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Liver Resection for Hepatocellular Carcinoma (HCC) with Direct Removal of Tumor Thrombi in the Main Portal Vein

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Since the tumor thrombus in the main portal vein appears in the terminal stage of hepatocellular carcinoma (HCC), any attempt to remove it surgically is thought to be impractical as the malignancy itself cannot be entirely removed. During the past 5 years, we have performed tumor thrombectomy combined with hepatectomy in 29 of 298 patients with HCC. This combined therapy was initially decided upon as an emergency measure to prevent impending rupture of esophageal varices, rather than to improve patient survival. Since portal flow was obtained after removal of thrombi, this condition enabled transcatheter arterial embolization (TAE) and/or percutaneous ethanol injection therapy (PEIT). Although improved patient survival was not the primary goal of the emergency operation and there was an operative mortality of 11%, half of the other patients in the present series had unexpectedly high survival rates of 1 year (52.2%), 2 years (23.2%), and 3 years (11.6%), which were significantly higher than in patients not undergoing operation (n = 22).

It is generally accepted that the principal route of hepatocellular carcinoma (HCC) dissemination is by the portal vein [1–5]. Intraportal spread of tumor thrombi is often encountered even in small HCC [6–8]. In advanced cases, the infiltrating tumor thrombi extends intraluminally toward the trunk and/or contralateral branches across the confluence. It is generally thought that liver resection is contraindicated in such patients, since complete removal of the malignancy cannot be accomplished. Transcatheter arterial embolization (TAE) is also contraindicated, since the portal flow is obstructed [9]. Consequently, in many patients with portal thrombi from advanced HCC, death results from the the rupture of the esophageal varices or hepatic failure. These appalling features of patients with tumor thrombus prompted us to perform tumor thrombectomy with hepatic resection as an emergency operation to decompress the portal vein pressure.

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During the past 5 years, we have performed this combined therapy in 29 patients with HCC. In the previous report, we discussed in detail the surgical techniques used in the removal of the portal vein tumor thrombi [10]. Since portal flow to the remnant liver was obtained after the removal of the portal thrombi, this condition further enabled us to perform TAE. Unexpectedly high survival rates of >1 year were obtained in half the cases in our present series and the longest survivor is now still alive >4 years postoperatively. This report discusses the significance and limitations of this operation relative to the clinical outcome of the long-term survivors.

Patients and Operative Techniques

Patients

During the past 5 years, from January, 1985 to April, 1990, we performed liver resection in 501 patients, including 298 patients with HCC. Among the latter number, there were 29 patients with portal thrombi treated by direct removal. Sixteen (55%) of 29 patients had liver cirrhosis and 6 (21%) others had chronic hepatitis as diagnosed by histological examination. That is, 76% of the patients in the present series had some form of chronic liver diseases in the background.

Another group of 22 patients with HCC with portal thrombi was selected from the same period in whom only conservative therapy such as sclerotherapy for esophageal varices was performed. These patients were designated as the non-operated group and were used to compare the survival rate.

The localization of the main tumors and the tumor thrombi are illustrated in Figure 1. In 16 patients the main tumors were located in the right lobe and in 13 patients in the left lobe. The tumor thrombi were confined in the first branch of the portal vein in 8 patients, extended to the confluence or trunk of the portal vein in 12 patients, and occupied the main trunk and extended across the confluence to the contralateral branches in the other 9 patients.

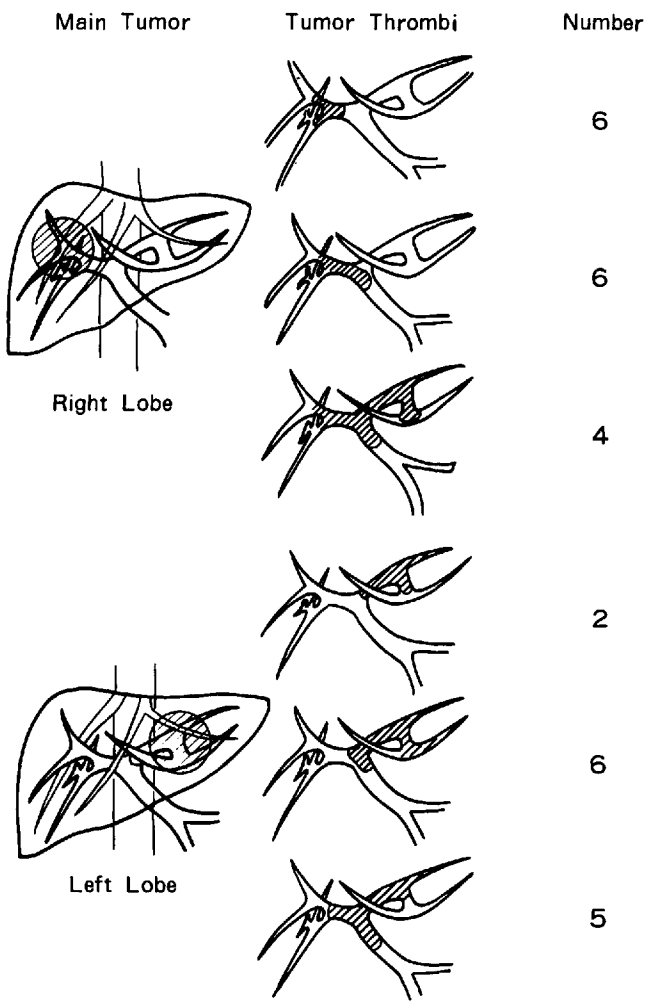

Fig. 1. Location of the primary tumors and tumor thrombi in the main branches of the portal vein.

Techniques for Removal of Tumor Thrombi

The operative techniques used are summarized in Figure 2. Some of them were previously reported [10].

Simple Hepatectomy Method (6 patients). If the tumor thrombi is wholly confined to the first branch of the portal vein, they are automatically removed when the portal vein is resected at the confluence using the conventional hemihepatectomy technique. Attention is focused at the time of portal vein occlusion not to nip the edge of the tumor thrombi, which would remain and spread in the portal flow to the other side.

Balloon Catheter Method (15 patients). After a balloon catheter (or Fogarty catheter) is applied to the portal vein, which is temporarily clamped, the tumor thrombi are removed by a spatula or suction through a window incised in the portal vein.

Bypass Method (3 patients). Bypass anastomosis is performed between the umbilical portion and the main portal trunk using an external iliac vein graft, with care taken to maintain the portal flow to the remnant liver during these procedures.

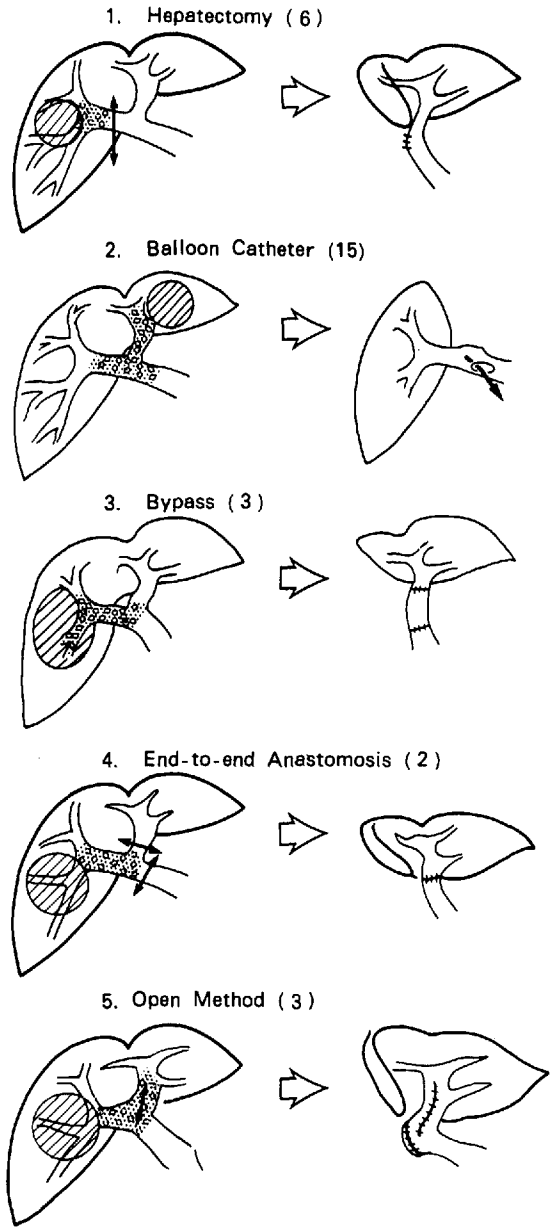

Fig. 2. Operative technique to remove the portal vein tumor thrombi and primary tumors. Figures in parentheses are number of patients undergoing this procedure.

Bypass between the P-point of the right portal vein to the portal trunk was performed in 1 patient. In these cases, the tumor thrombi are contained in the portal vein segment to be resected.

End-to-End Anastomosis Method (2 patients). When the tumor thrombi exists within a short segment of the confluence, they are removed by partial resection of the portal vein. This is done by temporary clamping the trunk and the first branch of the portal vein, before performing end-to-end anastomosis.

Open Method (3 patients). Under total vascular exclusion using an active pump-driven bypass (Biopump) from the portal vein and inferior vena cava area to the axillary vein, the portal vein

Table 1. Extent of liver resection for primary tumors and operative techniques for tumor thrombi.

Technique for removal of tumor thrombus	Extent of liver resection							
	Total	RT	ER	R	EL	L	Seg	M2
Simple hepatectomy	6	1	2	2	1	—	—	—
Balloon catheter method	15	—	2	3	2	4	3	1
Bypass method	3	1	1	—	—	1	—	—
End-to-end anastomosis method	2	—	—	—	—	2	—	—
Open method (Biopump)	3	1	2	—	—	—	—	—
Total	29	3	7	5	3	7	3	1

RT: right trisegmentectomy; ER: extended right lobectomy; R: right lobectomy; EL: extended left lobectomy; L: left lobectomy; Seg: segmentectomy; M2: resection of medial and anterior segment.

Table 2. Postoperative death within 30 days after operation.

Pt.	Age/ sex	Resection	Operative technique	Postoperative day	Complications
1	53 M	RT	Balloon	29	Pleural effusion; respiratory insufficiency
2	70 M	L	Balloon	27	Portal thrombus; liver insufficiency
3	58 M	R	Bypass	30	Liver insufficiency

See Table 1 for abbreviations. M: male.

Table 3. Major postoperative complications in 29 patients.

Complication	No. of pts.
Respiratory problems	6
Liver insufficiency	2
Intraabdominal bleeding	2
Bile leakage	1

is longitudinally incised to directly remove the tumor thrombus, and then closed with running suture of the vein. This method allows thrombectomy and hepatectomy without much blood loss [11].

Table 1 shows the extent of liver resection combined with extirpation of the portal thrombus. Most of the patients received major resections and resection of 1 segment was performed only in 3 cases.

Results

Postoperative Mortality, Morbidity, and Outcome

Three patients died within 30 days after operation, an operative mortality of 11% (Table 2). The first patient, a 53 year old male, had a large tumor in the anterior, posterior, and medial segment which invaded the confluence of both the portal vein and the bile duct. Thrombectomy with balloon catheter method was used combined with right trisegmentectomy and hepatoenteric anastomosis. Pleural effusion requiring respiratory support was observed on the fourth postoperative day. The patient died of respiratory insufficiency on the 29th postoperative day. The second patient, a 70 year old male, had a tumor which was localized in the left lobe. The tumor thrombi were removed from the confluence and trunk of the portal vein with a Fogarty catheter. The patient died of liver insufficiency on the 27th postoperative day due to the postoperative portal thrombi which were later confirmed by post-mortem examination. The third patient, a 58 year old male, had multiple tumors in the posterior segment and the tumor thrombi were removed with bypass method. Repeated portal clamping was done during operation to control intra-operative bleeding, but the bleeding continued postoperatively for 10 days. Bilirubin level increased gradually to a maximal of 37.5 mg/dl on the 21st postoperative day. The patient died of liver insufficiency on the 30th postoperative day.

By contrast, among the other 26 patients, uneventful postoperative courses were observed in 12 (46%) patients. Postoperative major complications including those observed in the above described patients who died within 30 days after operation are listed in Table 3. Respiratory problems such as pleural effusion and/or hypoxia requiring mechanical ventilation or pleural drainage were encountered in 6 (22%) patients in this series. Two of these patients died. Liver insufficiency was observed in 2 other patients. One was due to portal thrombus as described above, and the other patient had hyperbilirubinemia from the 10th postoperative day, even accepted oral intake, but died on the 35th postoperative day. Postoperative bleeding necessitating relaparotomy occurred in 2 patients. One patient deteriorated due to the multiple organ failure on the 47th postoperative day and the other patient tolerated subsequent subphrenic abscess and survived 474 days.

Figure 3 shows the cumulative survival curve of 29 patients in whom combined tumor thrombectomy and hepatectomy was performed in comparison to the non-operated group from the same period (n = 22). Half of the operated group died within 1 year after operation, but the others survived for significantly longer period than the non-operated group.

Pre-Operative Liver Function Tests

Pre-operative measurement of the tumor size, tumor markers, and other liver function tests are summarized in the Table 4. A comparison is made between the early recurrence group, in which patients died within 6 months, and the relatively long-term survivor group which lived >6 months. Tumor size was the only significant difference between the two groups.

Discussion

HCC has a noted propensity to invade the portal vein. The early intrahepatic spread of HCC via the portal vein, its main

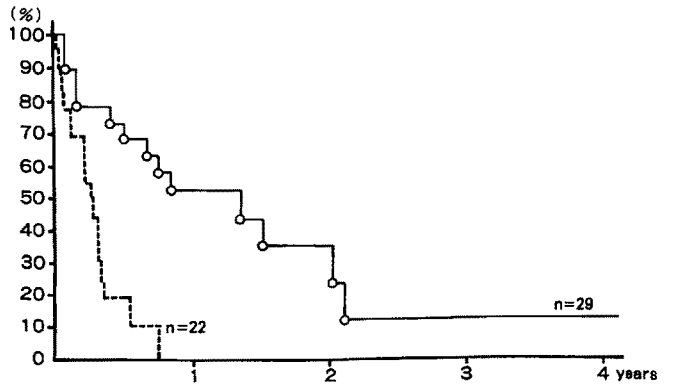

Fig. 3. Cumulative survival curves of patients with hepatocellular carcinoma. The solid line represents the operated group in this study, compared to the non-operated group represented by the dotted line.

Table 4. Pre-operative liver function tests comparing patients who died within 6 months and longer-term survivors.

Test (unit)	Patient survival	
	≤6 months	>6 months
GOT (IU/L)	111.8 ± 17.1	81.9 ± 9.4
GPT (IU/L)	57.4 ± 11.8	69.0 ± 10.4
ChE ($\times 10^2$IU/L)	1.85 ± 0.21	2.16 ± 0.26
Bil (mg/dl)	1.35 ± 0.15	0.83 ± 0.08
PTT (sec.)	12.7 ± 0.2	12.4 ± 0.2
Plt ($\times 10^9$/L)	15.2 ± 2.8	17.1 ± 2.7
Diameter of tumor (cm)	10.4 ± 1.6	6.8 ± 0.8 ($P < 0.05$)
AFP (ng/dl)	6095 ± 5672	4175 ± 3083

ChE: choline estelase; Bil: bilirubin; PT: prothrombin time; Plt: platelet; AFP: alphafetal protein.

drainage route, has been a major limiting factor in the indication for and the curability by resection [5, 8, 12]. Any attempt to remove the tumor thrombus or to resect the liver has generally been thought to be futile in such patients. Nagorney and coworkers [13], in their experience of 110 patients undergoing resection for HCC, reported a patient requiring tumor thrombectomy which ended in liver failure after a side-to-side portacaval shunt was done. Lin and colleagues [14], on the other hand, reported that it was possible to eliminate tumor thrombi from the portal vein surgically in 3 of their 207 patients who survived major hepatic resection.

It has been reported that the proliferation of tumor thrombi in the portal vein results in intrahepatic metastases as well as growth into the portal trunk [15]. Lin and associates [14] suggested that the relatively high mortality rate within 1 year of surgery is perhaps attributable to metastasis to the contralateral lobe via the portal vein. As to the relationship between the esophageal varices and tumor thrombi in HCC, it has been suggested that the occlusion of the main branch and trunk of the portal vein by tumor thrombus results in the creation of new arterioportal shunts which allow arterial blood to flow into the portal vein, thus accelerating the formation of varices and possibly triggering their rupture [15, 16].

Our attempt to remove the tumor thrombus was based on the assumption that if we could relieve the portal pressure, we would be able to prevent the fatal rupture of the esophageal varices. In all patients in the present series, we were successful in achieving decompression of the portal pressure which was monitored during surgery. Since no variceal bleeding was encountered postoperatively, we were satisfied that we had attained our primary goal of treating the impending rupture of esophageal varices. When we did a follow-up study of patients treated with TAE and percutaneous ethanol injection therapy (PEIT) [17] as postoperative adjuvant therapies, though, we noticed an unexpectedly large number of long-term survivors, hence we decided to do the present analysis of that patient population.

In the present study, the operative procedure adopted in each case varied. Bismush and coworkers [18] applied the balloon catheter method with intra-operative ultrasound to prevent the tumor thrombi from scattering to the other portal segments. We also used the balloon catheter method to prevent the dispersion of tumor thrombi to segments 2, 3, and 4 when the tumor thrombus extended toward the left branch from the right side of the portal vein. In this procedure, we inserted the balloon catheter into the umbilical portion of the portal vein and sprayed a saline solution from the catheter tip to drive the tumor thrombi out of the window incised in the main portal trunk. In patients with more advanced disease, however, we usually used a Fogarty catheter to remove the tumor thrombus [10, 19]. Bypass method is a reasonable approach since the remnant liver receives portal supply during liver resection and the tumor thrombus is contained in the portal vein segment to be resected. We also employed the open method since it is a relatively safe procedure with little blood loss even in patients with cirrhosis [11].

Hsu and colleagues [20] have suggested that tumor size is an important factor in determining the prognosis in patients with HCC, and that a tumor 5 cm in diameter should be regarded as distinguishing. They also pointed out that intrahepatic tumor invasion and intraportal spread were frequent and particularly extensive in patients with large diameter HCC. When the patients in this series were compared with regard to pre-operative parameters such as tumor size, tumor markers, and other liver function tests (Table 4), it was observed that the only significant difference that could be found was in tumor size, not in the other parameters examined. This finding would therefore suggest that the operative procedure described in the present report should not be applied to patients with huge tumors, even if they were deemed technically operable.

Of interest in the analysis of nuclear DNA contents measured by flow cytometry in another series of 34 patients with HCC in our clinic. This revealed that 61% (11 of 18) of the patients with aneuploid tumors had associated portal vein thrombi, which was significantly higher than the 6% (1 of 16) of patients with diploid tumors [21]. It is impossible to obtain pre-operative data by the present methods, however.

In conclusion, in order for the proposed operation to be accepted as a form of surgical treatment for HCC, not merely as an emergency life saving procedure, it is necessary to establish a pre-operative standard by which surgeons can distinguish between patients likely to have early recurrence from those likely to be long-term survivors.

Résumé

Lorsqu'il existe un thrombus dans la veine porte au cours d'un carcinome hépatocellulaire (CHC), l'exérèse est généralement déconseillée car le plus souvent la tumeur n'est pas enlevable chirurgicalement. Au cours de ces 5 dernières années, nous avons effectué une thrombectomie associée à une hépatectomie dans 29 des 298 cas de CHC. Cette attitude thérapeutique était, à l'origine, destinée à prévenir la rupture imminente des varices oesophagiennes plutôt qu'à améliorer la survie. Une fois la circulation portale a été ré-établie, l'embolisation par cathéter artériel et/ou par injection percutanée d'éthanol a été possible. Alors que l'amélioration de survie n'était pas le but initial de ce geste thérapeutique, et que la mortalité périopératoire a été de 11%, près de la moitié des patients ayant survecu la période périopératoire ont eu une survie significativement plus longue que les patients non opérés (n = 22): 52.2% à un an, 23.2% à deux ans et 11.6% à trois ans.

Resumen

Puesto que el trombo tumoral en la vena porta principal aparece en el estado terminal del carcinoma hepatocelular (CHC), cualquier esfuerzo destinado a removerlo por medios quirúrgicos se considera poco práctico teniendo en cuenta que la neoplasia no puede ser totalmente resecada. En el curso de los últimos 5 años hemos realizado la trombectomía tumoral combinada con hepatectomía en 29 de 298 casos de CHC. Esta modalidad de terapia combinada fue adoptada inicialmente como una medida de emergencia destinada a prevenir la ruptura de várices esofágicas, y no con miras a incrementar la sobrevida del paciente. El hecho de lograr flujo portal después de la remoción del trombo hace posible la embolización arterial por catéter y/o la inyección percutánea de etanol. Aunque el logro de una mayor tasa de sobrevida no constituyó el objetivo primario de la operación de emergencia y aunque se observó una mortalidad de 11%, la otra mitad de los pacientes en esta serie tuvo una inesperada mayor tasa de sobrevida a 1 año (52.2%), 2 años (23.2%) y 3 años (11.6%), cifras significativamente superiores a las del grupo de pacientes que no fueron operados (n = 22).

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