Budd- Chiari Syndrome with Emphasis on Space Occupying Lesion in The Liver: Analysis 30 Cases

Yusuf BAYRAKTAR, Ferhun BALKANCI, Emin KANSU, Burhan KAYHAN, Serap ASLAN, Muzaffer ERYILMAZ, Hasan TELATAR

Summary: *We reported our experience from 30 adult patients, with Budd-Chiari syndrome (BCS) which is a rare and serious disorder, characterized by hepatic outflow obstruction caused by many different conditions.*

The diagnosis was based on the clinical data, ultrasonography (US), vena cavography and hepatic venography, computed tomography (CT), and liver biopsy. Behçet's disease (BD) was found in ten patients with BCS as an underlying disease, and the use of oral contraceptive drugs in 2, liver tumor in 2 patients (HCC and liver lymphoma), chronic lymphocytic leukemia in 1 patient, and despite full investigation, we could not find any obvious underlying cause in the other 15 patients.

Our results suggest that 1) BCS must be considered as a possible complication in patients with Behçet's disease when they have hepatomegaly even if there weren't any cardinal manifestations of the disease at the time of admission, and BD is the most common etiologic factor in BCS (33 %) in Türkiye where the incidence of Behçet's disease is relatively high, 2) anti - aggregant treatment seems to be effective in many instances, 3) there were space occupying lesion like appearances in the liver of the seven cases on CT and US examination in the acute stage, and they disappeared on the follow-up CT and US in five patient, but continued in two. BCS should be differentiated from other liver lesions, and 4) there were other great vessel involvements in 43 percent of the cases, mostly venous, only one pulmonary arterial oclussion.

Key Words ; Budd- Chiari syndrome, Behçet's Disease, inferior vena caval obsruction,

Department of Internal Medicine and Radiology
Hacettepe University School of Medicine, Ankara-Türkiye

Budd - Chiari syndrome (BCS) is a rare disorder characterized by hepatomegaly, abdominal pain, ascites and hepatic histopathologic features demonstrating zone 3 sinusodal distention and pooling. The disorder can be the result of hepatic venous outflow obstruction and the obstruction can be located either within the liver or in the IVC between the liver and right atrium (1). Functional hepatic venous outflow obstruction caused by congestive heart failure and chronic pericarditis are not included within the definition of the syndrome. Obstruction caused by thrombosis is usually asssociated with myeloproliferative disorders such as polycythemia, both primary and secondary, essential thrombocytosis and chronic leukemia. This syndrome is also associated with systemic lupus erythematousus (2), Behçet Disease (3), paroxysmal nocturnal hemoglobinuria (PNH) (4), the use of oral contraceptives, blunt abdominal trauma and as is seen more often in the orient vena caval webs (5). In many cases, the etiology may be unexplained (6).

There are usually acute and chronic form. In the acute form, the patient often suffers from some other condition such as hepatoma, renal carcinoma or polycythemia and the clinical presentation is severe, if hepatic venous occlusion is total, delirium and hepatic coma are inevitable. In chronic form, clinical feature is characterized by pain over an enlarged tender liver, ascites and jaundice.

In this report, we present our experience from 30 adult patients with BCS seen at the De-

partments of Gastroenterology and Radiology of the Hacettepe University Hospital between 1970-1991.

MATERIAL and METHODS

During the period of 1970 to 1991, 30 patients sixteen males and 14 females whose ages ranged from 18 to 58 were diagnosed as having BCS, at the Hacettepe University Hospital, Department of Gastroenterology and Radiology. The mean age at the diagnosis was 35 years.

Diagnosis of the BCS was based on clinical data, liver biopsy and conventional venography (including cavography) prior to 1985 (only in three patients) and since 1985 computed tomography, cavography and hepatic venography with Digital Subtraction Angiograhy (DSA), and ultrasonography were introduced. Three patients diagnosed prior to 1985 as having BCS were analyzed in a retrospective fashion. Following the introduction of DSA and sonography in 1985,patients with BCS were evaluated prospectively. We have diagnosed 27 patients with BCS during the period 1985 to 1991 after using sonography and DSA.

For most patients, diagnosis was established after exclusion of primary liver cirrhosis, congestive heart failure and constructive pericarditis. For all patients, routine liver function tests, ascitic fluid analyzes if present, were done. Twenty of the 30 patients had liver biopsy. In 22 patient, hepatic venography was done in order to demonstrate the hepatic venous occlusion or typical "Spider web" appearance of intrahepatic collateral veins. At the same time we tried to obtain inferior and superior venocavography to demonstrate possible thrombotic occlusion of the vena cava, its compression by the congested liver and membranous webs.

Real-time ultrasonography was performed in twenty- seven patient with the commercially available machines (Toshiba SAL-90, and Shimadzu SL 300). Transducer frequency was 3.5 mHZ. Special attention was given to the morphology of the liver, caudate lobe, hepatic veins (especially clinically and radiologically when inferior vena cava obstruction was present) portal veins, the inferior vena cava, spleen and ascites.

The diagnosis of malignant liver disease was made by sonography guided liver biopsy. In patients with unknown etilogy, all test, related to PNH- SLE, polycythemia vera and essential trombocytemia were all negative, and in ten of these 15 patients with unknown etiology, protein C levels were also studied.

Computed tomography was performed in 17 of the thirty patients with BCS, by using Philips Tomoscan 350, IV and oral with and without contrast, at 9 mm intervals from upper part of diaphragm to the inferior pole of the kidneys.

Diagnosis of Behçet's syndrome was made according to International Criteria (7).

RESULTS

The most common presenting symptoms were ascites and right upper quadrant pain . The findings at initial presentation included hepatomegaly and jaundice. As seen Table 1, in fifteen patient, causal factors were Behçet's syndrome (in ten cases), liver malignant disease (one hepatocellular carcinoma, one lymphoma involved liver), and the use of oral contraceptive drugs (two). In 15 patient, no definite etiologic factor was found. In one female patient with Behçet's disease, after using oral contraceptives, clinical course deteriorated significantly. all the patients with Behçet's syndrome had a complete form of the disease (8).

Nineteen of the 27 patients performed US demonstrated modification of the liver morphology on US study. The most common appearance was the association of right lobar atrophy (three cases), and left and right lobar

Tablo -1. Clinical Features of Patients with Budd-Chiari Syndrome

No	Age	Sex	Jaundice	Ascites	HSM*	Underlying disease	Involved Vessels
1	28	M	+	+	+	BS	IVC + SVC + HVs
2	30	M	+	+	+	BS	IVC + HVs
3	35	M	+	+	+	BS	HVs
4	25	M	+	+	+	BS	IVC + HVs
5	30	M		+		BS	IVC + 2HVs
6	20	F	+	+	+	BS	HVs
7	32	M	+	+	+	BS	IVC + HVs
8	38	M	+	+	+	BS	HVs
9	26	M	+	+	+	HCC	HVs
10	58	M	+	+	+	Lymphoma	HVs
11	22	M	+	+	+	?	HVs
12	18	F	+	+	+	?	PA + HVs
13	19	F	+	+	+	?	HVs
14	22	F	+	+	+	?	HVs
15	22	F	+	+	+	?	IVc + HVs
16	35	F	+	+	+	?	IVc + HVs
17	20	F		+		?	HVs
18	30	M	+	+	+	?	IVc + HVs
19	29	F	+	+	+	Oral Cont	HVs
20	29	F		+		?	Ivc + HVs
21	25	M	+	+	+	?	HVs
22	30	M		+		?	Hep. IVC
23	18	M	+	+	+	?	HVs +
24	39	F		+		?	HVs + IVCO + IVC ANEu
25	45	F	+	+	+	BD	HVs
26	35	M	+	+	+	leuc. + B.M. Tr	HVs
27	24	F		+		?	HVs
28	28	F		+		Oral Cont	HVs
29	22	F	+	+	+	?	HVs + IVC
30	18	M	+	+	+	BD	HVs + IVC

IVC ; Inferior vena cava, HVs ; hepatic veins, HCC; hepatocellular carcinoma, BD; Behçet's Disease, Oral Cont ; the use of oral contraceptive, B.M. Tr; bone marrow transplantation

hypertrophy in the liver (20 cases). The caudate lobe was enlarged in all 27 patients, but markedly in 10 cases. In only one patient, all three hepatic veins were markedly dilated in which constructive pericarditis was considered. Inferior vena cavography clearly showed total occlussion in hepatic portion of IVC, correlating with the result of sonographic sudy (Fig. 1-2). In patients with inferior vena caval obstruction, sonography was very

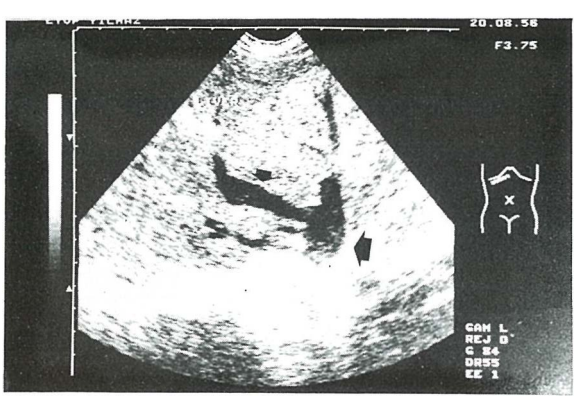

Fig. 1 US shows enlarged hepatic veins and occluded

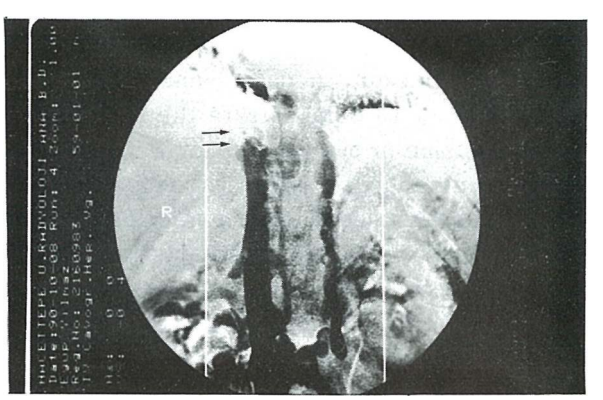

Fig. 2 Cavography with DSA shows total occlusion of IVC at the level of hepatic portion of IVC (arrows)

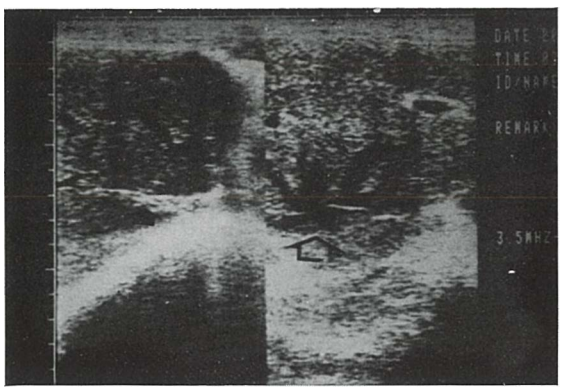

Fig. 3 US demonstrating hepatic veins occlusion (left, arrow) and dilatation of the caudate lobe veins (right, arrows)

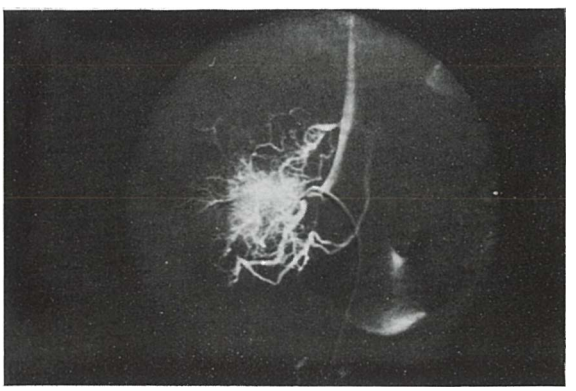

Fig. 4 Hepatic venogram shows typical "spider web" appearance of caudate lobe veins

Tablo II. Anatomy of Hepatic Venous Outflow Obstruction

Involved vessels	Patient Numbers	%	Definition
Only hepatic veins	17	56	interlobular and large hepatic veins cannot be visualized by hepatic venogram and US, and segmental dilatation on sonography
Hepatic veins+IVC	10	30	a segment of IVC that is in contact with the entry level of the right middle and left hepatic vein shown by DSA and involved hepatic vein by US
Hepatic IVC	1	3.3	Open left, right and middle hepatic vein sonographically but hepatic segment of IVC obstructed on US and DSA
Hepatic veins + PA	1	3.3	Involvement of all hepatic veins shown by US and DSA
HVs + IVC+SVC	1	3.3	Aneurysm and obstruction shown by US and cavography.
HVs+IVC+IVC Aneu.	1	3.3	

helpful in demonstrating patency of hepatic veins. US studies showed at least one of the following signs : stenosis (ten occurences), dilatations (seven), thick wall echoes (seventeen), dilated veins in caudate lobe (two, Fig. 3). Inferior vena cavography showed good correlation with US studies demonstrating caval obstruction. Also hepatic venography showing the typical "spider web" apperance of intrahepatic veins veins (Fig. 4), when performed, correlated well with the US study. When hepatic venography was performed, the catheterization of veins having thick wall on US was not possible. Occasionally, very small anastomotic veins could be opasified, but US study failed to detect these small veins.

Among chronic patients hepatic veins usually were not visible ; in three cases dilated veins were present in the caudate lobe. In these three patient, after administration of Aspirin an Dipyridamol, the veins of caudate lobe have been obvious (Fig. 3) and ascites has disappeared gradually, especially two cases did not need treatment for ascites any more.

The inferior vena cava was seen on all ultrasonographies either patent or occluded. In ten cases, obstruction was detected these findings and showed other abnormalities which were missed on US studies: some lumboazygeal ret-

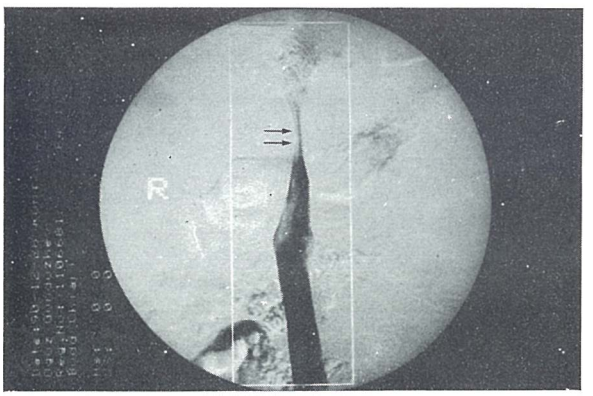

Fig. 5 Cavography shows compression of hypertrophied caudate lobe on IVC (arrows)

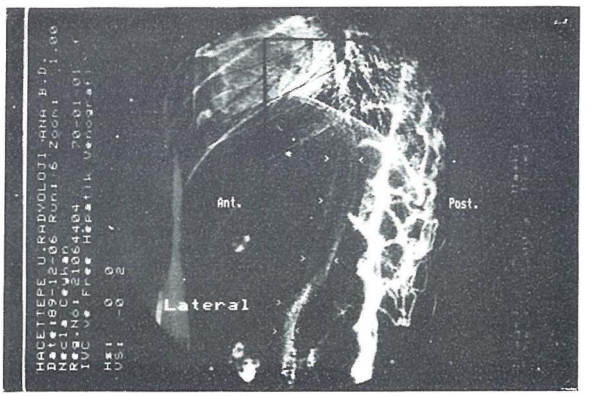

Fig. 6 Cavography Demonstrates total occlusion of IVC and retrograde filling of lumboazygous system (small arrow heads)

rograde flow and other collateral, and especially extrensic compression by the caudate lobe (Fig. 5-6). As seen in Table 1 ascites was present in all cases. Normal patency of the portal system was correctly assessed in all cases by US. In seven cases who had hepatic and caval involvement, there were multiple nodule - like masses (Fig. 7) suggesting space occupying lesions. Sonography - guided liver biopsies from these lesions demonstrated no malignancy but congestion and sinusoidal dilatation which were compatible with BCS.

For the further evaluation, these patients were studied with computed tomography and showed hypodense areas like space occupying lesions (Fig 8-9). These lesions disappeared in 5 of seven patients on the control CT and US. In one of these seven cases, left lobe liver cyst 5 cm in diameter developed during the course of the disease. In this case, concomitantly as long as space occupying lesions diminished, the veins of the caudate lobe dilated and ascites disappeared (Fig 3, Fig. 10 a-b)

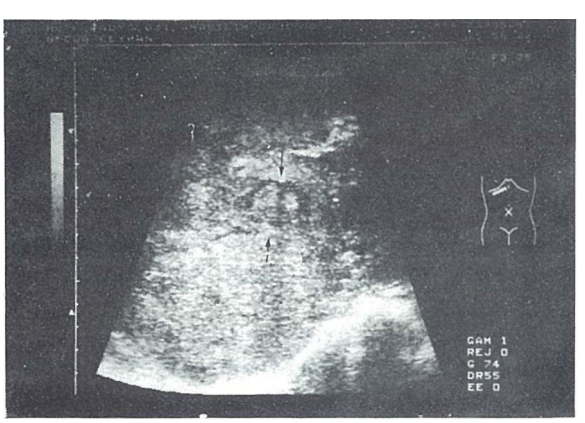

Fig. 7 Showing relatively well defined lesion on US (arrows)

DISCUSSION

Budd - Chiari syndrome is an uncommon disorder which occurs due to large number of conditions such as primary congenital obstruction of the hepatic vein, or inferior vena cava, by webs or bands, Behçet's disease, trauma, polycythemia vera, pregnancy, tumors,chronic leukemia, and use of oral contraceptives. In two thirds or half of the cases no definite etiology can be demonstrated. In this study, one third of the cases were found to have Behçet's disease which is a relatively common disease in Turkey. Although viral, immunologic, and immuno-genetic causes (9-15) have been postulated in the literature, the cause of Behçet's disease still remains an enygma. Thrombophlebitis is a frequent complication of Behçet's disease (3) and the pathogenesis of the vessel occlusions has not been explained. In all affected tissues, vasculitis is still remains the

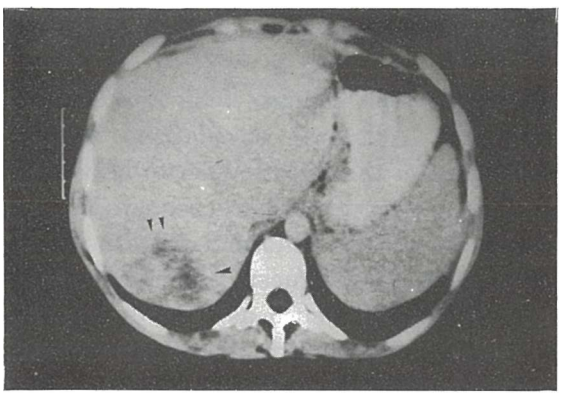

Fig. 8 Showing hypodense lesion in the right hepatic lobe on CT (arrow heads)

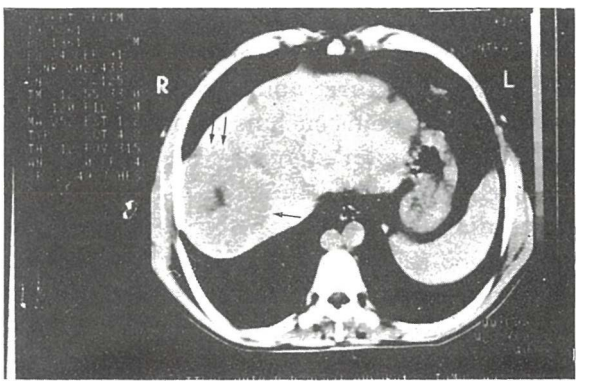

Fig. 9 CT demonstrates the hypodense lesion in the right hepatic lobe (arrows)

main feature of the disease. Kansu et al reported (16-17) that endothelial cell dysfunction due to possible immune mediated vasculitis could play a significant role in the thrombotic vascular complications such as BCS seen in Behçet's disease. As seen in Table 1, it was possible to find out the underlying disease in 15 patient. In the remaining fifteen patient, there was no clear cause for the syndrome.

The clinical diagnosis can be difficult since the classic triad of abdominal pain, ascites and hepatomegaly are not always found particularly in the chronic cases. Additionally, as in our patient, accompanied vessel involvement and primary disease can change the classical picture. Most patients presented with portal hypertension, jaundice, and hepatosplenomegaly. In the series, 10 patients had IVC obstruction besides the hepatic veins involvement and liver biopsy and US were the diagnostic modalities.

Although the patients with the congenital protein C deficiency have recently been shown to have a high risk for venous thrombosis (18), we were unable to detect low protein C activity in the ten patients studied.

Classically definitive diagnosis of this syndrome has been made with the liver biopsy and hepatic venography (19,20). Recently, a

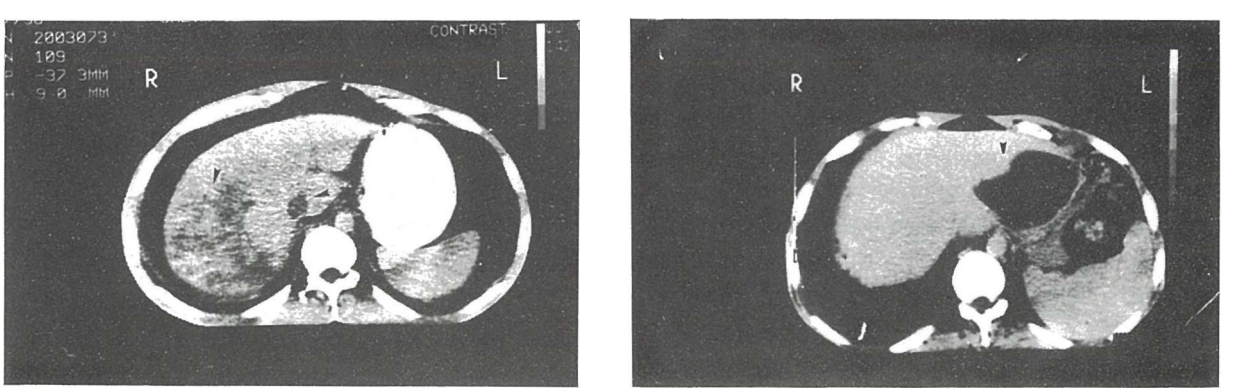

Fig. 10 a) CT shows multiple hypodense lesions in the right lobe of the liver in a patientwith BD, b) control CT demonstrates no visible lesions and left lobe liver cyst (arrow) in the same patients

great number of studies have shown the value of non-invasive modalities such as US (21-23) and CT (24-26). US may demonstrate changes in hepatic structure, and specific abnormalities of hepatic veins such as thrombosis, webs, wall thickening, or stenosis. (22, 27-29). It is also well established that US is the first tool in the diagnosis of BCS. After introducing of US in 1985 the diagnosis of BCS has been increasing in our hospital, and our findings are correlated well previously published studies (21-22). As seen Fig. 2, US was helpful not only in the demonstration of the hepatic veins but also thrombus formation in IVC. Beside this, it was informative in demonstrating IVCO and liver lesions. In seven cases, there were multiple lesions relatively well defined, in the liver. Sonography guided liver biopsies were compatible with BCS. Control sonograms and CT scans at different period (at least six months intervals) were showed no visible lesions in 5 of seven cases. This can be explained by reneuval collaterals and liver drainage.

The appearance of the BCS on CT scans has been defined in previous studies (22, 30-31) which consists of abscence of visualization of the hepatic veins and patchy enhancement of the central area of the liver (30, 32). Moreover, CT feature seems to be different in acute stage than in chronic stage of the syndrome. In our patients, in the acute stage, liver was always found to be enlarged with caudate lobe hypertropy. In the seven of 17 patients who had CT examination, the liver showed multiple hypodense lesions in the contrast and non-contrast studies which were similar to malignant lesion. Follow - up CT and US scans demonstrated no abnormality but in two patient, there were the same appearances. To our knowledge, these CT and US findings of the acute stage have not been previously reported and can be considered to be important in differentiating benign lesions from malignant liver lesions.

Inferior venocavography is especially important before deciding on therapy, because it reveals either the degree of obstruction of the IVC or the narrowing is relative to the enlargement of the caudate lobe and demonstrates the collateral circulation, enables opacification of the hepatic vein to be visualized. When retrograte hepatic venography fail to show clearly the abnormal pattern of the hepatic veins, the diagnosis was made clearly by other modalities such as liver biopsy and US, caudate lobe hypertrophy compressing to IVC demonstrated by cavography.

It was interesting to note that thirteen of 30 patients (43 %) had a great vessel involvement, such as IVC obstruction (in ten cases), pulmonary artery occlusion, SVC obstruction and IVC aneurysm. It is possible to explain the great vessel involvement in patients with Behçet's disease which is a multi-systemic disease, consisting of basically vasculitis. For other patients we could not find any explanation why there were multiple vascular involvement.

Although spontaneous remissions had been observed during the natural course of BCS, it is often severe and could be fatal. Medical management, including diuretics, heparin or thrombolytic therapy is rarely effective. We treated the patients with diuretics if ascites was present. Daily aspirin 300 mg with dypridamol 75 mg t. id. were given regardless of etiology. The combination therapy with an anti-aggregating drug, seemed to be more effective in most patients. None of them underwent surgical intervention. Three patients needed Lee-Veen shunt operation for the treatment of intractable ascites but in a relatively short time all the Lee-Veen shunts were occluded.

We conclude that Behçet's disease is the most common etiologic factor in BCS in Turkey. Space occupying lesions which are similar to the malignant shadows can also be seen in BCS during the acute stage.

REFERENCES

1. Ludwig J, Hashimoto E, McGill DB, Heerden JA. Classification of hepatic venous outflow obstruction : Ambiguous terminologiy of the Budd-Chiari Syndrome. Mayo Clin Proc, 1990; 65: 51-55
2. Nakamura H, Uehara H, O Kada et al : Occlusion of small hepatic veins associated with systemic lupus erythematosus ith the lupus anticoagulant and anti-cardiolipin antibody. Hepato-gastroenterol. 1989; 36: 393-397
3. Bayraktar Y, Balkancı F, Dündar S, Kansu E, Telatar H. The Angiographic findings of great vessel involvement in Behçet's Disease. Vascula Surgery 1991; 25: 119-125
4. Vala D, Dhumeaux D, Babany G, et al : Hepatic vein thrombosis in paroxsysmal nocturnal hemoglobinuria. Gastroenterology 1987; 93: 569-575
5. Terabatashi H, Okuda K, Nomura F, Ohnishi K, Wong P. Transformation of inferior vena caval thrombosis to membranous obstruction in a patient with the lupus anticoagulant. Gastroenterology 1986; 91: 219-224
6. Gentil - Kocher S Bernard O, Brunelle O, et al : Budd -Chiari syndrome Report of 22 cases. The Journal of Pediatrics 1988; 113: 30-38
7. International Study Group for Behçet's Disease. Criteria for diagnosis of Behçet's Disease. Lancet 1990 ; 335: 1078-1080
8. O' Duffy JD, Robertson DM, Goldstein NP. Chlorambucil in the treatment of uveitis and meningoencephalitis of Behçet's disease. Am. J. Med. 1984; 76:75
9. Denman AM, Fialkow PJ, Pelton BK, Salo AC, Appleford DJ. Attempts to establish a vial etiology for Behçet's syndrome. In : Lehner T, Barnes C. (eds). Behçet's syndrome. London : Academic Press, 1979, p91
10. Goolamali SK, Comaish JS, Hassanyek F, Stephens A. Familial Behçet's syndrome. Br. J Dermatol 1985 1985; 113: 319-321
11. Saito H, Honma T, Sato T, Fujiko Y. Autoimmune mechanisms as apossible aetiology of Behçet's syndrome an electron microscopic study of the oral mucosa. Virchows Arch 1971 ; 353: 216-272
12. Chajek T, Fainaru M. Behçet's disease. Report of 41 cases and a review of the litrature. Medicine 1975; 54: 179-196
13. O'Duffy JD, Carney WA, Deodhar S. Behçaet's disease, report of cases, with new manifestation. Ann Intern Med 1971; 75: 561-570
14. Lehner T Almedia ID, Levinsky RJ. Damaged membrane fragments and immune complexes in the blood of patients with Behçet's disease. Clin Exp Immunol 1975; 91:185
15. Lehner T, Fortune F, Studd M. T cel immunoregulation in Behçet's disease and consideration of microbial aetiology involving herpes simplex virus, head shock protein and streptococcal antigens. Behçet's disease Fifth Internationl Conference Rochestre,Minnesota, September 14-15, 1989
16. Kansu E, Sivri B, Şahin G et al : Endothelial cell dysfunciton in Behçet's disease.Behçet's disease, Fifth Internationl Conference. Rochester, Minnosota September 14-15 1989
17. Kansu E, Çelenigil H,Ruacan Ş, et al : Characterization of pripheral blood Iymphocytes and immunohistologic analysis of oral ulcer in Behçet's disease. Behçet's disease Fifth Inernational Conference Rochester, Minnesota, Sempember 14-15, 1989
18. Broekmans AW, Veltkamp JJ, Bertina RM. Congenital protein C deficiency and venous thrombo- embolism : a study in three Dutch families. NEngl J Med 1983; 309:340-
19. Kreel L, Freston JW, Clain D. Vascular radiology in Budd-Chiari syndrom. Br J Radiol 1967; 40: 755-759
20. Deutsch E, Rosenthal T, Adar R, Mozes M. Budd - Chiari syndrome ; study of angiographic findings and remarks on etiology. AJR 1972; 116: 430-439
21. Menu Y, Alison D, Lorphelin JM, at al : Budd - Chiari syndrome : US evaluation . Radiology 1985; 157: 761-764
22. Harter LP, Gross BH, Hilaire JS Filly RA, Goldberg HL. CT and sonographic appearance of hepatic vein obstruction. AJR 1982; 139: 176-178
23. Gran EG, Perrella R, Tessle FN, Lois J, Busuttil R. Budd-Chiarisyndrome : the results of duplex and color doppler imaging. AJR; 152: 377-381
24. Mathieu D, Vasile N, Menu Y, et al : Budd-Chiari syndrome : Dynamic CT. Radiology; 165; 409-413
25. Vogelzang RL, Anschuetz SL, Gore RM. Budd-Chiari syndrome : CT observation. Radiology 1987; 163: 329-333
26. Mori H, Maeda H, Fukuda T, et al. Acute thrombosis of the inferior vena cava and hepaticveins in atients with Budd-Chiari syndrome : CT demonstation. AJR; 153: 987-991
27. Yang PJ, Glazer GM, Bowerman RA. Budd-Chiari syndrome : Computed tomographic and ulrasonographic findingis. J Comput Assist Tomogr 1983; 7: 148-150
28. Baert AL, Fevery J, Marchal G, et al. Early diagnosis of Budd-Chiari syndrome by computed tomography and ultrasonography : report of five cases. Gastroenterology 1983; 84: 587-595
29. Makuuchi M, Hasegawa H, Yamazaki S, Monyama N, Takayasu K, Okazak M. Primary Budd-Chiari syndrome : ultrasonographic demonstration. Radiology 1984; 152: 775-779
30. Rossi P, Sposito M, Simonetti G, Sposato S, Cusumano G. CT diagnosis of Budd-Chiari syndrome. J Comput Assist Tomogr 1981; 50 366-369
31. Murphy FB, Stein berg HV, Shires GT, Martin LG, Bernardino ME. The Budd-Chiari syndrome : a review. AJR 1986; 147: 9-15
32. Becker CD, Scheidegger J, Marincek B. Hepatic vein occlusion : morphologic features on computed tomography and ultrasonography. Gastrointest Radiol 1986; 11: 305-311