

Thoracic Duct Lymph of a Patient with Dubin-Johnson Syndrome

Minoru MIZUTA, Tetsurō SASAYAMA
and Toshinori HARADA

*The First Division, Department of Internal
Medicine, Yamaguchi University School of Medicine,
Ube, Japan*

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Secondary rise of plasma bromsulphalein (BSP) concentration on BSP retention test is one of the characteristic phenomena for Dubin-Johnson syndrome,¹⁾ but the mechanism of this phenomenon is still not clear.

Two major routes of regurgitating BSP from the liver to blood stream are possible, one of them is direct route from the liver cells and the other is that through hepatic lymph and thoracic duct lymph. The secondary rise of plasma BSP appears on or after 60 minutes and the re-elevated BSP mainly is the conjugated form.²⁾

Then, it is reasonable to consider that the hepatic lymph passway is one of the main regurgitation route to blood stream.

In this article we have discussed about the role of lymphatic passway at the secondary rise of plasma BSP concentration in a patient with Dubin-Johnson syndrome.

PATIENT STUDIED

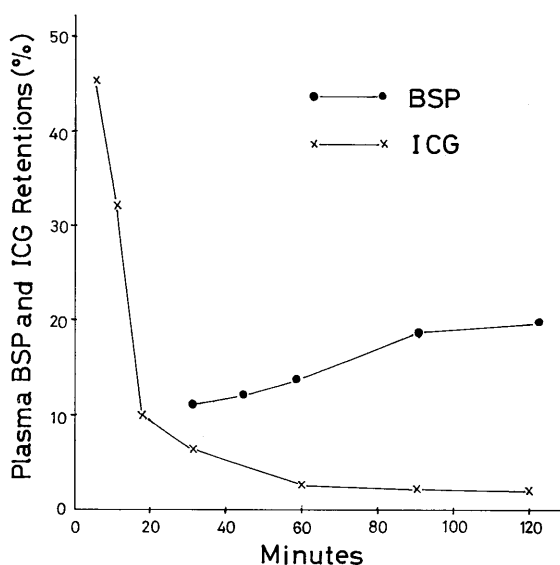
A 34 years old Japanese male patient was firstly noted with jaundice one years ago. Laparotomy was performed for the likelihood of extrahepatic obstructive jaundice seven monthes ago. There was nothing recorded on previous illness and family history could be referred.

The blood findings : Erythrocyte 370×10^4 , leukocyte 3,200, hematocrit 37.6 %, iron 146 mcg %, protein 7.9 gm %, albumin 3.7 gm %, globulin 4.2 gm%, total bilirubin 4.3 mg %, 15 minutes bilirubin 3.1 mg %, alkaline phosphatase 3.7 Bodansky units, cholesterol 140 mg %, glutamic pyruvic transaminase 11 Mizobe units (normal value below 10 units),³⁾ cephalin-cholesterol flocculation test +1, blood sugar 82 mg %, urea N 10 mg %, NPN 21 mg %, phenol turbidity test 6 units, leucine aminopeptidase 38 units and lactic dehydrogenase 20 units. On paper electrophoresis of plasma proteins : Albumin 46.4 %, α_1 -globulin 4.5 %, α_2 -globulin 11.5 %, β -globulin 18.5 %, γ -globulin 1.1 %.

α_2 -globulin 8.5 %, β -globulin 11.4 % and γ -globulin 29.2 %.

Bromsulphalein retention test shown in **Fig. 1**, 5 mg per kilograms of body weight of BSP was injected and, the concentrations in plasma were retained at level of 13 per cent on the first 45 minutes and rised higher on or after 60 minutes. Indocyanine green (ICG) clearance test, 0.5 mg per kilograms of body weight dossaged and no secondary elevation presented in plasma concentration, but a slight hepatic excretory dysfunction indicated by 10 per cent of retention at 15 minutes. The relative hepatic storage of BSP and maximal biliary transport of BSP were estimated with two kinds of rates infusion followed by Adams and his co-workers,⁴⁾ in which the former scarcely shown normal in level of 57.5 mg per 100 ml of plasma BSP concentration and the later shown low level at 1.53 mg per minute.

Fig. 1. BSP and ICG Tests



Microscopically, biopsy of the liver shows in Dubin-Johnson syndrome characterized by the brown coarse granule particularly surrounding the area of central veins. A slight eosinophilic degeneration, Mallory's body and inflammatory cells infiltration were also presented. (**Fig. 2**)

Liver tissue degenerations in nature of granule, dilation of bile canalicular lumen, decreased microvilli of bile canaliculi and dilation of intracellular spaces were appeared through the electron microscopy. (**Fig. 3**)

The clinical data obtained on the above indicated that the patient had been suffering from the latent hepatitis. Hepatic damage from hepatitis seemed not so heavy and did not bring much influences to the experimental data in the case of Dubin-Johnson syndrome.

Fig. 2. Microscopic findings of the liver (H. E. stain) .

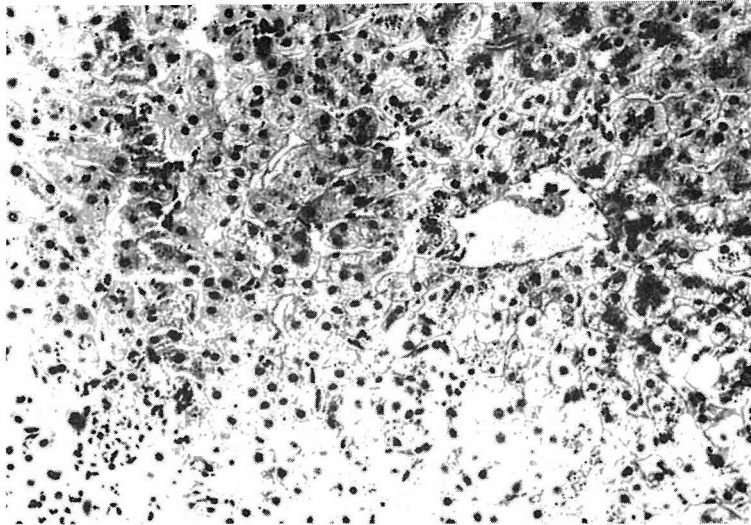
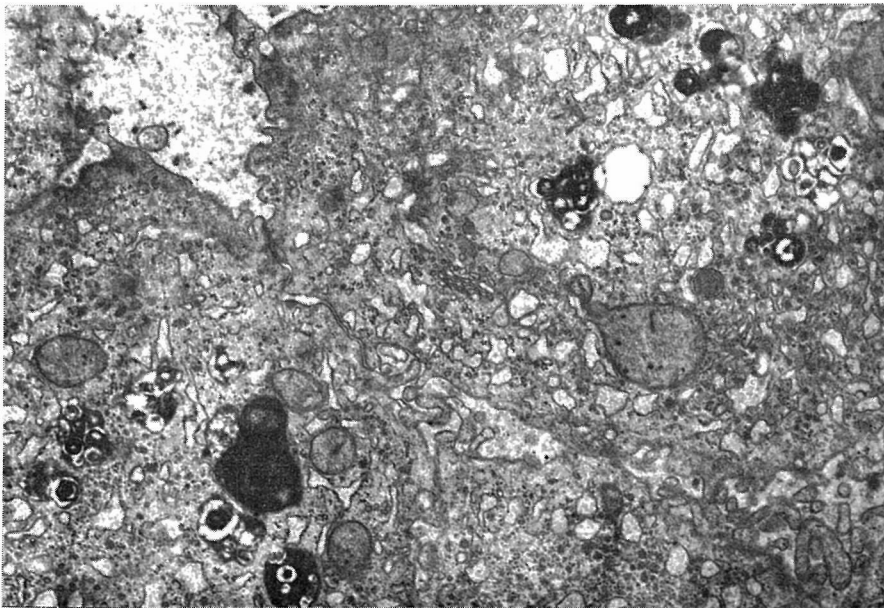


Fig. 3. Electron microscopic findings of the liver



EXPERIMENTAL PROCEDURES

A short time drainage was performed in the thoracic duct at the neck of the patient and the ordinary BSP retention test also was taken followed by two hours later the canulation. Bromsulphalein concentrations both plasma and heparinized thoracic duct lymph were estimated at 30, 45, 60, 90 and 120 minutes after the injection. Bromsulphalein concentrations were measured by means of alkalized sample of lymph and plasma with 580 millimicrons wave length of spectrophotometer. Meanwhile the conjugated and unconjugated BSP in lymph were also assayed with paper chromatography.⁵⁾

The protein concentration, bilirubin concentration, and flow rate in the thoracic duct lymph and flow pressure at clavicular level of thoracic duct were estimated. The lymph protein analysis was also examined with electrophoresis.

The normal range of all data referred were illustrated by other investigators.⁶⁾⁻¹¹⁾

RESULTS

Results obtained from thoracic duct lymph were shown in **Tab. 1**. The lymph flow rate of thoracic duct was in normal level of 1 ml per minute, the flow pressure was scarcely normal level of 20 cm H₂O. The total bilirubin concentration in lymph was 3.0 mg per 100 ml, 15 minutes bilirubin 1.8 mg per 100 ml. The total bilirubin level in lymph as 70 per cent as the level of plasma bilirubin was indicated. Total protein level in thoracic duct lymph was 8.3 gm per 100 ml and 105 per cent as the level as in plasma.

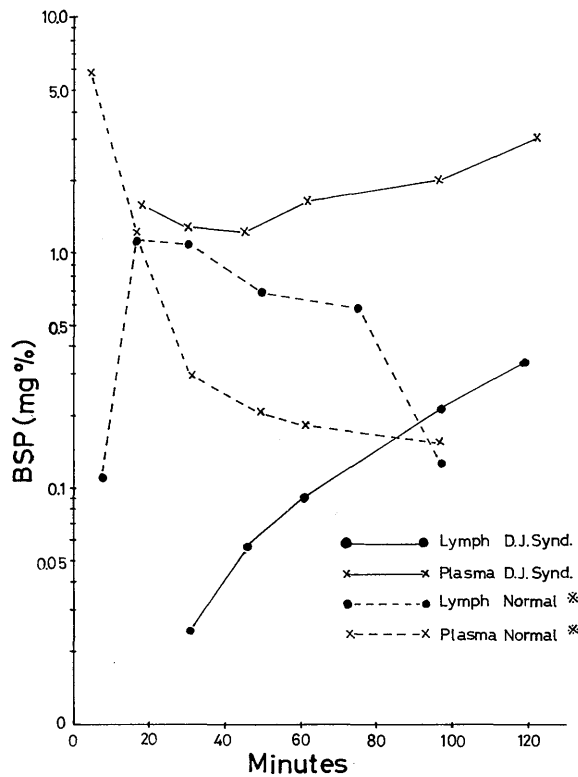
Table 1. Thoracic duct lymph

	Flow ml/min	Pressure cmH ₂ O	Protein (% plasma)	45 min BSP (% plasma)
Normal ⁸⁾⁻⁹⁾	1 (0.6~1.6)	10 (5~18)	70 (60~80)	—
Congestive heart failure ¹⁰⁾	7 (3~11)	37 (17~80)	50 (21~75)	—
Liver cirrhosis without varix bleeding ^{8) 11)}	6 (1~10)	28 (10~40)	57 (40~80)	74±15
Liver cirrhosis with varix bleeding ^{8) 11)}	8 (1~15)	30 (10~60)	34 (10~60)	29±17
Dubin-Johnson syndrome	1	20	105	5

The following values of proteins of thoracic duct lymph were detected : Albumin 42.7, α_1 -globulin 6.2, α_2 -globulin 9.6, β -globulin 17.2 and γ -globulin 24.7 per cent. Obviously the level of thoracic duct lymph protein of this patient was little higher than normal and considerably higher than liver cirrhotic cases, and the protein showed the similar nature as plasma protein.

As shown in **Fig. 4** the levels of BSP in thoracic duct lymph at 30, 45, 60, 90 and 120 minutes after injection were 0.025, 0.06, 0.09, 0.22 and 0.33 mg per 100 ml, which indicated both delayed appearance and decreased excretion of BSP in the lymph. The secondary rise of plasma BSP concentration was also shown by draining the thoracic duct lymph from the body. Furthermore, the BSP level of the thoracic duct lymph at 45 minutes as the percent as in plasma level of 5 per cent was indicated. Bromsulphalein in the lymph was only showing a conjugated form.

Fig. 4. BSP concentrations in plasma and thoracic duct lymph



* Dumont, A.E. & Witte, M.H. (1966)

DISCUSSION

Under the normal state, BSP concentration in thoracic duct lymph is equivalent to that in plasma at 15 and 20 minutes after the injection. In the case of obstructive jaundice, BSP also markedly moved into thoracic duct lymph.^{1,2)} In the case of Dubin-Johnson syndrome, however, delayed appearance of BSP into the lymph and decreased excretion of BSP into the lymph were noted.

By the observation of the decreased maximal biliary transport of BSP it was shown that the patient has disturbance of biliary excretion of BSP. Meanwhile alteration in the hepatic lymph also presented of the BSP transference and, the secondary rise of plasma BSP concentration was shown even by draining the thoracic duct lymph from the body.

Accordingly, the secondary rise of plasma BSP concentration is not resulted from the lymphatic regurgitation but could be resulted from the direct regurgitation of BSP from hepatic parenchymal cells to blood stream. It agrees with the fact that the plasma BSP at the secondary rise is mainly consisted of the conjugated type.^{1,2)}

CONCLUSION

On the thoracic duct lymph of a patient with Dubin-Johnson syndrome, the normal or slight raised pressure, increased protein concentration, normal flow rate and disturbed BSP excretion were observed. By means of BSP retention test, the secondary rise of plasma BSP concentration was studied with or without draining the thoracic duct lymph from the body. And it suggested that the secondary rise of plasma BSP concentration resulted in direct regurgitation from hepatic parenchymal cells to blood stream.

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