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Research Paper

An evaluation of the diagnostic value of CA19-9 and CEA levels in patients with pancreatic cancer

Zhenhua Ma*, Qingyong Ma, Zheng Wang
Department of Hepatobiliary Surgery, the First Affiliated Hospital, Medical School of Xi' an Jiaotong University, Xi' an 710061, China
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Abstract

Objective: The use of a combination of tumor markers may be an important tool in the early diagnosis of pancreatic cancer, which is the key to improving prognosis. The study aim was to investigate the diagnostic value of carbohydrate antigen 19-9(CA 19-9) and carcinoembryonic antigen(CEA) levels in patients with pancreatic cancer. **Methods:** An immunoradiometric assay was used to homochronously measure the serum CA19-9 and CEA levels in 78 pancreatic cancer cases and 64 healthy examinees in hospital. The normal reference values were CA19-9(0-39 U/ml) and CEA(0-3.4 ng/ml). **Results:** Mean serum CA19-9 and CEA levels in patients with pancreatic cancer(406.55±60.18 U/ml, 12.43 ± 1.25 ng/ml) were significantly higher($P < 0.01$) than those in healthy examinees(16.54 ± 1.95 U/ml, 2.37 ± 0.17 ng/ml). The sensitivity of the combined detection of CA19-9 and CEA (92.31%) was significantly higher($P < 0.05$) than that of either marker alone (79.49%, 71.79%, respectively). In addition, the sensitivity to diagnose pancreatic cancer by detecting the serum CA19-9 and CEA levels was higher($P < 0.05$) in stage ⅡB + Ⅲ + Ⅳ(87.04%, 79.23%) than stage Ⅰ + ⅡA(62.50%, 54.17%). **Conclusion:** The combined detection of CA19-9 and CEA could overcome the deficiency of using single marker detection by improving the sensitivity to diagnose pancreatic cancer. At the same time, CA19-9 and CEA detection could be used to assess mesenteric artery invasion and the metastasis of lymphatics and distant organs in pancreatic cancer.

Keywords: pancreatic cancer; carbohydrate antigen19-9; carcinoembryonic antigen

INTRODUCTION

Due to the onset of delitescence, atypical symptoms, high malignancies and early lymph node metastasis of pancreatic cancer, it is usually at an advanced stage when clinically diagnosed. This results in a low rate of surgical resection and a poor prognosis[1-3]. Therefore, the key to improving the rate of surgical resection and the prognosis is early detection[4-7]. For this reason, it was necessary to integrate the results of ultrasound, imaging and endoscopy, and to detect abnormal levels of tumor markers [8-10]. We retrospectively analyzed the serum carbohydrate antigen 19-9(CA 19-9) and carcinoembryonic antigen(CEA) levels in 78 pancreatic cancer patients and 64 healthy examinees at the same time. The goal was to evaluate the early diagnostic value of the detection of two tumor markers, CA19-9 and CEA, in pancreatic cancer.

MATERIALS AND METHODS

Clinical materials

We collected data on 78 patients with pancreatic cancer who were treated from January 2003 to December 2007 in the First Affiliated Hospital of the Medical School of Xi' an Jiaotong University. Their ages ranged from 31 to 86 years old, and 26 were females and 52 were males. All the cases were confirmed by surgical or pathological examination and staged according to the International Union Against Cancer (6th edition). There were one case of stage Ⅰ, 23 cases of stage ⅡA, 2 cases of stage ⅡB, 30 cases of stage Ⅲ, and 22 cases of stage Ⅳ. We also selected 64 healthy examinees in the same time. Their ages ranged from 25

*Corresponding author.
E-mail address: mzh@mail.xjtu.edu.cn

to 66 years old, and 31 were female and 33 were male.

Evaluation of tumor markers

The serum was stored in a -20℃ freezer after collecting a 5ml fasting blood sample from the medial cubital vein. The CA19-9 and CEA levels were detected by an immunoradiometric assay. The kits were purchased from the Institute of Atomic Energy(China) and the assays were carried out following the manufacturer's instructions. The normal reference values, which were 0-39 U/ml(CA19-9) and 0-3.4 ng/ml(CEA), and the above-range values were determined using the standards applied in the First Affiliated Hospital of the Medical School of Xi'an Jiaotong University.

Statistical analysis

We selected SPSS11.5 statistical software for statistical treatment. The mean serum CA19-9 and CEA level were presented as mean ±SD and differences between means were compared by Student's *t* test. The values of sensitivity, specificity and accuracy were compared by chi-square tests. $P < 0.05$ was considered statistically significant.

RESULTS

Serum CA19-9 and CEA levels

Mean serum CA19-9 levels in healthy examinees and patients with pancreatic cancer were 16.54 ± 1.95 U/ml and 406.55 ± 60.18 U/ml, respectively. Mean serum CEA levels in healthy examinees and patients with pancreatic cancer were 2.37 ± 0.17 ng/ml and 12.43 ± 1.25 ng/ml, respectively. The serum CA19-9 and CEA levels in patients with pancreatic cancer were significantly higher than those in healthy examinees ($P < 0.01$).

The diagnostic value of tumor markers in patients with pancreatic cancer

The diagnostic sensitivity of tumor detection using the combination of CA19-9 and CEA was higher than either marker alone($P < 0.05$), while the specificity of tumor detection using the combination of CA19-9 and CEA was not significantly different when compared to either marker alone($P > 0.05$)(***Table 1***).

Table 1 **The diagnostic efficacy of using single and combined markers for tumor detection in patients with pancreatic cancer(%)**

Tumor markers	Sensitivity	Specificity	Accuracy	Positive predictive value	Negative predictive value
CA19-9	79.49(62/78)*	95.31(61/64)	85.42(123/144)	95.39(62/65)	79.22(61/77)
CEA	71.79(56/78)*	93.75(60/64)	80.56(116/144)*	93.33(56/60)	73.17(60/82)*
CA19-9+CEA	92.31(72/78)	89.06(57/64)	89.58(129/144)	91.14(72/79)	90.48(57/63)

Compared with CA19-9+CEA, *$P < 0.05$.

The levels of serum tumor markers in different TNM stages of pancreatic cancer

The mean serum CA19-9 level was 357.31 ± 107.03 U/ml in stage Ⅰ+ⅡA pancreatic cancer and 428.43 ± 73.22 U/ml in stage ⅡB+Ⅲ+Ⅳ($P > 0.05$). However, the sensitivity of diagnosing pancreatic cancer by detecting the serum CA19-9 level was higher in stage ⅡB+Ⅲ+Ⅳ(87.04%) than stage Ⅰ+ⅡA(62.50%) ($P < 0.05$).

The mean serum CEA level was 11.38 ± 2.53 ng/ml in stage Ⅰ+ⅡA pancreatic cancer and 12.89 ± 1.43 ng/ml in stage ⅡB+Ⅲ+Ⅳ($P > 0.05$). As with CA19-9, the sensitivity of diagnosing pancreatic cancer by detecting the serum CEA level was higher in stage ⅡB+Ⅲ+Ⅳ(79.23%) than stage Ⅰ+ⅡA(54.17%) ($P < 0.05$).

DISCUSSION

Tumor markers are antigens and bioactive substances produced by tumor cells because of the abnormal expression of correlated genes. They are either not produced, or only minimally produced, in normal tissues, and can be detected in tissues, body fluids and excreta of patients with cancer. CA19-9, an intracellular adhesion molecule with a molecular weight greater than 500,000, mainly exists in the gastrointestinal tract, pancreas and biliary tract. The serum content was reported to be especially high in the patients with pancreatic and biliary tract cancers[11-15]. Goonetilleke and Siriwadena performed a systematic review of the MEDLINE database and found that the average diagnostic sensitivity of CA 19-9 of pancreatic cancer was 79% and the specificity was 82%[16]. CEA is a soluble glycoprotein, which has been reported to be markedly elevated in patients with digestive tract cancer, most conspicuously those involving the colon and rectum[17,18]. CEA had a relatively low sensitivity for the diagnosis of pancreatic cancer.

Because there has been no important breakthrough in the search for a new pancreatic cancer-specific antigen in recent years, the search for laboratory tests to diagnose pancreatic cancer at an early stage has shifted to detecting a combination of markers to overcome the deficiencies of using single markers, and thus improve the test sensitivity and specificity. Research results have

shown that the detection of a combination of tumor markers could greatly increase the diagnostic efficacy when compared to single marker detection[19-21]. Therefore we evaluated the diagnostic value of CA19-9 and CEA levels in patients with pancreatic cancer. Our research showed that the diagnostic sensitivity was markedly improved by using the combination of CA19-9 and CEA, but not the specificity. Overall, the use of a combination of the two markers, CA19-9 and CEA, could improve the diagnostic efficacy in pancreatic cancer, and could be of great significance in screening high-risk groups for early diagnosis.

Tumor markers are not only important for the diagnosis of pancreatic cancer, but can be of much value in detecting tumor recurrence and metastasis, and in the evaluation of therapeutic efficacy:①Tumor recurrence and metastasis after an operation could be found in time by determining the levels of several tumor markers in serum; ②The levels of tumor markers have been used to help determine the surgical method before an operation[22-25]. Zhang *et al*[11] performed a study to evaluate the value of serum CA19-9 levels in predicting the resectability of pancreatic cancer and found that a serum CA19-9 level of 353.15 U/ml could be used as a resectability cutoff, which was similar to the study of Kiliç *et al* [26]. Our study found that, with the progression of tumor, there was no significant difference in the serum CA19-9 and CEA levels, but the diagnostic sensitivity of CA19-9 and CEA was significantly different between stage Ⅰ+ⅡA and stage ⅡB + Ⅲ+ Ⅳ pancreatic cancer. This indicates that the sensitivity of using CA19-9 and CEA to diagnose pancreatic cancer increased with mesenteric artery invasion, and lymphatic and distant organic metastasis.

The early diagnosis of pancreatic cancer is a complicated and urgent problem, which must be improved upon to improve current treatment of this particularly deadly cancer. Thus, research on the use of combined tumor markers is getting more and more attention. Comprehensive utilization and rational analysis of the results of these tumor marker tests could overcome the deficiencies of single marker detection. Combined tumor marker tests could be of great significance for early diagnosis, and perhaps aid in determining the staging of pancreatic cancer when screening high-risk groups.

References

[1] Wilkowski R, Wolf M, Heinemann V. Primary advanced unresectable pancreatic cancer. *Recent Results Cancer Res* 2008; 177:79-93.

[2] Traverso LW. Pancreatic cancer: surgery alone is not sufficient. *Surg Endosc* 2006;20:S446-9.

[3] Krysa J, Miller M, Kukreja N, Steger A. Pancreatic cancer-is an aggressive approach justified? *Ann R Coll Surg Engl* 2005; 87:163-6.

[4] Noto M, Miwa K, Kitagawa H, Kayahara M, Takamura H, Shimizu K, Ohta T. Pancreas head carcinoma: frequency of invasion to soft tissue adherent to the superior mesenteric artery. *Am J Surg Pathol* 2005;29:1056-61.

[5] Karachristos A, Scarmeas N, Hoffman JP. CA 19-9 levels predict results of staging laparoscopy in pancreatic cancer. *J Gastrointest Surg* 2005;9:1286-92.

[6] Moniaux N, Chakraborty S, Yalniz M, Gonzalez J, Shostrom VK, Standop J, *et al.* Early diagnosis of pancreatic cancer: neutrophil gelatinase-associated lipocalin as a marker of pancreatic intraepithelial neoplasia. *Br J Cancer* 2008;98:1540-7.

[7] Lee JK. Screening and diagnosis for pancreatic cancer. *Korean J Gastroenterol* (in Korean)2008;51:84-8.

[8] Laurell H, Bouisson M, Berthelemy P, Rochaix P, Dejean S, Besse P, *et al.* Identification of biomarkers of human pancreatic adenocarcinomas by expression profiling and validation with gene expression analysis in endoscopic ultrasound-guided fine needle aspiration samples. *World J Gastroenterol* 2006;12:3344-51.

[9] Zhang GW, Zhou J, Li CL, Huang YQ. Diagnosis and treatment of pancreatolithiasis: report of 16 cases. *Hepatobiliary Pancreat Dis Int* 2005;4:135-8.

[10] Miura F, Takada T, Amano H, Yoshida M, Furui S, Takeshita K. Diagnosis of pancreatic cancer. *HPB(Oxford)* 2006;8:337-42.

[11] Zhang S, Wang YM, Sun CD, Lu Y, Wu LQ. Clinical value of serum CA19-9 levels in evaluating resectability of pancreatic carcinoma. *World J Gastroenterol* 2008;14:3750-53.

[12] Duraker N, Hot S, Polat Y, Höbek A, Gençler N, Urhan N. CEA, CA 19-9, and CA 125 in the differential diagnosis of benign and malignant pancreatic diseases with or without jaundice. *J Surg Oncol* 2007;95:142-7.

[13] Cwik G, Wallner G, Skoczylas T, Ciechanski A, Zinkiewicz K. Cancer antigens 19-9 and 125 in the differential diagnosis of pancreatic mass lesions. *Arch Surg* 2006;141:968-74.

[14] Harder J, Kummer O, Olschewski M, Otto F, Blum HE, Opitz O. Prognostic relevance of carbohydrate antigen 19-9 levels in patients with advanced biliary tract cancer. *Cancer Epidemiol Biomarkers Prev* 2007;16:2097-100.

[15] Shukla VK, Gurubachan, Sharma D, Dixit VK, Usha. Diagnostic value of serum CA242, CA 19-9, CA 15-3 and CA 125 in patients with carcinoma of the gallbladder. *Trop Gastroenterol* 2006;27:160-5.

[16] Goonetilleke KS, Siriwardena AK. Systematic review of carbohydrate antigen(CA 19-9) as a biochemical marker in the diagnosis of pancreatic cancer. *Eur J Surg Oncol* 2007;33: 266-70.

[17] Fernandes LC, Kim SB, Matos D. Cytokeratins and carcinoembryonic antigen in diagnosis, staging and prognosis of colorectal adenocarcinoma. *World J Gastroenterol* 2005,11: 645-8.

[18] Ren JQ, Zhou ZW, Wan DS, Lu ZH, Chen G, Wang GQ, *et al.* Univariate and multivariate regression analyses of recurrence and metastasis of colon cancer after radical resection. *Ai Zheng* (in Chinese) 2006;25:591-5.

[19] Ni XG, Bai XF, Mao YL, Shao YF, Wu JX, Shan Y, *et al.* The

clinical value of serum CEA, CA19-9, and CA242 in the diagnosis and prognosis of pancreatic cancer. *Eur J Surg Oncol* 2005;31: 164-9.

[20] Liao Q, Zhao YP, Yang YC, Li LJ, Long X, Han SM. Combined detection of serum tumor markers for differential diagnosis of solid lesions located at the pancreatic head. *Hepatobiliary Pancreat Dis Int* 2007;6:641-5.

[21] Jiang XT, Tao HQ, Zou SC. Detection of serum tumor markers in the diagnosis and treatment of patients with pancreatic cancer. *Hepatobiliary Pancreat Dis Int* 2004;3:464-8.

[22] Kang CM, Kim JY, Choi GH, Kim KS, Choi JS, Lee WJ, Kim BR. The use of adjusted preoperative CA 19-9 to predict the recurrence of resectable pancreatic cancer. *J Surg Res* 2007; 140:31-5.

[23] Niedergethmann M, Hildenbrand R, Wostbrock B, Hartel M, Sturm JW, Richter A, Post S. High expression of vascular endothelial growth factor predicts early recurrence and poor prognosis after curative resection for ductal adenocarcinoma of the pancreas. *Pancreas* 2002;25:122-9.

[24] Smith RA, Bosonnet L, Ghaneh P, Sutton R, Evans J, Healey P, *et al.* The platelet-lymphocyte ratio improves the predictive value of serum CA19-9 levels in determining patient selection for staging laparoscopy in suspected periampullary cancer. *Surgery* 2008;143:658-66.

[25] Matsumoto G, Muta M, Tsuruta K, Horiguchi S, Karasawa K, Okamoto A. Tumor size significantly correlates with postoperative liver metastases and COX-2 expression in patients with resectable pancreatic cancer. *Pancreatology* 2007;7:167-73.

[26] Kiliç M, Göçmen E, Tez M, Ertan T, Keskek M, Ko M. Value of preoperative serum CA 19-9 levels in predicting resectability for pancreatic cancer. *Can J Surg* 2006;49:241-4.