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Brief Note

Changes in Reticuloendothelial Function and Plasma Endotoxin Levels after Interventional Angiography

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Key words : reticuloendothelial system (RES) — endotoxin — interventional angiography — transcatheter arterial embolization (TAE) — partial splenic embolization (PSE)

Recently, advances and improvements in angiographic techniques and instruments have made performance of superselective angiography easier. In addition, there have also been improvements in pharmacological angiography, which is done using Prostaglandin E1. These improvements have enhanced the diagnostic value of angiography. Furthermore, angiography is also being widely used therapeutically. Comprehensively, this field of angiography is called interventional angiography (IA), and includes the following modes of antineoplastics : one shot intraarterial injection, balloon occluded intraarterial infusion, one shot intraarterial injection with lipiodol, continuous intraarterial infusion and transcatheter arterial embolization (TAE). Among these modes, TAE has had a marked effect on prolonging the life of patients with hepatocellular carcinoma (HCC). However, it may bring about hepatic failure in some cases of HCC with severe liver dysfunction. The author has previously described findings indicating the occurrence of a decrease in the function of the reticuloendothelial system (RES) and a reciprocal increase in plasma endotoxin levels after TAE and the disappearance of these signs/adverse effects in cases without hepatic failure 3 days after TAE, but their continuance in cases with hepatic failure even 7 days after TAE.[1] It was reported that the onset of hepatic failure after TAE might be associated with lowered RES function.[2] This study was intended to investigate changes in RES function and plasma endotoxin levels after IA to determine what factors lower RES function.

MATERIALS AND METHODS

The following seventy cases were included in this study : 6 cases undergoing hepatic angiography alone (4 with HCC complicated by liver cirrhosis and 2 with hepatic hemangioma); 4 cases undergoing one shot intraarterial injection of an antineoplastic (one shot) (3 with HCC complicated by liver cirrhosis and 1 with pancreatic carcinoma) ; 4 cases undergoing one shot intraarterial injection of an antineoplastic in combination with lipiodol (Lp one shot), all suffering from HCC complicated by liver cirrhosis ; 6 cases undergoing partial splenic embolization (PSE) (2 with liver cirrhosis, 3 with HCC complicated by liver cirrhosis and 1 with Budd-Chiari syndrome), and 50 cases undergoing TAE (45 with HCC complicated by liver cirrhosis and 5 with HCC).

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Seldinger's method was used for hepatic angiography. Doxorubicin 30 mg or cispiatin 50 to 100 mg was used for one shot. Lipiodol was used at a dose of 3 to 20 ml ; the antineoplastic used in combination with lipiodol was doxorubicin 10 to 50 mg. PSE was performed by inserting a catheter into the hilum of the spleen and using a gelatin sponge 1 to 2 mm square, to embolize about 70% of the spleen. TAE was performed by intraarterially injecting the antineoplastic and lipiodol and embolizing the hepatic artery with gelatin sponge particles, 1 to 2 mm square.

RES function was investigated by carrying out a lipid emulsion test (LET) according to the method of Kim *et al.*[3] Briefly, 10% lipid emulsion was injected intravenously (2 ml/kg), and then blood samples were collected 3, 6 and 9 minutes after injection. Next, the halftime ($T_{1/2}$) of the lipid emulsion was calculated, and then the phagocytic index (KLET) was computed using the formula KLET = log $2/T_{1/2}$.

Plasma endotoxin levels were measured by performing a quantitative limulus test (Toxicolor test®).

Computation of the KLET and measurement of plasma endotoxin levels were done before and 1 day, 3 days, and 7 days after IA.

The paired Wilcoxon's test was performed to determine whether there were significant differences.

RESULTS AND DISCUSSION

Serial changes in the KLET after IA are shown in Fig. 1. No significant change was noted after IA in this variable of cases undergoing hepatic angiography alone, one shot, or Lp one shot. In cases undergoing PSE or TAE, however, the KLET was significantly lowered 1 day after PSE or TAE and showed a tendency to recover with time.

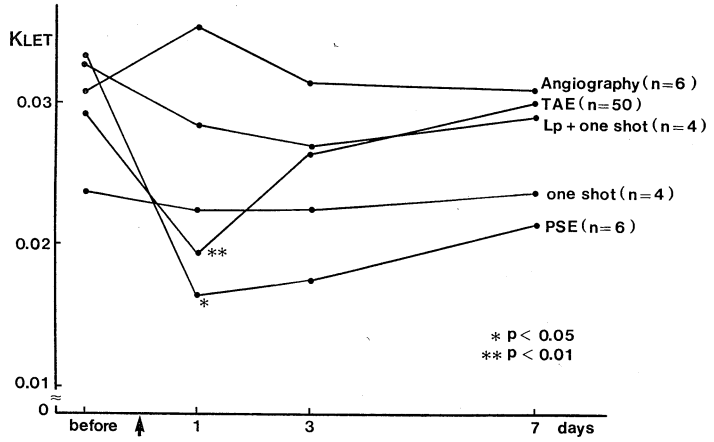

Fig. 1. Serial changes in KLET after interventional angiography.
one shot: one shot intraarterial injection of an antineoplastic
Lp+one shot: one shot intraarterial injection of an antineoplastic in combination with lipiodol
PSE: Partial splenic embolization
TAE: Transcatheter arterial embolization

The time courses of the plasma endotoxin levels are shown in Fig. 2. Like the KLET, this variable did not show any significant changes after IA in cases undergoing hepatic angiography alone, one shot, or Lp one shot. However, plasma endotoxin levels were significantly elevated on the first day after TAE or PSE and tended to be return to preteatment levels on the 7th day.

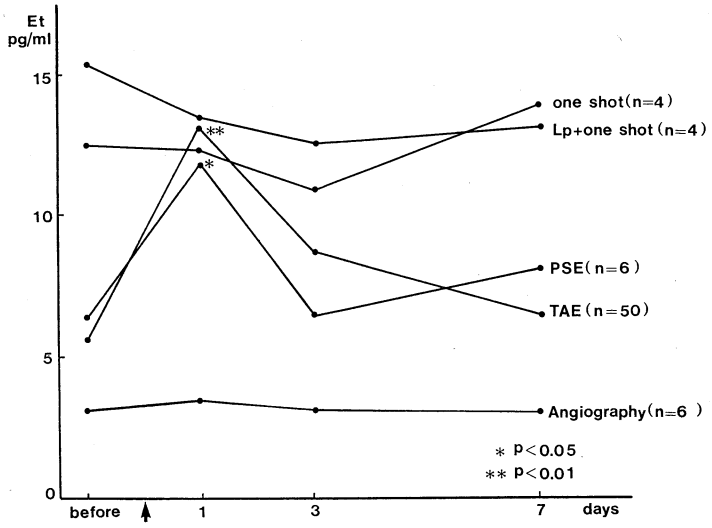

Fig. 2. Serial changes in plasma endotoxin levels after interventional angiography.
one shot: one shot intraarterial injection of an antineoplastic
Lp+one shot: one shot intraarterial injection of an antineoplastic in combination with lipiodol
PSE: Partial splenic embolization
TAE: Transcatheter arterial embolization

In this study, there were no significant differences in RES function or plasma endotoxin levels in cases undergoing hepatic angiography alone, one shot or Lp one shot in whom necrosis of tumors was hardly noted. On the other hand, a transitory decrease in RES function and a reciprocal increase in plasma endotoxin levels after PSE or TAE were noted.

PSE was devised by Spigos *et al.*[4] in 1979 to treat cases with hypersplenism. The splenic artery is a terminal artery. If it is embolized with a gelatin sponge particles, the splenic tissue becomes necrotic. Azuma *et al.*[5] reported that the KLET did not show any change after PSE. However, this finding was obtained when the KLET was measured more than 1 week after PSE. Changes in the KLET within 1 week after PSE were not investigated. On the other hand, the hepatic tissue is supplied by the hepatic arterial blood and the portal blood, while HCC is almost entirely supplied by the hepatic arterial blood. This means that HCC becomes necrotic after TAE.

The author previously pointed out that the decrease in RES function and the increase in plasma endotoxin levels on the day following TAE were more marked in cases with HCC who had largersized major tumors and reported that RES blockers produced from necrotic tumors might be responsible for the lowered RES function after TAE.[1] In this study, lowered RES function and

elevated plasma endotoxin levels were noted one day after treatment in cases who had tissue showing a necrotic change after PSE or TAE. These variables gradually returned to the normal range after that. Gut *et al.*[6] carried out a study on RES blockers using Frog virus 3 and reported that RES function was most greatly lowered 24 hours later and then tended to be restored. The results that we obtained from cases undergoing PSE or TAE were the same as the findings Gut *et al.* obtained.

All these findings suggest that RES blockers produced from necrotic tissue may be responsible for lowered RES function after PSE or TAE. Furthermore, the transitory elevation of plasma endotoxin levels only in cases with lowered RES function indicates that RES may play an important role in the disposal of endotoxin.

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