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Extraordinarily elevated serum levels of CA 19-9 and rapid decrease after succesfull therapy: A case report and review of literature

Olağanüstü yüksek serum CA 19-9 düzeyleri ve tedavi sonrası hızlı düşüş: Vaka sunumu ve literatürün gözden geçirilmesi

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Carbohydrate antigen 19-9 is most valuable as a serum marker for pancreatic and biliary cancer, but increased concentrations occur in several other gastrointestinal malignancies. A carbohydrate antigen 19-9 value of >1,000 U/ml usually indicates a digestive cancer and has been reported to have a specificity greater than 99% for pancreatic cancer; nevertheless, false-positive results owing to benign diseases such as pancreatitis or liver cirrhosis have been noted. We present a patient with cholelithiasis and choledocholithiasis with acute cholangitis who had very high serum levels of carbohydrate antigen 19-9 (9586 IU/ml). The rapid decrease in carbohydrate antigen 19-9 after successful treatment was as interesting as the pretreatment high serum level of carbohydrate antigen 19-9.

Key words: Ca 19-9, cholangitis, choledocholithiasis

CA 19-9 her ne kadar bazı gastrointestinal malignitelerde yükselse de asıl olarak pankreatik ve biliyer kanser olgularında değerli bir tümör belirtecidir. 1000 IU/ml üzerindeki CA 19-9 düzeyleri hemen her zaman sindirim kanalı kökenli bir maligniteye işaret eder. Pankreas kanseri için %99'dan fazla özgüllüğe sahip olsa da pankreatit, karaciğer sirozu gibi benign hastalıklara ait yalancı pozitif olgular da bildirilmiştir. Burada safra kesesi ve koledok taşı ile beraber akut kolanjit atağı geçiren olağanüstü yüksek CA 19-9 düzeyleri olan (9568 IU/ml) ve CA 19-9 düzeyinin başarılı tedavi sonrası kısa sürede hızla düzeldiği bir olguyu sunuyoruz.

Anahtar kelimeler: CA 19-9, kolanjit, koledokolitiyasis

INTRODUCTION

Carbohydrate antigen 19-9 (CA 19-9) is a kind of glycosphingolipid that is a specific sialyzed derivative of the Le^a blood group and shown as Le^{xa}. The CA 19-9 antigen was first isolated by Koprowski et al. (1, 2) using a monoclonal antibody generated against colonic carcinoma cell lines. Subsequently, a radioimmunometric assay was developed by Del-Villano et al. (3) to quantify CA 19-9.

CA 19-9 is most valuable as a serum marker for pancreatic and biliary cancer, but increased concentrations occur in several other gastrointestinal (GI) malignancies, e.g., gastric, colorectal and liver cancer and also in breast, lung and gynecological cancers (4-10). However, elevated levels may also occur in benign diseases (11-15). A CA 19-9 value of >1,000 U/ml usually indicates a digestive cancer and has been reported to have a specificity over 99% for pancreatic cancer (16); nevertheless, false-positive results owing to benign diseases such as pancreatitis or liver cirrhosis have been noted (17,18). Murohisa et al. (19) reported a case of acute cholangitis with a CA 19-9 level of 6000 IU/ml, which had decreased in six weeks after successful biliary drainage.

We present a patient with cholelithiasis and choledocholithiasis with acute cholangitis who had very high serum levels of CA 19-9 (9586 IU/ml). The rapid decrease in CA 19-9 after successful treatment was as interesting as the pretreatment high serum level of CA 19-9.

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CASE REPORT

A 76-year-old female patient was admitted to our hospital with symptoms of shaking chills, fever, abdominal pain, pruritus, fatigue, and dark urine. Physical examination revealed scleral icterus, jaundice and epigastric tenderness. Body temperature was 38°C. Complete blood test results were as follows: white blood cells 16000/ mm^3 and blood hemoglobin 14.2 g/dl. Biochemistry results were: aspartate aminotransferase (AST): 202 IU/L, alanine aminotransferase (ALT): 228 IU/L, gamma glutamyl transpeptidase (GGT): 296 IU/L, alkaline phosphatase (ALP): 866 IU/L, total bilirubin: 14.3 mg/dl, direct bilirubin: 10 mg/dl, amylase: 36 IU/L, lipase: 38 IU/L, protein: 7 g/dl, albumin: 3.8 g/dl, and serum CA 19-9: 9586 IU/ml (normal range: 0-37). Ultrasonographic examination of the liver and biliary system showed cholelithiasis, choledocholithiasis, dilatation of common bile duct and intrahepatic biliary ducts, and portal hilar lymph nodes. Abdominal computerized tomography revealed a stone in the common bile duct. Endosonography showed dilatation of the common bile duct (10 mm), choledocholithiasis and multiple stones in the gallbladder. Endoscopic retrograde cholangiography showed cholelithiasis and choledocholithiasis. Ceftriaxone 2 g/day was started. Sphincterotomy and extraction of biliary stone was performed for biliary drainage. After this procedure, her symptoms gradually disappeared within 10 days. Follow-up laboratory examination on the sixth day of admission revealed AST: 58 IU/L, ALT: 86 IU/L, GGT: 138 IU/L, ALP: 441 IU/L, total bilirubin: 2 mg/dl, direct bilirubin: 1.1 mg/dl, amylase: 38 IU/L, lipase: 36 IU/L, and CA 19-9: 50.0 IU/ml (normal range: 0-37).

The patient's written consent to the study, the procedures and to the publication of anonymous data was obtained.

DISCUSSION

CA 19-9 is considered the most valuable serum test used in the diagnosis and management of pancreatic cancer. In addition, it is the most useful test in distinguishing between benign and malignant pancreatic disorders (16). The upper limit of normal for CA 19-9 antigen is 37 to 40 U/ml, and with this limit, the assay has an overall mean sensitivity of 81% and a mean specificity of 90% for the diagnosis of pancreatic cancer. A CA 19-9 value of >1,000 U/ml usually indicates a digestive cancer and has been reported to have a specificity over 99% for pancreatic cancer (16).

Moderately high serum levels of CA 19-9 can be detected during benign diseases of the liver, pancreas and biliary tract, but enormously high serum levels of CA 19-9 for these diseases were found in only a few cases, such as cirrhosis and acute cholangitis (16,19,20). The duration for normalization of elevated CA 19-9 level is varied. This period may differ according to the type and localization of the disorder, coexisting infection, medical and surgical treatment modalities, and the delay between development of disease and the treatment.

The mechanisms for the increase in serum CA 19-9 during acute cholangitis are not clear, but there are a few possible explanations:

1. CA 19-9 production by irritated bile duct cells exposed to increased biliary pressure may be enhanced (21); 2. Inflammation may cause the increased proliferation of epithelial cells leading to increased production of CA19-9 (22); 3. Obstruction may cause accumulation of CA 19-9 in the biliary lumen (19); 4. Reflux of CA 19-9 into the circulation may be induced by obstruction (22); and 5. The inflammatory cytokines produced in sepsis due to cholangitis probably have some contribution.

It is difficult to assess the exact cause of the CA 19-9 increase due to a malignant versus benign condition. Although some authors declare that using a combination of CA 19-9, carcinoembryonic antigen (CEA) and CA 125 levels can differentiate the malignant-benign cause, other authors disagree (23).

In conclusion, CA 19-9 can be used in the diagnosis of pancreaticobiliary disorders. CA 19-9 levels >1000 IU/ml usually indicate GI system malignancy and especially pancreatic cancer. In rare conditions, very high serum levels of CA 19-9 can be detected in benign biliary and pancreatic disorders, and successful treatment of these conditions may result in sudden normalization of serum CA 19-9 levels.

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