Morphological Studies on Atherosclerotic Changes in Swine

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Abstract. Morphological studies on atherosclerotic lesions were carried out on 50 cases of slaughtered swine. Intimal elevations and fibrous plaques were notable in elastic vessels. Intimal elevations revealed hemispherical protuberance of the intima macroscopically, and a tendency to occur in young swine. Histologically, the elevations represented an increase of mesenchymal elements and occasionally hyperplasia of smooth muscle cells in the intima. Large grubular cells were also observed occasionally. The fibrous plaques were observed in old swine, and revealed roughened intimal thickening macroscopically. They were prominent in elastic hyperplastic thickening and extracellular lipid accumulation in the intima histologically. In the muscular vessels, fatty streaks and fibrous plaques were notable. Fatty streaks were recognizable in the intima of abdominal aorta in younger swine and also other main arteries of rather old one, and represented slight intimal thickening macroscopically. The lesions were composed of an increase of mesenchymal elements in the intima histologically. Fibrous plaques were noted in the intima of abdominal aorta and a few arteries of rather old swine. The lesions were irregularly thickened in the intima macroscopically. Elastic hyperplastic thickening, fat deposition and calcification were histologically noted.

Atherosclerosis, generic term for arterial thickening, has been occurred in many species of domestic animals [7]. The terms, intimal elevations [9], gelatinous elevations [9], fatty streaks [1, 4, 9, 16], fibrous plaques [1, 9] and atherosclerotic plaques [16] were in general use to express atherosclerotic lesions in swine. However, there were no established coincidence between morphologically morphological and histological classifications and the terminology. The occurrence of the disease in swine was estimated to be closely associated with the dietary composition ingested or an advancing in age [1—3, 8, 10—13]. Moreover, atherosclerotic lesions were dominantly recognized in thoracic and abdominal aortas and coronary, brachiocephalic and iliac arteries [1, 2, 4, 5, 8—13, 16].

The present report deals with histopathological examination on atherosclerotic lesions of main vessels in 50 cases of swine. The purpose of this paper is to investigate the distribution and classification of the lesions, and to discuss on pathogenetic correlation among the lesions.

Materials and Methods

Blood vessels from slaughtered swine of 50 cases were used for the present studies, which were 3 males and 47 females of Landrace crossbreed, and obtained in routine meat inspection at Kitakami abattoir during a period March 1975 through March 1977. The examined cases were well nourished and revealed no clinical symptoms except 5 cases of paralysis. They were also composed of one case in one year old, 12 in 2 years, 8 in 3 years, 14 in 4 years, 5 in 5 years, 9 in 6 years and one in 7 years.

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豚の動脈硬化性変化に関する形態学的研究：伊藤澤夫・藤田紀弥（盛岡保健所食肉衛生検査所）
years, respectively. Aortas and main arteries of large caliber, which were removed from the carcasses, were fixed in 10% solution of formalin after macroscopical observation, dissecting along the longitudinal direction. The materials of some cases were stained with the gross stain, oil red O, to find out easily atherosclerotic lesions before the fixation. On the other hand, slender arteries which were fixed together with each organ were observed on transverse sections by dissecting microscope. Paraffin sections were made and stained with hematoxylin and eosin, toluidine blue, azan, orcein, aldehyde fuchsin, azan, Gomori's silver impregnation, alcian blue, periodic acid Schiff (PAS), phosphotungstic acid hematoxylin, Kossa and Prussian blue. Moreover, carbowax or gelatin sections made from some regions of each case were stained with oil red O.

Results

1. Gross observations

Elastic vessels

Brachiocephalic trunk and thoracic aorta: Intimal elevations, focally whitish hemispherical protuberance, were noted in the intima of young swine. The lesions were abruptly moulded from the intima, and their surfaces were smooth. They were spindle in shape and 2 to 5 mm in size. They amounted to about 10 in the vessels frequently. The lesions were faintly stained about the basis of them by the gross stain (Fig. 1). On the other hand, fibrous plaques, irregular intimal thickening with roughened surface, were also recognized in above vessels and the ostium of left brachial artery of an aging swine. The lesion was also reddish in the gross stain.

Muscular vessels

Abdominal aorta: Fatty streaks, slightly linear thickening in the intima, were whitish or pale yellowish in color. The lesions were several millimeter in width and a few to several centimeter in length. They revealed reddish color in the gross stain distinctly. These lesions were noted in younger cases. They were frequently occurred around the branching orifices of the aorta and most in the distal half of the organ. On the other hand, fibrous plaques were found in several cases of aging one. The lesions represented irregularly roughened and thickened intima. The lesions were stiff in dissection and reddish color in the gross stain (Fig. 2). They were dominantly developed in distal half of the organ and specially about the orifice to the trifurcation.

Arteries: Fatty streaks, linear or ovoid thickening of intima, were sharply stained with the gross stain, which were dominant in external and internal iliac arteries of younger swine (Fig. 3). The linear streaks were also seen in coronary, hepatic, splenic, renal, lingual, gastro-duodenal, pancreaticoduodenal, and anterior mesenteric arteries in the observations using dissecting microscope. Fibrous plaques were noted in external and internal iliac arteries of aging swine. Focally mineralized areas were also recognized in right external iliac artery of two cases, which were a soybean in size, opaque in color and stiff in the dissection.

2. Histological findings

Elastic vessels

Intimal elevations revealed focal thickening of intimal cushion. They were composed of the meshworks of fine collagens and fragmented elastic materials. Foam cells containing lipid droplets were also dispersed. Large globular cells were also observed densely or dispersedly. These cells possessed pyknotic nucleus, and contained coarse granules which were hematoxylinophilic, bluish in azan stain and positive in alcian blue and PAS stains (Fig. 4). Further, the elevations composed of elastichyperplastic or conspicuous musculo-elastic layer were also recognizable in some cases (Fig. 5). In these lesions, large globular cells were unrecognized. On the other hand, fibrous plaques, irregularly thickened
intima, were developed with an advance of age. Typical fibrous plaques were recognized in brachiocephalic trunk, thoracic aorta and the ostial region of left brachial artery in old swine over 5 years old. The intima was composed of beaded elastic elements and meshworks of collagens. Proliferation of smooth muscle cells was less prominent (Fig. 6). Cholesterol crystal clefts were also dispersed in the region of the intima adjacent to the media. Foam cells with lipid and an accumulation of extracellular lipid were also noted in the basal area. Mucopolysaccharide stained with alcian blue was observed in fibrilar meshwork and smooth muscle cells of the lesion.

Muscular vessels

Abdominal aorta: An initial lesions of fatty streaks represented a focal slight thickening of the intima, in which beaded elastic fragments and an increase of mesenchymal elements were noted (Fig. 7). Mucopolysaccharide was precipitated in fibrilar matrix. Elastica interna was linear, fenestrated or disappeared. Lipid deposition occurred in foam cells and fibrillar matrix. Mononuclear cells and fibroblasts were occasionally present. Smooth muscle cells were also gradually increased with an advance of lesions. Fibrous plaques revealed prominent collagenization and fat precipitation in the intima (Fig. 8). In severely advanced plaques, endothelial cells were fragmentary, necrotic or absent occasionally. The intima showed a well-developed elastic-hyperplastic layer, but a distinct separation from muscular-elastic layer was rarely seen. The intima was composed of much collagens, fragmentary elastic fibers and fat droplets. Foam cells and mononuclear cells were dispersed. Proliferation of smooth muscle cells was observed in medial and basal regions of the intima. Mucopolysaccharide was faintly accumulated in superficial and basal regions of the intima. Elastica interna was swollen, fragmentary or disappeared. Mineralization was recognized in the intimal media, the base adjacent to the lamina, and occasionally the lamina itself (Fig. 9). Mineralized area was stained with Kossa's and PAS stains. Mucopolysaccharide was co-existent in the area densely. Cholesterol crystal clefts appearing needle-like vacuoles were also observed in adjacent regions to the lamina occasionally. The intima of the ostia branched to the iliac arteries revealed severe fibrous thickening frequently.

Arteries: Fatty streaks were most frequently noted in external and internal iliac arteries, and represented slight thickening of the intima, in which beaded elastic fibers and fine collagens and occasionally foam cells were observed. Mucopolysaccharide was notable in fibrilar matrix. Elastica interna was linear or fenestrated. Smooth muscle cells were increased in the intima with the advance of lesion and formed occasionally musculo-elastic layer. Extracellular lipid was also seen. Fatty streaks of coronary artery revealed irregular thickening of the intimal cushion. Elastic-hyperplastic layer or a thinly zonal arrangement of beaded elastic elements were newly formed in subendothelial area. Collagenous meshwork and dispersed elastic fragments were also noted. Moreover, musculo-elastic layer, zonal proliferation of smooth muscle cells, was frequently noticed. Inner limiting lamella of elastic element was also formed on this layer frequently. Elastica interna was linear, fragmentary or disappeared (Fig. 10). Mucopolysaccharide was recognized in fibrilar matrix and muscle cells. Extracellular lipid was rarely present. Both layers were developed with an age, but they did not accompany with
severe fat accumulation, collagenization and calcification in any cases. Other main arteries as hepatic, splenic, renal, lingual, gastroduodenal, pancreatino-duodenal, uterine and anterior mesenteric arteries showed also similar findings to above coronary artery. Fatty streaks of arteries of the brain were observed in basilar and anterior coronal artery, posterior communicating artery of internal carotid artery, artery of corpus callosum, middle cerebral artery and interior meningeal artery of aged swine (Fig. 11). Generally, the occurrence of elastic-hyperplastic layer was less obvious, but musculo-elastic one was remarkable. Mucopolysaccharide was prominent in fibrilar meshwork and muscle cells.

Fibrous plaques were recognizable in external and internal iliac arteries of many cases over 5 years old. Intima was thickened and revealed elastic-hyperplastic thickening (Fig. 12). Smooth muscle cells and foam cells were also numerous present. Inter-cellular and extracellular lipid were noted. Mucopolysaccharide was faint frequently and dense occasionally in collagenous meshwork. Elastica interna disturbed the original arrangement. Calcification and cholesterol clefts were noted in the inside of elastica interna. Right external iliac artery of two cases of 5 years old was severely calcified. Calcified lesion was present in the area including the intima and media, in which medial atrophy was noted (Fig. 13). The lesion was covered with necrotic, edematous and swelled collagenous matrix. Mucopolysaccharide was densely coexistent in the lesion which was circumscribed with lipid.

**Discussion**

Atherosclerotic lesions in 50 cases of slaughtered swine were histomorphologically investigated in the present studies. The lesions were divided into intimal elevations and fibrous plaques in elastic vessels, and fatty streaks and fibrous plaques in muscular vessels from the gross findings.

Intimal elevations [9] were unique in gross findings, and also termed hemispherical pinhead-sized plaques [11], small raised spots or streaks [4] or fatty streaks [16]. The lesions were noted in the intima of elastic vessels of swine alone, but not in that of other animals [9]. They were also differentiated into two kinds histologically [4]. The pathogenesis was unknown [9]. In the present studies, the lesions were characteristic in gross findings. A variety was also seen in the structure of the lesion in the histological findings. The lesions were essentially composed of fibrilar meshwork, and rarely accompanied with prominent musculo-elastic layer. Frequently, large globular cells were noted in the lesion without prominent musculo-elastic layer. Further, large globular cells were also termed as globular cells [4] or foam cells [11]. The similarity to monocytes [4] or granular cell myoblasts [9] was pointed out. In the present studies, the cells were different from foam cells in their cytological characteristics. The cells were found out in elastic vessels alone, and in an initial lesion of younger swine. The cells should be a kind of macrophage from cytological findings. On the other hand, fibrous plaques in elastic vessels revealed remarkably elastic-hyperplastic thickening, which were lacking of large globular cells and less prominently accompanied with proliferation of muscular cells. Moreover, it was suggested that some of the intimal elevations should be transformed to fibrous plaque.

Although it is very difficult to differentiate clearly between fatty streaks and fibrous plaques, the term, fatty streaks was applied to any macroscopic lesion in the intima.
stained distinctly by fat-soluble dye [1]. Fibrous plaques were also applied to any firm, elevated intimal lesion in gross findings, which was pale gray, glistening and translucent [1]. Moreover, fatty streaks were defined as an early atherosclerosis, and fibrous plaques were a successive change from the streaks [1, 7, 16]. In the present studies, fatty streaks revealed a tendency to occur in young cases and fibrous plaques in aged one. These lesions were frequently coincident in anatomical topology of the occurrence of them.

Histologically, fatty streaks were composed of collagens, elastic fibers, smooth muscle cells, mucopolysaccharide and fat [7]. Fibrous plaques were accompanied with severe collagenization and fat deposition [7]. On the other hand, initial changes of atherosclerotic lesions were set out in the disturbance of elastica interna. The formation of beaded or fragmentary elastic tissue and occurrence of smooth muscle cells were noted in the intima [5]. Musculo-elastic and elastic-hyperplastic thickenings were occurred as the succeeding change to above findings [4, 5]. The latter was developed on the superficial layer of the former [5]. In the present cases, atherosclerotic lesions were different with advance of lesions. Intimal changes of fatty streaks in coronary and slender arteries were prominent in well developed musculo-elastic layer which were clearly separated from elastic-hyperplastic layer. Further, fibrous plaques in the vessels with large diameter were noticeable in development of elastic-hyperplastic layer and severe accumulation of fat in the intima. In these vessels, formation of musculo-elastic layer was less distinct that clear separation in elastic-hyperplastic layer from the layer was not obvious.

Fibrous plaques were divided into physiologic sclerosis (uncomplicated intimal sclerosis) and complicated intimal sclerosis (early human artherosclerosis) [2]. The atherosclerosis in swine was almost under the category of the former, but the latter was rarely noted in an experimental case of miniature swine 38 months old [2], and a sow of large white breed [5], and naturally occurring case of 36 months old and 7 years old sow [8]. In the present studies, severe fat accumulation, calcification and cholesterol deposition were also found out in some cases. However, atheromatous gruel or thrombotic fibrotic calcified ulcerated plaque as usual in human [7] was unrecognizable.

Histochimically, mucopolysaccharide and intercellular and extracellular accumulations of lipid were noted in the intima of atherosclerotic lesions [2, 4, 5, 9–11, 14, 15]. Intercellular lipid accumulation was noted in foam and muscle cells and macrophage [4]. The foam cells, termed also as Langhans’ cells [2], were originated from smooth muscle cells [2, 11, 14, 15], monocyte [3, 17] or macrophage [18], which were took part in fibrosis [2] and elastic and reticulin formation [11]. In the present cases, mucopolysaccharide was also observed in the intima of atherosclerosis characteristically. The accumulation of lipid was recognized in foam and muscle cells, and fibrillar matrix of the intima.

As to the distribution of the lesions, thoracic [2, 4, 5, 8–13, 16] and abdominal [2, 5, 6, 8, 10, 12, 13] aortas, brachiocephalic trunk [2, 6, 11, 16] and coronary [1, 2, 4, 5, 8–11, 13, 16] and iliac [2, 9, 11, 16] arteries were dominantly affected, and bronchial [12], intercostal [4], left brachial [2, 11], splenic [12], uterine [11], cerebral [11] and renal [12] arteries rarely. Moreover, the lesion was apt to occur initially in the region of the aortic valve ring, lesser carvature of the aorta, base of the great vessels
of the head and neck, about intercostal vessels, and orifices and trifurcation of the aorta [3]. In the present studies, atherosclerotic lesions were observed in aortas and many main arteries. Moreover, it should be noticeable that the lesions were observed in lingual, gastro-duodenal, pancreatico-duodenal and mesenteric arteries. Further, the lesions originated initially in abdominal aorta, brachiocephalic trunk and thoracic aorta, and specially in the bifurcations and trifurcation of the organs. They spread over other arteries with the advance of age.

References


Explanation of Figures

Fig. 1. Intimal elevations (arrows) in thoracic aorta. Oil red O stain.

Fig. 2. Fibrous plaque of abdominal aorta and external and internal iliac arteries. Oil red O stain.

Fig. 3. Fatty streaks (arrows) in right external iliac artery. Oil red O stain.

Fig. 4. Intimal elevation in thoracic aorta. Large globular cells (arrow) are noted numerously. Hematoxylin and eosin stain (H-E), ×320.

Fig. 5. Intimal elevation in thoracic aorta revealing prominent musculo-elastic thickening. H-E, ×120.

Fig. 6. Fibrous plaque of thoracic aorta. Elastic-hyperplastic thickening is recognized in intimal cushion. Azan stain, ×100.

Fig. 7. Fatty streak of abdominal aorta. H-E, ×240.

Fig. 8. Fibrous plaque of abdominal aorta. An accumulation of fat droplets is observed. Oil red O and hematoxylin, ×90.

Fig. 9. Fibrous plaque of abdominal aorta. Elastic-hyperplastic thickening and calcification are present. H-E, ×170.

Fig. 10. Fatty streak of coronary artery. Musculo-elastic layer is prominent. Aldehyde fuchsin and H-E, ×60.

Fig. 11. Fatty streak in basilar artery in the brain. Musculo-elastic thickening is remarkable. Aldehyde fuchsin, alcian blue and hematoxylin stain, ×50.

Fig. 12. Fibrous plaque in left external iliac artery. An increase of collagen is prominent in the intima. Azan stain, ×160.

Fig. 13. Fibrous plaque in right external iliac artery. Calcified plaque is prominent in the area including the intima and media. Peripheral area of the plaque is necrotic and edematous. Aldehyde fuchsin, alcian blue and hematoxylin stain, ×35.