The Effect of "Pseudo-Clolangiocarcinoma Sign" on Serum Bilirubin and Alkaline Phosphatase Levels in Patients with Cavernous Transformation of the Portal Vein

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Özet: *PORTAL VENDE KAVERNOMATÖZ TRANSFORMASYON OLAN HASTALARDA SERUM BİLİRUBİN VE ALKALEN FOSFATAZ SEVİYELERİNE "PSÖDOKOLANJİOKARSİNOMA BELİRTİSİ" NİN ETKİSİ*

Portal venin kavernomatöz transformasyonu (PVKT) çok nadiren gözlenir. Genellikle portal ven trombüsüne sekonder gelişir, ancak konjenital da olabilir. Son 8 yılda değişik nedenlerle ortaya çıkmış portal hipertansiyonu olan 1247 hasta tarama testi olarak ultrasonografi (US) kullanılarak incelendi.1247 hastadan 44 ünde PVKT tespit edildi. Bu 44 hasta prospektif olarak incelendi ve tümünde tanı dijital substraksiyon anjiografi (DSA) uygulanarak portografiyle desteklendi (ya splenoportografi ya da arteryel portografi). Tüm hastalara artmış alkalen fosfataz ve bilirubin seviyelerini sebebini araştırmak için detaylı inceleme yapıldı. Ayrıca 44 hastanın 36 sında endoskopik retrograd kolanjiopankreatografi (ERCP) ile, hastaların tümünde US ile ve 19 hastada da komputerize tomografiyle biliер sistem değerlendirildi. Hipersplenizm ve/veya özefagus varis kanaması nedeniyle splenektomi yapılmış 10 hastadaki cerrahi bulgular ultrasonografik, ERCP ve tomografi bulgularıyla karşılaştırıldı.

PVKT olan 44 vakada altta yatan etiolojik sebep 7 hastada Behçet Hastalığı, 4 vakada kronik karaciğer hastalığı 5 vakada konjenital hepatik fibrozis, 1 vakada protein C eksikliği ve 1 vakada da kolelitiazis nedeniyle uygulanmış abdominal cerrahi olarak belirlendi. Geriye kalan 26 hastada karaciğer biyopsisi de normal olarak değerlendirildi ve bu vakalarda tüm araştırmalara rağmen predispozan faktör belirlenemedi. Bu 26 vakda serum bilirubin ve alkalen fosfataz seviyelerindeki artış aşırı değildi, ancak altta yatan sebep tespit

Summary: *Cavernous transformation of the portal vein (CTPV) is a rare condition which is generally secondary to portal vein thrombosis and may also be a congenital anomaly. A total of 1247 patients with portal hypertension resulting from different etiologies were examined by ultrasonography (US) as a screening test during the last 8 years. In 44 of the 1247 patients, CTPV was recognized using US. These 44 patients were prospectively studied and the diagnosis of cavernous transformation was confirmed by portography, either splenoportography or arterial portography, with digital subtraction angiography (DSA) in all cases. To discover the underlying disorder of CTPV, all patients were given a thorough examination particularly with regard to elucidating the etiology of direct hyperbilirubinemia and increased alkaline phosphatase (ALP) levels. In order to determine the cause of increased serum bilirubin and ALP levels, the biliary system was evaluated by endoscopic retrograde cholangiopancreatography (ERCP) in 36 of the 44 patients, by US in all patients and also by computed tomography in 19 of these 44 patients. The surgical findings in ten patients who had undergone splenectomy for either hypersplenism and / or bleeding from esophageal varices were compared with those of ultrasonographic, portographic and ERCP findings.*

In 44 patients with CTPV, the underlying disorder of cavernous transformation seemed to be Behçet's disease in 7 cases, chronic liver disease in 4 cases, congenital hepatic fibrosis in 5 cases, protein C deficiency in one case, and abdominal operation for cholelithiasis in one case. Despite full investigation, predisposing factors remained unknown in the remaining 26 patients who had no parenchymal liver disease on liver biopsy specimens. In these 26 patients, increases in the levels of serum bilirubin and ALP ranged from mild to moderate but these values changed from moderately to highly increased levels in 18 patients having an un-

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edilmiş olan 18 hastada orta veya aşırı derecede artmış değerler gözlendi. ERCP yapılan 36 hastanın 34 ünde ondülasyon, düzensizlik, daralma ve nodüler ekstrinsik defektler, yani "psödokolanjiokarsinoma belirtisi" tespit edildi. Karaciğer sirozuna bağlı portal hipertansiyon olan 10 vakada benzer görünüm yoktu. Splenektomi yapılan 10 vakada ultrasonografik, ERCP, portografik görünümler cerrahideki görünümle korrele idi.

Sonuçlar, etiolojisi bilinmeyen PVKT olgularında alkalen fosfataz ve direk bilirubin seviyelerindeki hafif dereceli yükselmeni kollateral damarlar ve portal trombusların bası yapmasıyla oluan, koledok boyunca yayılan kolaniokarsinomayı taklit eden "psödokolanjiokarsinoma belirtisi" nedeniyle oluştuğunu, ve bu belirtini altta yatan etiolojik sebep olan vakalardada etkili olabileceğini gösterdi. Splenomegalisi olup parankimal karaciğer hastalığı olmayan bir hastada artmış direk bilirubin ve alkalen fosfataz seviyeleri varsa PVKT olası tanı olmalı ve trombus nedeniyle ekstrahepatik safra sistemine bası düşünülmelidir.

Anahtar kelimeler: Kavernöz transformasyon, psedocholongiocarcinoma sign, bilirubin, alkalen fosfatoz.

derlying pathology. There were irregularity, undulation, narrowing and nodular extrinsic defects, the so-called "pseudo- choangiocarcinoma sign" in 34 of the 36 patients who underwent ERCP. Similar ERCP findings were not observed in ten patients with portal hypertension due to liver cirrhosis. The ultrasonographic, portographic and ERCP findings corresponded to the surgical findings in ten patients who had undergone splenectomy.

The results indicate that mildly increased ALP and D. bilirubin levels were caused by the "pseudocholangiocarcinoma sign" resulting from compression by thrombosis of the portal vein and the collateral vessels, mimicking cholangiocarcinoma spreading along the common bile duct in CTPV patients with unknown etiology, and this sign can contribute to the increase of these values in patients having an underlying disorder with CTPV. When a patient with splenomegaly but without parenchymal liver disease has increased direct bilirubin and ALP, CTPV should be suspected and these values should be attributed to incomplete obstructon of the extrahepatic biliary ducts due to the compression by thrombosis.

Key words: Cavernous transformation, pseudocholangiocarcinoma sign, bilirubin, alkaline phosphatase.

Many clinical disorders are associated with direct hyperbilirubinemia and increased ALP. Although several organs such as the liver, bone and placenta are the source of alkaline phosphatase, the hepatobiliary system is the suspected organ system when direct hyperbilirubinemia is present. Serum hepatic ALP may be distinguished from bony phosphatase by frationation into iso-enzymes, but this is not routinely carried out. A rise in gamma-glutamyl transpeptidase (GGT) confirms that the likely source of alkaline phosphatase is the hepatobiliary system. Its levels parallel serum alkaline phosphatase in cholestasis.

Extrahepatic obstruction to the biliary apparatus such as obstructive gallstones, carcinoma of the head of pancreas and inflammatory stenosing strictures and "pure cholestasis, e.g., the use of oral contraceptives and Dubin-Johnson and Rotor syndomes, are the main causes of direct hyperbilirubinemia. Some very rare conditions such as cavernous transformation of the portal vein (CTPV) can cause incomplete obstruction, and accordingly mildly or moderately increased indirect bilirubin and ALP levels can be seen. The finding of mildly increased levels often leads to over-investigation of elevated levels in an otherwise healthy person who has never had parenchymal liver disease or a true obstruction in the biliary tree. Additionally, as the patients with CTPV have splenomegaly, increased levels can be attributed to the liver diseases and other systemic disorders.

CTPV is a rare condition resulting from extrahepatic portal vein thrombosis with recanalization and collateral vein formation to bypass the occlusion. Regardless of its etiology (1-3), after obstruction, the preexisting periportal and paracholedocal vessels begin to enlarge and form a collateral circulation. The collaterals and throm-

boses cause extrinsic impressions. Although there have been many studies related to diagnosis and how it develops, few reports have described to what extent the biliary tree system is affected (4-5) and why direct hyperbilirubinemia and mildly increased serum ALP are produced by this rare condition.

This prospective syudy is designed to investigate the cause of increased alkaline phosphatase and bilirubin levels in 44 patients with CTPV diagnosed by sonography and portography in whom 18 had underlying disorders. ERCPs were carried out in 36 of them. The surgical findings were compared with those of the ERCPs and portographies in ten patients.

MATERIAL AND METHODS

Patients

One thousand-two hundred forty three patients with portal hypertension presenting with various clinical findings between December 1986 to June 1994 were carefully evaluated by using ultrasonography as a screening test. Splenoportography, inferior and superior vena cavography, abdominal computed tomography, surgery, peritonoscopy, and liver biopsy were performed for futher evaluation if necessary. Diagnosis of Behçet's disease (BD) was made according to international criteria (6).

Procedures

Patients were fasted and examined in a supine position and scans were obtained by a real time sonograph at 3.5 MHz. The portal vein system and its patency, the common bile duct, pancreas and vascular structures of the porta hepatis were carefully examined. In 44 patients (twenty four male, twenty female, mean age 34 yr, raing from 8 to 64 years) cavernous transformation of the portal vein was diagnosed by ultrasonography. We prospectively studied these 44 patients. To confirm the diagnosis, either splenoportography or arterial portography with digital subtraction angiography (DSA) was carried out in all 44 patients, by using a Phillips DVI device. Splenoportography was performed using a fine needle as described previously (7). Digital images were obtained in different positions. On arterial portography, a "side-winder" catheter was introduced via the femoral artery. DSA of the celiac and superior mesenteric artery was obtained after selective injection of 35 ml of 50% diluted contrast medium (Omnipaque 300) at a rate of 8ml/s. Digital images were recorded for 25 s at a rate of one frame /s during the arterial, arteriocapillary and venous phases.

In 19 of the 44 patients with CTPV, abdominal computed tomography was performed by using a tomography device providing images 5 mm in space.

After the diagnosis of cavernous transformation had been confirmed, ERCPs were carried out in 36 of the 44 patients with a side - viewing duodenoscope (Olympus JF-IT 20). In 8 of the 44 patients, ERCPs could not be performed either for technical reasons or problems related to the patients. After cannulation of the papilla of Vater, a contrast material, Conray 60, was injected through the cannula under fluoroscopic guidance. We obtained the radiograms of the biliary tract and pancreatic ducts from different positions with the same techniques, ERCPs were also performed in eleven patients with portal hypertension due to liver cirrhosis and in two patients with idiopathic portal hypertension.

Sonography-guided liver biopsy was performed in 40 of the 44 patients for evaluation of parenhymal liver diseases. In the remaining 4 patients, the general condition was poor, so we could not perform liver biopsy in these patients with BD. The diagnosis of Budd-Chiari syndrome (BCS) was made by sonography in which the caudate lobe should be bypertrophic and two or all of the hepatic veins should be occluded and hepatic venography should demonstrate the "spider web" appearance which is very specific for BCS. When the inferior vena cava was occluded, we performed the procedures via the jugular vein. In the case of inferior vena caval obstruction, we easliy demonstated the ocluded area by using the femoral vein as the access site.

Biochemical and serological tests

Routine blood and urine analyses were tested once every six months. Serial liver function tests

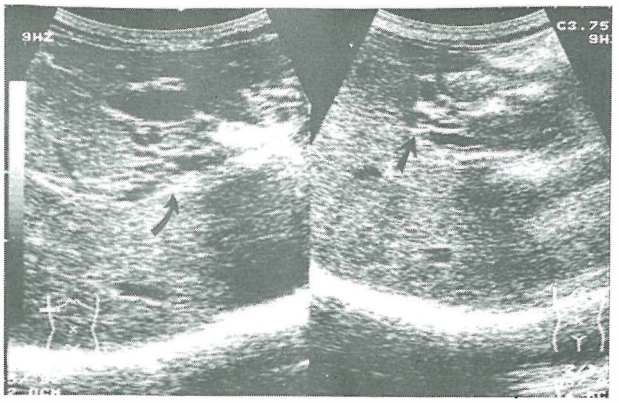

Fig. 1: Ultrasonography, a transverse sonogram, level of porta hepatis, shows echogenic band (arrows) resulting from fibrosis of portal vein branches and tubular structures replacing the main portal vein.

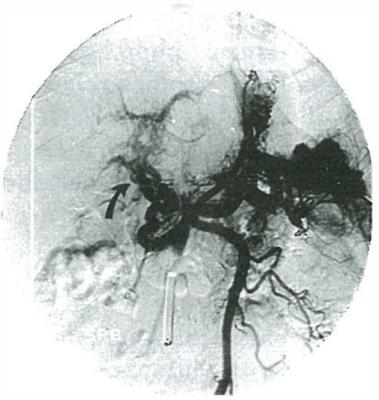

Fig. 2: Splenoportography of the same patient as in Fig. 1, reveals hepatofugal collateral flow and many tortuous vessels at the porta hepatis (arrows).

including serum ALT, GGT and bilirubin levels were studied. During the follow-up period, we considered two values-the lowest and highest of ALP-and direct bilirubin. Tumor markers such as Alpha Fetoprotein (AFP) and carinoembryonic antigen (CEA) and 19-9 (in 10 patients only), were also tested. The markers of hepatitis B virus, (HBV), hepatitis D virus and hepatitis C virus (in 21 patients) were investigated. To explain the reason for thrombosis in the portal vein, the thrombocyte count, prothrombine, anti-thrombin III, and protein C and S activities were also tested. As seen in Table 1 and 2, the patients weredivided into two groups according to the most probable underlying disorders of portal thrombosis.

All patients gave written informed consent before all procedures, including liver biopsy, were performed.

Statistical Analysis

The study of the relationships between the variables examined was performed using the student's test. We compared the values of ALP and direct bilirubin of the patients, both upper and lower levels, with each other and with upper limits of expected normal values.

RESULTS

Table 1 and 2 show some clinical features, sex and age distribution of the patients with CTPV. As seen in table 1, in 18 of the 44 patients (group 1;9 female, 9 male mean age 32.9±13.7 years, ranging from 9 to 67 yrs) there was an underlying disorder of cavernous transformation. Behçet's disease in 7 patients, congenital hepatic fibrosis in 5 patients, chronic liver disease in 4 patients, protein C deficiency in one patient and finally abdominal operation for gallbladder stone in one patient seemed to be the responsible disorder for portal vein thrombosis. Five of the 7 patients with BD died of vascular complications of BD. One of the remaining two patients has been followed-up and is doing well, the other is still alive but in poor condition. As seen in table 1, five of the 7 patients with BD also had other great vessel involvements in addition to the portal vein.

Despite full investigation, in 26 of the 44 patients (15 male 11 female mean age 30.5±11, ranging from 18 to 55 years), we could not find any etiologic factor for portal thrombosis. In these patients there was no history of pancreatitis, umbilical vein catheterization during the perinatal period, previous abdominal infection, but all the patients' social levels were lower or middle class. Umbilical sepsis might be an important factor in the development of portal vein thrombosis. All these 26 patients have been followed-up and are doing well, and the median follow-up period is 4 yrs. No systemic or local disorders could be detected in these patients during the follow-up period. Liver function tests were normal in this group except for ALP and direct bilirubin levels. As shown in table 2, most biliru-

Table 1- Sex and age distribution and the results of imaging modalities and some labaratory features of the CTPV patients having an underlying disorder.

Case	Sex/age	Viral status	Other vascular inv.	US	Port	ERCP	ALP (41-133) U/L	D. B. (0.2-0.7) mg/dl	LB	Ass.Dis
1H.A	M/30	-	-	+	+	+	140-234	1.0-3.2	N	BD
2 HM	M/31	HBsAg+	-	+	+	+	200-254	2.3-4	C	Cirr.
3 EE	M/25	-	IVCO+BCS	+	+	≠	247-458	1.7-5.3	≠	BD
4 EE	M/50	-	+BCS	+	+	≠	198-378	1.3-4	B	BD
5 HA	F/67	-	IVCO+BCS+SVO	+	+	≠	389-567	2.7-4.7	≠	BD
6 AG	F/12	-	IVC+BCS	+	+	≠	145-247	1.8-3.5	≠	BD
7 YA	M/32	-	M.A.O	+	+	≠	387-847	1.7-4.6	B	BD
8 HO	M/42	-	-	+	+	≠	231-245	1.3-1.8	≠	BD
9 MY	M/35	HBsAg+	-	+	+	+	144-156	0.7-1.2	C	Cirr.
10 NK	F/34	HBsAg+ anti-HDV+	-	+	+	+	98-144	0.6-2.4	C	Cirr.
11 PI	F/30	-	-	+	+	+	177-234	0.8-1.9	F	CHF
12 FK	F/30	-	-	+	+	+	155-187	0.9-1.8	F	CHF
13*AD	F/17	-	-	+	+	+	247-648	1.1-5.6	F	CHF+Car
14 ÖC	M/9	-	-	+	+	PTC	258-457	2.3-4.5	F	CHF+Car
15 FK	F/42	-	-	+	+	+	125-189	0.9-1.9	F	CHF
16 SB	F/30	-	Spl. vein	+	+	+	178-234	0.1-2.5	N	PrC
17 YA	F/30*	-	IVCO+BCS	+	+	+	765-867	0.9-4.3	C	Cirr
18*HÖ	M/47	-	-	+	+	+	349-431	3.3-6.7	Ch	Abd.Op

Total 26 patients Mean 30.577±11.035 Value	Lowest level Highest level	240±163 356±229	1.312±0.714 3.225±1.299

Case no. 13 and 18 were not included in estimating bilirubin and alkaline phosphatase because there were stones in CBDs and they were dilated*.
L. B.; Liver biopsy, N; normal liver biopsy, C; cirrhosis in liver biopsy, ≠; could not perform the procedure, BD; Behçet's Disease, CHF; congenital hepatic fibrosis, Pr C; Protein C deficiency, Ch; cholangitis, IVCO; inferior vena caval obstruction, Abd Op; abdominal operation for gallstone, B; Liver biopsy compatible with BCS, PTC; percutaneous transhepatic cholangiography, F; congenital hepatic fibrosis in liver biopsy

bin levels are higher than the normal upper limits and mean values (lower and upper limits) of D. bilirubin obtained from the patients were 0.992±0371 and 1.731±0.574 mg/dl respectively. When these values are compared with the lower and upper limit of the normal values, the differences were statistically significant ($p<0.001$). As seen in the same table, the patients' mean values of upper and lower limits of ALP (152±38.3 and 211.5±60.8) were higher than normal values. The differences were also significant statistically ($p<0.001$).

These values of ALP were, as seen in table 1, high in patients with CTPV complicated with an underlying disorders when compared with those

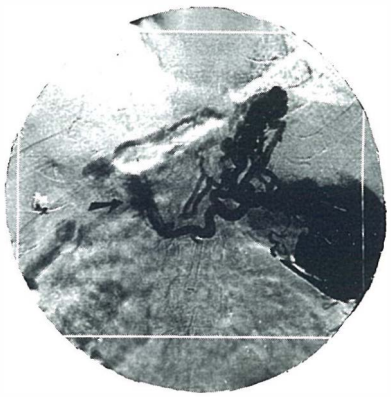

Fig. 3: Portography demonstrates cavernomatous replacement of the portal vein (arrows) and hepatofugal flow.

having only CTPV (152±38.3 vs 240±163; 211.5±60.8 vs 35±229, $p<0.05$). When we compared the mean value of D. bilirubin lower levels of the two groups (0.992±0.371 vs 1.312±0.714) the difference was not significant ($p>0.05$) but when the mean values of upper limits were compared, the difference was significant ($p>0.01$). In the two groups, GGT was not elevated in most cases. There was no strong correlation between ALP and GGT. In table 1, two patients (case no. 13 and 18) were exluded during the estimation of statistical analysis because these two patients had common bile duct stones and accordingly bile duct dilatation and increased bilirubin and ALP levels beside CTPV and underlying disorders. In this group, obviously the mean values of ALP and D. bilirubin levels were higher than normal ($p<0.001$).

In all but one patient coagulation factors including protein C and S, and Anti-thrombin-III, were normal (Table 1, ase No. 16). In this case it seems that protein deficiency was the responsible factor for portal and splenic vein thrombosis. Most patients had thrombocytopenia. In 15 of the 44 patients, the number of the thrombocytes was lower than 60.000 mm3.

AFP and CEA levels were within normal limits in all patients, including those with chronic liver diseases. The markers of HBV were positive in 6 patients (anti-HBs positive in 3 cases and HBsAg in 3 cases), and anti-HDV total was positive in only one patient (Table 1, cases no 10). Needle liver biopsy showed no parenchymal abnormalities in 28 of the 40 patients who underwent liver biopsy. In the remaining 12 patients, it demonstrated liver cirhosis in 3 patients, chronic active hepatitis in one patient, congenital hepatic fibrosis in five patients, and cholangitis in one patient. In four of the 7 patients with BD, we could not perform liver biopsy because of their poor general condition. The biopsies obtained from 2 Behçet patients were compatible with BCS in which there were central vein congestion and dilatation, and one biopsy was normal.

On ultrasonography, in all 44 patients, the main portal vein was not demonstrated, and multiple tortuous structures were located with a high echo wall located in the porta hepatis (Fig. 1). It was difficult to distinguish the collateral vessels from the extrahepatic biliary tree in 42 of the 44 patients because of multiple tubular structures alongside the portal vein. In two cases, the common bile duct was enlarged due to common bile duct stone, one of them also had multiple intrahepatic cystic dilatation Sonography was very informative in the case of Budd-Chiari syndrome and inferior vena caval obstruction in which the hepatic vein occlusions, thick wall echoes, central dilatation and thrombosis in the vena cava are the main findings.

Arterial portography (in 13 patients) at the venous phase demonstrated that the veins over the head of the pancreas drain into many tortuous worm-like veins extending along the portal veins to the portal vein radicles in the liver and there was a hepatofugal blood flow in most cases. In 31 patients, splenoportography revealed extrahepatic portal vein obstruction with filling of multiple tortuous hepatopetal collateral vessels which replaced the main portal vein (Fig. 2-3).

In 36 of the 38 patients studied, ERCPs revealed narrowing, undulation, nodular extrinsic defects, and irregularity along the common bile duct (8) (Fig. 4-6). As seen in the figures, in all patients the common bile duct was narrower than the proximal part of the common hepatic duct, and in most cases, narrower than the intrahepatic ducts. In some special cases, the ducts seem to be bilaterally compressed (Fig. 6).

Table 2- Sex and age distribution and the results of imaging modalities and some labaratory features of the patients with CTPV of unknown etiology

Case	Sex/age	Viral status	Other vascular inv.	US	Port	ERCP	ALP (U/L) (41-133)	D. B. (mg/dl) (0.2-0.7)	LB	Follow-up (yr)
1 T. B	F/30	-	-	+	+	+	150-230	1.6-2.9	N	3
2 T. E.	M/8	-	-	+	+	@	132-286	1.2-1.7	N	4
3 G. C.	F/35	-	-	+	+	+	128-189	0.9-1.3	N	3
4 GT	F/28	HBsAg+	-	+	+	+	235-321	1.1-1.7	N	3
5 M. B	F/40	-	-	+	+	+	120-169	1.1-1.5	N	4
6 HA	M/37	-	-	+	+	+	130-159	0.8-1.3	N	5
7 MG	F/33	-	-	+	+	+	98-134	0.5-1.2	N	5
8 YK	F/50	-	-	+	+	+	135-231	0.8-1.5	N	3
9 EB	M/18	-	-	+	+	+	238-321	1.4-2.1	N	6
10 OK	M/28	-	-	+	+	+	148-312	1.4-1.7	N	3
11 AD	M/45	antiHBs+	-	+	+	+	147-213	0.7-0.9	N	6
12 ŞÇ	F/25	-	-	+	+	+	213-267	0.8-1.7	N	4
13 MD	M/28	-	-	+	+	+	118-165	0.5-2.7	N	3
14 HK	M/35	-	-	+	+	+	187-321	0.8-2.9	N	17
15 HE	M/18	-	-	+	+	+	122-164	0.7-1.4	N	4
16 IA	M/40	-	splenic vein	+	+	@	123-167	0.6-1.8	N	4
17 ŞK	F/29	-	-	+	+	+	156-186	0.7-1.0	N	5
18 KK	M/23	-	-	+	+	+	165-176	0.6-1.1	N	4
19 CP	M/21	antiHBs+	-	+	+	+	123-154	0.6-1.3	N	3
20 AH	M/23	-	-	+	+	+	188-231	1.3-2.5	N	1
21 RG	M/19	-	-	+	+	@	132-198	1.4-1.9	N	2
22 HT	F/30	-	-	+	+	+	213-259	1.5-2.3	N	1
23 ÜG	M/18	-	-	+	+	+	116-143	1.3-1.9	N	3
24 KK	F/45	antiHCV+	-	+	+	+	145-189	1.2-1.8	N	2
25 NS	F/34	antiHBS+	-	+	+	+	158-169	1.7-2.0	N	1
26 HA	M/55	-	-	+	+	+	120-145	0.6-0.9	N	5
Total 26 patients										
Mean 30.577±11.035 Value			Lowest level				152±38.3	0.992±0.371		4
			Highest level				211.5±60.8	1.73±0.574		

ERCP, endoscopic retrograde cholangiopancreatography; @, ERCP could not be performed, -**, there was a large bile duct due to stone;

Fig. 4: ERCP of the patient in Fig. 1 reveals narrowing and extrinsic compression along the common bile duct, and the intrahepatic bile ducts are narrower than the common bile duct (arrows).

Fig. 5: ERCP shows a narrow common bile duct along with a long segment mimicking sclerosing cholangitis or cholangiocarcinoma (arrows) (the same patient as in Fig. 3).

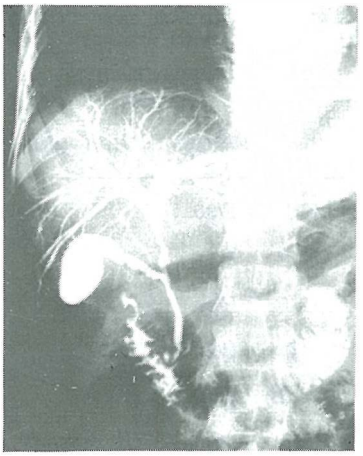

Fig. 6: ERCP demonstrates irregularity, narrowing and undulation along the common bile duct. Note : the common bile duct seems to be compressed bilaterally.

These findings were more predominant in cirrhotic patients complicated with CTPV. On the other hand, the ERCP findings of ten patients with idiopathic portal hypertension were normal. All patients had splenomegaly of varying degress. Five patients had hepatomegaly due to impaired outflow from the liver. Esophageal varices, although variable in degree, were also seen in all 44 patients during endoscopy of the upper gastroentestinal tract, and duodenal varices were seen in nine patients.

In ten patients in whom splenectomy was performed because of either hypersplenism (in seven cases) or massive bleeding from esophageal varices (in three cases), occluded veins and massive collaterals at the porta hepatis were observed and were found to be compressing the common bile duct. In these ten patients, ERCPs and portographic findings correlated with those of surgery.

DISCUSSION

In this prospective study, we examined 44 patients with CTPV and evaluated these patients in two groups : (1), 16 patients having an etiologic factor for portal vein thrombosis (2) and, 28 patients without an etiologic factor to explain the portal thrombosis. In both groups direct bilirubin and alkaline phosphatase were higher than normal levels. As seen in table 1 and 2, these values were higher in group 1 than in group 2. Although primary liver pathology can play an important role in increasing the levels, narrowing of the common bile duct has contributed to these values. When we compared the mean values of the two groups considering the lower normal limits, the difference was not significant statistically ($p>0.05$), showing that the lowest levels are almost the same in the two groups. As stated earlier, incomplete obstruction along the common bile duct has been found in 18 patients in addition to our first 16 cases of series (8). In other words, 34 of the 44 patients with CTPV demonstrated the "pseudocholangiocarcinoma sign" on ERCP which is responsible for hyperbilirubinemia. In 8 patients we could not perform the ERCP because of technical reasons and the poor medical condition of the patients. Whatever the reason for cavernous transformation or portal thrombosis (9-11), extensive collateral veins due to portal vein occlusion and thrombosis as observed during surgical procedures may compress and narrow the extra-

hepatic biliary tract and may cause obtructive jaundice (4, 12, 13). As shown in Fig. 4-6, the obstruction is sufficient to produce hyperbilirubinemia. When we consider only 28 patients without underlying disorders in whom the mean follow up period is 4 years, it is clear that the "pseudo-cholangiocarcinoma sign" seems to be responsible for hyperbilirubinemia and mildly inreased ALP since all liver function tests and liver biopsy are normal and no disorder developed during the follow- up period.

It is obvious that these ERCP findings resulted from the compression of paracholedocal varices and the presence of epicholedocal varices (5, 14-17) had cavernous transformation of the portal vein. In the remaining 5 cases, the causes of the varices were varied. In this current study, we report 44 additional cases including our previous report (8) in which the diagnosis was verified angiographically, ten of them anatomically. Besides cavernous transformation, lymphoma, submucosal tumors, extrinsic lesions such as lymph nodes, vessels crossing the bile duct and hydatic cyst which comunicates with biliary trees may cause incomplete obstruction of the common bile duct. Parasitic organisms (17) may inhabit the biliary tree and cause chronic direct hyperbilirubinemia. In evaluating direct hyperbilirubinemia as we did, the causes of "pure cholestasis" should be excluded. In differentiating this condition from others, liver needle biopsy is mandatory.

The mean follow-up period was about 4 yrs for our cases. During this period in the second group of patients, direct bilirubin and ALP were rarely within normal limits but mostly higher than the upper normal limits. The same laboratory findings and cholangiographic appearances can be seen in chronic cholangitis, benign strictures, chronic pancreatitis, the segmental variety of primary sclerosing cholangitis (18,19) and especially in cholangiocarcinoma, which spreads along the bile duct (20). In our cases however there was no attack of cholangitis or any other disease. In addition, serial liver function tests and liver biopsies were normal. On the other hand, in the cases of congenital hepatic fibrosis, serum protein, bilirubin and transaminase levels are usually normal but ALP values are sometimes increased (21). When we exclude the case of Caroli's disease complicated by common bile duct stone in our series, the others have increases of not only ALP but also direct bilirubin. We believe that these increased values should be attributed to the presence of CTPV.

As stated in the literature (3), congenital protein C deficiency can be a cause of venous thrombosis, but we found this decreased enzyme activity in only one patient who had splenic vein thrombosis in addition.

Five of the 7 Behçet patients had not only portal involvement but also other great vessel obstruction. Thrombophlebitis is a frequent omplication of BD (22), but the pathogenesis of the vessel obstructions has not been explained. In all affected tissue, vasculitis remains the main feature of the disease. Endothelial cell dysfunction (23,24) due to possible immune- mediated vaculitis could play a significant role in the thrombotic vascular complication such as the Budd-Chiari syndrome in which BD is the most common etiologic factor in Turkey (25). In six of the 7 Behçet patients, increased values of ALP and bilirubin can be attributed to other conditions such as BCS, but one case with only CTPV also had increased values. Thus, it is possible to say that CTPV is the responsible pathology in creating these high values.

To our knowledge, this is the largest series in the literature aiming to explain the increase of ALP and D bilirubin levels in extrahepatic portal hypertension caused by CTPV.

We conclude that the increased levels of bilirubin and ALP of 44 patients with CTPV are related to compression by thrombosis and collateral vessels which are responsible for the development of the "pseudo-cholangiocarcinoma sign". When faced with a patient with splenomegaly without parenchymal liver disease, CTPV should be suspected, and these moderately increased values should be attributed to incomplete obstruction of the extrahepatic biliary ducts due to the compression by thrombosis.

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