THE ETIOLOGY OF NON-CIRRHOTIC PORTAL HYPERTENSION. A STUDY OF 105 CONSECUTIVE PATIENTS

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Abstract

Background and aims. *Non-cirrhotic portal hypertension (NCPHT) represents an entity that is still incompletely studied as a whole. The aim of the present study is to obtain information on the prevalence, etiology, clinical and biological features of the NCPHT.*

Methods. *This is a prospective cross-sectional study of a population of 105 consecutive patients with NCPHT admitted in the Third Medical Clinic in Cluj-Napoca, Romania from October 2004 to October 2006. As control group, 105 consecutive cirrhotic patients admitted in the same clinic from September 2006 to October 2006 were studied. In this two-year period a total of 1474 patients with portal hypertension (PHT) were admitted.*

Results. *Non-cirrhotic PHT was present in 105/1474 (7.12%) of the patients with PHT. Solid cancers had represented the dominant etiology of PHT (58%). Venous thrombosis (35.2%), extrinsic compression (31.4%) and vascular tumor invasion (28.5%) were almost equally responsible for the NCPHT. Prehepatic PHT was dominant (83.8%) and 33.3% of the patients had segmental PHT in the NCPHT group. The gastric varices (12/69 patients v. 0/100 patients) and the associated esophageal + gastric varices (10/69 patients v. 5/100 patients) were significant more frequent in NCPHT than in cirrhosis ($p<0.05$). The mean value of platelet count (249,904±13,281/mm^3) was normal in the NCPHT group while in the cirrhotic group thrombocytopenia (108,215±65,069/mm^3) was noticed. A significant difference was found between the platelet count in NCPHT group and cirrhosis group in patients with spleen diameter over 120 mm (243,240±126,328 v. 106,175±66,470) ($p<0.001$) as well as a diameter less than 120 mm (214,333±75,191 v. 128,306±54,663) ($p<0.001$). A negative correlation was found between the platelets count and spleen size in the cirrhosis group ($r=-0.292$; $p=0.002$), but not in the NCPHT group ($r=0.016$; $p=0.871$).*

Conclusion. *Patients with NCPHT represented 7.12% from the patients with PHT. Thrombosis, tumor invasion and extrinsic compression were equally responsible for the NCPHT. One third of the patients with PHT had segmental PHT. The patients with NCPHT had normal platelets value. In contrast, thrombocytopenia was found in those with cirrhosis, which was negatively correlated with spleen size (might not be caused by PHT but by advanced hepatic fibrosis).*

Keywords: non-cirrhotic portal hypertension, etiology, platelets, spleen size, esophageal varices, gastric varices.

ETIOLOGIA HIPERTENSIUNII PORTALE NON CIROTICE. STUDIUL A 105 PACIENŢI CONSECUTIVI

Rezumat

Obiective. *Hipertensiunea portală non cirotică (HTPNC) reprezintă o entitate încă nestudiată ca şi întreg. Scopul acestui studiu este de a obţine informaţii despre prevalenţa, etiologia şi aspectele clinice şi biologice ale HTPNC.*

Metode. *Acesta este un studiu prospectiv transversal a 105 pacienţi cu HTPNC,*

internaţi în Clinica Medicală III din Cluj Napoca în perioada octombrie 2004-octombrie 2006. Ca şi grup de control au fost studiaţi 105 pacienţi cu ciroză hepatică de diverse etiologii, internaţi în aceeaşi clinică, în aceeaşi perioadă.

Rezultate. *În această perioadă de 2 ani au fost internaţi 1.474 pacienţi cu hipertensiune portală (HTP). HTPNC a fost prezentă la 105/1.474 (7,12%) din pacienţii cu HTP. Cancerele solide au reprezentat etiologia predominantă a HTPNC (58%). Tromboza venoasă (35,2%), compresia extrinsecă (31,4%) şi invazia vasculară tumorală (28,5%) au fost responsabile în proporţii egale de HTPNC. În grupul HTPNC a fost predominantă HTP prehepatică (83,8%), iar 33,3% din pacienţi au avut HTP segmentară. Varicele gastrice (12/69 pacienţi v. 0/100 pacienţi) şi asocierea varice esofagiene + varice gastrice (10/69 pacienţi v. 5/100 pacienţi) au fost semnificativ mai frecvente în HTPNC, decât în ciroză ($p<0,05$). Valoarea medie a trombocitelor a fost normală (249.904±13.281/mm^3) în grupul HTPNC, în timp ce trombocitopenia (108.215±65.069/mm^3) a fost comună la pacienţii din grupul cu ciroză. O diferenţă semnificativă a fost descoperită între valoarea trombocitelor la grupul cu HTPNC, comparativ cu grupul de pacienţi cu ciroză, atât cu splomegalie (243.240±126.328 v. 106.175±66.470) ($p<0,001$), cât şi cu splină normală (214.333± 75.191 v. 128.306±54.663) ($p<0,001$). O corelaţie negativă a fost descoperită între valoarea trombocitelor şi mărimea splinei în grupul celor cu ciroză ($r=-0,292$; $p=0,002$), dar nu şi în grupul celor cu HTPNC ($r=0,016$; $p=0,871$).*

Concluzii. *Pacienţii cu HTPNC reprezintă 7,12% din pacienţii cu HTP. Tromboza, invazia tumorală şi compresia extrinsecă sunt responsabile în proporţii egale de HTPNC. O treime din pacienţii cu HTPNC au de fapt HTP segmentară. Pacienţii cu HTPNC au valori normale ale trombocitelor. În contrast, trombocitopenia a fost prezentă la cei cu ciroză hepatică, fiind corelată negativ cu mărimea splinei.*

Cuvinte cheie: hipertensiune portală non cirotică, etiologie, trombocite, dimensiunile splinei, varice esofageale, varice gastrice.

Introduction

Portal hypertension is defined as an increase in the porto-caval gradient (difference between blocked and free hepatic venous pressure) over 5 mmHg with secondary formation of porto-systemic derivations [1]. Clinically significant PHT is defined as an increase with more than 10 mmHg of the porto-caval gradient (difference between blocked and free hepatic venous pressure). Presence of esophageal varices, hemorrhage from these varices and/or ascites is considered as indicator of clinically significant PHT [2]. Cirrhosis represents the main cause of PHT, but there are other diseases that can induce PHT. Non-cirrhotic PHT is defined as the presence of PHT in the absence of cirrhosis. Segmental PHT is defined as the presence of PHT in only one sector of portal venous system. Even if described in the 50', NCPHT was not analyzed as a whole regarding the etiology, clinical aspects and laboratory investigations [3]. Extrahepatic obstruction of the portal vein [4], idiopathic PHT [5,6] and Budd-Chiari syndrome [7,8] are the only ones carefully studied. The present study aimed to obtain data on the etiology, clinical and biological features of patients with NCPHT.

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Patients and methods

This is a prospective and cross-sectional study of all consecutive patients with NCPTH admitted in the Third Medical Clinic in Cluj-Napoca Romania from October 2004 to October 2006. The control group was represented by an equal number of consecutive cirrhotic patients admitted in the same period. In this two-year period 1474 consecutive patients with PHT were admitted in the clinic; the patients with multiple admissions in this period were counted only once, considering data on first admission. The patients with segmental PHT of the mesenteric vein from the NCPHT group were not considered for the analysis of hematological parameters in relation to the spleen size.

The study group included 105 patients diagnosed with NCPHT. They all met the inclusion criteria regarding presence of PHT as demonstrated by evidence of porto-systemic vascular derivations (at ultrasonography or endoscopy) and/or complete obstruction in the portal venous system (at ultrasonography and/or CT scan) and/or inversed blood flow in the portal vein (at Doppler ultrasonography). Liver cirrhosis was excluded by one of the following investigations: liver biopsy; the macroscopic aspect of the liver during surgical intervention; the ultrasonographic aspect of the liver (absence of diffuse nodular structure).

The control group (cirrhosis group) included 105 patients. The inclusion criteria for the cirrhosis group were

the presence of cirrhosis diagnosed by one of the following investigations: liver biopsy; macroscopic aspect of the liver during surgical procedure; imaging aspect of the liver.

An informed consent was obtained from all patients prior to the study. The study protocol was accepted by the Ethics Committee of the University.

Statistics: Descriptive and inferential statistic methods were used for the analysis of the data. Quantitative variables were expressed as mean±standard deviation. Non-parametric tests (Chi square and Fisher) and parametric tests (Student, ANOVA) were applied. A $p<0.05$ was considered statistically significant. Correlation was studied using Pearson regression analysis. SPSS 15 (The Predictive Analytics Company, Chicago, USA) was used for statistical analysis of the data.

Results

Multiple characteristics were evaluated at inclusion in all patients: age, sex, disease responsible for PHT, type of PHT according to anatomical classification (prehepatic, intrahepatic, posthepatic), type of PHT according to physiopathological classification (presinusoidal, sinusoidal, postsinusoidal), extension of PHT (global, segmental), clinical signs and symptoms, laboratory data and endoscopic signs of PHT.

Cirrhosis was caused by alcohol abuse in 43/105 patients (40.9%), viral hepatitis in 41/105 (39.2%), alcohol + viral hepatitis in 6/105 patients (5.7%), cryptogenic in 9/105 patients (8.5%) and other etiologies in 6/105 patients (5.7%). According to the modified Child-Turcotte classification, 50/105 patients (47.6%) were in class Child A, 28/105 patients (26.7%) were in class Child B and 27/105 patients (25.7%) were in class Child C.

The patients with NCPHT (105) represented 7.12% of the 1474 patients with PHT admitted in the two-year period. In this group, the mean age of the patients was 56.9±12.8 years (range 20-82) and 71 of the 105 patients (67.6%) were males. In the cirrhosis group, the mean age of the patients was 56.6±10.4 years (range 19-78) and 67 of the 105 patients (63.8%) were males. No significant differences were found between the two groups regarding age ($p=0.85$) and gender ($p=0.56$).

The etiology of non-cirrhotic portal hypertension in the NCPHT group was dominated by solid cancers and venous thrombosis (Table 1).

Table 1. Etiology of the non-cirrhotic portal hypertension in the 105 patients studied.

Etiology of non-cirrhotic portal hypertension	No of cases	%
Solid cancers	26	24.7
Solid cancer with vascular invasion	30	28.5
Lymphoproliferative diseases	3	2.8
Venous thrombosis	26	24.9
Lymphoproliferative diseases associated with venous thrombosis	6	5.7
Solid cancers associated with venous thrombosis	5	4.8
Other etiology (pancreatic pseudocyst, idiopathic portal hypertension)	9	8.6
TOTAL	**105**	**100%**

Asthenia was the most frequent symptom present at the moment of diagnosis in both groups (Table 2). Abdominal discomfort as the first symptom was present in 76/88 (86.3%) of the patients with prehepatic PHT, but only in 8/17 (47%) of those with intrahepatic/posthepatic PHT ($p<0.001$). Blood pressure was significantly lower in the cirrhotic group and vascular spiders were almost exclusive found in the cirrhosis group (Table 2).

Segmental PHT was present in 35/105 (33.3%) of the cases with NCPHT. In most cases (21/35 patients; 60%) it was localized at the splenic level; some patients had segmental PHT on the superior mesenteric vein (10/35 patients; 28.5%) and only a few had associated segmental PHT on the splenic and superior mesenteric vein (4/35 patients; 11.5%). Segmental PHT was caused by venous thrombosis (8/35 patients; 22.8%), extrinsic compression (11/35 patients; 31.4%) and tumor invasion (16/35 patients; 45.8%). Pancreatic pathology was the dominant etiology (31/35 patients; 88.5%) for the segmental PHT ($p<0.001$). Acute pancreatitis caused more frequently segmental PHT (7/35 patients; 20%) than global PHT (3/70 patients; 4.2%) ($p<0.001$). Chronic pancreatitis represented the etiology

Table 2. Symptoms and clinical signs presents in the NCPHT and the cirrhosis group.

	NCPHT group (N = 105 patients)	Cirrhosis group (N = 105 patients)	p
Asthenia	92 (87.6%)	97 (92.4%)	p=0.25
Abdominal discomfort	84 (80%)	49 (37.1%)	**p<0.001**
Nausea	41 (39%)	28 (26.7%)	p=0.05
Jaundice	28 (26.7%)	42 (40%)	**p=0.040**
Abdominal distension	11 (10.5%)	22 (20.9%)	**p=0.037**
Upper digestive hemorrhage	6 (5.7%)	24 (22.8%)	**p=0.001**
Blood pressure (mmHg)*	127/77±21/13 mmHg	115/72±14/9 mmHg	**p=0.003**
Superficial abdominal venous collateral circulation	19 (18.1%)	64 (60.9%)	**p<0.001**
Mobile dullness	17 (16.1%)	31 (29.5%)	**p=0.032**
Vascular spiders	1 (0.9%)	81 (77.1%)	**p<0.001**
	Number of patients (percent)	Number of patients (percent)	

* Values represent mean ± standard deviation

for segmental PHT in 6/35 (17.1%) of the patients and for global PHT in 6/70 (8.5%) of the patients. Ascites detected by ultrasonography was present in 10/35 (28.5%) of the patients, in comparison with 40/105 (38%) of the patients in the cirrhotic group (p=0.31).

Regarding location of the obstacle in the afferent or efferent hepatic venous system, prehepatic PHT was dominant in NCPHT group (88/105 patients; 83.8%), followed by intrahepatic PHT (14/105 patients; 13.3%), while posthepatic PHT was present only in 2.9% (3/105 patients) of cases. Prehepatic PHT was caused by venous thrombosis (36/88 patients; 40.9%), tumor invasion (30/88 patients; 34.1%), extrinsic compression (19/88 patients; 21.6%) and increase in hepatic flow (3/88 patients; 3.4%). All the cases of intrahepatic PHT were determined by extrinsic compression (14/14 patients; 100%) and one case of posthepatic PHT by venous thrombosis (1/3 patients; 33.3%).

The obstruction in the venous system at presinusoidal, sinusoidal and postsinusoidal level (102/105 patients; 97.1%) was dominant, while an increase in the hepatic afferent flow was present in only 3/105 (2.9%) of the cases. Venous thrombosis (37/105 patients; 35.2%), extrinsic compression (33/105 patients; 31.4%) and tumor invasion (30/105 patients; 28.5%) shared almost equal responsibility for the obstruction of the afferent and efferent hepatic venous system.

The platelet count and white blood cells were significantly diminished in the cirrhosis group when compared to the NCPHT group (Table 3). In the NCPHT group, cholestasis was significantly more important in patients with tumoral etiology (invasion: AP = 1,016 U/l, GGT = 510 U/l; extrinsic compression: AP = 871 U/l, GGT = 466 U/l) when compared to those with extrahepatic portal vein thrombosis (AP = 576 U/l and GGT = 202 U/l) (p<0.001).

The mean value of the spleen size was 138.6±22.2 mm in the NCPHT group and 148.4±28.2 mm in the cirrhosis group (p=0.008). In the subgroup of patients with spleen over 120 mm, the mean value of spleen size was 144.9±20.3 in the NCPHT group and 155.1±25.6 mm in the cirrhosis group (p=0.006). Splenectomy had been anterior performed in 4/105 (3.8%) of the patients in NCPHT group and in 2/105 (1.3%) of the patients in cirrhotic group. We present the value of hematological tests in relation with the spleen size in Tables 4-7.

In the NCPHT group, no significant correlation (r=0.016; p=0.87) was found between platelets and spleen size. In the cirrhosis group, we found a significant negative correlation (r=-0.292; p=0.002) between platelet counts and spleen size.

In the subgroup of cirrhotic patients with a spleen size less than 120 mm (15 patients) we found normal hemoglobin level in Child A (14.9±1.2 g/dl) and Child B

Table 3. Biochemical data of the patients from the NCPHT and the cirrhotic group (mean±standard deviation).

	NCPTH group (N = 105 patients)	Cirrhotic group (N = 105 patients)	p
Hemoglobin (g/dl)	11.7±2.8	12.4±3	p=0.08
White blood cells (/mm^3)	9,320±9,310	5,920±2,898	**p<0.001**
Platelets (/mm^3)	249,904±132,381	108,215±65,069	**p<0.001**
Glycaemia (mg/dl)	121±53	123±44	p=0.76
AST (U/l)	71±75	91±131	**p<0.001**
ALT (U/l)	79±115	61±52	**p<0.001**
T Bil (mg/dl)	3.6±6.3	2.6±4	p=0.14
C Bil (mg/dl)	2.4±4.9	1.2±2.4	**p=0.028**
AP (U/l)	785±908	338±157	**p<0.001**
GGT (U/l)	367±496	178±206	**p<0.001**

AST = aspartate aminotransferase; ALT = alanine aminotransferase; T Bil = total bilirubinemia; C Bil = conjugated bilirubinemia; AP = alkaline phosphatase; GGT = gamma-glutamyltransferase

Table 4. Hematological tests in patients with spleen over 120 mm (mean±standard deviation).

	NCPTH group (N = 79 patients)	Cirrhotic group (N = 88 patients)	p
Platelets (/mm^3)	243,240±126,328	106,175±66,470	**p<0.001**
White blood cells (/mm^3)	9,688±10,623	5,752±3,000	**p=0.002**
Hemoglobin (g/dl)	11.8±2.8	12.1±3.1	p=0.46

Table 5. Hematological tests in patients with spleen less than 120 mm (mean±standard deviation).

	NCPTH group (N = 12 patients)	Cirrhotic group (N = 15 patients)	p
Platelets (/mm^3)	214,333±75,191	128,306±54,663	**p=0.002**
White blood cells (/mm^3)	8,463±2,929	6,744±1,830	p=0.07
Hemoglobin (g/dl)	11.3±3.2	14.1±1.8	**p=0.017**

Table 6. Hematological tests data for the NCPHT group in relation with spleen size (mean±standard deviation).

	Spleen > 120 mm (N = 79 patients)	Spleen < 120 mm (N = 12 patients)	p
Platelets (/mm^3)	243,240±126,328	214,333±75,191	p=0.44
White blood cells (/mm^3)	9,688±10,623	8,463±2,929	p=0.69
Hemoglobin (g/dl)	11.8±2.8	11.3±3.2	p=0.60

Table 7. Hematological tests data for the cirrhosis group in relation with spleen size (mean±standard deviation).

	Spleen > 120 mm (N = 88 patients)	Spleen < 120 mm (N = 15 patients)	p
Platelets (/mm^3)	106,175±66,470	128,306±54,663	p=0.22
White blood cells (/mm^3)	5,752±3,000	6,744±1,830	p=0.21
Hemoglobin (g/dl)	12.1±3.1	14.1±1.8	**p=0.002**

(14.0±1.5 g/dl) and significantly lower level in Child C (10.8±1.2 g/dl, p=0.002 and p=0.015 respectively). The white blood cells mean value was among normal ranges in all patients. The platelets mean value was 141,733±62,117/mm^3 for patients in Child A class, 103,750±47,055/mm^3 for patients in Child B class and 117,000±5,656/mm^3 for patients in Child C class, with no significant difference between groups (p=0.52).

In the cirrhotic patients with the spleen larger than 120 mm (88 patients) we found normal hemoglobin level in Child A class (14.0±2.0 g/dl) and significant lower level in Child B class (11.1±2.8 g/dl, p<0.001) and Child C class (9.9±3.1, p<0.001). The white blood cells mean value was among normal ranges in all patients. The platelets mean value was 107,875±65,710/mm^3 for Child A class, 91,116±63,823/mm^3 for Child B class and 118,400±82,392/mm^3 for Child C class, with no significant difference between groups (p=0.35).

The ascites detected by ultrasonography was present in 39/105 (37.1%) patients in the NCPHT group and in 40/105 (38%) patients in the cirrhotic group (p=0.88).

The presence of esogastric varices was evaluated by endoscopy in 69 of the patients with NCPHT and in 100 of the patients with cirrhosis. Esophageal varices were more frequent in the cirrhotic group and gastric varices in the NCPHT group (Table 8).

Discussion

We described and analyzed comparatively 105 patients with NCPHT and 105 control patients with PHT due to liver cirrhosis.

The proportion of patients diagnosed with NCPHT proves the importance of non-cirrhotic etiology in PHT (105/1474; 7.12%). Our data are similar to other studies which found a frequency of 7.8% for thrombosis of portal vein [9] and of 5-10% for extrahepatic portal vein obstruction [10] in the etiology of PHT. There was no significant difference of age between groups, but a dominance of male in both our groups is notable.

Solid cancers (with or without vascular invasion or venous thrombosis) represented the dominant etiology of NCPHT in our study, with more than half of the cases (58%). Non-malignant venous thrombosis was the second most frequent etiology of NCPHT; hematological malignancies and other diseases (benign tumors, idiopathic portal hypertension) were less frequent. In the cirrhosis group, the alcohol consumption and hepatitis viruses were the predominant etiologies.

The most frequent symptoms in both groups were non-specific, asthenia being dominant. Abdominal discomfort and nausea occurred more frequent in the NCPHT group, while jaundice and weight increase were more frequent in the cirrhosis group. Abdominal discomfort was significantly more frequent in prehepatic PHT than in intrahepatic and posthepatic PHT. Upper digestive tract hemorrhage as first symptom was significantly more frequent in the cirrhosis group that in the NCPHT group. This might be explained by the alteration of hepatic function in the cirrhosis group. Our results are similar to those of other studies, where the most frequent symptoms were: abdominal pain (71%) and ascites (38%) in portal vein thrombosis [11], ascites (83-95%) and abdominal pain (62-72%) in Budd-Chiari syndrome [12,13] and digestive tract hemorrhage (64.9-72%) in non-cirrhotic liver fibrosis [14,15].

Vascular spiders, mobile dullness and superficial abdominal venous collateral circulation were significantly more frequent in cirrhosis than in NCPHT group. In fact,

Table 8. Data on varices detected at endoscopy.

	NCPHT group (69 patients)	Cirrhosis group (100 patients)	p
No varices	12 (17.4%)	2 (2%)	**p<0.001**
Esophageal varices	35 (50.7%)	93 (93%)	**p<0.001**
Gastric varices	12 (17.4%)	0 (0%)	**p<0.001**
Esophageal + gastric varices	10 (14.5%)	5 (5%)	**p=0.033**

the vascular spiders were found almost exclusively in cirrhotic patients. We also noted a mean blood pressure significantly lower in the cirrhotic group than in the NCPHT group. This suggests that hypotension observed in cirrhosis might be related to the advanced hepatic disease.

About 1/3 of our patients had segmental PHT with the dominance of the splenic location. This is a rather important percentage and reflects the frequent obstruction of portal venous system in only one sector. The obstruction at the splenic level is associated with the presence of gastric varices, hemorrhage at this level being technically more difficult to be stopped. The dominant etiology for segmental PHT was pancreatic pathology and therefore, if a segmental obstruction of the portal system is identified, the pancreas should be the first organ to investigate. Beside chronic pancreatitis, segmental PHT was rather frequently described in pancreatic cancer and pancreatic pseudocyst [16]. Ertugrul et al reported 28.4% of the portal venous system thrombosis as being localized in the splenic vein [17].

Mesenteric vein thrombosis is a rare cause of hypertension in the mesenteric vein system [18] and it can be caused by systemic diseases or by local conditions. In our study, an obstruction (thrombosis or tumoral vascular invasion) of the mesenteric vein was found in all the patients with segmental PHT at this level.

In our patients with NCPHT, prehepatic PHT was more frequent than intrahepatic PHT and posthepatic PHT. A possible explanation is the fact that liver biopsy was not performed to exclude cirrhosis in all potentially eligible patients. In other studies, extrahepatic portal venous system obstruction is appreciated to be the second most frequent cause of PHT (5-10% in western countries and 30% in developing countries) [10]. In the pediatric population, extrahepatic portal venous system obstruction can be responsible for up to 70% of the cases of PHT [19]. Sarin et al described in India relatively equal proportions of non-cirrhotic liver fibrosis (9.6%) and extrahepatic portal vein obstruction (11%) in 2137 patients with PHT [20].

Thrombosis, extrinsic compression and vascular tumor invasion were relatively equally responsible for the NCPHT in our study, while the increase of the prehepatic blood flow and a posthepatic obstacle were responsible for the NCPHT in only a few cases.

Laboratory workup revealed discrete liver cytolysis and hyperbilirubinemia and a moderate cholestasis in the NCPHT group. Cholestasis was more important in the case of tumoral etiology than in extrahepatic portal vein thrombosis. It was more important in NCPHT group than in cirrhosis group. This might be explained by the important percentage of tumoral etiology of the NCPHT.

We found normal values for the platelets count in NCPHT group, while cirrhotic patients from the control group were thrombocytopenic. The difference between the mean of platelet counts from NCPHT group (normal) and cirrhosis group (thrombocytopenia) was significant for the patients with the spleen > 120 mm and for the patients with the spleen < 120 mm. No significant difference was found between the platelet counts in the patients with the spleen < 120 mm and in those with the spleen > 120 mm from NCPHT group (normal value) and from cirrhosis group (thrombocytopenia). At the same time, in the cirrhosis group, the mean value of platelet counts was not related to the spleen size or Child class. There was a negative correlation between platelets count and spleen size in the cirrhotic group, but not in the NCPHT group. Normal values of platelets in the majority of patients with extrahepatic obstruction of the portal vein had already been described by Bajaj et al [21]. On the other hand, Dhimann et al reported thrombocytopenia of less than 100,000/mm^3 in 50% of the patients with non-cirrhotic portal fibrosis [14]. All these data suggest that thrombocytopenia in PHT is correlated only with an advanced liver disease (probably with an advanced hepatic fibrosis) and for these patients (and only for these) there is moderate negative correlation between spleen size and platelets count. In conclusion, the thrombocytopenia might not be caused by PHT or splenomegaly, but by advanced hepatic fibrosis and a low platelets count could be an indicator of advanced hepatic fibrosis.

The ascites was detected with the same frequency in both groups (NCPHT and cirrhosis) and it was less frequent in the case of segmental PHT. This result is similar with other studies which reported the presence of ascites in 13% of the patients with portal vein thrombosis [22] and suggests that ascites in PHT is only the consequence of a mechanical effect.

It is known that hemorrhage from varices (even if large and reddish varices) is less frequent in patients with portal vein thrombosis than in the cirrhotic ones [23]. We also found that superior digestive tract hemorrhage as the first sign of PHT was significantly less frequent in NCPHT group than in cirrhosis group. The explanation could be a good preservation of the liver function in the patients with NCPHT when compared with cirrhotic patients. We found that absence of varices, gastric varices and esophageal varices associated with gastric varices were more frequent in the NCPHT group and the esophageal varices alone were significantly more frequent in the cirrhosis group.

Conclusion

In our study, NCPHT was present in 7.12% of the patients with PHT. The etiology of NCPHT is heterogeneous, with the predominance of the prehepatic PHT. Venous thrombosis, tumoral vascular invasion and extrinsic compression of the venous system (portal, suprahepatic and inferior vena cava) are responsible in almost equal proportions for the NCPHT. Segmental PHT was present in about one third of the patients with NCPHT. Absence of varices, gastric varices and esophageal varices associated with gastric varices were more frequent in NCPHT patients

than in cirrhotic patients. In contrast with the cirrhotic patients, who presented thrombocytopenia, the patients with NCPHT had normal platelet counts. Thrombocytopenia did not correlate with PHT, but with an advanced hepatic fibrosis; in NCPHT patients, there was a negative correlation between the spleen size and platelets count.

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