A Multicentric Development Of Intraductal Papillary Mucinous Neoplasm Treated By Repeated Pancreatectomy

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Citation

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Abstract

There are few reports of multicentric recurrence after resection of lesions of intraductal papillary mucinous neoplasms (IPMNs) of the pancreas. We report a case of repeated pancreatectomy for recurrent IPMN showing multicentric development in the pancreatic remnant after resection of the initial lesion. In February 1999 a 70-year-old man underwent distal pancreatectomy for a cystic neoplasm in the pancreatic tail. Histological examination revealed invasive intraductal papillary mucinous adenocarcinoma (IPMC) with lymph node metastasis. Forty-seven months later, a cystic mass with an intracystic nodule was detected during surveillance by computed tomography. The patient underwent completion pancreatectomy. Histological examination demonstrated IPMC with neural invasion. In immunohistochemical staining, the initial specimen was positive for proteinase-activated receptor 2, but the second specimen was not. The present case helps elucidate the multicentric development of IPMN of the pancreas. We recommend careful surveillance for the recurrence of IPMN in the pancreatic remnant after resection.

INTRODUCTION

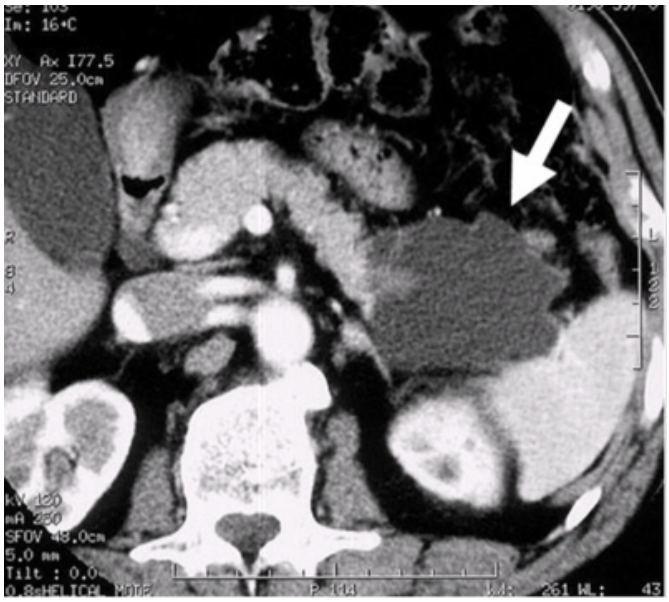
Intraductal papillary mucinous neoplasm (IPMN) is a well-characterized entity of mucinous cystic neoplasms of the pancreas with malignant potential. The clinicopathological features of IPMNs have been reported frequently in the last decade ([1,2,3]). Because IPMN is usually a slow-growing neoplasm with low malignancy, surveillance after surgical resection has tended to be less than vigilant. There are several recent reports of recurrence after resection of IPMN ([4,5,6]). The sites of IPMN recurrence are distant organs or the pancreatic remnant. Although multiple lesions of IPMN in the pancreas are often encountered ([7,8]), few reports have discussed metachronous or multicentric recurrence in the pancreatic remnant after resection of IPMN. We report a case of recurrence showing the progress of the multicentric development after resection of the initial IPMN.

CASE REPORT

In February 1999 a 70-year-old man was referred to our hospital for treatment of a cystic neoplasm in the pancreas. Abdominal computed topography (CT) revealed an IPMN 6 cm in diameter in the tail of the pancreas (Fig. 1).

Figure 1

Figure 1: Computed tomography reveals a cystic mass 6 cm in diameter with intracystic mural nodules in the pancreatic tail (white arrow).

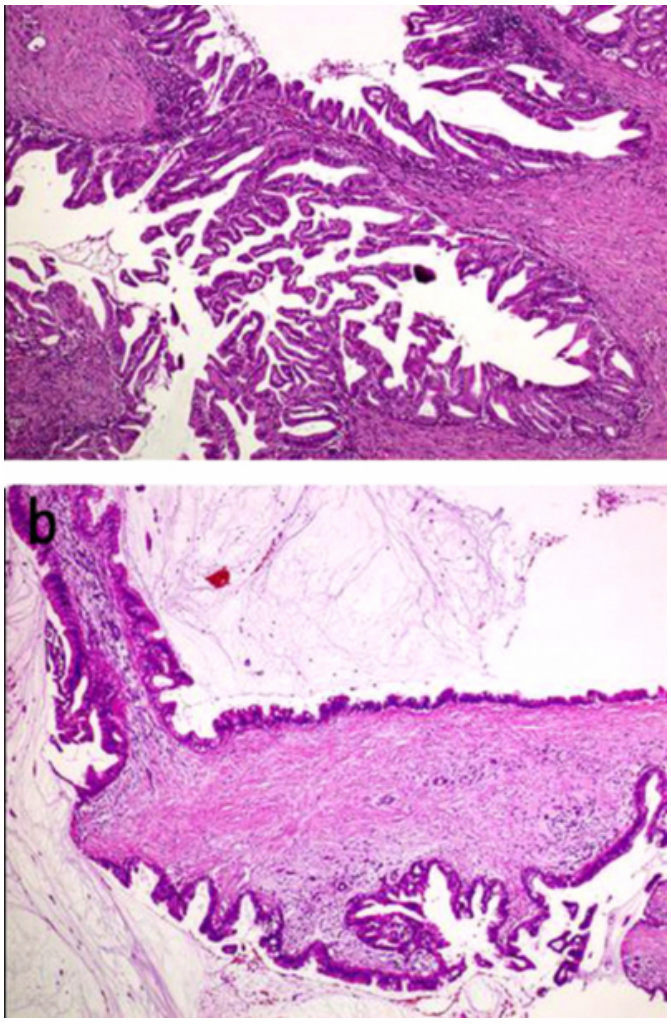


Endoscopic retrograde cholagiopancreatography (ERCP) showed a normal main pancreatic duct without communication to the cystic mass. Endoscopic ultrasonography revealed mural nodules in the cystic wall.

The patient underwent distal pancreatectomy with splenectomy and extended lymph node dissection. Postoperative histological examination showed intraductal papillary mucinous adenocarcinoma invading the pancreatic parenchyma with peripancreatic lymph node metastasis (Fig. 2a).

Figure 2

Figure 2: Histological appearances of both intraductal papillary mucinous adenocarcinoma (IPMC) (H&E, x40). The atypical grade of IPMC in the pancreatic tail (a) is higher than that in the pancreatic uncus (b).

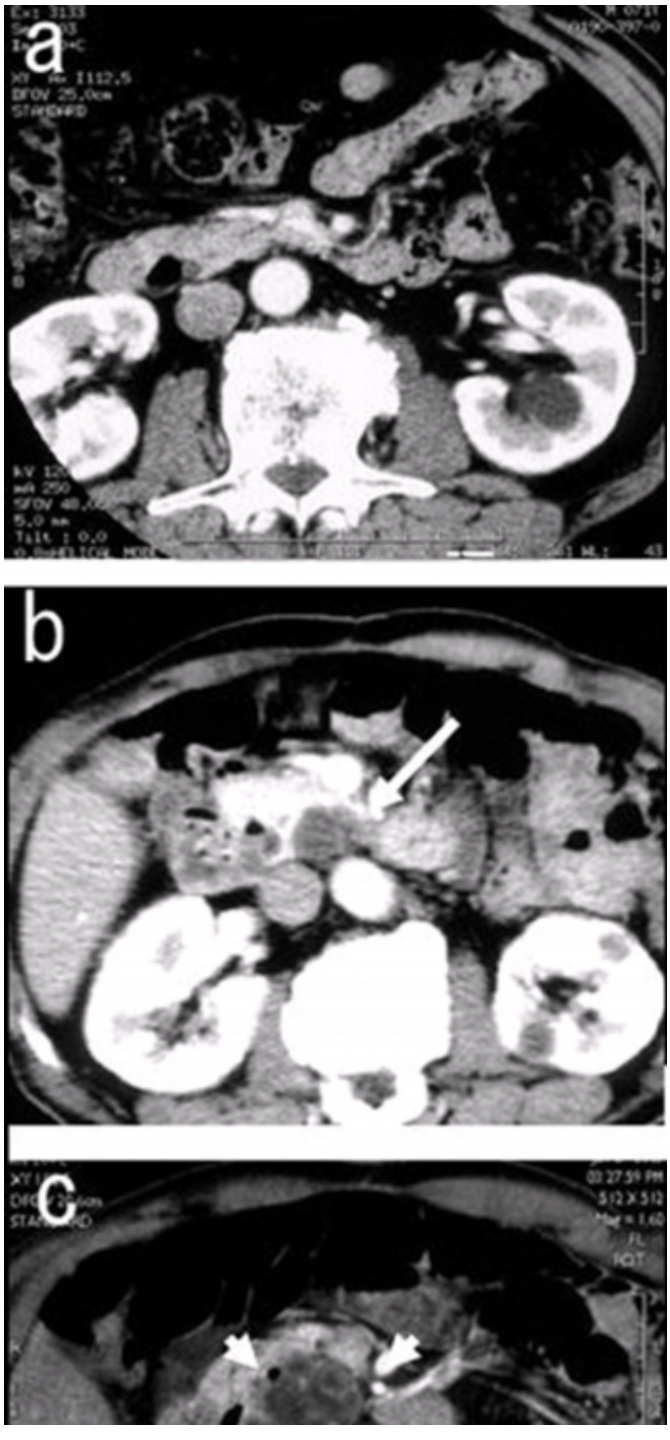


The surgical cut margin showed no atypical cells in either the intra- or post-operative histological examination. In addition, no ovarian stroma was noticed. The postoperative course was uneventful, and the patient was discharged.

Thirty months after resection of the IPMN in the tail of the pancreas, surveillance by abdominal CT revealed a small cystic mass in the uncus of the pancreas. Seventeen months later, the cystic mass had grown to 4 cm in diameter with an intracystic mural nodule (Fig. 3a, b, c).

Figure 3

Figure 3: Computed tomography for surveillance after resection of the initial lesion. (a) No cystic mass was detected just after the initial surgery. (b) Cystic mass was detected in the pancreatic uncus 30 months after the initial resection (white arrow). (c) Cystic mass enlarged and had a mural nodule in the cystic neoplasm 17 months after the detection (white arrow head).

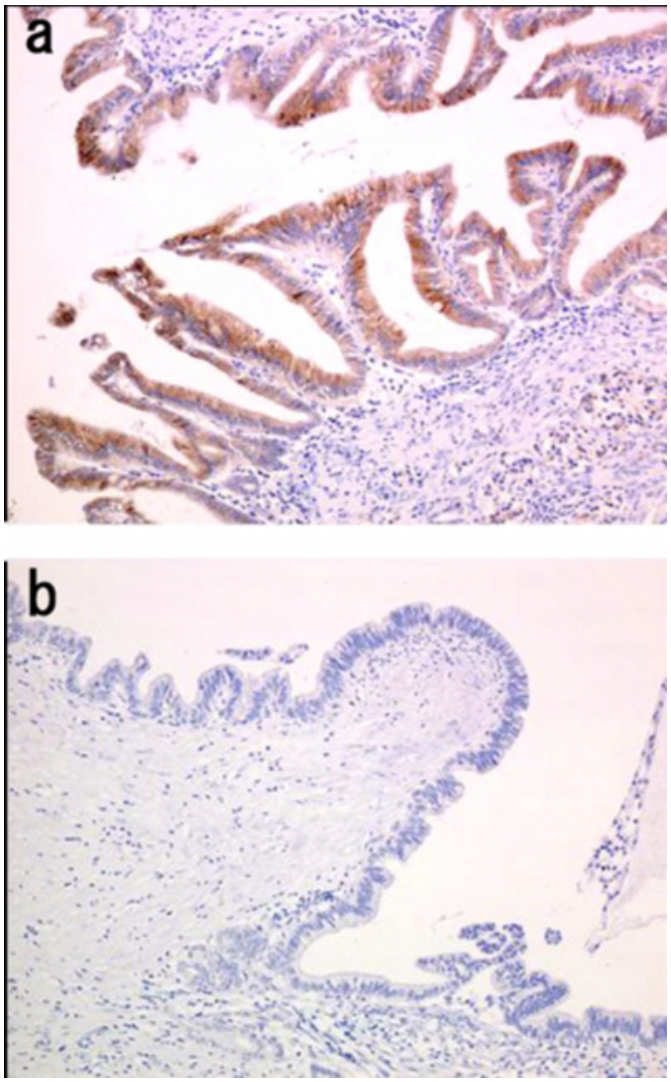


The lesion was considered a recurrent IPMN in the pancreatic remnant. The patient underwent completion pancreatectomy with extended lymph node dissection. Postoperative histological examination showed intraductal papillary mucinous adenocarcinoma with perineural invasion (Fig. 2b).

Lymph node metastasis was not noticed. Immunohistochemical stainings of Ki-67, p53, DPC4 ([9]), and proteinase-activated receptor 2 (PAR-2) ([10,11]) were performed. Positive expression of PAR-2 was noticed in the initial specimen, but not in the second specimen (Fig. 4).

Figure 4

Figure 4: Immunohistochemical staining of proteinase-activated receptor-2 shows positive expression in intraductal papillary mucinous adenocarcinoma (IPMC) in the pancreatic tail (a) but negative in the pancreatic uncus (b).



Other molecular factors were stained without differences between the two specimens. Although the patient now has diabetes, but he is healthy and there has been no recurrence of the neoplasm 36 months after the second surgery.

DISCUSSION

IPMNs of the pancreas are characterized by papillary proliferation of the pancreatic epithelium, with a tendency toward slow invasive growth and metastasis. However, few reports have investigated the long-term outcome after IPMN lesions have been resected ([5,12]). The mechanism underlying recurrence in the pancreatic remnant remains unknown. Two mechanisms underlying this recurrence have been proposed. One is a continuous lesion forming the remnant marginal tumor, and the other is the formation of a multicentric neoplasm. In a study by Falconi et al of 4 patients with local recurrences, all of the recurrent tumors resulted from remnant dysplasia ([13]). There are some reports of recurrences after partial pancreatectomy for noninvasive IPMN, in which the cut margin showed normal epithelium ([5,12]). In the present case, the recurrent site after resection for invasive IPMN had no previous cystic lesions. As we reported previously, the progressive lesion was resected because of malignant behaviors, inducing growth to more than 30 mm in size and an intracystic mural nodule ([14]). Since the cut margin had no atypical cells at the initial surgery and the recurrent lesion grew progressively from the branch-duct side on CT images, we considered it highly likely that the recurrence developed from multicentric foci. We reported that PAR-2 might correlate with proliferative activity of pancreatic neoplasms ([11]). In this case, the positive expression of PAR-2 was showed in the initial lesion, but not in the recurrence. The differences in immunohistochemical analysis of PAR-2 between the two lesions suggested that the recurrence in the present case was a multicentric development.

Chari et al. found no recurrence after total pancreatectomy for noninvasive IPMN in 13 patients ([5]). In the past, total pancreatectomy was considered for patients with invasive IPMN to prevent recurrence in the pancreatic remnant. However, the impaired metabolic outcome and the limited risk of recurrence discouraged the use of total pancreatectomy for patients with a definitive local lesion and a negative margin. Sites of recurrence after extended resection of invasive IPMN were almost always in distant organs such as liver or lymph nodes. Total pancreatectomy does not seem to improve the survival of patients with invasive IPMN. Recurrent IPMN is believed to be

resectable, and the prognosis after the second resection might be relatively good. To undertake curative surgery for IPMN, there must be no atypical cells at the cut margin by intraoperative frozen histological examination.

Recurrence after resection is likely to occur late because IPMN is usually a slow-growing and low-grade malignancy. Until now, recurrence has been evaluated through short-term surveillance. Salvia et al. found 6 recurrences in the pancreatic remnant appearing at a median of 50 months after the initial resection ([15]). Reports on short-term surveillance might reveal a low rate of recurrence for benign or noninvasive IPMN. Therefore, long-term surveillance may be required to determine the recurrence rate, especially for IPMNs showing multicentric development.

CONCLUSION

In summary, we report a patient who underwent completion pancreatectomy for recurrent IPMN showing multicentric development. IPMN is a unique neoplasm that is often discovered incidentally and that has a malignant potential warranting curative resection. Long-term postoperative surveillance is recommended to detect a recurrent lesion in the pancreatic remnant without delay.

CORRESPONDENCE TO

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