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Original article

Acinar cell cystadenoma of the pancreas: A retrospective analysis of ten-year experience from a single academic institution

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ABSTRACT

Background/objective: Acinar cell cystadenoma (ACA), also referred to as "acinar cystic transformation", is a rare and newly recognized cystic lesion of the pancreas displaying apparent acinar cell differentiation with benign outcomes. We summarized our experience with the diagnosis, clinicopathologic feature, treatment and prognosis of ACA to provide a reference for the disposal of this uncommon condition.
Methods: We retrospectively analyzed the clinical data from eight patients with ACA treated in our hospital between March, 2005 and January, 2015.
Results: Among eight patients, five of whom were female and the age at diagnosis ranged from 33 to 67 years (mean, 49.8 y). The most commonly clinical symptom was abdominal pain. Eight lesions were unifocal and either unilocular (n = 5) or multilocular (n = 3) with average size of 10.5 cm (range, 5.1–19.7 cm). All the patients were treated surgically and a definite diagnosis of ACA was obtained by the histopathological, histochemical and immunohistochemical tests. The length of stay range was from 11 to 17 days and there were no perioperative deaths. At a median follow-up of 57.3 months, all the patients were alive and there was no evidence of recurrence, distant metastasis or malignant transformation.
Conclusions: Appropriately preoperative differential diagnosis of ACA remains challenging and the final result is usually gained by the histopathology and immunohistochemistry. Although the origin of ACA is still contradictory, surgery is actively advocated as the most effective method for relieving the symptoms and preventing the tumor from local extension or malignant transformation so as to obtain an optimal long-term survival.

Introduction

With the continuous improvement in modern imaging techniques, more and more cystic lesions of the pancreas have been identified and emphasized clinically with the incidence being about 1 in 100 hospitalized patients in America [1]. Pancreatic cysts, characterized by different features of biology, etiology and morphology, usually have a broad spectrum of non-neoplastic lesion and cystic neoplasm. Although the vast majority of these cysts are non-neoplastic, 10%–15% represent cystic neoplasms of the pancreas [2]. Cystic neoplasms of the pancreas are relatively uncommon compared with solid tumors of the pancreas, but constitute an increasingly important category including benign and malignant tumors represented mainly by mucinous tumors and serous cystadenomas with a challenging differential diagnosis [3,4]. In recent years, an uncommon and novel cystic change of the pancreas, referred to as acinar cell cystadenoma (ACA), has become the new research focus of worldwide pancreatic surgeons and pathologists. ACA was first described by Zamboni in 2002 which was also known as "acinar cystic transformation" [5]. The exact etiopathogenesis of ACA is still not clear. As the benign counterpart of

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acinar cystadenocarcinoma, ACA shares the common features of obvious acinar differentiation of the epithelial cells, unrelation to the majorductal system, absence of distinct cellular atypia, focal or diffuse involvement of the pancreas and a good prognosis without any aggressive behavior including uncontrollable growth and metastasis inclination [5]. The size and complexity of the lesion vary considerably. Nevertheless, the neoplastic versus non-neoplastic origin of this lesion still remains unclear and contradictory [2,5,6]. Thus far, we retrospectively reviewed and analyzed the clinical results of eight patients with ACA treated in our hospital between March, 2005 and January, 2015. The aim of the present research was to report our experience with the diagnosis, treatment and prognosis of ACA and attempt a summary of the current literature. We hypothesize that our study could raise the awareness of surgeons about the existence of such a distinctive entity that is readily confused with other pancreatic tumors as well as provide a clinical reference for the management of this rare disease.

Methods

This study protocol was approved by the Institutional Review Board of the first affiliated hospital of Harbin Medical University. We retrospectively collected and analyzed the general characteristics, clinical presentation, imaging findings, surgical data, pathological features, postoperative course and long-term survival of eight patients histopathologically, histochemically and immunohistochemically diagnosed of ACA submitted to surgical resection in our department between March, 2005 and January, 2015. ACA was defined as pancreatic cystic lesion lined predominantly by acinar-type epithelium without cellular atypia. Gross pathological reports were assessed for the location, number, and size of cysts as well as the extent of pancreatic involvement. Outpatient records combined with telephone interviews were used for the clinical follow-up and all the patients were informed and agreed to participate in our research.

Results

Patient characteristics

A total of eight ACAs were identified during the study period. Of the eight patients, five (62.5%) were female and the age at diagnosis ranged from 33 to 67 years (mean 49.8 years). The clinical manifestations were non-specific, including abdominal pain (87.5%), abdominal distension (37.5%), weight loss (37.5%), anergy (62.5%), jaundice (12.5%), vomiting (12.5%), dyspepsia (12.5%) and constipation (12.5%). One patient whose ACA was found during routine healthy examination was asymptomatic. Palpable masses in the abdominal cavity were detected in four of the eight patients (50%) during the physical examinations. The clinical features of all the eight patients were listed in Table 1.

Laboratory and imaging findings

Each patient underwent laboratory and imaging tests after hospital admission and received a comprehensive assessment of the surgical risks. Among the patients, serum total bilirubin, carbohydrate antigen 19-9 (Ca-199), carcinoembryonic antigen (CEA) and amylase levels were enhanced in 3 cases, 2 cases, 1 case and 3 cases, respectively (Table 1). Besides, cystic fluid analyses guided by endoscopic ultrasonography (EUS) were performed in 4 cases and the levels of CEA, Ca-199 and amylase were elevated in 1 case, 2 cases and 2 cases, respectively (Table 1). Cytologic tests were used and 3 cases were nondiagnostic, while the fourth was reported as “no malignant cells found” (Table 1). In other words, the malignant lesions could not be completely ruled out. Radiological investigations were performed after admission, mainly including computered tomography (CT), magnetic resonance imaging (MRI), ultrasonography (US) and magnetic resonance cholangiopancreatography (MRCP), etc. CT and MRI displayed focal cystic lesions in different parts of the pancreas (Figs. 1 and 2). MRCP was exerted in three patients which showed the cysts of the pancreatic head accompanied by dilated bile ducts to different degrees (Fig. 2). Of all, two cases received endoscopic retrograde cholangiopancreatography (ERCP) and the results revealed that the cystic lesions did not communicate with the pancreatic ducts. Based on the imaging findings, the cystic lesions were classified as unilocular ($n = 5$) or multilocular ($n = 3$) variants and ranged in size from 5.1 to 19.7 cm (average size of 10.5 cm). Besides, the locations of pancreatic cysts involved the head in 2 cases, neck in 1 case, neck/body in 1 case, body/tail in 2 cases and tail in 2 cases, respectively. Before the operation, none of the patients obtained a definitive diagnosis and we also could not determine the real nature of these cystic lesions.

Surgical procedure

Due to the presence of abdominal symptoms, dubious malignancy and uncertain diagnosis with tumor size of larger than 5 cm, all the patients underwent laparotomy under general anesthesia. We performed pancreaticoduodenectomy in 3 cases, central pancreatectomy in 1 case, distal pancreatectomy combined with splenectomy in 3 cases and spleen-preserving distal pancreatectomy in 1 case, respectively. The total surgery duration ranged from 150 to 330 min. All the intraoperative data were listed in Table 2.

Histopathological, histochemical and immunohistochemical features

Grossly, the tissular samples revealed well-circumscribed cystic lesions of the pancreas containing serous fluid with no solid areas or papillary projections which did not infiltrate the pancreatic parenchyma. Besides, the internal surface was shiny and smooth (Fig. 3). There was no gross communication of the cysts with the pancreatic ducts, but with acinar structures. Hematoxylin and eosin-stained (HE) slides were tested to evaluate the histologic features. Histopathological views showed unilocular or multiple cysts lined by typical clusters of epithelium displaying apparent acinar cell differentiation, which were lack of distinct cellular atypia, nuclear mitotic figure, necrosis and infiltrative growth. The epithelium presented the characteristic central single nucleoli and the striking eosinophilic granularity of the cytoplasm reflected the presence of cytoplasmic zymogen granules. Besides, the primary cryptae could also be detected in some HE slides showing the process of forming an incipient acinus (Fig. 4-1). Histochemical staining analysis for periodic acid-Schiff with diastase pretreatment (PAS-D) was performed to support acinar origin and differentiation of the epithelial cell and the results showed that pink zymogen granules in the apical cytoplasm of the epithelium were seen (Fig. 4-2). The immunohistochemical analyses were also performed in all eight cases and the findings demonstrated typically positive staining for β-catenin, cytokeratin (CK) 7, lipase, Ki-67(labeling index was <1%), trypsin and chymotrypsin (Fig. 4-2). The expression of CK7 is the single identifiable difference from normal acinar cells which are CK7 negatively stained. β-catenin has a unique staining style of chicken-weired structure. The positive staining for Ki-67 means it is a benign behavior. In trypsin and chymotrypsin positively stained cells, tiny brown particles could be seen which are characteristic for acinar cells. In summary, the overall histopathological, histochemical and immunochemical profiles supported the definitive diagnosis of ACA.

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