A Case of Common Bile Duct Stone with Cholangitis Presenting an Extraordinarily High Serum CA19-9 Value

Toshimitsu Murohisa, Hitoshi Sugaya, Isando Tetsuka, Takuji Suzuki and Takashi Harada

A 63-year-old male complained of right upper abdominal pain and jaundice. Laboratory data on admission showed hyperbilirubinemia, elevation of biliary enzymes and an extraordinarily high value of serum CA19-9 (60,000 U/ml). Diagnostic imaging modalities including abdominal ultrasonogram, abdominal CT and PTC suggested a stone impaction of the common bile duct. Jaundice subsided after PTC-drainage in association with decreasing serum CA19-9 value, which returned to the normal level six weeks later. Spontaneous delivery of the stone via the fistula was confirmed by cholangiography through the drainage tube. Though there are few reports of such a high serum CA19-9 level, the possibility of benign biliary tract disease should be considered in patients showing an extraordinarily high serum CA19-9 value.

Key words: benign biliary tract disease, tumor marker

Introduction

Carbohydrate antigen CA19-9 is known as one of the serum tumor markers which shows a high positivity in pancreato-biliary malignancies (1-7). However, elevation of serum CA19-9 is occasionally found in benign diseases of the liver, pancreas and biliary tract, especially in cases with gall stone disease in which the high rate of its elevation has been reported in an acute stage, but the value is usually below 5,000 U/ml (2, 5, 6, 8-11). We report a case of common bile duct stone with cholangitis presenting an extraordinarily high serum CA19-9 value with special reference to differential diagnosis from malignancies.

Case Report

A 63-year-old male visited our clinic complaining of right upper abdominal pain and dark colored urine of five days duration. He had been treated for hypertension with medication for 15 years and had a history of peptic ulcer of the duodenum at age 48. He had an episode of right back pain which was spontaneously relieved in 1988. He suffered abrupt colicky pain from the epigastric region to right hypochondriac region on Jan. 30, 1989. The pain occurred independent of ingestion of foods without fever, and was not relieved by medication. Also he noticed dark colored urine on Jan. 31, and acholic stool on Feb. 3. He was admitted to our clinic on Feb. 4, 1989.

Physical examination showed a slightly obese man with marked jaundice but no anemia. Body temperature, pulse rate and blood pressure were 36.6°C, 96/min, and 160/80 mmHg, respectively. The liver with a sharp edge was softly palpable one finger breadth below the right costal margin; the spleen was not palpable. There was no muscle guarding, rebound tenderness or Courvoisier’s sign, but only slight spontaneous pain was present in the right hypochondriac region.

Laboratory data on admission are shown on Table 1. Slight elevation of serum transaminase activity, high values of biliary enzymes and hyperbilirubinemia with dominant conjugated bilirubin were outstanding findings of the liver function test. In peripheral blood analysis, leukocytosis (10,900/μl) with neutrophilia (83%) was found. C-reactive protein (CRP) was strongly positive (16.8 mg/dl) and the one-hour value of erythrocyte sedimentation rate (ESR) was 58 mm. These data strongly suggested the presence of inflammatory process in this case. Serum CA19-9 value was 60,000 U/ml, which was extraordinarily high. We suspected the presence of obstructive jaundice caused by gall bladder stone disease.
CBD Stone with High Serum CA19-9

Table 1. Laboratory data on Admission

<table>
<thead>
<tr>
<th>Test</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>GOT</td>
<td>92 KU</td>
</tr>
<tr>
<td>GPT</td>
<td>86 KU</td>
</tr>
<tr>
<td>ALP</td>
<td>29.5 KAU</td>
</tr>
<tr>
<td>LAP</td>
<td>381 GRU</td>
</tr>
<tr>
<td>LDH</td>
<td>259 WU</td>
</tr>
<tr>
<td>γ-GTP</td>
<td>255 UL</td>
</tr>
<tr>
<td>T-Bil</td>
<td>17.5 mg/dl</td>
</tr>
<tr>
<td>D-Bil</td>
<td>17.5 mg/dl</td>
</tr>
<tr>
<td>TBA</td>
<td>168.4 μmol/l</td>
</tr>
<tr>
<td>ZTT</td>
<td>4.8 KU</td>
</tr>
<tr>
<td>ch-E</td>
<td>148 IU/l</td>
</tr>
<tr>
<td>T-P</td>
<td>5.8 g/dl</td>
</tr>
<tr>
<td>BUN</td>
<td>13 mg/dl</td>
</tr>
<tr>
<td>Na</td>
<td>134 mEq/l</td>
</tr>
<tr>
<td>K</td>
<td>3.9 mEq/l</td>
</tr>
<tr>
<td>Cl</td>
<td>94 mEq/l</td>
</tr>
<tr>
<td>Ca</td>
<td>3.8 mEq/l</td>
</tr>
<tr>
<td>P</td>
<td>2.0 mg/dl</td>
</tr>
<tr>
<td>Uric acid</td>
<td>1.2 mg/dl</td>
</tr>
<tr>
<td>Creatinine</td>
<td>0.5 mg/dl</td>
</tr>
<tr>
<td>Amylase</td>
<td>174 Dye.u/dl</td>
</tr>
<tr>
<td>Glucose</td>
<td>144 mg/dl</td>
</tr>
<tr>
<td>T-Cholesterol</td>
<td>165 mg/dl</td>
</tr>
<tr>
<td>E-Cholesterol</td>
<td>28 mg/dl</td>
</tr>
<tr>
<td>F-Cholesterol</td>
<td>137 mg/dl</td>
</tr>
<tr>
<td>TG</td>
<td>179 mg/dl</td>
</tr>
<tr>
<td>NEFA</td>
<td>0.40 mEq/l</td>
</tr>
<tr>
<td>β-Lip</td>
<td>372 mg/dl</td>
</tr>
<tr>
<td>PL</td>
<td>304 mg/dl</td>
</tr>
<tr>
<td>IgG</td>
<td>1,150 mg/dl</td>
</tr>
<tr>
<td>IgA</td>
<td>485 mg/dl</td>
</tr>
<tr>
<td>IgM</td>
<td>101 mg/dl</td>
</tr>
<tr>
<td>Albumin</td>
<td>47.8%</td>
</tr>
<tr>
<td>α1 Globulin</td>
<td>6.3%</td>
</tr>
<tr>
<td>α2 Globulin</td>
<td>12.3%</td>
</tr>
<tr>
<td>β Globulin</td>
<td>15.8%</td>
</tr>
<tr>
<td>γ Globulin</td>
<td>17.7%</td>
</tr>
<tr>
<td>α FP</td>
<td>5 ng/ml</td>
</tr>
<tr>
<td>CEA</td>
<td>2.5 ng/ml</td>
</tr>
<tr>
<td>CA19-9</td>
<td>60,000 U/ml</td>
</tr>
</tbody>
</table>

or pancreatobiliary malignancy, and performed the following diagnostic procedures.

Abdominal urtrasonogram (US) showed dilatation of intrahepatic bile ducts in both lobes of the liver (Fig. 1a) and common bile duct, but intestinal gas precluded delineation of the distal part of the common bile duct (Fig. 1b). The gall bladder appeared slightly swollen, but there were no findings of wall thickening; gall stones were not present. CT of the abdomen showed dilated intrahepatic bile ducts in both lobes of the liver as well as on abdominal US, and further showed a high density area in the distal part of the common bile duct (Fig. 2). On the third day of hospitalization percutaneous transhepatic cholangiography (PTC) showed a dilated common bile duct and a filling defect in the distal part of the common bile duct.

Course after Hospitalization

After hospitalization his temperature became elevated (38°C); administration of antibiotics had no effect on the fever, but did relieve right hypochondralgia. Abdominal US showed dilated intrahepatic bile ducts, so PTC-drainage (PTC-D) was employed on the third hospital day. Our diagnosis was obstructive jaundice due to impacted gall stone in the common bile duct based on the PTC findings and results of other diagnostic procedures including laboratory data. After PTC-D, fever subsided with concomitant improvement of jaundice. Three weeks later the serum total bilirubin reached to 1.2 mg/dl from the initial value of 17.5 mg/dl, and cholangiography through the drainage tube revealed no filling defect in the distal part of the common bile duct. Clamping of the

Fig. 1. Ultrasonogram of the upper abdomen. Dilatation of the common bile ducts is 17 mm in diameter. Distal end is not clear (a). Intra-hepatic bile duct is markedly dilated (b).
PTC drainage tube did not aggravate jaundice. These clinical features suggested delivery of the gall stone. Six weeks later, duodenoscopy showed slightly swollen, reddish papilla and a fistula located in the oral side of the papilla. ERC (Fig. 4) revealed fistula communication between the duodenum and common bile duct, but no gall stones (Fig. 5); presumably the stone was spontaneously delivered from the fistula. Chronological changes of serum total bilirubin, ALP, body temperature, abdominal pain and CA19-9 are shown in Fig. 6. Laboratory data on admission showed
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Fig. 6. Clinical course. Concomitant with the improvement of jaundice, the serum CA19-9 level decreased rapidly. BT: body temperature, T-Bil: total bilirubin, PTCD: percutaneous transhepatic cholangiography and drainage.

elevation of total serum bilirubin (17.5 mg/dl), CRP of 16.8 mg/dl and leukocytosis (10,900/µl), which suggested the presence of cholangitis. The value of serum CA19-9 on admission was 60,000 U/ml, which rapidly decreased after PTC-D; it was 1,540 U/ml one week later and 130 U/ml after two weeks. After three weeks serum CA19-9 was 49 U/ml and negative CRP and normalization of leukocyte count were found. After six weeks it was normalized to 29 U/ml when serum total bilirubin returned to normal value (0.8 mg/dl). There was no recurrence of abdominal pain or fever during the hospitalization.

Discussion

CA19-9, carbohydrate antigen which was defined by monoclonal antibody to the cultured cell from human colonic cancer, was termed by Korprowski in 1979 (12). Initially it was considered to be a tumor marker associated with colonic cancer. Thereafter, many reports have discussed an elevated CA19-9 in the sera of patients with digestive diseases, especially in those with pancreatobiliary malignancies (1–7). CA19-9 is now considered to be one of the useful tumor markers of pancreatobiliary malignancies. In contrast, it is also well known that elevated CA19-9 in the sera may occur in various benign diseases such as gall bladder (GB) stone disease (8–11), chronic pancreatitis, hepatitis, liver cirrhosis, renal failure, duodenal ulcer, gastric polyps, colonic polyps and renal cyst. The rate of elevated CA19-9 in GB stone was reported to be from 11.8% to 66.7% (1–11). From our experience, the rate for common bile duct stone and gall bladder stone on admission is 50% and 23.5% respectively. These values are similar to those of other investigators (3–5, 8, 9, 11). It is likewise noteworthy that the rate of occurrence of the common bile duct stone is higher than that of gall bladder stones, and the maximum value in the patients with common bile duct stone tends to be higher. The percentage of patients with a serum CA19-9 level of over 10,000 U/ml is reported to be 6–31% in pancreatic cancer and 0–30% in biliary tract cancer (1–4, 6, 9). There are few reports however, of gall stone patients with such a high serum CA19-9 value in Japan; to our knowledge only two reports have discussed a serum CA19-9 value of over 10,000 U/ml: a case with common bile duct stone (13), and a case with gall stone disease (14). The clinical course of these two cases is similar to the present case with respect to the improvement of jaundice and subsidence of the coexisting infection followed by improvement of the serum CA19-9 value. Further, there has been only one case of common bile duct stone with a serum CA19-9 level of over 10,000 U/ml in the English literature (15), but the details of that case are not described.

Production and secretion of CA19-9 from malignant cells are considered to be responsible for the high serum CA19-9 level in malignancies. Several additional mechanisms have been postulated to be factors in the high serum CA19-9 value in the gall stone disease. These postulated factors include 1) leakage of condensed CA19-9 due to biliary tract obstruction from the bile into blood circulation (16), 2) leakage of CA19-9 from the bile duct epithelium where a small amount of this substance is normally present (17), 3) enhanced production of CA19-9 in the bile duct epithelium and the mucosa of gall bladder induced by the inflammatory process (11), and 4) reflux of CA19-9 from bile duct epithelium into the blood stream presumably due to the elevated pressure of the biliary tract (10). At present, most highly agreed opinion is the elevated pressure of the biliary tract associated with inflammation. In studies of obstructive jaundice, however, inconsistent results have been reported in the correlation between the serum total bilirubin value and serum CA19-9 value (8, 11). In the present case a positive correlation was found between CRP, total bilirubin and the CA19-9 value. These results suggested that both the elevated pressure of the biliary tract and inflammation might have been responsible for the high serum CA19-9 value. In general, an increased serum CA19-9 value will return to the normal level after improvement of jaundice in gall stone disease, but in malignancies this does not necessarily occur (8, 18). Furthermore, it may be possible to make a differential diagnosis between benign and malignant disease by simultaneous measurement of other serum tumor markers (2, 7, 19).

The present patient showed an abnormally high serum CA19-9 value of up to 60,000 U/ml on admission, and the value became normal in accordance with improve-
ment of jaundice and inflammation. However, there are few patients with an extraordinarily high serum CA19-9 level among cases with benign biliary obstruction and inflammation; the precise mechanism for this abnormally high elevation remains to be clarified.

References