Case report

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Serous cystadenocarcinoma of the pancreas with portal thrombosis

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Abstract

Serous cystadenocarcinoma of the pancreas is a rare entity. We report on a primary tumor of the pancreas in a 74-year-old male. Computerized tomography showed an abdominal mass within pancreatic head, portal vein infiltration and absence of metastatic lesions. Patient underwent Whipple's procedure and portal vein thrombectomy. Pathologic examinations of the specimen showed it to be serous cystadenocarcinoma. To the knowledge of the authors, serous cystic neoplasms of the pancreas have been uniformly benign in biologic behaviour. However, serous cystadenocarcinoma of the pancreas has been reported as a new entity. The current report is the first among 22 cases described to present portal vein thrombosis and might support the local malignant behaviour of this controversial class of tumours.
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Case report

A 74-year-old man was admitted to our Department in March 2007 presenting with a left upper quadrant abdominal mass. He did not have a significant history before admission except for abdominal aortic stenosis. On admission computerized tomography (CT) scan (Fig. 1A) showed the presence of an expansive solid lesion at the pancreatic head with regular margins infiltrating portal vein. Ultrasonography and CT were indicative of cystadenoma. Other laboratory investigations, such as those of biochemical and tumour markers, including CA 19-9, indicated no abnormalities. Interestingly, plasmatic chromogranin was significantly elevated (180 UI/l) whereas immunohistochemical analysis showed no positivity for chromogranin. In addition, the patient presented no cystic lesions or evident metastases in other organs. Laparotomy revealed a large mass involving the head and the body of the pancreas surrounding the pyloric region and infiltrating the portal vein (Fig. 1B). Patient underwent Whipple's procedure with Liagasure and portal vein thrombectomy followed by portal plastic (Fig. 1A). The surgical procedures had 6 hours duration, minimal blood loss; the patient experienced a good recovery and was dismissed following 8 days after the operation. Six months following operation, the patient was re-evaluated for the presence of metastases and biochemical parameters. These set of clinical exams showed no hepatic metastases and a thrombus in two pulmonary arterioles; all biochemical parameter including chromogranin were within normal range.

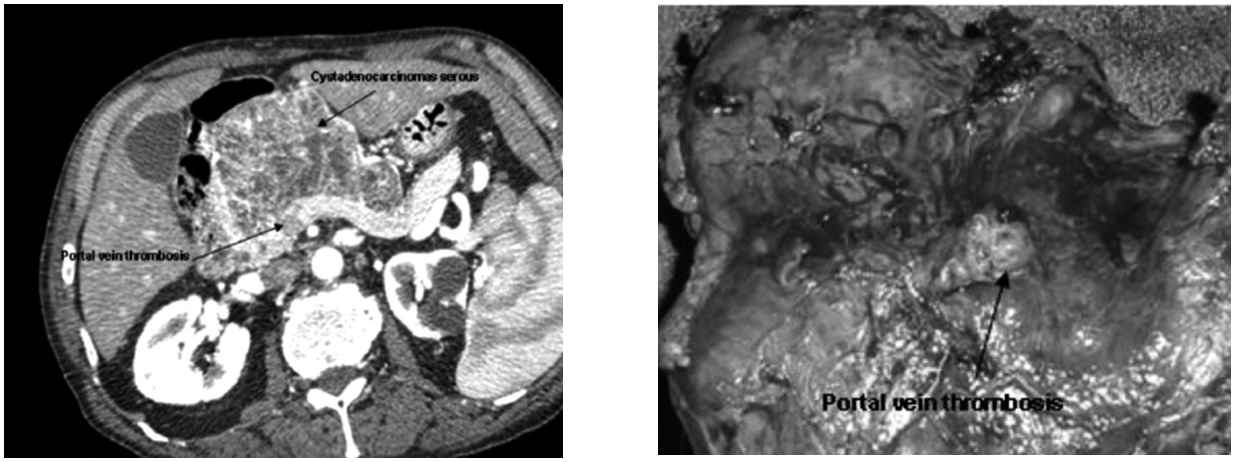

Fig. 1. (A) Computerized tomography scan showing the presence of an expansive solid lesion at the pancreatic head with regular margins infiltrating portal vein. (B) Large mass involving the head and the body of the pancreas surrounding the pyloric region and infiltrating the portal vein.

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Pathologic findings

A polycystic sponge-like tumor, measuring 8 x 8.5 x 9 cm, replaced the head and the body of the pancreas. On the cut surface, the tumor was separated by a fibrous capsule from the tissue that indicated the normal pancreas (Fig. 2). The most striking feature on the microscopic examinations was the presence of multiple cysts separated by loose fibrous connective septa. The cysts ranged in size from more than 5 mm to less than 1 mm in diameter. The cyst walls were lined by a single layer of cuboidal epithelium with clear cytoplasm (Figs. 3A and 3B), feature consistent with serous microcystic adenoma, but focal nuclear pleomorphism and papillary areas were also found (Fig. 3C). The nuclei were round and uniform. The tumor was surrounded by a fibrous capsule without evidence of invasion of pancreatic parenchyma nor duodenal wall. The examination of 15 regional lymph nodes revealed no metastatic tissue. Portal resected tract was filled by neoplastic thrombus in occlusive fashion (Fig. 3D). No sign of mucin secretion nor chromogranin expression was evidenced. The presence of papillary areas, the mild nuclear pleomorphism and, by far mostly, the portal thrombus led to diagnosis of pancreatic cystadenocarcinoma.

Fig. 2. A polycystic sponge-like tumor, measuring 8 X 8.5 X 9 cm, replacing the head and the body of the pancreas. On the cut surface, the tumor was separated by a fibrous capsule from the tissue that indicated the normal pancreas.

Discussion

In the current case, the resected pancreatic neoplasm was basically serous cystadenocarcinoma, showing the typical cells with slight nuclear atypia and papillary structures.

George et at.(1) reported an autopsy case of serous cystadenocarcinoma of the pancreas as a new entity. However, in their case, the pancreatic tumor invaded the gastric walls and the histological characteristics of the neoplasm in the pancreas showed a typical appearance as serous cystadenoma. For diagnosis of the current case as primary serous cystadenocarcinoma of the pancreas, the possibilities of other neoplasms (primary and metastatic) should be excluded. Furthermore, we excluded mucinous cystadenocarcinoma following staining for mucins. In addition, because of the cystic appearance, it was easy to distinguish it from the acinar cell cystadenocarcinoma, which is characterized by columnar cells with eosinophilia and zymogen granules, and the papillary cystic tumor, which is characterized by the papillary structure and the solid sheets with eosinophilic cytoplasm and prominent nucleoli. Finally, the possibility that the pancreatic tumor was metastatic tumour from other organs such as kidney was excluded from various examinations, including CT scan.

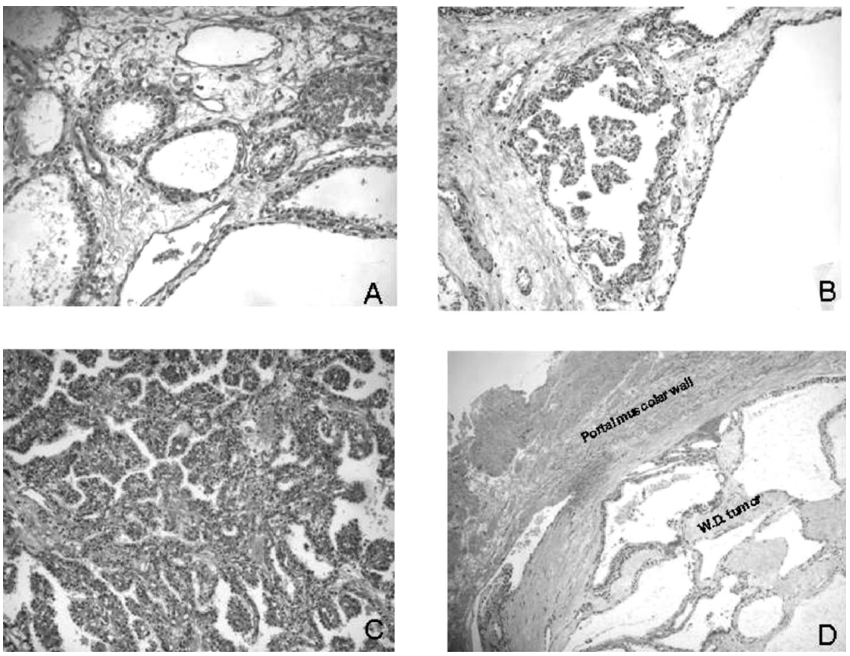

Fig. 3. Microphotographs showing the cyst walls lined by a single layer of cuboidal epithelium with clear cytoplasm (A and B), feature consistent with serous microcystic adenoma, but focal nuclear pleomorphism and papillary areas were also found (C). Portal resected tract was filled by neoplastic thrombus in occlusive fashion (D).

In our case, the patient was diagnosed to have a serous cystadenocarcinoma of the pancreas because the microscopic examination of the surgical specimen showed an invasion of tumor cells into portal vein, although typical histological features of microcystic adenoma were present throughout the whole neoplastic tissue. Clinically, the tumor behaved benign with a long history of unspecific symptoms before diagnosis, indicating a slow rate of tumor progression and no signs of malignancy as local or systemic metastases. In this case, as in most of the other reported cases, the diagnosis could only be made postoperatively. Because of the difficulty in preoperative diagnosis of serous neoplasms on the one hand and well documented cases of malignant behaviour on the other hand, attempts have been made to find preoperative criteria that are able to determine whether a cystic lesion is malignant or benign. Using imaging studies including CT and magnetic resonance imaging, radiologists are capable of distinguishing cystic neoplasms from pancreatic pseudocysts and mucinous from serous cystic lesions if they show a typical microcystic appearance (2-4). Radiological and histological diagnosis are further complicated by the existence of a macrocystic variant of serous cystadenoma that appears as unilocular cyst and is frequently misdiagnosed as mucinous neoplasm (5, 6). Although radiological imaging is very useful for the differential diagnosis between serous and mucinous tumours, the assessment of the grade of malignancy is generally not possible. There are no radiological criteria that allow the certain diagnosis of a malignant cystic lesion, unless tumor infiltration or metastasis is obvious. The analysis of cyst fluid obtained by needle aspiration provides additional preoperative information. Typically the cyst fluid of mucinous neoplasms appears viscous and contains high levels of CEA, whereas in serous cystadenomas CEA levels are almost always low (7). Cytological examination shows epithelial cells with a positive mucin stain as opposed to cuboid epithelial cells with abundant periodic acid Schiff-positive glycogen in serous cystadenomas (8). Thus, mucinous neoplasms and therefore tumours with an obligatory pathway to malignancy can be detected with a relatively high accuracy. Because serous tumours were previously believed to be exclusively benign, this distinction so far seemed to be sufficient to make a decision regarding surgical therapy. In an attempt to develop preoperative markers to reliably discriminate malignant lesions, several tumor markers have been found markedly elevated in mucinous cystadenocarcinomas (8). However, with the possibility of malignant transformation of serous cystadenomas it becomes even more important to find preoperatively available markers that are also applicable to serous cystic lesions. In none of the reported serous cystadenocarcinomas has cystic fluid analysis been performed. Some authors have tried to determine possible markers for malignancy by immunohistochemical staining. Ishikawa et al. (9) examined the surgical specimen of 7 serous cystadenomas, 1 of which was clinically malignant and 2 histologically showed mild cell atypia. Immunohistochemical examinations for CEA and p53 were negative in all cases. Two specimens were stained focally with anti-CA 19-9, whereas the localization pattern over the entire surface of the cells seemed to be indicative of malignancy. Fuji et al. (10) retrospectively examined the expression of tumor markers on serous cystadenocarcinomas published until then. Only 1 case was positive for anti-CEA staining and 2 cases were positive for anti-CA 19-9 staining. Serum tumor markers also showed inconsistent results. Comparing all values of the published reports, no clear correlation can be found. The elevation of serum CA 19-9 may be suggestive of malignancy, but results are varying among the reported cases. Consistently with these observations, the present case showed normal levels of CEA and CA 19-9 (Table 1).

In summary, immunohistochemical analysis and serum tumor markers may be useful in determining malignancy of serous neoplasms. However, only a small number of cases has been examined thus far, and more extensive studies on larger collectives will be necessary. Using the presently available diagnostic tools, the preoperative differentiation between a benign and a malignant cystic lesion still cannot be done unequivocally. Because not only mucinous but increasingly also serous lesions undergo malignant transformation, some authors favour an aggressive surgical approach to all patients diagnosed with a cystic neoplasm of the pancreas. In a retrospective cohort analysis of 25 patients, Horvath and Chabot (11) examined the perioperative morbidity and mortality after surgery for cystic neoplasms of the pancreas and reported low occurrences of perioperative complications and no perioperative mortalities. The authors concluded that all cystic neoplasms of the pancreas should be resected, provided that the patient is medically suitable to undergo surgery. Nevertheless, the overall perioperative complication rate was 40%, and 1 of the patients had a total pancreatectomy, which caused a major perioperative complication of severe exocrine and endocrine pancreatic insufficiency. Although an increasing number of malignant serous lesions has been reported in the past decade, the overall prevalence of serous cystadenocarcinoma is assumed to be only about 1% of all cystic neoplasms. Yoshimi et al. (12) suggested that this low prevalence of malignancy among serous cystadenomas does not justify surgical resection in any case. Serous cystadenocarcinomas are relatively low-malignant tumours with a slow rate of tumor progression indicated by a long course of history with unspecific symptoms before diagnosis and a low expression of proliferation markers. To avoid over treatment of serous cystadenomas but still not dismiss possibly malignant serous lesions, we suggest to make surgical treatment dependent on the relative growth of the lesion. Infiltrative growth or an increase of 4 mm in diameter per year force resection. In cases where resection is necessary, the complex armamentarium of partial pancreatic resections including atypical resections are available. We agree with Yoshimi's conclusions, in fact the choice of the surgical procedure decision was dictated by the local invasion of the portal vein and infiltration of the pyloric region.

Because of the low occurrence of serous cystadenocarcinomas and inconsistently reported histological and immunohistochemical features, more extensive studies will be necessary to develop criteria for differential diagnosis. Our case may support the hypothesis described by George et al. (1), that serous cystadenocarcinoma truly exists in the pancreas. There is the possibility that all cystic tumours of the pancreas and ovaries have malignant potentials and that serous cystadenocarcinoma of the pancreas has a biologic

Table 1. Clinical features of previous reported serous cystoadenocarcinoma compared to the present case report.

	Previous Reports		Present case
Number of patients	22		1
Age (Mean ± SD)	66.82 ± 7.73		74
Gender	M (n=6) F (n=16)		M
Initial Symtoms/Signs (%)	Abdominal Pain	27.27%	Palpable Mass; Abdominal Pain
	Palpable Mass	22.72%	
	Weigh loss	18.18%	
	Incidental Detection	9.1%	
	Hemorrhage	4.54%	
	Enlarged lymph nodes	4.54%	
	Elevated liver function tests	4.54%	
	Jaundice	4.54%	
	Diarrhea	4.54%	
Malignant Findings (%)	Metastases in the liver	36.36%	Portal vein invasion
	Metastases in other organs	27.27%	
	Metastases in Lymph nodes Vascular	13.63%	
	Invasion	9.1%	
	Neural Invasion	4.54%	
Tumor Size (Mean ± SD)	9.5 ± 4.84 cm		8.5 cm
Tumor Location	(Pancreatic Tumor)		Head and Body
	Body	22.72%	
	Body and Tail	22.72%	
	Tail	9.1%	
	Entire Pancreas	13.63%	
	Head	13.63%	
Procedure	DP	45.45%	PD
	TP	9.1%	
	PPPD	4.54%	
	PD	4.54%	
	Enucleation	4.54%	
Outcome	No recurrence	45.45%	No recurrence 6 months later
	Death	4.54%	
	Not Stated	50%	

behaviour similar to that of adenoma malignum of the uterine cervix. However, the accumulation of additional cases resembling the current case may be necessary to establish serous cystadenocarcinoma as a new entity of the malignant pancreatic neoplasm and to clarify that the development of serous cystadenocarcinoma results from the transformation of serous cystadenoma in pancreas.

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