

Extremely high values of CA 19-9 in liver hydatidosis and frank biliary rupture

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Elevation of carbohydrate antigen 19-9 has been observed in jaundiced patients with benign biliary tract diseases. No clear answer has explained that relationship. Patients with liver hydatidosis and frank intrabiliary rupture could present obstructive jaundice due to the presence of liver cyst material in the bile duct. We present two cases of huge elevation of carbohydrate antigen 19-9 in jaundiced patients with liver hydatidosis and biliocystic communication, and we assess the different theories presented in the medical literature today.

Key words: Carbohydrate antigen 19-9, hydatidosis, jaundice, surgery

Karaciğerin hidaditozisi ve safra yoluna aşikar açılımı olan vakada son derece yüksek CA 19-9 değerleri

Benign safra yolu hastalığı olan ikterli vakalarda karbonhidrat antijen 19-9 düzeylerinde artış görülebilmektedir. Bu ilişkiye net bir açıklama getirilememiştir. Karaciğer hidaditozisi olan ve safra yoluna aşikar açılımı olan hastalar safra yoluna dökülen kist materyali nedeni ile tıkanma sarılığı ile başvurabilirler. Burada karaciğer hidaditozisi ve bilio-kistik ilişkisi olan ve karbonhidrat antijen 19-9 düzeyleri son derece yüksek olan iki vaka sunulmuştur. Ayrıca literatürdeki bu konu ile ilgili farklı teoriler irdelenmiştir.

Anahtar kelimeler: Karbonhidrat antijen 19-9, hidaditozis, sarılık, cerrahi

INTRODUCTION

Hydatidosis is an endemic zoonosis in multiple areas of the world caused by the cestode *Echinococcus* sp. (1,2). In Spain, in the vast majority of patients, *E. granulosus* has caused cystic liver disease. Carbohydrate antigen (CA) 19-9 is the carbohydrate determinant of a circulating oligosaccharide antigen. It was detected originally using a monoclonal antibody in human colon cancer cells growing in cell culture (2,4,5). Only 2% of healthy subjects show abnormal levels of CA 19-9 (2). It is remarkable that some patients with benign biliary tract disease showed levels of CA 19-9 above cut-off and they are usually jaundiced patients. However, it is exceptional to observe extremely high levels in patients without cancer (4-7).

We present two patients with extremely high values of CA19-9 in the course of acute cholangitis (jaundice and fever) due to frank rupture of a hydatid cyst into the intrahepatic bile duct, with presence of cyst material (membranes, scoleces, debris) in the bile duct and posterior normalization after surgery. We discuss the hypothetical reasons that could explain this elevation of CA 19-9.

CASE REPORTS

CASE 1

A 73-year-old male presented in our hospital with nausea and jaundice. Among the blood test results, the following were remarkable: eosinophilia

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5.1%, aspartate aminotransferase (AST) 173 IU/L, alanine aminotransferase (ALT) 194 IU/L, gamma-glutamyl transpeptidase (GGT) 681 IU/L, AF 924 IU/L, and total bilirubin 6 mg/dl. We request CA 19-9 in all jaundiced patients during their admission. The result was 25.991 IU/L. An ultrasound and computed tomography (CT) scan were requested, in which two liver lesions of 9 and 6 cm were visualized in the left hemiliver with intra- and extrahepatic bile duct dilatation, suggesting liver hydatid cysts. During the sphincterectomy in endoscopic retrograde cholangiopancreatography (ERCP), hydatid cysts and pus were visualized through the papilla. Later, an open left hepatectomy was performed in our Hepato-Pancreato-Biliary (HPB) Unit. The postoperative course was uneventful and the patient was discharged five days later. In the outpatient clinic, a new blood test sample demonstrated the normal rate of CA 19-9 and normal liver test.

CASE 2

A 54-year-old male presented with abdominal pain, fever and jaundice. Blood tests showed: eosinophilia 4.6%, AST 203 IU/L, ALT 484 IU/L, GGT 315 IU/L, AF 1054 IU/L, total bilirubin 6.3 mg/dl, and CA 19-9 572.3 IU/L. Ultrasound and CT scan showed a lesion 5.6 cm in segment VII with intra- and extrahepatic bile duct dilatation. ERCP demonstrated hydatid membranes in the papilla. After sphincterectomy, a total closed cystectomy was performed without any remarkable event during the postoperative period. One month later, during the follow-up in the outpatient clinic, the blood test showed a normal value of CA 19-9.

DISCUSSION

Intrabiliary rupture is one of the most common complications of liver hydatid cyst. The true incidence is unknown, but it has been reported to range from 5% to 25%. The complication between the cyst and the biliary tree has been classified as major and minor. A major (or frank) complication is characterized by the content of the cyst draining directly into a major biliary duct, causing symptoms (cholangitis, pancreatitis, etc.) or serum abnormalities, depending on intermittent or complete obstruction of the duct (8). In our two cases, intrabiliary rupture caused an episode of acute cholangitis with fever and jaundice.

CA 19-9 elevation in benign biliary tract disease has frequently been reported, but a very high level

of CA 19-9 (>500 IU/ml) in such cases has rarely been observed (3-7,9). Mirizzi's syndrome and acute cholangitis are the usual definitive diagnoses of patients with these extreme values (4,7). Hyperbilirubinemia has been associated with a further deterioration in the specificity of CA 19-9, so special consideration was necessary in order to interpret the results in jaundiced patients; however, the relationship between jaundice and elevation of CA 19-9 is not yet clearly explained (6,8-10).

Very few reports of elevated CA 19-9 levels in liver hydatidosis have been described, and no correlation with jaundice was noted in these series (1-3). Pfister et al. (2) showed that 11% of the patients with liver hydatidosis caused by *E. granulosus* presented an abnormal value of CA 19-9. On the other hand, Yuksel et al. (1) noticed in their series of 40 patients that 65% presented a value above cut-off. However, the maximum value was 120 IU and the median value was 45.1 ± 3 U/l, very near the cut-off values, which implies a moderate elevation over cut-off (1). That author demonstrated the clear relationship between infection and elevation of CA 19-9 because he confirmed the normalization of the marker after surgery, as also occurred in our patients (1).

Many theories have been put forth to explain why CA 19-9 elevates in patients with liver hydatidosis:

- The theory of Pfister et al. (2) is that the blood from the patients with an *Echinococcus* infection may contain substances originating from the parasites, which have been sialylated either by the host's or parasite's metabolism. The epitope recognized by anti CA 19-9 antibodies is the sialylated Lewis-a antigen. This antigen ends with a characteristic carbohydrate sequence, and very similar sialylated fucose-containing glycans have been found in hydatid membranes of *E. granulosus* (2). These substances may bear the Lewis-a antigen or closely related structures, which are recognized by anti CA 19-9 antibodies, producing an elevation of CA 19-9 (11).
- Sheen et al. (4) postulated that several factors could produce the elevation of CA 19-9 in patients with acute cholangitis: CA 19-9 production by irritated bile duct cells exposed to increased biliary pressure may be enhanced; inflammation may cause the proliferation of epithelial cells leading to more production of CA 19-9; obstruction may cause accumulation of CA 19-

9 in the lumen; reflux of CA 19-9 into the circulation may be induced by obstruction; or there may be a collateral role of inflammatory cytokines produced in sepsis (4).

We think that the extremely high values of CA 19-9 obtained in our cases are multifactorial. Several

factors (hyperbilirubinemia due to obstruction, liver hydatidosis infection, acute cholangitis related to frank intrabiliary rupture of the cyst and inflammation) caused an elevation of CA 19-9 that disappeared after surgery when these factors were eliminated.

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