World Journal of Gastroenterology

Submit a Manuscript: http://www.wjgnet.com/esps/
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
DOI: 10.3748/wjg.v20.i33.11904

World J Gastroenterol 2014 September 7; 20(33): 11904-11909
ISSN 1007-9327 (print) ISSN 2219-2840 (online)

CASE REPORT

Total pancreatectomy for metachronous mixed acinar-ductal carcinoma in a remnant pancreas

Tatsuya Shonaka, Mitsuhiro Inagaki, Hiromitsu Akabane, Naoyuki Yanagida, Hiroki Shomura, Nobuyuki Yanagawa, Kensuke Oikawa, Shiro Nakano

Tatsuya Shonaka, Mitsuhiro Inagaki, Hiromitsu Akabane, Naoyuki Yanagida, Hiroki Shomura, Shiro Nakano, Division of Surgery, Hokkaido PWFAC Asahikawa-Kosei General Hospital, Asahikawa 78-8211, Japan
Nobuyuki Yanagawa, Gastroenterology Endoscopic Center, Hokkaido PWFAC Asahikawa-Kosei General Hospital, Asahikawa 78-8211, Japan
Kensuke Oikawa, Department of Pathology, Asahikawa Medical University, Asahikawa 78-8510, Japan
Author contributions: Shonaka T wrote the manuscript; Inagaki M reviewed the paper; Akabane H operated on and treated the patient as an attending doctor; Yanagida N and Shomura H reviewed the paper and provided care to the patient; Yanagawa N completed the image evaluation and made the preoperative diagnosis; Oikawa K performed pathological examinations; Nakano S was supervised the entire process.
Correspondence to: Tatsuya Shonaka, MD, Division of Surgery, Hokkaido PWFAC Asahikawa-Kosei General Hospital, 1 Jodori, 1-24, Asahikawa 78-8211, Japan. tatsusho@yacht.ocn.ne.jp
Telephone: +81-166-337171 Fax: +81-166-336075
Received: January 21, 2014 Revised: March 28, 2014
Accepted: April 21, 2014
Published online: September 7, 2014

Abstract

In October 2009, a 71-year-old female was diagnosed with a cystic tumor in the tail of the pancreas with an irregular dilatation of the main pancreatic duct in the body and tail of the pancreas. A distal pancreatectomy with splenectomy, and partial resection of the duodenum, jejunum and transverse colon was performed. In March 2011, a follow-up computed tomography scan showed a low density mass at the head of the remnant pancreas. We diagnosed it as a recurrence of the tumor and performed a total pancreatectomy for the remnant pancreas. In the histological evaluation of the resected specimen of the distal pancreas, the neoplastic cells formed an acinar and papillary structure that extended into the main pancreatic duct. Mucin5AC, α1-antitrypsin (α-AT) and carcinoembryonic antigen (CEA) were detected in the tumor cells by immunohistochemistry. In the resected head of the pancreas, the tumor was composed of both acinar and ductal elements with a mottled pattern. The proportions of each element were approximately 40% and 60%, respectively. Strongly positive α-AT cells were detected in the acinar element. Some tumor cells were also CEA positive. However, the staining for synaptophysin and chromogranin A was negative in the tumor cells. Ultimately, we diagnosed the tumor as a recurrence of mixed acinar-ductal carcinoma in the remnant pancreas. In conclusion, we report here a rare case of repeated pancreatic resection for multicentric lesions of mixed acinar-ductal carcinoma of the pancreas.

Key words: Mixed acinar-ductal carcinoma; Pancreatic cancer; Acinar carcinoma; Total pancreatectomy

Core tip: We report a rare case of multicentric mixed acinar-ductal carcinoma lesions of the pancreas. The patient lived for 39 mo after the first operation without a second recurrence.

Shonaka T, Inagaki M, Akabane H, Yanagida N, Shomura H, Yanagawa N, Oikawa K, Nakano S. Total pancreatectomy for metachronous mixed acinar-ductal carcinoma in a remnant pancreas. *World J Gastroenterol* 2014; 20(33): 11904-11909 Available from: URL: http://www.wjgnet.com/1007-9327/full/v20/i33/11904.htm DOI: http://dx.doi.org/10.3748/wjg.v20.i33.11904

INTRODUCTION

Although several cases of mixed acinar-endocrine carcinoma of the pancreas, which is composed of both

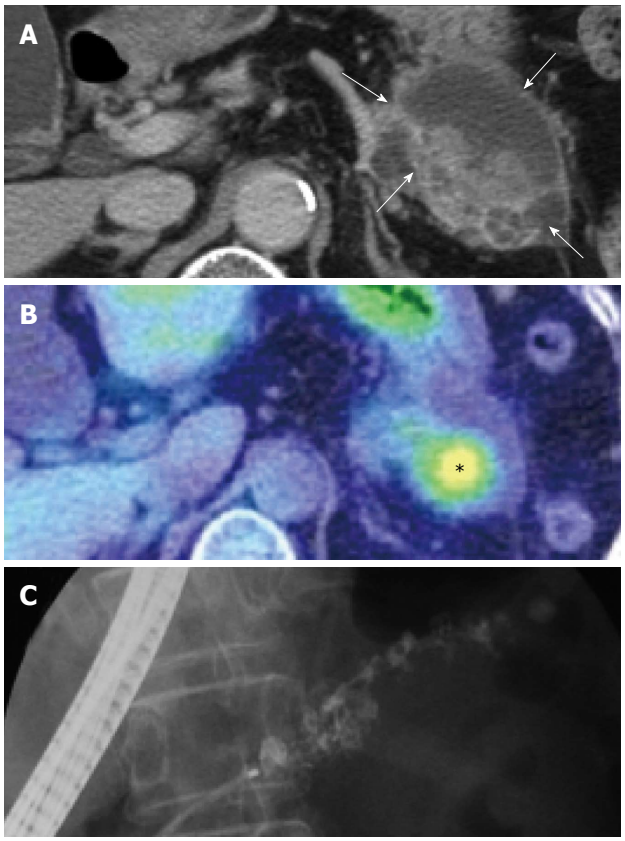

Figure 1 Diagnostic imaging before the first operation. A: Computed tomography showed a low density area (approximately 6 cm) in the pancreas tail (arrow); B: Positron emission tomography-computed tomography showed abnormal uptake of fluorodeoxy glucose (asterisk) in the low density area observed on computed tomography; C: Endoscopic retrograde cholangiopancreatography showed irregular dilatation of the main pancreatic duct in the body and tail.

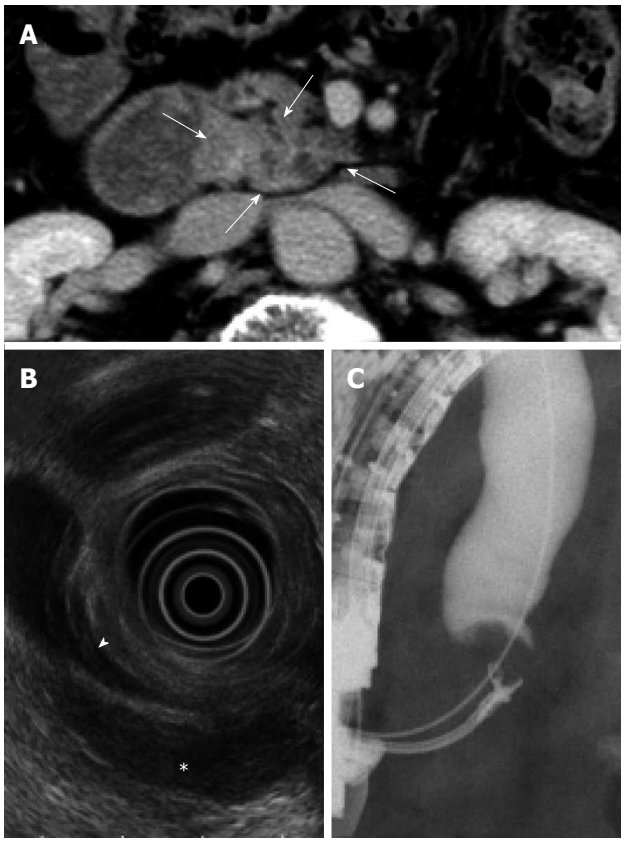

Figure 2 Diagnostic imaging before the second operation. A: Computed tomography showed a low density area at the uncus of the pancreas (arrow); B: Endoscopic ultrasound showed a 3 cm hypoechoic mass (asterisk) at the main pancreatic duct near the common bile duct (arrowhead); C: Endoscopic retrograde cholangiopancreatography showed the presence of inferior common bile duct stenosis.

acinar and endocrine tumor cells, have been reported[1], there have only been a few cases of resected mixed acinar-ductal carcinoma worldwide. According to the World Health Organization (WHO) classification, mixed acinar-ductal carcinoma is considered to be a sub-class of acinar cell neoplasms[2]. Mixed acinar-ductal carcinoma is defined in cases where greater than 25% of the tumor exhibits acinar and ductal elements in the pathological findings. Mixed acinar-ductal carcinoma usually exhibits an aggressive behavior, and it has a poor prognosis[3].

Herein we report a case of repeat pancreatectomy for multicentric lesions diagnosed as mixed acinar-ductal carcinoma, discuss the clinicopathological features, and present a review of the literature.

CASE REPORT

Clinical features

A 71-year-old female presented with epigastric pain in October 2009. Abdominal computed tomography (CT) showed a cystic lesion with a solid component in the tail of the pancreas (Figure 1A) and positron emission tomography-CT (PET-CT) showed intense fluorodeoxy glucose (FDG) uptake at the solid lesion (Figure 1B). Endoscopic retrograde cholangiopancreatography (ERCP) revealed irregular dilatation of the main pancreatic duct in the body and tail of the pancreas (Figure 1C). We diagnosed the patient with intraductal papillary mucinous neoplasms. During the operation, we found that the pancreas tumor was adhered to the duodenum, jejunum and transverse colon. We did not want to peel away the tumor, so we performed a distal pancreatectomy with splenectomy and partial resections of the duodenum, jejunum and transverse colon.

In March 2011 (15 mo after the first operation), the patient had did not exhibit any symptoms, but a follow-up CT examination showed a low density area at the uniciate process of the pancreas (Figure 2A). FDG/PET-CT revealed intense FDG uptake in the same region (data not shown). An endoscopic ultrasound examination showed a hypo-echoic lesion in the uniciate process of the pancreas that was approximately 3 cm in diameter, and this tumor compressed the inferior common bile duct (Figure 2B). ERCP revealed the presence of inferior common bile duct stenosis, and adenocarcinoma was suggested by a biopsy of the tumor lesion (Figure 2C). Based on these findings, we suspected a recurrence of mixed-acinar ductal carcinoma. Total resection of the remnant pancreas was performed. The patient was discharged successful on postoperative day 32. She re-

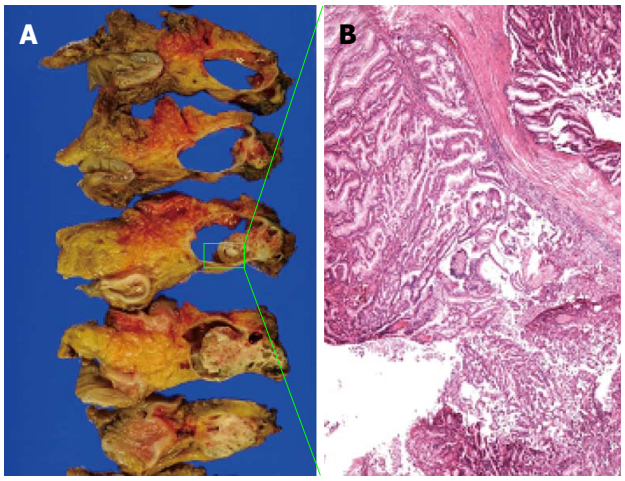

Figure 3 The resected specimen and pathological findings from the first operation. A: The resected specimen had a cystic lesion with a solid component; B: HE staining showed a mucus-type epithelium with an extension of intraductal papillary growth of the tumor cells. Scarce mucus-producing cells were also present (HE, × 40).

mained alive 21 mo after the second operation and had no recurrence.

Gross and pathological findings

During the distal pancreatectomy, a cystic lesion that was 7.2 cm in diameter with a partial solid component was noted in the specimen (Figure 3A). Hematoxylin and eosin (HE) staining showed both papillary and acinar-like structures in the solid component that extended into the main and the branch pancreatic duct (Figure 3B). In the former region, cube-shaped or high columnar cells exhibiting with mucin production formed the papillary structure resembling intraductal papillary neoplasms. Acinar-like structures were also observed in certain areas. No malignant cells were detected in the proximal stump of the pancreas. The tumor was localized to the pancreas without invasion into the duodenum, jejunum or, colon. We used an EnVision™ FLEX system for immunostaining. We assessed the ductal and acinar elements using immunohistochemistry. The results showed, positive staining for α1-antitrypsin (α-AT) and carcinoembryonic antigen (CEA). The gastrointestinal element was negative for mucin 2 (MUC2). Mucin 5AC (MUC5AC) was minimally detected in the tumor cells; however the we thought intraductal papillary mucinous neoplasm was negative (Figure 4). The islet element was negative for synaptophysin and chromogranin A (data not shown). Based on these histological findings, we diagnosed the tumor as a mixed acinar-ductal carcinoma. Extended papillary growth outside the cystic lesion was also observed. A total of 8 lymph nodes were extracted, but no metastasis of the resected lymph nodes was detected. The pathological stage was ⅢⅠb (T3N0M0) based on the 7th edition criteria of the Union for International Center Control[4].

The specimen taken during the second operation revealed another tumor approximately 3 cm in diameter tumor in the head of the pancreas (Figure 5A). Acinar-like structures and papillary growths were observed, with a mottled pattern were observed(Figure 5B). Some regions of the tumor had a papillary growth pattern (Figure 5C).

Some of the tumor cells with mild atypia showed poor mucus production with eosinophilic cytoplasm. The tumor exhibited a papillary proliferation pattern, with delicate fibervascular stroma and acinar-like structure pattern in some regions (Figure 5D). The tumor exhibited an almost solid growth, and the glandular lumen was unclear. We detected abundant mitotic figures in the tumor. In the microscopic findings, approximately 40% of the tumor had an acinar-like structure, and 60% of it exhibited a papillary growth pattern. There was intense α-AT staining in the acinar-like part of the tumor. MUC5AC was not detected. Mild positive staining for mucin1 and CEA was observed (Figure 6). The staining for synaptophysin A and chromogranin were negative (data not shown). The tumor showed both an acinar-like and papillary growth pattern in the main pancreatic duct. As a result, we diagnosed the tumor as a mixed acinar-ductal carcinoma in the remnant pancreas. A total of 7 lymph nodes were extracted, but metastasis was not detected.

DISCUSSION

Combined acinar and ductal phenotype carcinoma of the pancreas is very rare[5-7]. The WHO classification categorizes mixed acinar-ductal pancreatic carcinoma as a sub-class of acinar cell neoplasms[2]. Mixed carcinomas of the pancreas have distinctive histological features suggesting more than one line of differentiation. Mixed acinar-ductal carcinomas are defined as those in which at least 25 percent of the neoplastic cells show an acinar and ductal line of differentiation[2,8].

Stelow *et al*[3] reported a study of 11 cases of mixed acinar-ductal carcinoma. In their report, all cases showed significant evidence of acinar and ductal differentiation that were, estimated to include at least 25% of the neoplastic cells. In the present case, acinar differentiation was shown to involve 40% of the tumor, with the remaining portion exhibiting ductal differentiation during the second operation. All but one of the carcinomas showed predominantly acinar differentiation, based on routine histological and immunohistochemical analyses[3]. The 18 previously reported cases of mixed-acinar ductal carcinoma in the English and Japanese literatures are summarized in Table 1[3,9-11]. In five cases, the tumors were present in the tail of the pancreas, while in the remaining cases, the tumors were located in the head of the pancreas (the tumor diameters ranged from 35-72 mm). With regard to treatment, only one case received radiotherapy, and the other cases underwent surgical resection. There were no reports of a recurrence of the tumor or additional resection of the remnant pancreas.

Kobayashi *et al*[12] reported an intraductal growth of tumor cells into the main pancreatic duct with acinar endocrine carcinomas. For this reason, it is possible that mixed acinar and ductal phenotype carcinoma is biologi-

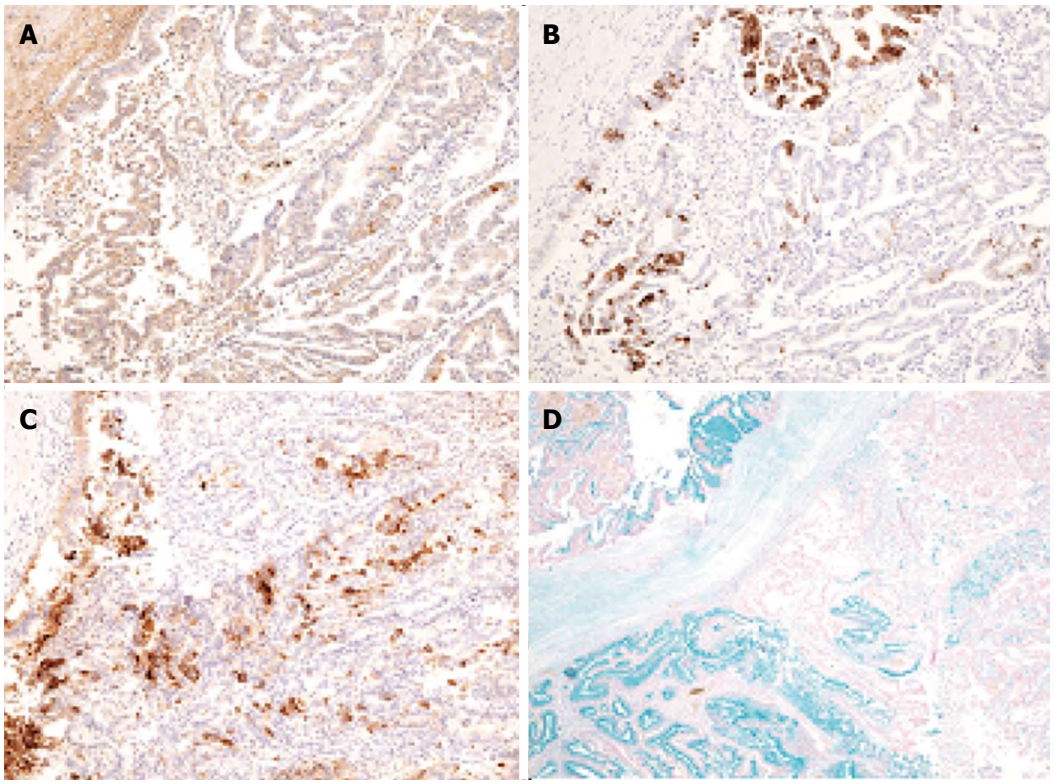

Figure 4 Immunohistochemical and pathological findings from the first operation. A: α1-antitrypsin (× 100): regions of both strongly positive and weakly positive cells were present; B: Mucin5AC (× 100): only part of the tumor was positive; C: Carcinoembryonic antigen (× 100): a portion of the tumor was positive; D: Alcian blue (× 100): staining was positive in the region with poor mucus production.

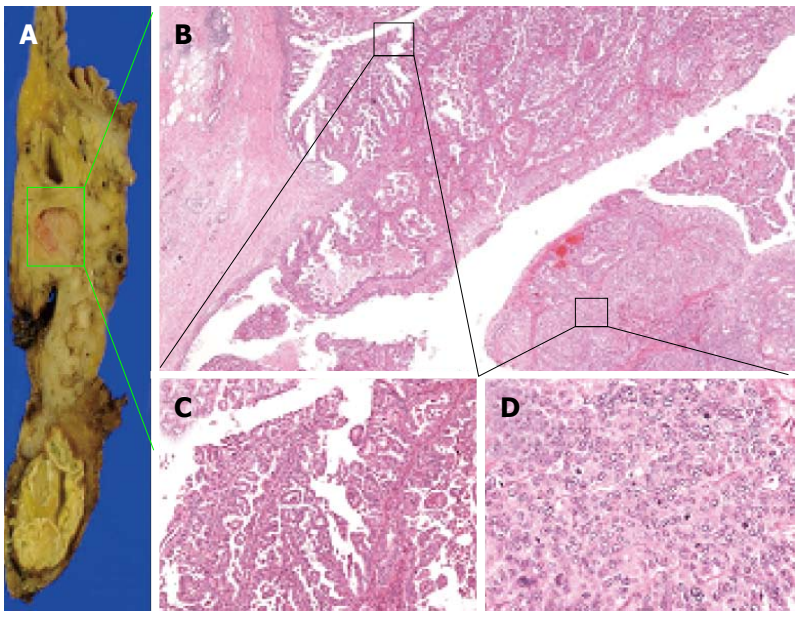

Figure 5 The resected specimen and pathological findings from the second operation. A: The resected specimen from the second operation showed a 3 cm solid mass in the head of the pancreas; B: There was a region with acinar-like structures (bottom right) that showed papillary growth (upper left) (HE, × 40); C: Dysplastic cells with poor mucus production exhibited papillary proliferation (HE, × 200); D: Acinar structures and cell division were observed (HE, × 400).

cally more closely related to acinar cell carcinoma than to pancreatic duct carcinoma. Five of the previously reported cases had a "mucinous acinar cell carcinoma" pattern that, which is characterized by the production of mucin in the acinar cell carcinoma. Six cases were reported to exhibit a "combined acinar ductal" pattern which finds mottled component of acinar cell carcinoma and ductal carcinoma. Our case was a "mucinous acinar cell carcinoma" at the first operation and a "combined acinar ductal carcinoma" at the second operation[3].

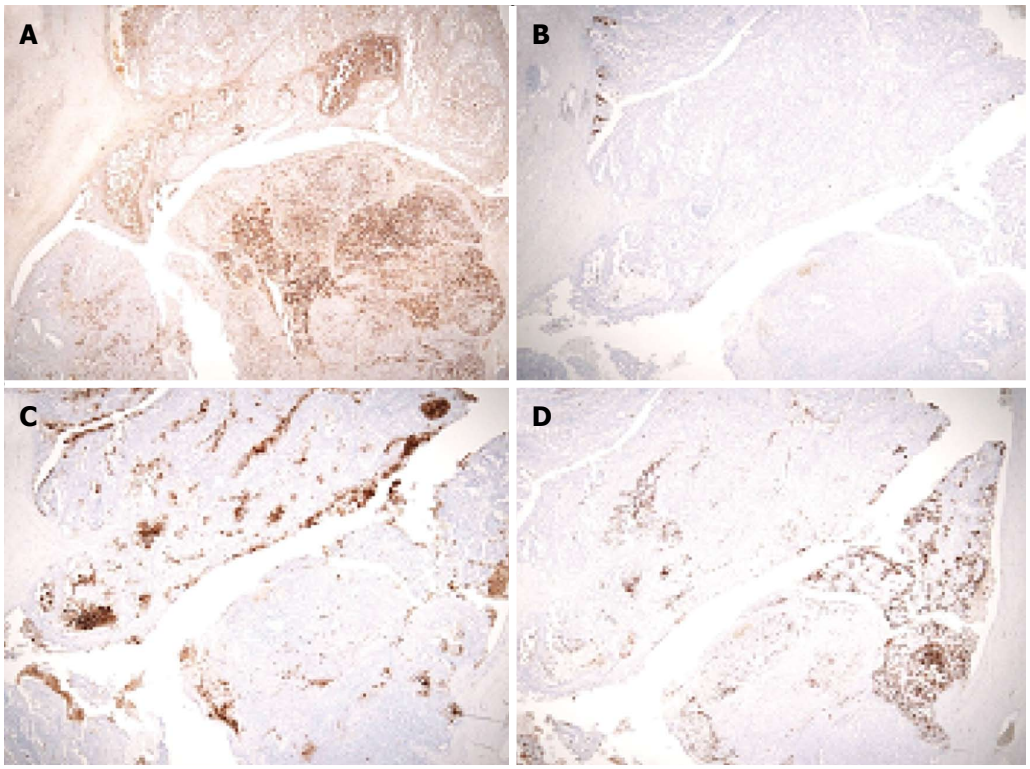

Figure 6 Immunohistochemical and pathological findings from the second operation. A: α1-antitrypsin (× 40): the acinar structure in the lower right area was strongly positive; B: Mucin5AC (× 40): only a small part of the tumor was positively stained; C: Carcinoembryonic antigen (× 40): only a portion of the area was positively stained; D: Mucin1 (× 40): some positive staining was observed.

Table 1 The 18 previously reported cases of mixed-acinar ductal carcinoma in the English and Japanese literatures

Case	Age	Sex	Symptoms at presentation	Size	Location	Treatment	Follow-up	Prognosis	Reference
1	74	M	Painless jaundice	31	Head	RTx, CTx	20	Alive	[3]
2	75	M	Weight loss and diarrhea	25	Head	RTx, CTx	39	Dead	[3]
3	73	M	Not available	20	Tail	RTx, CTx	52	Dead	[3]
4	74	M	Weight loss and diarrhea	40	Head	RTx, CTx	51	Dead	[3]
5	70	M	Pain	40	Head	RTx, Rdx	38	Dead	[3]
6	77	F	Weight loss	30	Head	Rdx	9	Dead	[3]
7	77	M	Weight loss and pain	37	Head	RTx	0.5	Dead[1]	[3]
8	52	M	Pain	55	Head	RTx, CTx	12	Dead	[3]
9	76	M	Painless jaundice	35	Head	RTx, CTx	8	Dead	[3]
10	79	M	Painless jaundice	34	Head	RTx, CTx	11	Alive	[3]
11	69	M	Painless jaundice	54	Head	RTx, CTx	36	Alive	[3]
12	71	M	Not mentioned	30	Head	-	12	Dead	[10]
13	51	F	Not mentioned	-	Tail	-	3	Dead	[10]
14	51	F	Not mentioned	30	Tail	-	4	Dead	[10]
15	85	M	Not mentioned	-	Tail	-	6	Dead	[10]
16 (J)	63	M	Abdominal pain	65	Head	RTx	39	Alive	[11]
17 (J)	63	M	Worsening of diabetes	35	Head	RTx	8	Dead	[12]
18	71	F	Epigastric discomfort	72	Tail	RTx	36	Alive[2]	
				35	Head	RTx			

[1]Deceased due to a post operative complication; [2]Recurrence in the remnant pancreas 18 mo after the first operation. J: Japanese article; M: Male; F: Female; RTx: Resection; Rdx: Radiation; CTx: Chemotherapy; -: Not mentioned.

Mucin production was observed in all cases, with a high positive rate of immunostaining for MUC1 and CEA that, was useful in the diagnosis. This was also the case consistent with our patient. The clinical course was considered to be aggressive, and seven of the previous patients died at a mean of 29 mo after the operation[3]. However, our patinet remained alive without recurrence 39 mo after the first operation.

Our patient underwent repeated pancreatectomy due to a metachronous mixed acinar-ductal carcinoma. A metachrounous tumor in the remnant pancreas of mixed acinar-ductal carcinoma has not previously been reported,

although repeated pancreatectomy for some cases of pancreatic duct carcinoma, intraductal papillary, mucinous tumors and endocrine tumors has[13-18]. There was only one previous case of a recurrence of acinar carcinoma[14].

In conclusion, we reported a rare case of mixed acinar-ductal carcinoma. The patient developed metachrounous tumors in the remnant pancreas and underwent a repeated resection. She remained alive 39 mo after the first operation without a second recurrence.

ACKNOWLEDGMENTS

We thank Tomoko Mitsuhashi (Department of Surgical Pathology, Hokkaido University Hospital) for her expertise regarding this case.

REFERENCES

1 **Ohike N**, Jürgensen A, Pipeleers-Marichal M, Klöppel G. Mixed ductal-endocrine carcinomas of the pancreas and ductal adenocarcinomas with scattered endocrine cells: characterization of the endocrine cells. *Virchows Arch* 2003; **442**: 258-265 [PMID: 12647216]

2 **Bosman FT**, Carneiro F, Hruban RH, Theise ND. WHO Classification of Tumours of the Digestive System. 9th ed. Lyon: IARC/WHO, 2010: 279-337

3 **Stelow EB**, Shaco-Levy R, Bao F, Garcia J, Klimstra DS. Pancreatic acinar cell carcinomas with prominent ductal differentiation: Mixed acinar ductal carcinoma and mixed acinar endocrine ductal carcinoma. *Am J Surg Pathol* 2010; **34**: 510-518 [PMID: 20182344 DOI: 10.1097/PAS.0b013e3181cfcac7]

4 **Sobin L**, Gospodarowic M, Wittekind C. TNM Classification of Malignant tumours. 7th ed. New York: Wiley-Blackwell, 2009

5 **Schron DS**, Mendelsohn G. Pancreatic carcinoma with duct, endocrine, and acinar differentiation. A histologic, immunocytochemical, and ultrastructural study. *Cancer* 1984; **54**: 1766-1770 [PMID: 6089999]

6 **Okada Y**, Mori H, Tsutsumi A. Duct-acinar-islet cell tumor of the pancreas. *Pathol Int* 1995; **45**: 669-676 [PMID: 8548040 DOI: 10.1111/j.1440-1827.1995.tb03520.x]

7 **Tanakaya K**, Teramoto N, Konaga E, Takeuchi H, Yasui Y, Takeda A, Yunoki Y, Murakami I. Mixed duct-acinar-islet cell tumor of the pancreas: report of a case. *Surg Today* 2001; **31**: 177-179 [PMID: 11291717 DOI: 10.1007/s005950170207]

8 **Hruban RH**, Pitman MB, Klimstra DS. Tumors of the pancreas afip Atlas of Tumor Pathology. 4th Series Fascicle. Washington DC: American Registry of Pathology, 2007: 211-218

9 **Webb JN**. Acinar cell neoplasms of the exocrine pancreas. *J Clin Pathol* 1977; **30**: 103-112 [PMID: 845259 DOI: 10.1136/jcp.30.2.103]

10 **Inaba N**, Kasahara K, Kashii A, Kanazawa K, Yamaguchi T, Saito K, Kamisawa T. [Mixed ductal and acinar cell cancer of the pancreas head; report of a case]. *Nihon Geka Gakkai Zasshi* 1987; **88**: 773-778 [PMID: 3041198]

11 **Sakai M**, Takeda S, Ishikawa T, Kanazumi N, Inoue S, Kaneko T, Nakao A, Nagasaka T. Mixed duct-acinar cell carcinoma of the pancreas: Report of a case. *Jpn J Gastroenterol Surg* 2005; **38**: 1821-1827

12 **Kobayashi S**, Asakura T, Ohike N, Enomoto T, Sakurai J, Koizumi S, Watanabe T, Nakano H, Otsubo T. Mixed acinar-endocrine carcinoma of the pancreas with intraductal growth into the main pancreatic duct: Report of a case. *Surg Today* 2010; **40**: 380-384 [PMID: 20339996 DOI: 10.1007/s00595-009-4083-9]

13 **Inagaki M**, Aoyagi T, Nomura A, Yokoo H, Akabane M, Kawata A, Nakano S, Chiba A, Fujii T, Sakurai H, Tsukada T, Takahashi M. Surgical approach to tumor recurrence and metastatic lesions of the liver in a patient with malignant endocrine tumors of the pancreas: case report. *J Hepatobiliary Pancreat Surg* 2003; **10**: 325-328 [PMID: 14598155]

14 **Miura F**, Takada T, Amano H, Yoshida M, Isaka T, Toyota N, Wada K, Takagi K, Kato K. Repeated pancreatectomy after pancreatoduodenectomy. *J Gastrointest Surg* 2007; **11**: 179-186 [PMID: 17390170 DOI: 10.1007/s11605-006-0026-6]

15 **Kleeff J**, Reiser C, Hinz U, Bachmann J, Debus J, Jaeger D, Friess H, Büchler MW. Surgery for recurrent pancreatic ductal adenocarcinoma. *Ann Surg* 2007; **245**: 566-572 [PMID: 17414605 DOI: 10.1097/01.sla.0000245845.06772.7d]

16 **Inagaki M**, Obara M, Kino S, Goto J, Suzuki S, Ishizaki A, Tanno S, Kohgo Y, Tokusashi Y, Miyokawa N, Kasai S. Pylorus-preserving total pancreatectomy for an intraductal papillary-mucinous neoplasm of the pancreas. *J Hepatobiliary Pancreat Surg* 2007; **14**: 264-269 [PMID: 17520201 DOI: 10.1007/s00534-006-1146-9]

17 **Zacharias T**, Oussoultzoglou E, Jaeck D, Pessaux P, Bachellier P. Surgery for recurrence of periampullary malignancies. *J Gastrointest Surg* 2009; **13**: 760-767 [PMID: 19050979 DOI: 10.1007/s11605-008-0769-3]

18 Ogino T, Ueda J, Sato N, Takahata S, Mizumoto K, Nakamura M, Oda Y, Tanaka M. Repeated Pancreatectomy for Recurrent Pancreatic Carcinoma after Pylorus-Preserving Pancreatoduodenectomy: Report of Two Patients. *Case Rep Gastroenterol* 2010; **4**: 429-434 [PMID: 21060713 DOI: 10.1159/000321513]

P- Reviewer: Eysselein VE, Iacono C, Liu SH **S- Editor**: Gou SX
L- Editor: A **E- Editor**: Liu XM

Published by **Baishideng Publishing Group Inc**
8226 Regency Drive, Pleasanton, CA 94588, USA
Telephone: +1-925-223-8242
Fax: +1-925-223-8243
E-mail: bpgoffice@wjgnet.com
Help Desk: http://www.wjgnet.com/esps/helpdesk.aspx
http://www.wjgnet.com

ISSN 1007-9327