RELATIONS BETWEEN DISTURBANCES IN MICROCIRCULATION AND ACCUMULATION OF LIPIDS IN THE AORTIC WALL

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EXPERIMENTAL accumulation of lipids in the aortic wall varies from species to species^{1,2}. There is also the site of predilection in the aorta even in the same species³, though blood pressure and the constituents flowing in the aortic lumen are the same. This difference has recently been explained with disturbances in microcirculation in the aortic wall^{1,2,4}.

This work was done to study further the relations between disturbances in microcirculation and accumulation of lipids in the aortic wall.

MATERIALS AND METHODS

Thirteen rabbits weighing 2.4–3.4 kg were used. Nine of them were fed a 1% cholesterol and 5% coconut oil for either 2, 4, 10, or 16 weeks. Four rabbits were fed a normal diet as control up to 4 weeks.

The total serum cholesterol and body weight were measured at the beginning and the end of the experiment. After microangiography of vasa vasorum by the method reported previously⁵, the same specimens were stained with hematoxylin-eosin, elastica-Van Gieson, toluidine blue at pH 4.1 and 7.0, periodic acid-Schiff's reagent, phosphotungstic acid-hematoxylin and Mallory-Azan for histochemical study.

RESULTS

The total serum cholesterol increased to

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Predilection

300 mg/dl–1230 mg/dl in 2–16 weeks (Fig. 1). The body weight altered only slightly, however.

The vasa vasorum of the normal aortic wall were distributed to the outer coat of the media with a thin wall made up of 1–2 layers. The distribution of vasa vasorum in the normal abdominal aorta were less than that in the thoracic aorta. By microangiography, the vasa vasorum became less distributed and smaller in the diameter on sacrifice (Fig. 2), and the vasa vasorum were recognized in the middle portion of the media associated with thickening of the intima. In the adventitia and the periaortic tissue, intimal thickening and obstruction of vasa vasorum or lymphatics were observed partially. However, these lesions were limited, and little changes observed histologically in the greater part of vasa vasorum (Fig. 3).

An intimal thickening and a deposition of fat were observed initially in the portion branching from the aorta (Fig. 4), and lipids were then seen generally in the thickened intima and the inner media of the thoracic aorta after 4 weeks. In the abdominal aorta, these vascular lesions were mild in the proximal portion and scarce in the distal portion except for 2 after 10 and 16 weeks.

The aortic media decreased in thickness and numbers of the elastic lamina straightly in the distal direction, and was 40% of those in the ascending aorta in the distal portion of the abdominal aorta showing statistical difference (Figs. 5 and 6). The degree of intimal thickening was parallel with the medial thickness and numbers of the elastic lamina (Fig. 7 and Table I).

In the cross section of thickened intima, cells tended to be arranged radially and assume a long, slender shape with wide intercellular spaces

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Fig.1. Total serum cholesterol.

Fig.2. Microangiogram after 10 weeks fed a cholesterol and coconut oil.

Vasa vasorum are slender and tortuous. The arrow shows the distribution in the middle media with the intimal thickening. (Cross section. Original magnification: $\times 8$).
 L: aortic lumen. W: aortic wall. P: periaortic tissue.

Fig.3. No changes is seen in the vasa vasorum (arrow) of the outer coats after 16 weeks fed a cholesterol and coconut oil. (Sudan III stain. Original magnification: x200.)
A: adventitia. M: media.

Fig.4. Accumulation of lipids (↑) is observed in the portion of branching (↑↑) from the abdominal aorta after 10 weeks. (Sudan III stain. Original magnification: x50.)

(Fig. 8). In the inter cellular spaces, acid mucopolysaccharide was conspicuous by stain

with toluidine blue at pH 4.1 and 7.0, but the spaces were not stained with periodic acid-Schiffs

Fig.5. Thickness of the media in the each aortic part.
 ◐: Mean value with SEM.

reagent.

DISCUSSION

It is well agreed that the rabbit has a thin aortic wall, and that vasa vasorum are less distributed than those of humans or dogs^{2,6} The same findings were achieved in this experiment.

Jellinek et al. reported that disturbances in lymph drainage in the aortic wall might contribute to aggravation of arteriosclerotic lesions,

Fig.6. Numbers of the elastic lamina in the each aortic media.

◐: Mean value with SEM.

Fig.7. Thickness of the intima in the each aortic part.

The upper line shows the mean of 2 rabbits fed for 10 and 16 weeks presenting marked intimal thickening of the distal abdominal aorta. The lower line shows the mean of the other 7 rabbits.

TABLE I RELATION BETWEEN THICKNESS OF THE MEDIA OR NUMBERS OF THE MEDIAL ELASTIC LAMINA, AND THICKNESS OF THE INTIMA

	Thoracic aorta			Abdominal aorta		
	Ascendens (A)	Arch (B)	Descendens (C)	Proximal part (D)	Middle part (E)	Distal part (F)
Thickness of media (9 rabbits)	337±72	267±56	223±44	178±37	148±23	141±40
Decrease rate	100%	81.9±15.3%	69.4±15.9%	56.1±10.7%	48.3±10.1%	39.9±9.9%
Number of elastic lamina (9 rabbits)	23.2±4.3	19.8±1.8	18.4±2.5	15.0±3.4	12.8±1.4	10.1±1.6
Decrease rate	100%	85.6±10.8%	80.2±13.6%	67.6±13.4%	54.4±8.8%	40.2±6.6%
Thickness of intima (7 rabbits)	63±49	53±40	29±28	16±28	0	0
Decrease rate	100%	84.1%	46.0%	25.4%		
Thickness of intima (2 rabbits of 10 & 16 weeks)	208	120	113	93	70	35
Decrease rate	100%	57.7%	54.3%	44.7%	33.7%	16.8%

Mean of 7 or 9 rabbits in each group together with SEM.

Thickness of media [(A-C, D, E, & F), (B-D, E, & F), (C-E, & F): $P < 0.01$]. [(C-D): $P < 0.05$].

Numbers of elastic lamina [(A-D, E, & F), (B-D, E, & F), (C-E & F): $P < 0.01$]. [(C-D): $P < 0.05$].

Thickness of intima [(A-C & D), (B-C & D), (C-D): $P < 0.01$]. [(A-B): $P < 0.05$].

Fig. 8. Radial arrangement and long shape with wide intercellular spaces are seen in the inner coat after 10 weeks. The intercellular spaces are stained well with toluidine blue at pH 4.1. (Cross section. Original magnification: $\times 200$.)

based on the observation of lipids in the endothelial cells of the aortic lymphatics of rats fed an atherogenic diet.⁷ Changes in vasa vasorum observed by microangiography seemed to be caused by compression of the lipids deposited markedly in the periaortic tissue, because the changes were histologically mild in the greater part of vasa vasorum and periaortic lymphatics. So, it was not thought that the disturbances in vasa vasorum and lymphatics could become a trigger of early deposition of lipids in this series, though, in former experiments, accumulation of lipids occurred easily in the aortic wall of which the vasa vasorum had been disturbed previously.^{5,8}

Edematous thickening of the intima and radial arrangement of the intimal cells have usually been observed in the early phase of arteriosclerosis.⁹ The same findings were achieved in the thickened intima where vasa vasorum did not reach the middle and inner media, but no radial arrangement was seen in the thickened intima where vasa vasorum were observed in the middle part of the media. It suggested that a radial arrangement of intimal cells with wide intercellular spaces should be very convenient for the passage of fluids toward the outer coat, and that the permeability should be increased in the region.

There are many reports that the permeability increases with cholesterol and that arteriosclerotic lesions develop rapidly in the region with high permeability.^{3,10,11} An increase in permeability with cholesterol should be similar in the intimal surface, and an influx of plasma constituents into the wall should occur similarly, but there are marked differences in accumulation of lipids between different aortic regions. The intimal permeability and the degree of flowing-out of fluids from the wall differ in the site of aorta due to difference in the thickness of wall, arrangement of cells, intramural pressure and intramural P_{O_2} which is carried directly through its lumen or via vasa vasorum.¹²⁻¹⁶

From the above facts, it may be reasonable to presume that disturbances in microcirculation occurred in the aortic wall and the difference in the severity resulted in the difference in the site of predilection for accumulation of lipids.

SUMMARY

For the purpose of unraveling the relations between disturbances in microcirculation and deposition of lipids in the aortic wall, 9 rabbits

were fed a 1% cholesterol and 5% coconut oil at intervals up to 16 weeks, and 4 rabbits were used as controls. After microangiography of vasa vasorum, the same specimens were studied histochemically.

The distribution of vasa vasorum became poorer on sacrifice by microangiography. However, it could not be thought that disturbances in vasa vasorum was a cause in the early deposition of lipids, because lesions were histologically mild in the greater parts of vasa vasorum.

The sites of predilection for the vascular lesions were initially the branching part, and then the thoracic aorta. Thickness and numbers of the elastic lamina in the media decreased straightly in the distal direction, and the degree of intimal thickening and accumulation of lipids were parallel with the degree of the medial thickness. The intimal cells tended to be arranged radially with wide intercellular spaces in the cross section, suggesting the convenience for the passage of fluids.

From the above facts, it may be reasonable to presume that the difference in severity of disturbances of microcirculation resulted in the difference in the site of predilection.

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