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Relationship of CA 19-9 with choledocholithiasis and cholangitis

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Background/aims: *It is well known that increased concentrations of CA 19-9 can be found in benign disease of the liver, pancreas and biliary tract, especially in cases with gallstone disease with cholangitis. The aim of this study was to investigate the relation of CA 19-9 with the number and size of the stones, cholangitis and biliary obstruction in patients with choledocholithiasis.* ***Methods:*** *Seventy patients with radiologically proven choledocholithiasis were studied. Endoscopic retrograde cholangiopancreatography, sphincterotomy and stone extraction were applied to all patients. In each case, the parameters recorded included the levels of CA 19-9 and other laboratory tests before and after endoscopic retrograde cholangiopancreatography and the results of imaging techniques and immunoserologic tests. The correlations of these parameters were determined by SPSS 17 package program for statistical analysis.* ***Results:*** *Elevation of CA 19-9 was found in 32 patients (46%), while 8 patients (11%) had extraordinarily high levels (>1000 U/ml). CA 19-9 levels were correlated with serum alkaline phosphatase (r=0.5, p<0.01), gamma glutamyl transpeptidase (r=0.5, p<0.01) and bilirubin (r=0.4, p<0.01) levels but not with aspartate aminotransferase or alanine aminotransferase levels. There was also no association between serum CA 19-9 levels and the number and size of stones. Six patients had cholangitis. CA 19-9 levels were found higher in patients with cholangitis than others (100% vs. 41%, p<0.01) as well as alkaline phosphatase, gamma glutamyl transpeptidase and bilirubin levels. After stone extraction, CA 19-9 levels started to decrease and reached normal values 1-28 days later.* ***Conclusion:*** *In conclusion, CA 19-9 levels are associated with biliary obstruction and cholangitis but not with the number and size of stones in patients with choledocholithiasis.*

Key words: CA 19-9, choledocholithiasis, cholangitis, biliary obstruction

CA 19-9'un koledok taşları ve kolanjitle ilişkisi

Amaç: *Benign karaciğer, pankreas ve özellikle kolanjitle birlikte safra taşı olan bilier sistem hastalıklarında CA 19-9'un yüksek bulunabileceği iyi bilinmektedir. Bu çalışmanın amacı, koledok taşı olan hastalarda CA 19-9 ile taşların sayı ve büyüklüğü, kolanjit ve bilier obstrüksiyon arasındaki ilişkiyi araştırmaktır.* ***Yöntem:*** *Radyolojik olarak koledok taşı saptanmış 70 hasta çalışmaya alındı. Hastalara endoskopik retrograd kolanjiyopankreatografi, sfinkterotomi ve taş ekstraksiyonu uygulandı. Her hastada görüntüleme sonuçları, immünoserolojik testler ve endoskopik retrograd kolanjiyopankreatografi öncesi ve sonrası bakılan CA 19-9 seviyeleri ile diğer laboratuvar tetkikleri kaydedildi. İstatistiksel analiz için sonuçlar SPSS 17 programı kullanılarak karşılaştırıldı.* ***Bulgular:*** *CA 19-9 yüksekliği 32 hastada (%46) bulunurken, 8 hastada (%11) aşırı derecede yüksek seviyeler mevcuttu (> 1000 IU/ml). CA 19-9 seviyeleri, serum alkalen fosfataz (r=0.5, p<0.01), gamma glutamil transpeptidaz (r=0.5, p<0.01) ve bilirubin (r=0.4, p<0.01) seviyeleri ile korelasyon gösterirken, aspartat aminotransferaz ve alanin aminotransferaz seviyeleri ile korelasyon göstermiyordu. Serum CA 19-9 seviyeleri ile taşların sayı ve büyüklüğü arasında da bir ilişki saptanmadı. 6 hastada kolanjit vardı. Kolanjitli hastalarda CA 19-9 seviyeleri diğer gruba göre alkalen fosfataz, gamma glutamil transpeptidaz ve bilirubinde olduğu gibi daha yüksek (%100'e karşılık %41, p<0.01) bulundu. Taş ekstraksiyonundan sonra CA 19-9 seviyeleri düşmeye başladı ve 1-28 gün içinde normale döndü.* ***Sonuç:*** *Sonuç olarak, koledok taşı olan hastalarda yüksek serum CA 19-9 değerleri, bilier obstrüksiyon ve kolanjitle ilişkili, fakat taşların sayı ve büyüklüğü ile ilişkisizdir.*

Anahtar kelimeler: CA 19-9, koledok taşı, kolanjit, bilier obstrüksiyon

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INTRODUCTION

CA 19-9, a carbohydrate antigen that was defined by monoclonal antibody to the cultured cell from human colonic cancer, was termed by Koprowski in 1979 (1). Initially, it was considered to be a tumor marker associated with colon cancer, but later became a useful tumor marker for pancreatobiliary malignancies (2,3).

CA 19-9 is synthesized from normal human pancreatic, biliary, ductal, gastric, colonic, endometrial, and salivary epithelial cells (4-6). Kim et al. (7) reported a serum level of >37

U/ml in only 157 of 20,035 asymptomatic cases (0.78%). It is a tumor-associated not a tumor- specific marker and is associated with some malignant and nonmalignant diseases, although it is higher in cancer than in benign conditions (8). In a one-year retrospective study, CA 19-9 was found to be elevated in malignancies of the pancreas, colorectum, lung, liver, and ovary, and in benign conditions of the hepatobiliary system, pneumonia, pleural effusion, renal failure, and systemic lupus erythematosus (9).

It is well known that moderately increased concentrations of CA 19-9 can be found in 15-36% of patients with benign pancreatic, liver and biliary tract diseases (10). Furthermore, several benign tract diseases in which serum CA 19-9 elevation suggested malignancy were reported. Inflammatory liver pseudotumor with CA 19-9 levels at 1167.9 U/ml (11), Mirizzi's syndrome with high CA 19-9 levels mimicking cholangiocarcinoma (12-14), and increased CA 19-9 levels in mucinous pancreatic ductal ectasia (15) are case reports of interest. A high level of CA 19-9 was also found in autoimmune biliary diseases such as primary sclerosing cholangitis and autoimmune cholangitis, with normalization of the levels after methylprednisolone (16,17).

In addition to these reports, elevations of CA 19-9 to extraordinarily high levels without pancreatic or other gastrointestinal malignancies have also been reported in patients, particularly with choledocholithiasis and cholangitis (16,18-22). In light of the foregoing, it is impossible for the clinician not to consider malignancy when he is dealing with an older patient with obstructive jaundice and extremely elevated CA 19-9 levels.

In this respect, we planned this study to investigate the relation of CA 19-9 with the number and size of the stones, cholangitis and biliary obstruction in patients with choledocholithiasis.

MATERIALS AND METHODS

Patients

A prospective study was performed. The study was performed in accordance with the Declaration of Helsinki, and all subjects provided written informed consent. All patients with radiologically proven choledocholithiasis in our department from December 1, 2008 to May 30, 2009 were included in the study. Patients with a biliopancreatic space-filling lesion on ultrasound (US) or helical computed tomography (CT) or magnetic resonance cholangiopancreatography (MRCP) were excluded. Seventy patients met the inclusion criteria.

Methods

Patients included in our study underwent US, helical CT and MRCP before endoscopic retrograde cholangiopancreatography (ERCP). Although it is preferable to do endosonography before ERCP in cases with suspicion of choledocholithiasis, this could not be done because of technical problems and preferred MRCP. In patients with choledocholithiasis, serum CA 19-9, amylase, aspartate aminotransferase (AST), alanine aminotransferase (ALT), alkaline phosphatase (ALP), gamma glutamyl transpeptidase (GGT), and bilirubin were evaluated before and after ERCP. Other tumor markers (alpha-fetoprotein and carcinoembryonic antigen) and immunoserologic tests (ANA, AMA and SMA) were also recorded before ERCP. Finally, ERCP, sphincterotomy and stone extraction were applied to all patients. The results of ERCP and the number and size of stones were recorded. In patients with high CA 19-9 levels, serum CA 19-9, AST, ALT, ALP, GGT, amylase, and bilirubin levels were recorded again after ERCP on the 1st, 3rd, 7th, 14th, 21st and 28th days until their CA 19-9 levels had normalized. The patients were discharged along the process when their CA 19-9 levels reached normal values.

Statistics

Statistical analysis was performed using the SPSS 17 package program. Pearson correlation test was used for the correlation of demographic and general features of the patients. Categorical variables were compared using the chi-square and Mann-Whitney U tests. Friedman test was used in the analysis of follow-up data. The results were considered significant if $p<0.05$.

RESULTS

Seventy patients with choledocholithiasis were studied. There were 22 males and 48 females aged

20-83 years (mean: 56.2 ± 20.7). Ten patients had pancreatitis and 6 had cholangitis. Twenty-eight patients had biliary sludge with stones <2 mm. Twenty had 1 and 22 had ≥2 biliary stones. Sizes of stones were 2-10 mm in 26 patients and 11-20 mm in 16 patients. Demographic and general features of the subjects studied are shown in Table 1.

Normal values of CA 19-9, ALP, GGT, bilirubin, AST, ALT, and amylase in our laboratory varied from 0 to 37 U/ml, 35 to 129 U/L, 11 to 50 U/L, 0.2 to 1.1 mg/dl, 9 to 40 U/L, 7 to 40 U/L, and 25 to 125 U/L, respectively.

Elevation of CA 19-9 was found in 32 patients (46%), while 8 patients (11%) had extraordinarily high levels (>1000 U/ml). Other tumor markers and immunoserologic tests were negative in all patients. Before ERCP, serum levels of bilirubin and ALP were high in 38 patients (54%), serum levels of GGT were high in 56 patients (80%), and serum levels of AST and ALT were high in 40 patients (57%). There was a significant correlation between serum CA 19-9 levels and serum ALP (r=0.5, p<0.01), GGT (r=0.5, p<0.01) and bilirubin (r=0.4, p<0.01) levels, but CA 19-9 levels were not correlated with serum AST or ALT levels. There was also no association between serum CA 19-9 levels and the number and size of stones according to correlation matrix and variance analysis.

Table 1. Demographic and general features of the subjects studied

	Patients with choledocholithiasis
Number of cases	70
Mean age (yrs)	56.2 ± 20.7
Male/Female	22/48
Acute pancreatitis n (%)	10 (14.3)
Cholangitis n (%)	6 (8.6)
Number of stones (%)	
Sludge with stones <2 mm	28 (40)
One stone*	20 (28.6)
Two or more stones*	22 (31.4)
Size of stones (%)	
Sludge with stones <2 mm	28 (40)
2-10 mm diameter	26 (37.1)
11-20 mm diameter	16 (22.9)
CA 19-9 (U/ml)	233.3 ± 474.2
Median (min-max)	35 (0.6 - 2037)
ALP (U/L)	204.4 ± 147.8
Median (min-max)	158 (38 - 585)
GGT (U/L)	282.9 ± 251.2
Median (min-max)	209 (6 - 957)
Bilirubin (mg/dl)	2.7 ± 2.6
Median (min-max)	1.8 (0.2 - 9.3)
AST (U/L)	77.7 ± 68.3
Median (min-max)	55 (10 - 308)
ALT (U/L)	123.6 ± 115.8
Median (min-max)	64 (5 - 418)
Amylase (U/L)	151.2 ± 234.1
Median (min-max)	74 (32 - 1122)

*≥2 mm

CA 19-9 levels were high in all patients with cholangitis but in none of the patients with pancreatitis. Higher rates of CA 19-9, ALP, GGT, and bilirubin levels were found in patients with cholangitis than in those without cholangitis (Table 2). The mean age was also found to be high in the group with cholangitis. No statistical differences were determined between groups in AST and ALT levels. There was also no association between cholangitis and the number and size of the stones. Serum amylase levels were higher in the group of patients without cholangitis.

Mean CA 19-9, ALP, GGT, bilirubin, AST, and ALT levels before and after ERCP are reported in Table 3. After stone extraction, CA 19-9 levels started to decrease and reached normal values 1-28 days later. Serum ALP, GGT and bilirubin levels also reached normal values as with CA 19-9. The patients were discharged along the process as their CA 19-9 levels reached normal values. The numbers of patients with high levels of CA 19-9 were 24, 12, 10, 4, and 2 on the 1st, 3rd, 7th, 14th, and 21st days, respectively, while 32 patients had high levels of CA 19-9 before ERCP. On the 28th day, CA 19-9 levels were normal in all patients as were ALP, GGT, bilirubin, AST, and ALT levels.

Eight of 32 patients had extraordinarily high levels of CA 19-9 (>1000 U/ml) before ERCP. Four of them also had cholangitis. CA 19-9, ALP and bilirubin levels were higher and duration of normalization of CA 19-9 was longer in patients with cholangitis than in patients without cholangitis, in this group. Furthermore, the number of stones tended to multiply in patients without cholangitis. The results of the 8 patients with extraordinarily high levels of CA 19-9 and a comparison of the results of patients with and without cholangitis are reported in Table 4.

DISCUSSION

Elevated CA 19-9 serum concentrations have a sensitivity of 80-90% for pancreatic cancer and 60-70% for biliary cancer, at a cutoff value of 37 U/ml (6,7). Specificity of CA

Table 2. General features of the patients with and without cholangitis

	Patients with cholangitis (n=6)	Patients without cholangitis (n=64)	P value
Mean age (yrs)	72 ± 9.3	54.8 ± 20.9	< 0.05
Number of Stones (%)			Non significant
Sludge with stones <2 mm	2 (33)	26 (41)	
One stone*	2 (33)	18 (28)	
Two or more stones*	2 (33)	20 (31)	
Size of Stones (%)			Non significant
Sludge with stones <2 mm	2 (33)	26 (41)	
2-10 mm	-	26 (41)	
11-20 mm	4 (67)	12 (18)	
CA 19-9 (U/ml, mean ± SD)	1294.5 ± 772.6	133.8 ± 285.7	< 0.01
Median (min-max)	1500 (346.5 - 2037)	23.3 (0.6 - 1200)	
Number of patients with high CA 19-9 (%)	6 (100)	26 (40.23)	< 0.01
ALP (U/L, mean ± SD)	367 ± 141	189.2 ± 140	< 0.05
Median (min-max)	401 (195 - 505)	136 (38 - 585)	
GGT (U/L, mean ± SD)	661.7 ± 249.7	247.3 ± 221.9	= 0.01
Median (min-max)	626 (402 - 957)	188 (6 - 829)	
Bilirubin (mg/dl, mean ± SD)	5 ± 2.4	2.5 ± 2.5	< 005
Median (min-max)	4.1 (2.9 - 8.1)	1.3 (0.2 - 9.3)	
AST (U/L, mean ± SD)	96.7 ± 83.7	75.9 ± 67.2	Non significant
Median (min-max)	54 (32 - 204)	56.5 (10 - 308)	
ALT (U/L, mean ± SD)	91 ± 73	126.7 ± 119	Non significant
Median (min-max)	63 (27 - 183)	66 (5 - 418)	
Amylase (U/ L, mean ± SD)	47.7 ± 3.7	160.9 ± 242.7	< 0.01
Median (min-max)	49 (43 – 51)	74.5 (32 - 1122)	

*≥2 mm

Table 3. CA 19-9, ALP, GGT, bilirubin, AST, and ALT levels before and after ERCP

	Number (%) of patients with elevated CA 19-9	Mean ± SD Median (min-max) CA 19-9	ALP	GGT	Bilirubin	AST	ALT
Before ERCP	32 (46%)	233.3 ± 474.2	204.4 ± 147.8	282.9 ± 251.2	2.7 ± 2.6	77.7 ± 68.3	123.6 ± 115.8
n=70		35 (0.6 - 2037)	158 (38 - 585)	209 (6 - 957)	1.8 (0.2 – 9.3)	55 (10 – 308)	64 (5 – 418)
1st day	24 (34%)	159.6 ± 260	199.2 ± 112.4	276.6 ± 188	2.3 ± 1.8	55.6 ± 46.9	81.5 ± 99
n=32		81 (15.7-1100)	173 (50 – 387)	269 (10 – 621)	1.8 (0.2 – 6.3)	44 (10 – 201)	36 (8 – 353)
3rd day	12 (17%)	104.8 ± 162.7	186.2 ± 80.7	243.9 ± 129	1.8 ± 1	43.8 ± 30.7	74.7 ± 97.3
n=24		39.6 (24 – 620)	165 (71 – 285)	248 (30 – 406)	1.8 (0.2 – 3.6)	35 (12 -104)	30 (14 – 286)
7th day	10 (14%)	103.6 ± 86.7	153.2 ± 39.4	196.8 ± 64	1.4 ± 0.3	36 ± 18	59.8 ± 61.9
n=12		70.6 (31 – 279)	149 (100 – 200)	190 (120-300)	1.3 (1 – 1.8)	32 (20 – 70)	32 (15 – 185)
14th day	4 (6%)	74 ± 61.9	122 ± 29.3	111 ± 41.7	0.9 ± 0.8	28 ± 10.8	43.8 ± 36
n=10		36 (30 – 183)	110 (90 – 160)	80 (80 – 175)	0.9 (0.8 – 1.1)	20 (20 – 45)	30 (14 – 110)
21st day	2 (3%)	63.5 ± 30.6	117.5 ± 8.7	67.5 ± 26	0.7 ± 0.1	25 ± 5.8	15 ± 5.8
n=4		63.5 (37 – 90)	117 (110-125)	67 (45 – 90)	0.7 (0.6 – 0.8)	25 (20 – 30)	15 (10 – 20)
28th day	0	34.9 ± 0.1	87.5 ± 3.5	42.5 ± 3.5	0.7	35 ± 7	25 ± 7
n=2		34.9 (34.8-35)	87.5 (85 – 90)	42.5 (40 – 45)	0.7 (0.7 – 0.7)	35 (30 – 40)	25 (20 – 30)
P value (Friedman test)		< 0.001	< 0.001	< 0.001	< 0.001	< 0.001	< 0.001

19-9 for pancreatic cancer, especially when its serum level is >1000 U/ml, is about 99% (23). Furthermore, noncancerous conditions such as cirrhosis, cholestasis, cholangitis, and pancreatitis can be associated with increased concentrations of serum CA 19-9, but in these conditions, the concentrations are usually (but not always) <1000 U/ml (6). Jalanko et al. (10) reported that elevation of CA 19-9 levels had been found in 35% of 14 patients with choledocholithiasis; 10 of them (71%) had obstructive jaundice, but none had cholangitis. In that study, the highest CA 19-9 value was 440 U/ml. In our study, elevation of CA 19-9 was found in 46% of 70 patients with choledocholithiasis, and

Table 4. General features of the patients with extraordinarily high levels of CA 19-9 and a comparison of the results of the patients with and without cholangitis in this group

	All patients with extraordinarily high levels of CA 19-9 n=8	Patients with cholangitis n=4	Patients without cholangitis n=4	P value
Mean age (yrs)	62 ± 24	75.5 ± 3.3	48.5 ± 29	Non significant
Number of Stones (%)				< 0.05
Sludge with stones <2 mm	2 (25)	2 (50)	-	
One stone*	2 (25)	2 (50)	-	
Two or more stones*	4 (50)	-	4 (100)	
Size of Stones (%)				Non significant
Sludge with stones <2 mm	2 (25)	2 (50)	-	
2-10 mm	2 (25)	-	2 (50)	
11-20 mm	4 (50)	2 (50)	2 (50)	
CA 19-9 (U/ml, mean ± SD)	1471.8 ± 366.9	1766 ± 280.1	1177.5 ± 68.5	< 0.05
Median (min-max)	1380 (1100 – 2137)	1763 (1500 - 2037)	1175 (1100 - 1260)	
Duration of normalization of CA 19-9, Median (min-max)	13.5 ± 12 days 12 (1 – 28)	24.5 ± 4 days 24.5 (21 – 28)	2.5 ± 1 days 3 (1 – 3)	< 0.05
ALP (U/L, mean ± SD)	313.5 ± 170.5	453 ± 60	174 ± 110.9	< 0.05
Median (min-max)	335.5 (78 – 505)	453 (401 - 505)	174 (78 - 270)	
GGT (U/L, mean ± SD)	527.5 ± 378.2	679.5 ± 320.4	375.5 ± 411.7	Non significant
Median (min-max)	567 (19 – 957)	679 (402 - 957)	375.5 (19 - 732)	
Bilirubin (mg/dl, mean ± SD)	3.9 ± 2.9	6.1 ± 2.3	1.7 ± 1.4	< 0.05
Median (min-max)	3.5 (0.5 – 8.1)	6.1 (4.1 - 8.1)	1.7 (0.5 - 2.9)	
AST (U/L, mean ± SD)	77.8 ± 78	118 ± 99.3	37.5 ± 0.6	Non significant
Median (min-max)	37.5 (32 – 204)	118 (32 - 204)	37.5 (37 - 38)	
ALT (U/L, mean ± SD)	134 ± 129.6	105 ± 90.1	163 ± 169.7	Non significant
Median (min-max)	105 (16 - 310)	105 (27 - 183)	163 (16 - 310)	
Amylase (U/L, mean ± SD)	53 ± 9.8	47 ± 4.6	59 ± 10.4	Non significant
Median (min-max)	50.5 (43 – 68)	49 (43 – 51)	59 (50 - 68)	

*≥2 mm

38 (54%) of them had raised levels of bilirubin. The highest CA 19-9 value was 2037 U/ml, but 6 patients had cholangitis. In 64 patients without cholangitis, elevation of CA 19-9 levels was present in 40% of patients, and the highest CA 19-9 value was 1200 U/ml (Table 2). Thus, the results were similar except for the 4 patients with extraordinary high levels of CA 19-9 in patients without cholangitis.

McLaughlin et al. (24) reported that there was a significant correlation between CA 19-9 levels and ALP, AST, ALT, bilirubin, and GGT levels in benign and malignant conditions. However, Ng et al. (25) and Morris-Stiff et al. (26) reported that serum bilirubin was correlated with CA 19-9 levels in benign jaundice but not in malignant jaundice. We also found a significant correlation between CA 19-9 levels and serum ALP, GGT and bilirubin levels, but not with AST or ALT levels in patients with choledocholithiasis.

CA 19-9 is a serum glycoprotein and seems to be excreted in the biliary tract after being cleared by the liver (8,27-29). In cases of benign biliary obstruction, there is a direct correlation between serum bilirubin and CA 19-9 concentration. This is most likely due to impaired biliary excretion of CA 19-9 (8). Some factors are postulated in benign biliary tract diseases: 1) CA 19-9 production by irritated bile duct cells exposed to increased biliary pressure may be enhanced (30); 2) Inflammation may cause the increased proliferation of epithelial cells leading to more production of CA 19-9 (7); 3) Obstruction may cause accumulation of CA 19-9 in the biliary lumen (31); and 4) Reflux of CA 19-9 into the circulation may be induced by obstruction (7). The association between elevated serum bilirubin and CA 19-9 does not occur in malignant diseases, however, presumably because proliferating tumor cells synthesize CA 19-9 (8).

CA 19-9 cannot be employed to differentiate between malignant and benign extrahepatic jaundice (7,32). Therefore, elevations in CA 19-9 levels should be interpreted cautiously in patients with obstructive jaundice, unless the high levels persist after the obstruction has been removed (8,25).

There are a few reports related to extraordinarily

high levels of CA 19-9 and cholangitis (16,18-22). Although the real reason for the CA 19-9 elevation in cholangitis is not clear, several mechanisms as mentioned above have been postulated. The inflammatory cytokines produced in sepsis due to cholangitis are probably also a contributing factor (33). In our study, 6 patients had cholangitis, and all of them had elevated levels of CA 19-9. Furthermore, 4 of 6 patients with cholangitis had extremely high levels of CA 19-9 at the same time. Mean age and CA 19-9, ALP, GGT, and bilirubin levels were higher in patients with cholangitis (Table 2). There were no differences between the groups in AST or ALT levels. There was also no association between cholangitis and the number and size of the stones. Serum amylase levels were higher in the group of patients without cholangitis, probably due to having high rates of sludge with smaller stones. It seems that cholangitis is associated with biliary obstruction regardless of the number and size of stones. However, these results must be supported with more patients because some mistakes in statistical analyses may occur due to the limited number of patients.

As is known, smaller stones can cause pancreatitis while the larger stones can cause biliary obstruction. In the same way, it is expected that multiple (and larger) stones can obstruct the choledochus and even cause cholangitis. We planned this study with this in mind, but did not find any association between CA 19-9 levels and the number and size of stones in patients with choledocholithiasis, or in the patients with cholangitis. The number of stones tended to multiply in patients without cholangitis only in 8 patients with extremely high levels of CA 19-9 (Table 3). However, that was a very small group, and furthermore, extremely high levels of CA 19-9 in patients without cholangitis may be associated with biliary obstruction in close conjunction with multiple stones. New studies are necessary in order to explain the extremely high levels of CA 19-9 in patients without cholangitis.

After stone extraction, CA 19-9 levels started to decrease and reached normal values 1-28 days later (Table 3). Furthermore, serum ALP, GGT and bilirubin levels also reached normal values as with CA 19-9, as reported in the literature (25).

We had 8 patients with extraordinarily high levels of CA 19-9 (Table 4). Four of them had cholangitis and 4 did not. It is well known that extraordinarily high levels of CA 19-9 may be seen in patients with cholangitis (22). However, it is interesting that it was present in our patients without cholangitis as well. CA 19-9, ALP and bilirubin levels were higher and duration of normalization of CA 19-9 was longer in patients with cholangitis than in patients without cholangitis, in this group. Duration of normalization of CA 19-9 levels was 21–28 days in patients with cholangitis and 1–3 days in patients without cholangitis. Serum ALP, GGT and bilirubin levels also reached normal values as did CA 19-9. It seems that extraordinarily high levels of CA 19-9 seen in patients without cholangitis drop to normal values quickly after the stone extraction. However, in patients with cholangitis, this duration is prolonged; as seen in the literature, CA 19-9 levels return to normal levels in up to two months in patients with cholangitis (22).

In conclusion, considering that we studied only a few patients and the associated limitations, CA 19-9 levels were seen to be associated with biliary obstruction and cholangitis but not with the number and size of stones in patients with choledocholithiasis as well as in patients with cholangitis.

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