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Postoperative Changes of Serum Bile Acid Levels in a Case with Massive Hepatic Resection*)

Mitsuo HARADA[1)], Makoto TAKAHASHI[2)], Motomu KODAMA[1)],
Naotaka AKIMOTO[2)], Jiro AOYAMA[2)], Kazuro INAGAKI[1)]
and Haruo EZAKI[1)]

1) *The 2nd Department of Surgery, Hiroshima University School of Medicine, 1-2-3, Kasumi, Minami-ku, Hiroshima 734, Japan*
2) *The Department of Surgery, Chugoku Rosai Hospital, Kure 737-01, Japan*

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ABSTRACTS

Postoperative serum bile acids in a patient with hepatectomy were determined by gas-liquid chromatography. The results showed that two high peaks of serum bile acid levels were found respectively on the 2nd and 7th postoperative day, although serum bile acid levels returned to normal after the 15th postoperative day. The high peaks were considered to be due to the escape of necrotic hepatic intracellular bile acids into systemic blood stream, poor uptake of bile acids by hepatocytes and reabsorption of bile acids leaked from the residual liver into the peritoneal cavity.

INTRODUCTION

Massive hepatic resection may be indicated for hepatic carcinomas, liver-cell adenomas, hemangiomas or traumatic rupture of liver parenchyma. However, the effects of hepatic resection on bile acid metabolism have not been studied at all. Very recently, serum bile acids have been focussed on as a parameter of liver function[1,3,5,7,9,12-14]. Some authors have reported[5,13] that serum bile acids reflected the status of the liver functions very sensitively. In this paper, serum bile acids as well as other liver function tests were determined postoperatively in a patient with right hepatic lobectomy along Cantlie's line for the serious traumatic liver ruptures.

PATIENT AND METHODS

PATIENT: This healthy 31-year-old male was compelled to undergo an emergent operation for serious hepatic rupture due to the accident during labor. Soon after laparotomy, 2,000 ml of blood was aspirated from peritoneal cavity. Inspection and palpation of the liver revealed extensive and multiple traumatic ruptures of the right lobe without presence of any hepatic diseases, for example, chronic hepatitis etc., so that right hepatic lobectomy along Cantlie's line was carried out after cholecystectomy. The volume of the resected liver was about two-thirds of the whole liver. The abdominal wall was closed in layer after the insertion of a drain into the right subphrenic space. 2,300 ml of packed red blood cells was transfused during operation. Pathological result of the resected liver was normal except for hepatic ruptures. The postoperative course was very smooth and the drain was removed on the 14th postoperative day. The patient has been in good condition up to now.

ANALYTICAL METHODS FOR SERUM BILE ACIDS: Fasting blood samples were drawn for studying changes of serum bile acids and liver function tests every day until the 8th postoperative day and after that, every 1 week for a month. The procedure for serum bile acid analysis is outlined in Fig. 1. Each serum

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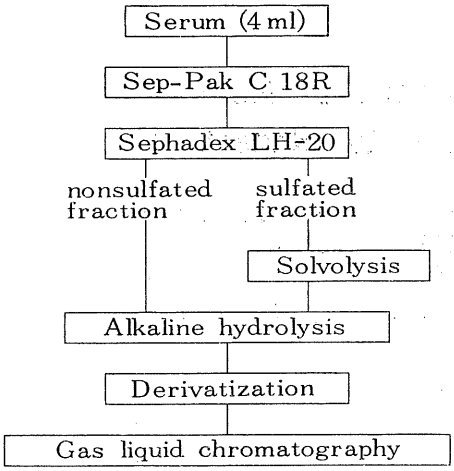

Fig. 1. Outline of procedure for analysis of bile acid profiles in systemic blood.

(4 ml) diluted with an equal amount of water was passed through the Sep-Pak C18R bonded cartridge[15]. After the cartridge was washed with 10–20 ml of water, bile salts were eluted with methanol through the cartridge. The resulting sodium salts were divided into two groups of differing polarity by column-chromatography on Sephadex LH-20, separating nonsulfated from sulfated fraction. The elution of nonsulfated fraction was achieved, with the solvent mixture chloroform/methanol (1 : 1, v/v), containing 0.01 M sodium chloride. Then a known volume of 5α-cholestane was added to each fraction as an internal standard. After the sulfated fraction was solvolyzed, the bile acids in both fractions were deconjugated by alkaline hydrolysis (for 3 hours at 120°). Then the bile acids were analyzed in gas-liquid chromatography as their methylester-trimethylsilyl derivatives. All gas-liquid chromatographic analyses were carried out on model GC-7A (Shimadzu Manufacturing Co., Kyoto, Japan) with 2% Poly I-110 and 3% OV-17 column.

RESULTS

The levels of serum bile acids after right hepatic lobectomy are shown in Table 1 and Fig. 2. Although total bile acid levels dropped on the 5th postoperative day after their steep elevation on the 2nd day, high peak appeared on the 1st postoperative week. This was the highest level during the entire course (115.6 μg/ml). After the 1st week, serum bile acid

Table 1. Levels of serum bile acids after hepatic resection

Postoperative day	TBA		CA	CDC	DC (μg/ml)
1	2.4	NS	1.1	1.3	—
		S	—	—	—
2	108.8	NS	53.2	55.6	—
		S	—	—	—
3	60.2	NS	4.8	50.9	1.8
		S	—	2.7	—
5	6.0	NS	1.1	3.5	—
		S	—	1.4	—
6	16.3	NS	6.8	9.5	—
		S	—	—	—
7	115.6	NS	63.6	52.0	—
		S	—	—	—
8	58.2	NS	30.2	28.0	—
		S	—	—	—
15	trace	NS	trace		
		S			
22	0.5	NS	—	0.5	—
		S	—	—	—
29	0.6	NS	—	0.6	—
		S	—	—	—

TBA: Total bile acids, CA: Cholic acid, CDC: Chenodeoxycholic acid, DC: Deoxycholic acid, NS: Nonsulfated bile acid, S: Sulfated bile acid

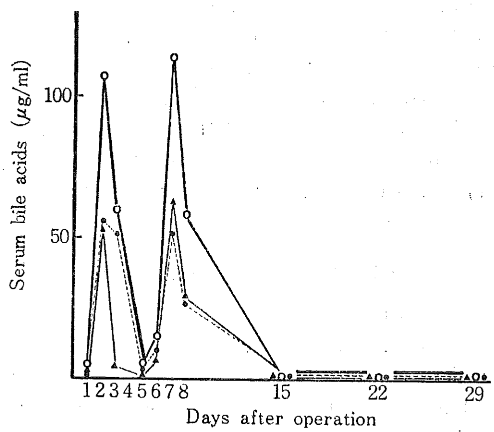

Fig. 2. Changes of serum bile acids following hepatic resection. ○—○ : Total bile acids, ▲—▲ : Cholic acid, ●--● : Chenodeoxycholic acid

level started to go down and it had been less than 1.0 μg/ml after the 15th day.

In composition of serum bile acids, cholic acid/chenodeoxycholic acid ratio indicated no fixed tendency. Fig. 3 shows postoperative changes of serum albumin and alkaline phosphatase, which were not paralleled to those of serum bile acids. Serum GOT, GPT levels rapidly returned to normal after their remarkable elevation on the 1st day as shown in Fig. 4. Serum total bilirubin levels were transiently elevated on the 1st week. The main component for the increase was due to that of unconjugated bilirubin. It returned to normal within 2 weeks (Fig. 5). The changes of serum total and esterified cholesterol were almost similar to those of bile acids as shown in Fig. 6. A linear correlation with statistical significance was found between serum total bile acid levels and serum cholesterol levels in this patient (Fig. 7)

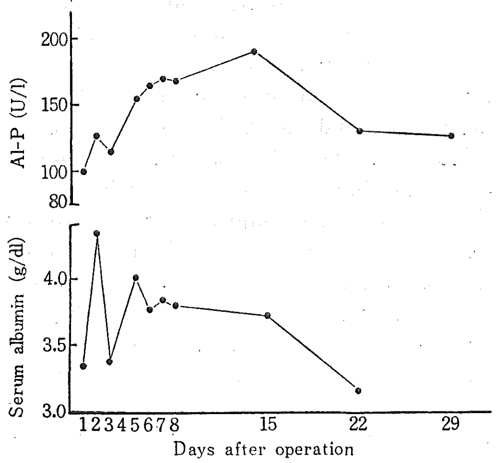

Fig. 3. Changes of serum alkaline phosphatase and albumin following hepatic resection. (normal range: alkaline phosphatase 60-270, albumin 3.6-5.1)

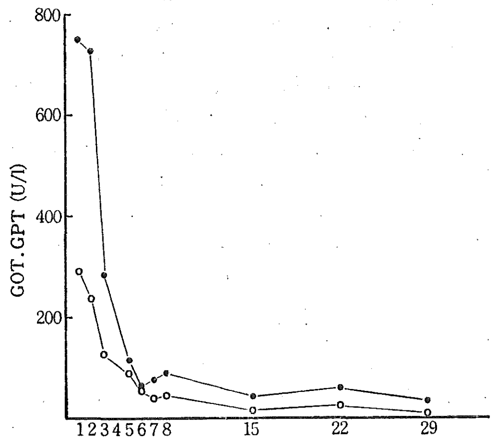

Fig. 4. Changes of serum GOT and GPT following hepatic resection. ●—● : GOT, ○—○ : GPT (normal range: GOT 5-35, GPT 0-30)

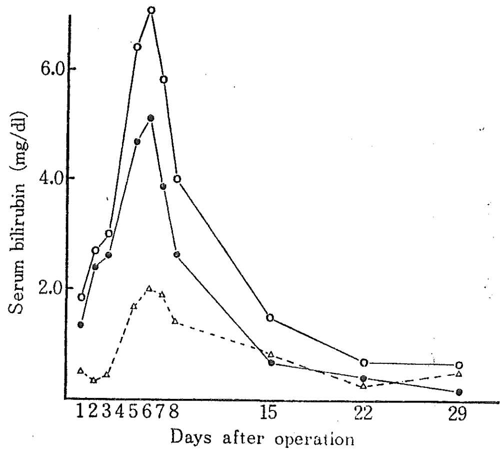

Fig. 5. Changes of serum bilirubin following hepatic resection. ○—○ : Total bilirubin, ●—●: Unconjugated bilirubin, △—△ : Conjugated bilirubin (normal range: Total bilirubin 0.2-1.0, Unconjugated bilirubin 0-0.6, Conjugated bilirubin 0.1-0.4)

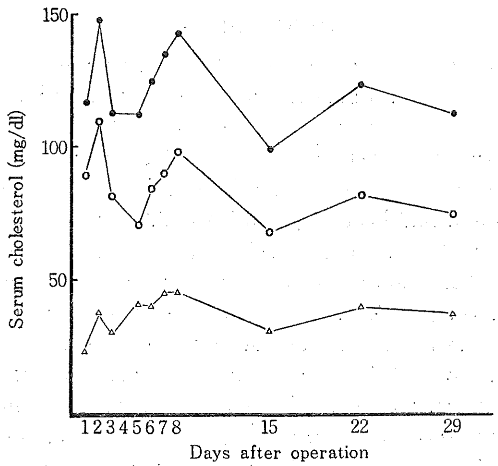

Fig. 6. Changes of serum cholesterol following hepatic resection. ●—● : Total cholesterol, ○—○ : Esterified cholesterol, △—△ : Free cholesterol (normal range: Total cholesterol 140-230, Free cholesterol 35-60)

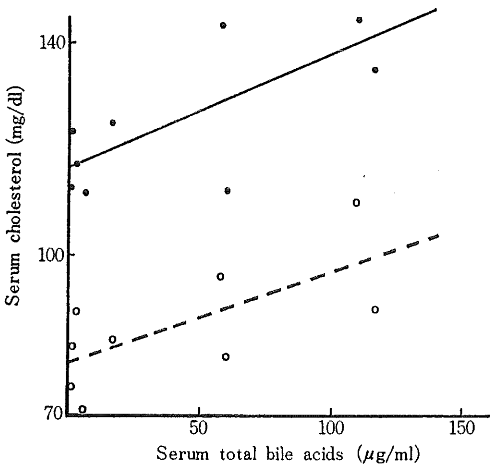

Fig. 7. Relationship between serum bile acid and serum cholesterol levels following hepatic resection. ● : Total cholesterol, ○ : Esterified cholesterol Closed symbols denote: $Y=0.21X+117.1$, $r=0.72$ ($p<0.05$) Open symbols denote: $Y=0.17X+79.9$, $r=0.69$ ($p<0.05$)

DISCUSSION

Fasting serum bile acid levels determined by gas-liquid chromatography in healthy individuals have been reported to be 0.29–2.26 μg/ml[10]. Although it returned to normal after the 15th postoperative day, serum bile acid levels in this patient had been high until the 8th day. Cause of high serum bile acid levels after hepatic resection might be traceable to the following reasons; 1) Accumulation of bile acids in serum secondary to excretory disturbance in renal dysfunction, 2) Cholestasis in the remained liver, 3) Escape of necrotic hepatic intracellular bile acids into blood stream, 4) Poor uptake of bile acids from the portal venous system by hepatocytes, 5) Peritoneal reabsorption of bile acids leaked from transected surface of the remained liver into the abdominal cavity.

In this patient, it is not to be imagined that renal dysfunction as described above was present after hepatic lobectomy, because serum BUN and creatinine levels were normal and enough urine was excreted through the whole clinical course. As serum alkaline phosphatase levels were within normal limits and conjugated bilirubin levels were not so high as unconjugated ones, the possibility of intra-and extra-hepatic cholestasis was considered to be negligible.

It is well accepted[6] that acute hepatitis frequently accompanies high level of serum bile acids as well as GOT, GPT. As shown in Fig. 2, two high peaks were found in serum bile acid levels after hepatectomy in this patient. It is considered that the lst high peak of serum bile acid curve shown on the 2nd postoperative day might be due to the escape of necrotic intracellular bile acids into systemic blood stream as well as serum GOT, GPT.

On the other hand, what is the mechanism of the 2nd steep rise of serum bile acid level found on the 7th day? It is generally recognized that serum bile acids exist as form bound to albumin[8]. Moreover, albumin-bound bile acids were described to be more efficiently taken up than non-albumin-bound bile acids by hepatocytes[2]. It has been reported that bilirubin competes with bile acids in the ability bound to albumin in serum[11]. Furthermore, unconjugated bilirubin possesses more ability to bind with albumin than conjugated one[4]. In this patient, the period of the highest serum bile acid level was well coincident with the peak of serum unconjugated bilirubin level (Fig. 5). Therefore, the 2nd peak of serum bile acid level may result from the poor uptake of non-albumin-bound bile acids by hepatocytes, secondary to competition theory with unconjugated bilirubin.

Postoperatively about 350 ml of serum bloody fluid was excreted a day from the drain inserted into the right subphrenic space and the drain was removed on the 12th postoperative day. Although the volume of bile acids discharged from the drain was not determined, it is probable that bile acids leaked from the transected surface of the residual liver into peritoneal cavity had some effect on the elevated levels of serum bile acids after hepatectomy by the mechanism of peritoneal reabsorption of bile acids.

In a comparison of serum bile acid level curve with other routine liver functional parameters, correlation only with serum cholesterol was found in this patient. However, the precise cause of this correlation is uncertain.

In conclusion, although postoperative serum bile acid levels showed two high peaks respectively on the 2nd and 7th day, they returned to normal after the 15th postoperative day. The following were considered as cause of steep rises of serum bile acids. 1) The lst peak possibly came from the escape of necrotic hepatic intracellular bile acids into systemic blood stream. 2) The 2nd peak might be due to the poor uptake of non-albumin-bound bile acids by hepatocytes secondary to the elevation of unconjugated bilirubin. However, it cannot be neglected that reabsorbed bile acids leaked from the transected surface of the residual liver into the peritoneal cavity had an effect on both peaks. As the postoperative clinical course was smooth, normal serum bile acid levels after the 15th postoperative day might suggest a good prognosis in this patient. Since the effects of hepatectomy on the bile acid metabolism have not been reported, further studies are required for understanding hepatic resection.

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