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Bile Acids in Ascites of a Case with Liver Cirrhosis*)

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ABSTRACT

Ascitic bile acids in a cirrhotic patient with hepatoma were determined by gas liquid chromatography. The bile acids in ascites were considered to originate from those in hepatic lymph transuded by postsinusoidal obstruction in liver cirrhosis.

INTRODUCTION

Many investigations about bile acids in body fluids have been reported with a view to elucidate the possible relationship between diseases and bile acids. Most of the samples employed in research of bile acids in clinical cases have been mainly obtained from bile, serum, urine and feces. In affected condition, bile acids are supposed to be present not only in fractions as described above but in other fractions, for example, in ascitic fluid with liver cirrhosis, although it has not been reported whether bile acids were found in ascites with liver cirrhosis. The aim of this paper is to study whether bile acids are present in ascitic fluid of a cirrhotic patient and their clinical significance.

PATIENT AND METHODS

PATIENT: This 61-year-old female had undergone medical treatment in a hospital for liver cirrhosis since ten years ago, when she was unaware of the abdominal distension. In September 1982, abdominal distension was suspected by the patient. Immediately after serious abdominal pain attacked the patient, she was sent to the Department of Internal Medicine, Chugoku Rosai Hospital, when she was almost in condition of hepatic coma with much ascites on October 31, 1982. Although the consciousness level was improved by conservative therapy, she complained of abdominal pain very often and there seemed to be a complication of panperitonitis. Then she was referred to the Department of Surgery for the purpose of surgical treatment. Laboratory data of liver and renal function at the time of her hospitalization are shown in Table 1. Although the cause of panperitonitis could not be diagnosed preoperatively, emergent laparotomy was performed to save the patient from acute abdomen.

No abnormality was found except for ascites, expanded gallbladder, and liver. Eighteen hundreds ml of ascitic fluid was aspirated from the peritoneal cavity. The expanded gallbladder had no gallstones and no inflammatory changes of the wall. Furthermore, communication of the gallbladder with common bile duct was intact. The liver was very atrophic and undoubtedly showed a severe cirrhosis with a hepatoma of the size of a pigeon-egg in the right lobe. However, no signs suggesting portal hypertension, that is splenomegaly or dilatation of portal venous system, were observed. It seemed likely that the expanded gallbladder was more or less related to panperitonitis, as it was about to burst with bile at any moment. So external

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Table 1. Liver and renal function data in serum before operation

T. Protein	6.1 g/dl (6.3-8.2)	LDH	1818 U/l (44-390)
Albumin	1.6 g/dl (3.6-5.1)	T. Bilirubin	6.3 mg/dl (0.2-1.0)
GOT	1241 U/l (5-35)	Conjugated B.	5.1 mg/dl (0.1-0.4)
GPT	296 U/l (0-30)	TTT	10 M.U (0-4)
Ch-E	0.11 △p H (0.65-1.2)	ZTT	41 K.U (4-12)
Al-p	650 U/l (60-270)	BUN	28 mg/dl (8-20)
γ-GTP	111 U/l (0-35)	Creatinin	2.33 mg/dl (0.7-1.5)
LAP	164 U/l (40-70)		

The numbers in parenthesis indicate normal range.

cholecystostomy and drainage from the peritoneal cavity were finally carried out after aspiration of 150 ml of the gallbladder bile, although the origin of panperitonitis could not be clearly determined. Unfortunately, she died due to hepatic come on the 3rd postoperative day.

METHODS: Gallbladder bile, ascitic fluid, peripheral venous blood, and urine were obtained for bile acid analysis during the operation. Bile acids of all samples were determined by gas liquid chromatography. Biliary bile acids were analyzed as described previously[2]. Serum, urinary and ascitic bile acids were determined with Makino's procedure[5], in which nonsulfated bile acids were separated from sulfated ones. In this procedure, however, Sep-Pak C 18R bonded cartridge[12] was used for the extraction of bile acids.

RESULTS AND DISCUSSION

Bile acid concentrations in each fraction of body fluids are shown in Table 2. In the ascitic fluid, considerable amounts of bile acids were detected almost conclusively as a nonsulfated fraction. Which compartment of body fluids were bile acids in ascites derived from? As ascites in this patient was not exudate but transudate from the features of ascites (Table 3), the cause of ascites is supposed to be due to liver cirrhosis.

In patients with liver cirrhosis, although the exact site of ascites formation has been controversial, Witte and his colleagues[13] reported that postsinusoidal obstruction leads to a tremendous increase in the formation of hepatic lymph and the hepatic lymph plays a prominant role in ascites formation whereas presinusoidal obstruction promotes portal hypertension, increases intestinal lymph and capillary filtration in extrahepatic portal bed, and results in ascitic fluid formation.

Ascites in this patient is assumed to originate from hepatic lymph, because no portal hypertension was present in the operative finding. On the other hand, as the molecular weight of albumin is very large, blood capillary is supposed to be less permeable to albumin. However, liver sinusoids are highly permeable to serum albumin, for they constitute a unique capillary bed. Therefore, it is suggested that

Table 2. Bile acid concentration of individual compartment in body fluids

	Ascites (μg/ml)		Gallbladder bile (μg/ml)	Serum (μg/ml)		Urine (μg/ml)	
	N.S.	S.		N.S.	S.	N.S.	S.
CA	7.46	ND	16.31	12.62	ND	0.36	0.27
CDC	16.62	ND	41.48	46.08	4.13	0.21	12.80
LCA	ND	ND	ND	ND	ND	ND	0.40
	24.08	—		58.70	4.13	0.57	13.47
Total	24.08		57.79	62.83		14.04	

CA: Cholic acid, CDC: Chenodeoxycholic acid, LCA: Lithocholic acid
N.S.: Nonsulfated bile acids, S.: Sualfted bile acids
ND: not determined

Table 3. Characteristics in ascitic fluid

Appearance:	cloudy yellow
Specific gravity:	1.009
Total protein:	2.8 g/dl
Albumin:	1.5 g/dl
Rivalta reaction:	negative
Bacterial culture:	sterile

serum albumin-bound bile acids, which were mostly present as that form in serum[7], passed across the sinusoidal wall into hepatic lymph and appeared in ascites because of postsinusoidal resistance to flow in liver cirrhosis.

Sulfated bile acids were not detected in ascites of this patient. They have been considered to be absent in portal venous system[1], so that bile acids found in ascites were thought to be derived from portal blood before being taken up by hepatocytes and sulfated in hepatocytes. This supports the above-mentioned mechanism that bile acids in ascites originated from the bile acids contained in hepatic lymph of this cirrhotic patient.

There is also a possibility that bile acids in ascites were transuded from the gallbladder, while it is supposed that bile acids in functioning gallbladder without inflammatory changes are not transported across the wall into the peritoneal cavity.

Gallbladder bile acid concentration was of an extremetely low level in this patient (Table 2). That might be due to the fact that bile acid synthesis is seriously decreased in liver cirrhosis[11], and that the hormones which increase the bile flow, such as secretin, are not inactivated under hepatic cirrhosis[3].

Serum bile acid concentration in this patient was of a remarkably high value in comparison with those in healthy individuals[8]. That might result from an extrahepatic collateral bypass in hepatic cirrhosis[6], and moderate obstructive jaundice[9] as shown in Table 1.

In all analyzed samples of this patient, chenodeoxycholic acid was major bile acid and deoxycholic acid was not determined. These results are consistent with those reported in previous papers[4,6,10] that chenodeoxycholic acid increases and deoxycholic acid decreases in biliary bile acid composition of liver cirrhosis.

Sulfation of bile acids is a kind of detoxifying mechanism in a living body. In this patient, ascitic bile acids were not present as sulfated form. Moreover, ascitic fluid was sterile (Table 3). Although there has been no report that cholic acid and/or chenodeoxycholic acid impair body tissues, nonsulfated bile acids might be harmful to peritoneum, for the cause of the panperitonitis without bacterial infection in this case was uncertain. Further study is needed to clarify whether bile acids are able to cause peritonitis as demonstrated in this case and whether they affect the reabsorption of ascites by peritoneum.

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