

Clinicopathological features of giant cell carcinoma of the pancreas

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BACKGROUND: Giant cell carcinoma of the pancreas (GCCP) as a tumor of high malignancy, large size, and inflammatory reaction occupies 2.1%–12.8% of all cases of pancreatic malignancies. This study was to analyze cases of GCCP collected in 8 years at our hospital in an attempt to describe some features of GCCP in Chinese people.

METHODS: The clinicopathological features of 19 patients who had been pathologically diagnosed as having GCCP from 1021 patients with pancreatic malignancies collected by Pancreatic Disease Research Group (PDRG) of Changhai Hospital were retrospectively analyzed compared with those of 96 patients with common pancreatic carcinoma (PC) who were randomly selected from 1002 patients with pancreatic carcinoma. The differences of location, clinical symptoms, imagings, laboratory test, operation and the prognosis of these two groups were defined.

RESULTS: Tumors in the head of the pancreas were found in 8 patients (42.1%), and those in the body or tail of the pancreas in 11 (57.9%). The initial symptom was abdominal pain in most patients (57.9%). Abdominal pain (73.7%), dyspepsia (63.2%), weight loss (36.8%) but jaundice were common at the time of diagnosis. The abnormal rates of routine laboratory tests in the GCCP group were lower than those in the common PC group. The assay of tumor markers between the groups of GCCP and common PC was approximately the same. The sensitivity and accuracy of ultrasonography, spiral computed tomography and magnetic resonance imaging were considerably high. Large carcinoma in stage IV was seen in 9 patients or 47.4% of the GCCP group, a rate higher than that in the common PC group. Osteoid formation was found microscopically in some patients, and poorly differentiated tumor cells were found in most patients. The 1-year survival rate was 17.6%, which was lower than that in the common PC group.

CONCLUSION: The clinicopathological features of GCCP are different from those of common PC. Imaging tests can be used together with the assay of tumor markers to diagnose GCCP as early as possible and to improve the prognosis of GCCP patients.

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KEY WORDS: pancreatic neoplasm; pathology; diagnosis; stage classification; prognosis

Introduction

Giant cell carcinoma of the pancreas (GCCP) is a rare tumor of high malignancy, large size, and inflammatory reaction, which accounts for 2.1%–12.8% of all cases of pancreatic malignancies. It has long been discussed whether it is of epithelial or mesenchymal origin and whether its prognosis is better than that of other exocrine tumors of the pancreas.^[1] GCCP generally is associated with a poor prognosis, and patients usually die within months despite intensive multimodality therapy. Some patients with GCCP, however, may survive longer when invasion of adjacent organs and distant metastases are absent. Surgical resection is an appropriate treatment for tumors with these favorable characteristics.^[2] This study was designed to analyze GCCP cases collected in about 8 years at this hospital, attempting to find some features of GCCP in Chinese people.

Methods

Nineteen patients with GCCP were identified from 1021 patients with pancreatic cancers who had been collected from 1994 to 2001 by the Pancreatic Disease Research Group of this hospital. All of the 19 patients were diagnosed as having GCCP pathologically and they had no severe disorders of the heart, liver, and kidney except that caused by tumor itself in late stage.

Ninety-six patients were randomly selected from the other 1002 patients with pancreatic carcinoma who had been diagnosed as having common pancreatic carcinoma (PC). The differences between the two groups were detected according to the sites of tumors, clinical symptoms, imaging results, laboratory findings, operative resectability, and prognosis.

Statistical analysis was performed using the SPSS software, mainly Student's *t* test, Pearson's product-moment correlation coefficient and the chi-square test.

Results

Sex, age, and tumor sites

In the 19 patients with primary GCCP (13 men and 6 women; aged from 34 to 77 years), 8 (42.1%) had GCCP located in the head of the pancreas and 11 (57.9%) had GCCP in the body or tail of the pancreas. In the common PC group (96 patients), 68 (70.8%) had PC in the head, 23 (24.0%) in the body or tail, 5 (5.2%) in the whole pancreas. Significant differences were observed between the two groups ($P < 0.05$).

Clinical symptoms

All of the 19 patients with GCCP showed symptoms characterized initially by abdominal pain (57.9%) and dyspepsia (36.8%). Abdominal pain (73.7%), dyspepsia (63.2%), weight loss (36.8%), abdominal distention (21.1%), jaundice (15.8%), diarrhea (15.8%), diabetes mellitus (10.5%) were prominent at the time of diagnosis. As an initial symptom abdominal pain was more common in the GCCP group than in the control group, but jaundice as an initial symptom was less common ($P < 0.05$).

Laboratory tests

In the GCCP group, the levels of serum bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), γ -glutamyltransferase (GGT), and albumin were 31.6%, 36.8%, 47.4%, 36.8%, 26.1%, respectively, which were lower than those but ALT in the common PC group. The increased level of serum amylase was 21.1%, and the increased levels of serum CEA and CA19-9 were 21.1%, 57.9%, respectively. No significant differences were observed between the two groups. In 5 patients who received examination of CA125, 2 patients had the level above the standard. Fasting blood glucose level above the standard was noted in 36.8% of the patients.

Imaging examinations

In the GCCP group, the sensitivities of abdominal ultrasonography, spiral computed tomography (SCT), endoscopic ultrasonography (EUS), magnetic resonance imaging (MRI), endoscopic retrograde cholangiopancreatography (ERCP) were 94.7%, 100%, 100%, 100%, 88.9%, respectively, which were higher than those in the common PC group. The accuracy of these methods was 78.9%, 83.3%, 64.3%, 81.3%, 55.6%, respectively, which were the same in the common PC group. No significant differences were found between the two groups. None of the 19 patients was examined angiographically.

Operation, stage and pathology

In the 19 patients, clinical stage of I, II, III, IV comprised 15.8%, 21.1%, 15.8%, 47.4%, respective-



Fig. Giant cell carcinoma of the pancreas (HE, original magnification $\times 100$).

ly, in contrast to 13.5%, 28.1%, 26.0%, 32.4% in the common PC group. No significant differences were observed between the two groups. Two of 8 patients with carcinoma in the head of the pancreas received pancreaticoduodenectomy, and 3 (26.3%) of 19 patients underwent palliative operation, with a total resectable rate of 21.1%. The tumor diameter varied from 4 to 23 cm (mean 7.4 cm). Nine patients (47.4%) had blood metastasis. The rate of low differentiation was 47.1% (8/17), and 4 patients were found osteoid formation by microscopic examination (Fig.).

Prognosis

In 17 of the GCCP group who had been followed up, the 0.5-, 1-, 2-, 3-, 4-, and 5-year survival rates were 23.5%, 17.6%, 11.8%, 0, 0, and 0, respectively, and those in the common PC group were 58.3%, 26.0%, 11.5%, 5.2%, 2.1%, and 1.0%, respectively. The survival rates of the GCCP group were lower than those of the common PC group, especially the half-year survival rate ($P < 0.05$). The mean survival time of the 17 patients was 4.7 months.

Discussion

Pathological features of GCCP were first reported by Sommers and Meissner.^[3,4] Early studies showed that it is a rare but highly malignant carcinoma.^[5,6] In this study, GCCP comprised 1.9% of the patients because of incomplete pathological diagnosis, and the actual rate may be higher. Researchers believe that GCCP has some features different from those of common PC.

First, the tumor is mostly originated from the body and tail of the pancreas in contrast to common PC which happens in the head of the pancreas.

Second, different symptoms are due to different tumor sites. Abdominal pain as an initial symptom is

prominent in patients with GCCP, whereas jaundice is much less common in patients with common PC. This may be attributable to occurrence of tumor mainly in the body or tail of the pancreas, which rarely causes bile duct obstruction or constriction. The high incidence of abdominal distention as an initial or main symptom may be related to the potential growth of the tumor to a giant mass. In 48 patients with GCCP reported before 1999 in Japan, 60% had a tumor diameter larger than 6 cm, the largest being 24.5 cm,^[7] which may be another characteristic of GCCP.

The assay of tumor markers showed that the increased levels of CA19-9, CEA in the GCCP group were lower than those in the common PC group, but no significant differences were observed between them. The sensitivities of abdominal ultrasonography, SCT, EUS, MRI, ERCP in the GCCP group were higher than those in the common PC group. The accuracy between GCCP and common PC was approximately the same and no significant differences were observed between the two groups. Ultrasound examination of GCCP revealed an irregularly low-resonance mass, and CT revealed low density and irregular enhancement.^[8]

As to tumor staging and prognosis, the ratio of stage I to the 1-year survival rate of GCCP patients were lower than that of common PC patients. Because of poor prognosis of pancreatic carcinoma, no significant differences were observed between the two groups except for the half-year survival rate.

Three features of GCCP were reported.^[7] First, inflammatory reaction of tumor syndrome or the levels of blood leucocytes, C-reaction protein (CRP) and interleukin (IL) increased. The increase of blood leucocytes and CRP accounted for 53% of all cases of GCCP reported in Japan in 1999. GCCP may have the property to secrete inflammatory mediators. Second, excessive blood vessels were seen angiographically in the region of tumor, with a tumor staining phenomenon, which was found in 58% of patients with GCCP reported in Japan before 1999. Excessive blood vessels were rarely seen in patients with common PC. Third, osteoid formation was found microscopically in some patients. Because of insufficient knowledge on GCCP, examination of inflammatory mediators and angiography were not performed in all patients of this study.

We believe that GCCP is easy to metastasize via blood, which may be one of the reasons for its poor prognosis.^[9-11] Researchers also found pathologically that osteoid formation and blood metastasis are two key factors of prognosis that the former is beneficial to the prognosis, whereas the latter is harmful. Four of the 19 patients with GCCP had osteoid formation. Their half-year survival rate was 75%.

Clinically, GCCP has the following characteristics: 2% in pancreatic carcinomas; over 50% in the body or tail of the pancreas; common in men; initial symptom

characterized by abdominal pain (>50%) in most patients; common symptoms including abdominal pain, dyspepsia, weight loss and abdominal distention; no highly specific methods for detection; secretion of inflammatory mediators; ultrasonography, SCT and MRI angiography detectable showing excessive blood vessels in the region of tumor; high blood metastasis, stage IV (1/2) other than in adenocarcinoma; large tumor (mean diameter 7.4 cm); osteoid formation found pathologically; poor prognosis compared with common PC; mean survival rate less than 5 months; osteoid formation beneficial to prognosis but blood metastasis harmful; and low- or medium-differentiated.

Competing interest

The author or authors do not choose to response to the statements listed in Instructions for Authors.

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