphism that was the same in each, thus confirming that the lesion represented recurrent tumor and not a second primary. The patient was not a candidate for completion pancreatectomy because of the cirrhosis. His case was presented at our interdisciplinary GI tumor board, and he was retreated with twice-weekly gemcitabine 50 mg/m², concurrent with radiotherapy in nonoverlapping fields. He received 45 Gy with 3-D conformal planning. The previous radiation plan was fused to avoid overdosing of critical structures. Conformal planning was chosen over IMRT to avoid radiation dose spillage into the previously treated tumor bed (Figure 2). The patient completed chemoradiotherapy (CRT) in September 2010 with a 50% reduction in tumor size and normalization of CA 19-9. Three of 12 planned doses of gemcitabine were cancelled for thrombocytopenia and/or diarrhea. Treatment was well tolerated, except for some weight loss and depression, which was managed with mirtazapine. Re-resection was considered, but the cirrhosis was thought to pose too great a surgical risk. The patient was subsequently followed up for recurrence with twice-yearly CT scans. The most recent scan demonstrated stable 1.5-cm hypodensity in the tail of the pancreas, with no evidence of progression or metastases (Figure 3), and CA 19-9 was 24 U/mL (normal, <34.9 U/mL). The patient remained alive and free of disease progression 48 months from the time of initial diagnosis and 34 months from the time of recurrence.

DISCUSSION
Despite advances in treatment, pancreatic adenocarcinoma carries a dismal prognosis. Surgery remains the only potentially curative treatment, but postresection recurrence rates range from 35% to 86%.² Therapy for recurrent disease is palliative, and survival is generally poor. Over the past decade, case reports have documented the outcome of re-resection for pancreatic remnant recurrence after partial pancreatectomy.³ – ⁷ These showed survival of 5 to 44 months after reoperation, with a median survival of 15.6 months.³ The use

Figure 1. Surveillance CT scan 7 months after pancreaticoduodenectomy, demonstrating tumor recurrence in the pancreatic remnant.
of adjuvant or neoadjuvant chemotherapy varies widely, and little mention is made of radiotherapy. These reports have prompted further investigation in larger retrospective series.

Strobel et al. reviewed re-resection of isolated local recurrence in 105 patients at a single institution, with 44% of the local recurrence being intrapancreatic and the remaining 56% involving the mesenteric axis (25%), paracaval or interaortocaval lymph nodes (20%), multiple viscera (7%), or celiac trunk (4%). Median overall survival after re-resection was 16.4 months; after R0 resection it was 30.5 months. The patients with confirmed recurrence received neoadjuvant or adjuvant chemotherapy or CRT. Notably, 9.1% of the patients who received neoadjuvant treatment had no viable tumor in the surgical specimen. In light of recent data demonstrating improved resectability with neoadjuvant CRT, it was postulated that CRT contributed to the overall success of re-resection in these patients.

Habermehl et al. evaluated the use of CRT to improve resectability of recurrence in 41 patients at a single institution. Both median overall survival and progression-free survival improved with the use of neoadjuvant CRT, with survival of 16.1 months overall and 28.3 months after successful re-resection. Neoadjuvant CRT allowed for resection in 12% of patients whose tumors were previously unresectable and induced a biopsy-proven complete remission in 15% of patients.

Wilkowski et al. published a retrospective study of 18 patients who received CRT for isolated local recurrence. Prior radiotherapy was an exclusion criterion, and only three patients had received adjuvant chemotherapy, yielding median progression-free survival of 14.7 months and median overall survival of 17.5 months, comparable to patients treated with CRT for initially unresectable tumors. The authors concluded that CRT can be as beneficial for isolated local recurrence as for initially unresectable disease.

In contrast to these studies, our case demonstrates prolonged survival with isolated local recurrence after pancreaticoduodenectomy followed by CRT alone. It is notable that this patient’s tumor was not deemed unresectable due to tumor characteristics, but rather because of comorbidity. However, given the biopsy-proven recurrence, survival of 34 months is significantly longer than that in most documented reports. This case illustrates that gemcitabine with radiotherapy is a treatment option for isolated local recurrence in select patients and that retreatment in nonoverlapping fields is feasible in those deemed not to be candidates for reoperation.

REFERENCES


Disclosures of Potential Conflicts of Interest

The authors indicated no potential conflicts of interest.