A Case of Klatskin Tumor with High Levels of CA 19-9

YÜKSEK CA 19-9 SEVİYELERİ İLE SEYREDEN KLATSKİN TÜMÖRÜ OLGUSU

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Abstract

Carbohydrate antigen 19-9 (CA 19-9) is used as a serum tumor marker for adenocarcinoma of the upper gastrointestinal tract, particularly primary adenocarcinoma of the pancreas. In addition, this tumor marker can be highly elevated in benign diseases such as acute pancreatitis, chronic pancreatitis, chronic liver disease and biliary tract disease. A 69 year-old man was hospitalized with jaundice, cola-colored urine, right-sided upper abdominal pain, weight loss and pruritus. Laboratory data revealed a high level of serum CA19-9 of more than 100 000 U/mL and a mass in the left lobe of the liver was detected on computed tomography. ERCP, PTCA and CT-guided biopsy yielded the diagnosis of Klatskin tumor. Review of the literature revealed that Klatskin tumor with high levels of CA19-9 over 100 000 U/mL was not reported.

Key Words: Klatskins tumor; antigens, tumor-associated, carbohydrate

Özet

Serum karbonhidrat antijen 19-9 (CA 19-9) üst gastrointestinal traktın adenokanser ve özellikle de primer pankreatik adenokanser tümör belirteçi olarak kullanılmaktadır. Ayrıca akut pankreatit, kronik pankreatit, kronik karaciğer hastalığı gibi benign hastalıklarda ve biliyer trakt hastalıklarında da yükselebilmektedir. 69 yaşında erkek hasta, sarılık, kola renginde idrar, sağ üst kadran ağrısı, kilo kaybı ve kaşıntı şikayetleri nedeni ile hastanemize yatırıldı. Laboratuvar verilerinde 100 000 U/mL'den daha yüksek düzeyde serum CA 19-9 değeri ve bilgisayarlı tomografide karaciğer sol lob kesiminde kitle lezyonu mevcuttu. Daha sonrasında ERCP, PTCA ve BT eşliğinde biyopsi işlemleri uygulandı ve klatskin tümörü tanısı kondu. Literatürü gözden geçirdiğimizde, 100 000 U/mL'den daha yüksek CA 19-9 düzeyleri ile seyreden Klatskin tümörü olgusu mevcut değildir.

Anahtar Kelimeler: Klatskin tümörü; karbonhidrat antijen

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Biliary tract cancer is the second most common primary hepatobiliary cancer, after hepatocellular cancer. Biliary tract cancers were traditionally divided into cancers of the gallbladder, the extrahepatic bile ducts, and the ampulla of vater, whereas intrahepatic bile-duct cancers were classified as primary liver cancers.[1]

Perihilar tumors involving the bifurcation of the hepatic duct are called Klatskin tumors, according to Klatskin's original description in 1965.[2] More than 95% of uch tumors are ductal adenocarcinomas; many patients present with unresectable or metastatic disease. The etiology of most bile duct cancers remains undetermined. Persistent inflammation, as with primary sclerosing cholangitis (PSC) or chronic parasitic infection, was suggested to play a role by inducing hyperplasia, cellular proliferation and ultimately, malignant transformation.

Despite aggressive anticancer therapy and interventional supportive care (ie, wall stents or percutaneous biliary drainage), median survival rate is low since most patients (90%) are not eligible for curative resection.

The perihilar bile-duct tumors were further classified by Bismuth et al as tumors below the confluence of the left and right hepatic ducts (type I), tumors reaching the confluence (type II), tumors occluding the common hepatic duct and either the right or the left hepatic duct (types IIIa and IIIb,

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respectively), and tumors that are multicentric or that involve the confluence and both the right and left hepatic ducts (type IV).[3]

A variety of markers were tested in bile and serum with limited success. Tumor marker CA 19-9 is a sialylated Lewis blood group antigen presented in normal pancreas, bile duct, gastric, cholic, and salivary epithelia. Due to its variable location, it may be misinterpreted as benign cholestasis in pancreatic and bile duct malignancies. CA 19-9 is currently widely used, particularly for detecting cholangiocarcinoma in patients with PSC.[4,5] Serum CA 19-9 levels greater than 100 U per milliliter (the normal level is less than 40 U per milliliter) were reported to have a sensitivity of 89 percent and a specificity of 86 percent for the detection of cholangiocarcinoma in such patients.[6]

We present a case with Klatskin tumor with marked elevation of CA 19-9 higher than 100.000 U/mL. To our knowledge, this might be the first case of Klatskin tumor associated with high levels of serum CA19-9 antigen.

Case Report

A 69-year-old man was admitted to the hospital with jaundice, cola-colored urine, right-sided upper abdominal pain, weight loss and pruritus. On physical examination, the blood pressure was 140/80 mmHg, the pulse rate was 78/min, temperature was 36.5°C, and the respiration rate was 18/min. His sclera was icteric, lungs were clear, abdominal examination revealed tender enlargement of the liver and jaundice was present at admission.

Laboratory tests were as follows: Hemoglobin 12.1 g/dL, hematocrit 29.5 percent, white blood cell count 11.700 per cubic millimeter and platelet count 202.000 per cubic millimeter. Blood urea nitrogen, creatinine, glucose, calcium, phosphorus, magnesium, sodium and potassium levels were normal. Alanine aminotransferase level was 386 u/L (0-42), aspartate aminotransferase was 131 u/L (0-37), alkaline phosphatase was 320 u/L (42-128), gamma-glutamyl transpeptidase 2157 u/L (7-49), total bilirubin was 10.5 mg/dL (0.0-1.2), and conjugated bilirubin was 9.5 mg/dL (0.0-0.4). Urinalysis was normal. Hepatitis B surface antibody, hepatitis B antigen and hepatitis C antibody were negative. The levels of tumor markers were alpha feto protein (AFP) 1.2 U/mL, carcinoembryonic antigen (CEA) 120.7 U/mL, and CA 19-9> 100.000 U/mL.

Abdominal ultrasound examination revealed that the liver has enlarged. A hypoechoic solid mass in the medial segment of the left lobe approximately 4 cm in diameter and with a lobulated contour was detected. Intrahepatic biliary tracts around the mass were dilated. A CT scan

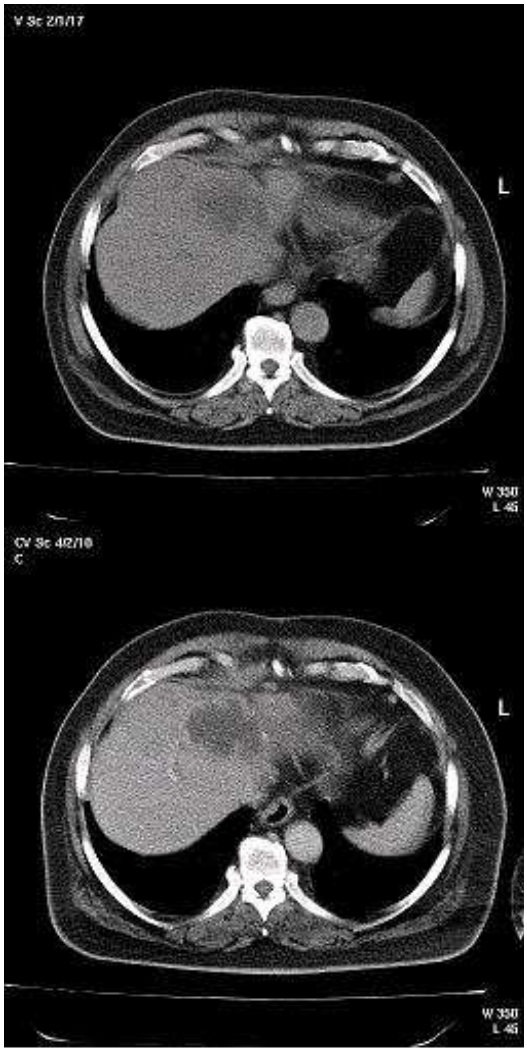

Figure 1 a, b. Nonenhanced contrast scanning of the liver left lobe medial segment detected a hypodense mass with an irregular border that could not be differentiated from the surrounding tissue. In addition, dilated tree of peripheral mass seen.

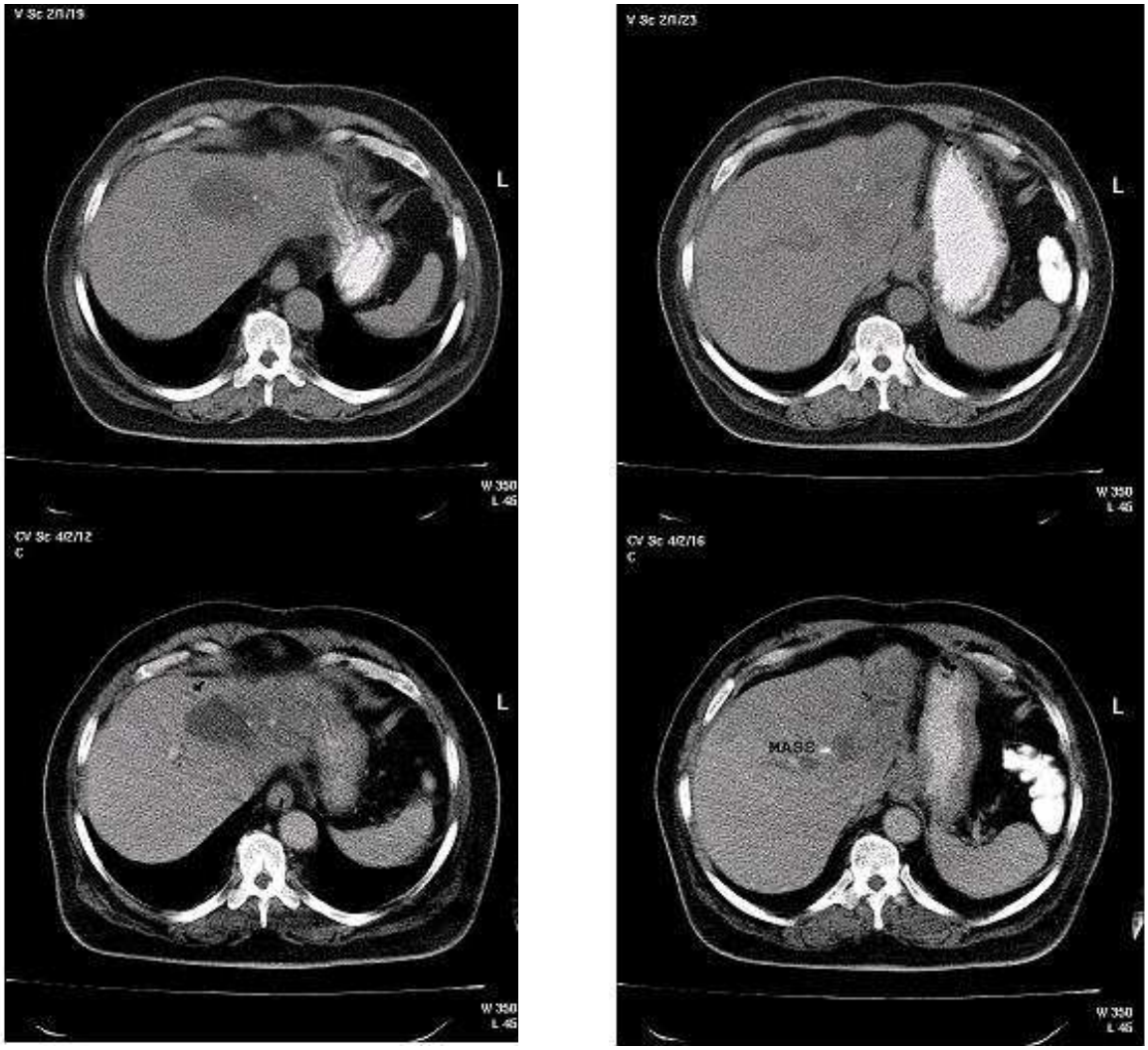

Figure 2 a-b, 3 a-b. Using contrast in the scannig didn't showed contrast enhanced on solid mass and at the portal venous phase (first sec.) irregularly thickened and minimally dense and dilated biliary tract seen. (fig.2a-b, 3a-b).

was performed to evaluate the hypoechoic solid mass in the left lobe of the liver; the cranio-caudal hepatic lobe length has increased to 17.5 cm. Nonenhanced contrast scanning of the liver left lobe medial segment detected a hypodense mass with an irregular border that could not be differentiated from the surrounding tissue. In addition, dilated tree of peripheral mass seen (Figure 1a, b). Using contrast in the scannig didn't showed contrast enhanced on solid mass and at the portal venous phase (first sec.) irregularly thickened and minimally dense and dilated biliary tract seen (Figure 2 a, b, 3 a, b). The density should be examined at the late phase.[7]

ERCP revealed normal pancreatic ducts. There was no passage of contrast material to the common bile ducts.

In PTCA, intrahepatic bile ducts were dilated. Common bile ducts was dilated up to the site of total obstruction at the proximal part. A 8 f drainage catheter was inserted into the intrahepatic bile duct with successful drainage from the catheter.

Following this, CT-guided biopsy was performed from the mass in the medial segment of the left lobe of the liver. Histopathological examination revealed adenocarcinoma of the biliary duct and the patient was referred to an Oncology department to determine the therapeutic approach.

Discussion

A large number of potential markers of biliary tract cancers were identified. Many markers, however, are not specific and may also be present under nonmalignant conditions. In the differential diagnosis of pancreatic cancer, CA19-9 appears to be the most sensitive and specific marker. Other serum markers were studied, but none seems to be as useful as CA 19-9. CA19-9 was also used to differentiate benign from malignant diseases of the pancreas. In the absence of jaundice and at levels greater than 1000 U/mL, the specificity is almost 100%. Levels higher than 1000 U/mL are very uncommon for benign diseases. However, significant elevations of CA 19-9 levels in the absence of pancreatic malignancy were also reported. Levels of CA 19-9 may be elevated in benign processes, such as acute pancreatitis, chronic pancreatitis, chronic liver disease, and biliary tract disease, but marked elevations are essentially limited to cirrhosis and acute cholangitis.[8-12]

Marked elevations of CA 19-9 were associated with obstructive cholangitis, but biliary obstruction in the absence of cholangitis does not usually produce significant elevations.[13-15]

A review of the literature indicated that very high levels of CA19-9 in cases with obstructive jaundice could be due to malignant as well as benign diseases. However, we found no case report with CA 19-9 levels higher than 100.000 U/mL in Klatskin tumor or pancreas malignancy. This case demonstrates that a markedly elevated serum level of CA 19-9 may occur not only in pancreatic malignancy but also in Klatskin tumor. Increased serum levels of the CA 19-9 may be due to the enhanced production of CA 19-9 from the biliary epithelial cells and its decreased hepato-biliary clearance because of cholestasis.

Since the extreme increase in CA 19-9 levels could lead to a misdiagnosis of pancreatic or biliary malignancy, CA 19-9 should never be considered the gold standard; however, it may be used as a helpful indicator when searching for biliary malignancy. This case confirmed that high serum CA 19-9 concentrations should be well interpreted considering clinical information, endoscopic and radiological investigations.

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