FACTORS AFFECTING SERUM LEVELS OF CA 19-9 WITH SPECIAL REFERENCE TO BENIGN HEPATOBILIARY AND PANCREATIC DISEASES


*The Department of Internal Medicine, Cancer Research Institute and **The First Department of Internal Medicine, School of Medicine, Kanazawa University, Kanazawa 921, Japan

Summary

In order to elucidate the factors affecting the serum levels of CA 19-9, we analyzed sera of 79 patients with pancreatic cancer and 169 with non-malignant diseases, chiefly consisting of hepatobiliary and pancreatic diseases. Serum CA 19-9 values in patients with pancreatic cancer had no relation to the location of the tumor or presence of jaundice. Similarly, no tendency was observed as to the location and size of tumor or to the grade of differentiation in 12 CA 19-9-negative patients with pancreatic cancer. Serum levels of CA 19-9 in patients with cholelithiasis complicated by cholangitis frequently showed markedly high values, but then rapidly normalized in parallel with the subsiding of inflammation. The behaviour of serum CA 19-9 showed little relation to renal or hepatic failures or to intrahepatic cholestasis. However, slightly elevated levels of the antigen were found in more than half of those patients with fulminant hepatitis showing massive necrosis. In chronic pancreatitis, the prevalence was only 8%; however, an increase was observed at the time of exacerbation in 2 of 5 positive patients. There was hardly any increase in serum levels of CA 19-9 after endoscopic retrograde cholangiopancreatography (ERCP), although serum levels of pancreatic enzymes rose after ERCP in almost all patients. Thus, it appears that CA 19-9 does not easily escape into the bloodstream, unlike pancreatic enzymes.

Key Words: Benign liver diseases, Cholelithiasis, CA 19-9, Pancreatic cancer, Pancreatitis.

Introduction

The carbohydrate antigen, CA 19-9, discovered by Koprowski et al.1,2) is a digestive cancer-related antigen defined by monoclonal antibody and has recently attracted attention as a tumor marker. With the development of the solid-phase, radioimmunometric sandwich assay, it has been made clear that this antigen in blood shows particularly high sensitivity and high values in pancreatic cancer3-15). Thus, a test using this antigen is gaining acceptance as an important diagnostic method for pancreatic...
cancer.

On the other hand, it is also known that there are some CA 19-9-positive patients with benign diseases such as pancreatitis, hepatitis and cholelithiasis\(^5\)-\(^12\). However, questions about the relationship of the clinical status of these diseases with positive CA 19-9, or whether CA 19-9 is affected by the metabolism in the liver and kidney remain obscure.

For the purpose of elucidating what factor affects the serum concentration of CA 19-9, we determined serum levels of CA 19-9 in pancreatic cancer and various benign diseases and studied their relationship to the clinical disease status.

**Subjects and Methods**

**Serum levels of CA 19-9 in various diseases**

A total of 248 patients were entered into this study. They consisted of 79 pancreatic cancer patients (inclusive of islet cell cancer 1) and 169 with various benign diseases: chronic pancreatitis (61 patients), cholelithiasis (29), fulminant hepatitis (7), acute hepatitis (10), chronic hepatitis (19), liver cirrhosis (32) and chronic renal failure (11). Of the 79 patients with pancreatic cancer, the lesions were confirmed pathologically by surgery or autopsy in 60 patients and the remaining 19 patients were diagnosed by radiological evidence on computed tomography (CT), endoscopic retrograde pancreatography (ERCP), and angiography. The diagnosis of chronic pancreatitis was based on an unequivocally abnormal ERCP and/or pancreatic malfunction, with a decrease in at least two of three parameters in the pancreozymin secretin test: output fluid volume, maximal bicarbonate concentration, and amylase output in duodenal aspirate. Cholelithiasis was diagnosed by such examinations as sonography and/or endoscopic retrograde cholangiography (ERC) and classified into cholecystolithiasis (22) and choledocholithiasis (7). Plasma exchange was performed for all 7 patients with fulminant hepatitis who had severely impaired liver function and hepatic encephalopathy; sera were obtained before plasma exchange. Other liver diseases were diagnosed by liver biopsy or peritoneoscopy in addition to serobiochemical examinations. Chronic renal failure originated from chronic glomerulonephritis; all patients were on hemodialysis, and sera drawn immediately before dialysis were used. Sera were preserved at \(-70^\circ\text{C}\) until determination.

CA 19-9 was determined with the CA 19-9 RIA kit supplied by Centocor (Malvern, U.S.A.). This kit is based on the solid-phase sandwich assay using beads. Levels over 37 units/ml were regarded as positive in accordance with reports by Del Villano et al.\(^5\).

**Serum CA 19-9 levels before and after ERCP**

ERCP was performed on 21 patients with various digestive diseases including chronic pancreatitis (2) and pancreatic cancer (2). Pre-ERCP sera were obtained on the morning of the day ERCP was performed and post-ERCP sera from 12 to 16 hours after ERCP. CA 19-9 was determined by the method mentioned earlier. As for pancreatic enzymes, amylase was determined by the blue-starch method (Shionogi, Osaka, Japan), elastase I by the double antibody radioimmunoassay (Dinabott, Tokyo, Japan), and lipase by nephelometry (Kokusai Shiyaku, Tokyo, Japan).

Statistical analysis of CA 19-9 concentration was made by the logarithmic scale, and Student's t-test was used to analyse the result. To correlate different quantitative data, a linear regression coefficient was calculated.

**Results**

**Serum CA 19-9 levels and clinical status in pancreatic cancer**

Seventy-nine patients were divided according to the location of their pancreatic cancers into