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Elevated carbohydrate antigen 19-9 levels in a patient with choledocholithiasis

Koledok taşı olan bir hastada artmış karbonhidrat antijen 19-9 düzeyleri

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Carbohydrate antigen 19-9 (CA19-9) has been used as a tumor marker in the diagnosis and differentiation of pancreatic cancers. However, significantly high levels of CA 19-9 in the absence of pancreatic malignancy have also been reported. We present a 50-year-old woman with a common bile duct stone and cholangitis, whose CA-19-9 level of 1.500 U/ml returned to normal after definitive treatment of choledocholithiasis.

Keywords: CA19-9, choledocholithiasis.

Karbohidrat antijen 19-9 (CA19-9) pankreas kanserlerinin ayırımı ve tanısında kullanılan bir tümör belirtecidir. Pankreas malinitesi olmayıp belirgin CA19-9 yüksekliği ile seyreden olgular bildirilmektedir. Bu yazıda tedavi öncesi Cal9-9 serum düzeyi 1500 U/l olup tedavi sonrasında tamamen normal düzeye düsen koledok taşlı 50 yaşında bir kadın olgu sunulmaktadır.

Anahtar kelimeler: CA19-9, koledok taşı.

INTRODUCTION

Serum carbohydrate antigen 19-9 (CA 19-9) has been used not only as a serum tumor marker for pancreatic and gastrointestinal carcinoma, but also to differentiate benign from malignant diseases of the pancreas (1-5). However, elevations of CA 19-9 to extraordinarily high levels without pancreatic or other gastrointestinal malignancies have also been reported especially in patients with choledocholithiasis and/or cholangitis (6-10). We present a case with a marked elevation of CA 19-9 in a benign condition.

CASE REPORT

A 50-year-old woman with no complaints until 10 days at the emergency department with jaundice, darkened urine, fatigue, loss of apetite and upper right abdominal pain. She reported that her complaints had gradually increased during these 10 days and that a fever of not more than 38 °C had developed in the previous two days. On the morning of her admission, she had fainted at home, which made her to come to the emergency room. Her past medical history was not significant. Her father had controlled type II diabetes mellitus and her mother was healthy.

Physical examination revealed only a sensitive right upper quadrant and apparent jaundice. Her pertinent initial laboratory tests were aspartate transaminase (AST): 83 U (N: 5-40), alanine transaminase (ALT): 130 U (N: 5-40), alkaline phosphatase (ALP): 792 U (N : 35-125), gama-glutamyl transferase (GGT): 239 U (N: 10-45), conjugated bilirubin (cBLB): 8 mg (N : 0- 0.2), unconjugated bilirubin (uBLB): 6.2 mg (N : 0.2- 0.8). Complete blood count and other biochemistry results were normal. Blood was also drawn for CA 19-9 and carcinoembrionic antigen (CEA), but the results were not obtained until after surgery.

An abdominal ultrasound performed in the emergency room revealed a heterogenous, hypoechoic mass lesion of 23mm x 16mm x 12 mm in size,

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with irregular margins, located at the distal end ofthe common bile duct (CBD). Both the CBD and intrahepatic biliary tree were dilated. Because ultrasonography did not differentiate between tumor and stone, a computerized tomographic (CT) scan was obtained and the result, although not positively confirming, was suggestive of an impacted stone. Because the size of the stone was large and the result ofthe CT scan did not confirm choledocholithiasis, surgery was planned instead ofendoscopic retrograde colangiopancreatography (ERCP) and the patient underwent cholecystectomy with CBD exploration and T-tube drainage. Surgical exploration revealed an impacted stone at the distal end of the CBD. Following cholecystectomy, the stone was extracted and a t-tube inserted into the CBD.

In the post operative T-tube cholangiogram, the calibration ofthe CBD and right intrahepatic duct were normal, while the left intrahepatic ducts were still somewhat dilated. The distal end of the CBD and the opening to the duodenum were found to be somewhat narrow.

When the results of CA 19-9 and CEA were obtained after surgery [CA 19-9 : > 1.500 U / ml (N: 0-29 U/ml) and CEA: 0.6 ng / ml (N :0-5 mg/ml)] the extremely high level of CA 19-9 and the persistently high bilirubin levels during the postoperative period prompted us to perform further evaluation. An ERCP was performed and the result was normal, without any sign of tumoral lesion and / or papillary obstruction.

On the 10th postoperative day her biochemistry started returning to normal. ALT : 132 U /L, AST: 190 U /L, ALP : 317 U /L, GGT : 87 U /L, cBLB: 0.5 mg / di, uBLB: 1.9 mg /di.

CA 19-9 level repeated on the 15th postoperative day was 282 U / ml, and was 43 U / ml one month after the surgery.

DISCUSSION

Serum carbohydrate antigen 19-9 rarely increases in healthy subjects or in benign conditions. In a study of 341 patients without malignant disease, the mean serum level of CA 19-9 was reported to be 8.73 ± 6.9 U/ml (11). Kim et al reported a serum level of > 37 U/ml in only 157 of 20,035 cases (0.78 %) (12). On the other hand high CA 19-9 levels have been reported previously in benign cases (12.8 % - 50 % in pancreatic diseases, 15 % - 38.8 % in biliary tract cases, 8.8 % in pulmonary disease) (12-14). Extremely high levels of CA 19-9 however have been observed more rarely and there have been some case reports. Akdoğan et al reported a 79-year-old woman who presented with cholangitis and a pancreatic pseudocyst with elevation of CA 19-9 up to 35,500 u/ml, which returned to normal following adequate treatment of her conditions (6). Tolliver and al noted a marked elevation of CA 19-9 due to et infectious process in a 42-year-old patient with a pancreatic mass suggestive of malignancy, which turned out to be chronic pancreatitis (8).

The findings in our patient were very similar to the case reported by Peterli et al (7). Their case also had a CBD stone and cholangitis. The only difference was that the level of CA 19-9 was exteremely high in their case (61,800 U/ml) although it returned to normal level after treatment.

Our patient had an impacted stone in the common bile duct and cholangitis, with a CA 19-9 level of more than 1,500 U/ml, which raised the question of a malignant condition. An exceedingly elevated level of CA 19-9 was detected just after surgery in our case and this finding prompted us to perform further evaluation to exclude malignancy. However, the results of both surgery and ERCP performed following surgery excluded a malignant condition and the CA 19-9 level returned to normal within three weeks. Considering the previous reports on high CA 19-9 levels in benign conditions, it might have been more appropriate to wait for some time before scheduling further evaluation for cancer in such patients. Further testing might not have been necessary in our case since CA 19-9 levels return to normal after definitive treatment in all cases with high CA 19-9 levels due to benign conditions. If persistently elevated CA 19-9 levels were seen despite treatment of the benign condition, then evaluation for cancer should have been prompted.

CA 19-9 is known to be the most sensitive and specific marker in the differential diagnosis of pancreatic cancer currently in use. However, as previous case reports suggest, even very high levels of CA 19-9 in cases with obstructive jaundice can be caused by benign conditions. With most other tumor markers (alpha-fetoprotein, carcinoembryonic antigen etc), exceedingly high levels are definitely suggestive of malignancy. However high levels of CA 19-9 can be caused by benign obstructive jaundice or other benign conditions (6,8,12-14), which reduces the value of CA 19-9 as a tumor marker.

In their study, Heptner et al (5) evaluated the specificity and sensitivity of CA 19-9 and reported that the specificity of CA 19-9 as tumor marker was 97 % in patients without gastrointestinal disease, but it was only 56 % in those with liver disease and 44 % in those with choledocholithiasis. They also noted that CA 19-9 failed to differentiate between the control group, chronic pancreatitis and carcinoma of the pancreas groups (5).

Although contrary reports have been published, indicating high sensitivity and specificity of CA 19-9 in detecting pancreatic carcinoma (15), the findings in our case along with previous reports suggest that even extremely high levels of CA 19-9 may not be caused by a malignant condition. Thus or with a better paraphrasing, benign conditions of the gastrointestinal tract may cause high levels of CA 19-9 which may mislead physicians.

In conclusion, we believe that caution is necessary in the interpretation of an elevated serum CA 19-9 value as a marker for malignancy, especially in patients with choledoholithiasis and / or cholangitis. The elevation in our case was due to obstructive cholangitis, rather than a malignant condition. We also believe that further diagnostic testing for malignancy may not be necessary if CA 19-9 levels are decreasing after definitive treatment of an obstructive process with or without inflammation.

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