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Protein Content of Liver Lymph in Patients with Portal Hypertension Secondary to Hepatic Cirrhosis

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Summary

Protein content of liver lymph was measured in 14 patients with portal hypertension secondary to advanced hepatic cirrhosis. An abnormally low concentration was found in each patient, averaging 52% of plasma levels. This finding reflects a decreased sinusoidal permeability to protein, the possible effect of "capillarization of the sinusoid" and may bear on development of portal congestion.

The fact that liver lymph and plasma normally contain approximately equal amounts of protein led *Starling* to recognize that there is no oncotic gradient across liver sinusoids: "Here a very small pressure is sufficient to produce a great transudation of lymph containing practically the same amout of protein as the blood plasma from which it is formed" (1). In patients with cirrhosis, increased hepatic venous outflow resistance is usually viewed as the predominant alteration underlying portal hypertension (2) and therefore increased formation of high protein liver lymph would be expected. Clusters of bulging lymphatics at the porta hepatis are in fact frequently encountered at laparotomy in such patients. But with the exception of brief references in passing (3, 4), protein content of the lymph in these distended vessels has been completely neglected. A recent retrospective analysis of clinical data acquired during the past 10 years provided this information in 14 patients with portal hypertension secondary to advanced cirrhosis and forms the basis for this report.

Methods

Fourteen adult patients undergoing laparotomy for a portacaval shunt were studied. In each case the diagnosis of advanced hepatic cirrhosis was confirmed by gross and microscopic appearance of the liver and by the results of biochemical tests of liver function. A history of bleeding from esophageal varices was present in 9 and the remainder had recurrent massive ascites. All patients gave a history of prolonged alcoholism.

Portal pressures were measured by cannulation of an omental or mesenteric vein and a saline manometer with a zero pressure level taken as 12 cm above the operating table. Liver lymph was obtained from periportal or hepatic capsular lymph vessels and protein concentration in this fluid and in plasma was measured by the Biuret method (5) or with a T/S refractometer.

Results

Distended lymph vessels at the porta hepatis and/or on the capsule of the liver were noted in each patient. Protein content of liver lymph ranged from 1 to 5.5 grams per 100 ml and averaged 2.9. Expressed as the fraction of simultaneous plasma levels, the corresponding values ranged from 17% to 81% and averaged 52% of plasma concentrations. Portal pressures ranged from 32 to 55 cm of H_2O. The data are summarized in Table 1.

Table 1. Protein Content of Liver Lymph and Plasma in Patients with Portal Hypertension

Patient	Ascites	Varix Bleeding	Portal Pressure cm H_2O	Plasma Protein (Grams %)	Liver Lymph Protein (Grams %)	L/P Ratio
JD		x	38.5	5.8	2.6	.44
GN	x		34	4.9	4.0	.81
LT		x	42	4.4	2.7	.61
AR	x	x	36	7.2	5.5	.76
TW	x		39	6.9	2.1	.30
CS	x		34	4.6	2.7	.50
IL	x		34	5.4	4.0	.74
BK	x	x	46	5.5	2.3	.40
RC	x	x	49	7.9	2.8	.35
GL	x	x	40	5.1	3.0	.58
JW		x	55	5.2	1.5	.28
AC	x		36	5.8	1.0	.17
LG		x	40	4.8	3.7	.77
JA		x	32	6.3	3.8	.60

Discussion

In experimental animals undergoing thoracic inferior vena caval constriction (3) and in patients with hepatomegaly secondary to right sided congestive heart failure (6) protein content of excess liver lymph is normal, averaging 90% of plasma levels. In contrast, in the 14 patient with portal hypertension secondary to Laennec's Cirrhosis reported here protein content of liver lymph averaged only 52% of plasma levels. Considered in the light of authoritative statements that hepatic venous outflow obstruction underlies portal hypertension (2), this is a curious and unexpected finding. An experimental attempt to reproduce this derangement in dogs with portal vein constriction superimposed on chronic thoracic caval constriction was not successful (3). Although these animals developed portal hypertension, protein content of the excess liver lymph remained at 90% of plasma levels. Moreover, in dogs undergoing portal vein constriction or ligation without caval constriction, protein content of liver lymph fell to 70% of plasma levels but hepatic hilar lymph vessels collapsed and formation of liver lymph diminished markedly.

In seeking to explain the low protein content of excess liver lymph in patients with portal hypertension secondary to cirrhosis it may be important to recall earlier electronmicroscopic studies of the cirrhotic liver (7). In advanced cirrhosis an abnormal deposition of connective tissue was found along the walls of sinusoids. As this extra lining appeared to resemble a basement membrane the alteration was designated "capillarization of the sinusoid". Decrease in the normal permeability of the sinusoid to protein would be expected under these circumstances and might account for the decreased protein content of excess liver lymph in the patients with portal hypertension reported here.

Free diffusion of plasma protein across liver sinusoids can be viewed as the key component of a physiologic mechanism which normally functions to regulate splanchnic plasma volume in the face of increased hepatic venous outflow resistance (8). This arrangement permits diversion of some of the excess plasma into liver lymph without the restraint of an oncotic gradient. Thus an expandable extravascular compartment is formed (in liver, distended lymph vessels and in ascitic fluid) from which plasma equivalent fluid is slowly returned to the systemic circulation. In patients with advanced cirrhosis, decrease in sinusoidal permeability to protein may impair the ability of this mechanism to compensate for reduced hepatic venous outflow. The net hemodynamic effect would be a tendency for splanchnic plasma volume to increase, leading in turn

to portal congestion. Support for this view derives from the finding that protein concentration in liver lymph was abnormally low in each one of 14 consecutive patients with portal hypertension secondary to hepatic cirrhosis, a close relationship which was overlooked in earlier reports based on findings in a smaller number of patients (3, 4). Although more information is needed, particularly with regard to protein content of liver lymph in patients with less advanced stages of cirrhosis, it is tempting to speculate that altered sinusoidal permeability to protein, however, obscure in origin, may be an important component of the mechanism underlying portal hypertension.

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High Concentration of Bilirubin in Post-Nodal Lymph Associated with Red Blood Cell Catabolism in Lymph Nodes of the Sheep

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Summary

Qualitative and quantitative analysis of post-nodal lymph of the sheep has shown that the distinct yellow colour of this fluid pool is due to the presence of relatively large amounts of bilirubin. In efferent lymph from the popliteal, prefemoral, prescapular, renal and intestinal lymph nodes total bilirubin concentrations were 3-8 times higher than the corresponding concentrations in blood plasma. In contrast the total bilirubin concentrations in afferent lymph from the lower leg and kidney were less than the corresponding concentrations in blood plasma. Histological examination of several popliteal and mesenteric lymph nodes revealed the presence of free iron and bilirubin in the cytoplasm of cells located near the lymphatic sinuses of the node. In addition, the concentration of bilirubin in efferent lymph from the popliteal node was observed to increase following an induced rise in the number of red blood cells reaching the node by way of the afferent lymphatic duct. These latter observations suggest that the bilirubin in post-nodal lymph is associated with the catabolism of extravascular red cells by reticulo-endothelial cells within the lymph nodes.