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2. Hepatic Circulation in the Experimental Allergic Hepatitis¹

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IN ORDER to clarify the pathogenesis of microcirculatory disturbances in the liver, hepatic changes of the rabbits were examined morphologically in the intravascular antigen-antibody reaction or anaphylaxis.

Based upon the Hamamoto's theory¹⁾²⁾ of "Intravascular Antigen-Antibody Reaction", anti-rabbit red cell guinea pig serum were injected intravenously through the hepatic artery and portal vein of rabbits in the reversed anaphylaxis.

In the active anaphylaxis, shock of the liver was induced experimentally by injecting the bovine erythrocytes into the hepatic artery and portal vein of the previously sensitized rabbits. Erythrocytic antigen were chosen as the most suitable antigen to produce intravascular antigen-antibody reaction, and Yoshimi³⁾⁴⁾ has reported on the histological changes in the liver which were induced by this reversed anaphylaxis, and the those of the active anaphylaxis were described by Shirasu⁵⁾.

The most severe histological changes in these reactions were as follows: a) parenchymal necrotic foci, b) various degree of degeneration of liver cells, c) serous inflammation, d) thrombosis, e) fibrinoid swelling of arterial walls.

No significant changes were found in the control animals.

For the purpose of clarifying the genesis of these parenchymal necrotic foci and degeneration of liver cells, the fibrin staining were carried out.

In general the thrombi were found in arterioles and sinusoid surrounding of necrotic foci. The fibrin thrombi in these cases are of a special nature and consist of strands of fibrin, in most instances occluding the lumen of the vessels.

It is suggested that the microcirculatory disturbances occur in this part and these intravascular fibrin deposition in hepatic arterioles is responsible for the necrosis and degenerations.

Then, an experiment was made to investigate these microcirculatory disturbances.

The 2% trypan blue solution was injected 3 hours after a single provocative injection of anti-serum, when permeable activity of the blood vessel walls had been increased most remarkable

Fig. 1. Showing hepatic changes of the experimental rabbits by injecting the dye after provocative injection (P.I.) of antiserum.

l: Accumulation of trypan blue dye in the liver. (arrow)

r: No accumulation of the dye. (arrow)

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TABLE I PERIODIC OBSERVATION OF THE HISTOLOGICAL CHANGES IN THE LIVER

	No.	Titer of the antiserum	Survival days	Route of the provocative injection	Parenchym							Glissons capsul							Capsel	
					Degeneration of hepatic cells	Dilatation of central vein	Dilatation of sinusoid	Serous inflammation	Massive necrotic lesion	Small necrotic foci	Megakaryocyte	Cell infiltration	Edematous swelling	Blood vessel						Thickening of wall
														Dilatation of vein	Hemor-rhage	Throm-bosis	Fibrinoid swelling of arterial walls			
I	411	32	90	<i>V. portae</i>	+	+	-	-	+	+	+	+	+	-	-	+	-	+	+	
	413	32	90	<i>A. hepatica</i>	+	+	-	-	+	+	-	+	+	-	-	-	-	+	+	
II	415	128	60	<i>A. hepatica</i>	+	+	+	-	+	+	+	+	-	+	-	+	-	+	-	
	418	128	60	<i>A. hepatica</i>	+	+	±	-	-	+	+	+	±	+	-	-	-	+	-	
	419	128	60	<i>V. portae</i>	+	+	+	-	+	+	+	+	+	+	-	+	+	+	-	
III	420	32	40	<i>A. hepatica</i>	±	+	+	-	-	+	+	+	+	+	-	+	+	+	-	
	421	32	40	<i>V. portae</i>	±	+	+	-	-	+	+	+	+	+	-	+	+	+	+	
	422	64	30	<i>A. hepatica</i>	±	+	+	-	-	+	+	+	+	+	-	+	+	+	+	
	423	64	30	<i>A. hepatica</i>	+	+	+	-	+	+	+	+	+	+	+	+	+	+	-	
	424	64	30	<i>V. portae</i>	+	+	+	-	-	+	-	+	+	+	-	+	-	-	+	
IV	426	64	15	<i>V. portae</i>	+	+	+	-	+	+	+	+	+	+	-	+	+	+	+	
				<i>A. hepatica</i>	+	+	+	-	-	+	+	+	+	+	-	+	-	+	+	
	427	64	15	<i>A. hepatica</i>	+	+	+	-	-	+	+	+	+	+	-	+	-	+	+	
	428	32	7	<i>V. portae</i>	+	+	±	-	-	+	+	+	+	+	-	+	+	+	+	
	429	32	7	<i>A. hepatica</i>	+	+	±	-	+	+	+	+	+	+	-	+	+	+	+	
	430	32	7	<i>A. hepatica</i>	+	+	+	-	+	+	-	+	+	+	-	+	+	+	+	

in the inflammatory area. The accumulation of injected trypan blue dye were found in the parenchymal necrotic foci in the liver of rabbits. And also, 2 % trypan blue solution was injected 4 days after the provocative injection of anti-serum, when parenchymal necrotic foci had been well developed. No accumulation of the dye was observed completely in the central area of large focal necrosis in the liver, but only microscopically the trypan blue dye was appeared in the sinusoid surrounding the necrotic foci.

In these animal experiments it was noted that hepatic damage could be recognized until 3 hours had elapsed after the provocative injection by promoting permeability of vessel walls, and that it made its development a few days after the provocative injection by formation of fibrin thrombi in arterioles.

Then 15 days after the granulation tissue with the giant cells were seen remarkably surrounding the large area of focal necrosis and fresh fibrosis were developed.

Ninety days after, the major changes were

remarkable fibrosis and the liver showed the post necrotic cirrhosis at least in part. But in other part of the liver lobules localized limited inflammatory processes were remained, and the cords of parenchymal cells were somewhat dissociated.

These hepatic changes above described resemble those of eclampsia⁶⁾ or generalized Schwartzman phenomenon⁷⁾ and are quite similar to those in the intravascular antigen-antibody reaction, particularly in reversed anaphylaxis.

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3. Studies on Action of Plasmin upon the Liver[†]

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SOME RESEARCHERS have reported that proteolytic enzyme, plasmin, played an important role in releasing of shock agents, and was highly activated in the state of shock or in allergic condition.

The author examined the pathogenicity of plasmin upon the liver tissue.

When plasmin extracted from dog's plasma following Shimizu's method was injected into the mesenteric vein of dog, firstly an ascent of portal vein pressure and then a descent of arterial pressure was observed. [Fig. 1]

Fig. 1.

When plasmin was injected into femoral vein a descent of arterial pressure was followed by an ascent of portal pressure.

Namely the results showed the same changes of the pressures as were observed in histamin-treated animals.

Histopathological examination of the liver was made.

Plasmotaxis in the central and portal vein was observed twenty-four hours after the injection of plasmin into the mesenteric vein.

Seventy-two hours after the injection, arterial thrombosis, partial destruction of the arterial wall, epithelial proliferation and swelling degeneration of the vascular wall was observed.

The development of spotty necrosis of parenchymal cells was recognized, but no massive necrosis was produced with the plasmin.

Under the electron microscope dilatation of

Fig. 2.

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