Case Report

Three Curative Pancreatectomies for the Metachronous Appearance of Pancreatic Invasive Ductal Adenocarcinoma

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Keywords

Repeated pancreatectomy · Pancreatic cancer · Local recurrence · Metachronous cancer

Abstract

We report a rare case of a patient who underwent 3 successful curative operations for the metachronous appearance of pancreatic cancer. In July 2007, a 54-year-old woman underwent pylorus-preserving pancreaticoduodenectomy. In March 2010, a tumor measuring 9 mm in diameter was detected in the tail of the pancreas on computed tomography (CT) and magnetic resonance imaging. The pancreas tail was subsequently resected while preserving the pancreatic body. In February 2011, CT revealed a cystic tumor measuring 2.5 cm in diameter in the remnant pancreatic body without any metastasis; therefore, total resection of the residual pancreas was performed in April 2011. The first resected tumor was histopathologically diagnosed as undifferentiated adenocarcinoma with osteoclast-like giant cells. Additionally, the third resected tumor had similar undifferentiated components. Contrarily, the second resected tumor was diagnosed as a well-differentiated tubular adenocarcinoma. We consider that the tumor from the third operation was an intra-pancreatic metastasis of the primary cancer and that the tumor from the second operation was the second primary cancer. The patient responded well with good control of surgical diabetes for 92 months since the last pancreatectomy. This case suggested that aggressive repeated resection for recurrent pancreatic invasive ductal adenocarcinoma is beneficial in limited cases.

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Introduction

Invasive ductal adenocarcinoma of the pancreas has a poor prognosis with a high rate of postoperative recurrences; therefore, only complete surgical resection is a possible cure [1, 2]. Treatment of recurrent pancreatic cancer remains difficult, although chemotherapy and irradiation have advanced [3]. Several reports on remnant pancreatectomy for recurrent or metachronous pancreatic cancer have been published [3–5]. Some authors report encouraging survival rates [6–8]; however, there is no consensus regarding the efficacy of surgical resection on recurrence or metachronous disease. In this study, we report a rare case of 3 successful curative pancreatectomies performed for isolated local recurrence and metachronous appearances of pancreatic adenocarcinoma.

Case Report

First Operation

A 53-year-old woman was admitted to our hospital in May 2008 with the chief complaint of epigastralgia. She was clinically diagnosed with pancreas head cancer concomitant with pancreatitis. After pancreatitis was cured, she was referred to the surgical division for operation, and pylorus-preserving pancreaticoduodenectomy was performed. The tumor was histopathologically diagnosed as anaplastic adenocarcinoma with osteoclast-like giant cells (Fig. 1A) and was classified as Stage 1 (pT1, pN0, M0) according to the UICC TNM classification [9]. The surgical margin was free from cancer cells, and no metastasis of the regional lymph node was noted. R0 resection was confirmed. A pancreatic intra-epithelial lesion (PanIN) was not identified in the specimen of the first resected tumor.

Fig. 1. Histopathologic findings of the resected specimen. **A** Specimen from the initial operation showed an aplastic carcinoma with osteoclast-like large cells. **B** Specimen from the second operation showed a well-differentiated tubular adenocarcinoma with glandular formation. **C** Specimen from the third operation showed an aplastic carcinoma similar to that of the initial operation.

Fig. 2. Images of the second operation. **A** Contrast-enhanced CT showing a small low-density lesion (10 mm in diameter) in the tail of the residual pancreas (arrow). **B** MRI showing small nodules in the tail of the pancreas (arrow), which had a low intensity on a T1-weighted image and iso-intensity on a T2-weighted image. The nodule was not enhanced by gadolinium EDTA.

Second Operation

The postoperative course was uneventful after the first operation, and adjuvant chemotherapy with gemcitabine (1,400 mg/body) was administered every 2 weeks for 36 courses. Subsequently, the titer of carbohydrate antigen 19-9 increased up to 70.4 ng/mL. Moreover, a small nodular lesion measuring 9 mm in diameter was observed in the tail of the residual pancreas on computed tomography (CT) (Fig. 2A) and magnetic resonance imaging (MRI) (Fig. 2B). ^{18}F -deoxyglucose positron emission tomography (FDG-PET) revealed a very small hot spot in the tail of the pancreas. In April 2010, we resected the pancreas tail while preserving the pancreas body and stomach. The second resected tumor was diagnosed as a well-differentiated tubular adenocarcinoma (Fig. 1B), T1, N0, M0, R0 Stage 1. The surgical margin was free from cancer cells, and no surrounding tissue invasion or regional lymph node metastasis was noted.

Third Operation

After the second operation (pancreas tail resection), the postoperative course was uneventful. The patient was followed up at the outpatient department without adjuvant chemotherapy according to patient self-determination. In February 2011, periodic CT showed a tumor measuring 2.5 cm in diameter with cystic components in the remaining pancreatic body (Fig. 3A) but with no distant metastasis or surrounding tissue invasion. The tumor intensity on MRI was iso and high on T1- and T2-weighted images, respectively (Fig. 3B). FDG-PET showed a hot spot in the body of the pancreas (Fig. 3C). We diagnosed it as a recurrent disease and performed total resection of the residual pancreas.

Pathological examination of the third tumor showed components of aplastic carcinoma similar to the microscopic findings of the specimen from the first operation (Fig. 1C). There were no continuous lesions in both ducts and parenchyma of the pancreas, and the surgical margin was free from tumor cells. The tumor was classified as Stage II with pT2, pN0, and M0. The postoperative course was uneventful, and the patient was discharged on the 39th postoperative day. The patient received adjuvant chemotherapy with gemcitabine for 3 years. After 92 months

Fig. 3. Images of the third operation. **A** CT scan during the third operation showing a tumor measuring 2.5 cm in diameter with cystic components in the remnant pancreatic body (arrow). **B** MRI after the third operation showing that the tumor had iso-intensity on a T1-weighted image and high intensity on a T2-weighted image (arrow). **C** FDG-PET showing a hot spot (arrow) in the body of the remnant pancreas.

since the last operation, she is doing well without any recurrent disease, and her insulin-deficient diabetes mellitus was stable with adequate administration of insulin preparation.

Discussion

The treatment of invasive ductal adenocarcinoma of the pancreas remains difficult, with a 5-year overall survival rate of <10% [1]. Complete resection of the tumor offers the only chance of cure for a patient with this disease [2]. Nevertheless, the resection rate is low, and the 5-year survival rate after curative resection is only 15–25%. The effectiveness of adjuvant chemotherapy combined with gemcitabine and 5-fluorouracil [10] or tegafur/gimeracil/oteracil potassium (TS-1[®], Taiho Pharma, Tokyo) [11] was recently reported, although the outcome of the treatment was not satisfactory.

The most frequent form of recurrence is liver metastasis followed by local and peritoneal recurrences, and the prognosis is approximately 3 and 7 months after the appearance of liver metastasis and local recurrences, respectively [12].

Currently, the combination of chemo-radiotherapy [13] and novel chemotherapy, such as FOLFIRINOX (leucovorin and fluorouracil plus irinotecan and oxaliplatin) [14], has improved the prognosis of unresectable pancreatic adenocarcinoma; however, the median survival time has increased only till 11 months.

Although there are few case reports on the repeated resection of the pancreas for recurrent cancer, most patients do not have long-term survival. Kleeff et al. [4] reported about 31 patients who underwent surgical resection for recurrent pancreatic carcinoma and concluded that re-resection did not have a positive effect on the overall survival. However, they suggested that a second resection may be potentially beneficial in patients aged <65 years with the disease recurring more than 9 months after the initial surgery.

Recently, some authors have reported the efficacy of aggressive surgery for metastatic pancreatic cancer [15] or recurrent pancreatic cancer in the remnant pancreas [12]. Miyazaki et al. [6] reported 11 cases of repeat pancreatectomy for isolated recurrence of pancreatic ductal cancer. The median survival in the resected group was longer than that in the unresected population (25.0 and 9.3 months, respectively). Strobel et al. [7] reported 55 cases of re-resection for isolated local recurrence of pancreatic cancer, including 24 cases of residual pancreatectomy, with a median survival was 26.0 months, and long-term survival was observed in 20% of the resected group. They concluded that repeated pancreatectomy for both local recurrence and new primary cancer in the pancreatic remnant could prolong survival. Although there were a few cases of 3 pancreatectomies reported in these studies, the patients rarely achieved long-term survival after the third pancreatectomy for recurrent pancreatic ductal adenocarcinoma.

It is not easy to distinguish local metastasis from metachronous de novo pancreatic cancer [8]. We regard the tumor from the second operation as a second primary cancer because the histological finding and location of the tumor were completely different from those of the tumors from the first and third operations. Contrarily, the tumor from the third operation seemed to be intra-pancreatic metastasis or intra-ductal dissemination of the primary tumor based on its histological similarity to the primary carcinoma of characteristic anaplastic adenocarcinoma. This was a curious case in which histologically different new primary lesions and recurrent tumor coexisted in the same patient.

Koizumi et al. [3] reported the usefulness of FDG-PET in detecting small solitary recurrence or metachronous pancreatic cancer in the remnant pancreas. This result is consistent with our case. Careful follow-up using FDG-PET allowed the early detection of the recurrent disease in the remaining pancreas.

The detailed operative procedure for remnant pancreatic cancer has not been established. While complete pancreatectomy was performed in most of the patients who underwent repeated pancreatectomy in the former study [7, 16], we preserved the pancreatic body at the second operation to maintain endocrine and exocrine functions of the pancreas and the quality of life of the patient. Therefore, we performed pancreas-preserving operation for the second tumor that was located in the distal portion of the pancreas tail, and the surgical margin was confirmed by intraoperative histopathologic examination of the frozen section. However, we had to remove the total residual pancreas in the third operation because of the size and location of the third tumor.

Conclusion

In summary, we report a rare case of 3 successful curative pancreatectomies for invasive ductal adenocarcinoma of the pancreas. Although there are no consensuses on the surgical treatment for recurrent pancreatic cancer, aggressive surgical treatment for recurrence is beneficial in select patients if curative (R0) resection is possible because only surgical resection enables long-term survival. Further investigation of the efficacy of surgical treatment for recurrent pancreatic cancer will be needed.

Statement of Ethics

Written informed consent was obtained from the patient for the publication of the present case report.

Disclosure Statement

The authors declare that they have no conflicts of interest.

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Author Contributions

All authors were involved in the preparation of this article. Yusuke Miyagawa, Masato Kitazawa, and Yuji Soejima wrote the manuscript. Hiroe Kitahara, Yukihiko Karasawa, and Takashi Orii were involved in the operation and administration of chemotherapy to the patient. All authors have read and approved the final manuscript.

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