HISTOLOGICAL STUDY ON THE VASCULAR NERVE IN DIABETIC RABBITS

by

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I. INTRODUCTION

Diabetic gangrene is observed in about 27 per cent of all diabetic patients according to HOWARD. It usually attacks peripheral parts of the body in the form of wet gangrene. This gangrene is characterized by a predisposition to infection, unsatisfactory demarcation and unfavorable prognosis.

Until recently, sclerotic occlusion of the peripheral arteries was believed to play a prominent role in the occurrence of diabetic gangrene. However, recent results of autopsies (HART, J, F.) and of animal experiments (DUFF, ALLEN, JONES, NAKAMURA, MUGITANI and others) failed to corroborate any relationship between arteriosclerosis and diabetes.

On the other hand, many studies (KESTERMANN, VOGT, HIRAYAMA, ITAYA and others) have shown a decreased resistance of diabetic patients and animals against infection. Also, MUGITANI has mentioned recently that infection is the principal cause of diabetic gangren in rabbits.

Various types of gangrene are caused by functional disorders of peripheral blood vessels. RAYNAUD's disease is known to be due to increased vasospasm. However, decreased vasocontraction in diabetes was described by MUGITANI in pharmacological experiments on rabbits with Alloxan diabetes (1957). To further investigate this vasoconstrictor disturbance, histological studies on the vascular nerves in diabetic rabbits were performed by the present authors. The results were as follows.

II. PRODUCTION OF DIABETES IN RABBITS

The experiment was performed using Alloxan diabetic rabbits. The method of producing diabetes was as follows. Adult male rabbits were used. After 12 hours fasting, 5 per cent Alloxan monohydrate (EASTMAN KODAK Co. Ltd.) solution was injected intravenously in the dosage of 200 mg per kg. The blood sugar of rabbits increased to a high concentration (average 300 mg/dl) several hours after injection, but thereafter suddenly fell to hypoglycemic levels leading to generalized convulsions. The convulsing rabbit was immediately injected with 20 per cent glucose solution in order to protect it from hypoglycemic death. This generalized convulsion was repeated several times during an 8 to 10 hour interval. Twenty-four hours after

injection of the Alloxan solution, the blood sugar resumed a high concentration of from 300 to 550 mg/dl. And then this hyperglycemia continued for a long time. Six rabbits which had Alloxan diabetes for 2 to 6 monthes were used in this experiment.

III. HISTOLOGICAL FINDINGS OF VASCULAR NERVES IN NORMAL AND DIABETIC RABBITS

Various tissue fragments (aorta, ventricle, large and small intestine, spleen, liver and ears of normal and diabetic rabbits) were fixed in 20 per cent neutral formalin solution. After fixation for several monthes, these tissues were sectioned from 35 to 40 microns thick and impregnated by a modified BIELSCHOWSKY's method (silver carbonate method of JABONERO).

I) Nerve fibers of capillary veins

In normal rabbits, capillary veins are frequently accompanied by nerve fibers or a nervous syncytium (Fig. 1). However, these fibers rarely twine around veins, and sometimes run to other tissues.

Also, in diabetic rabbits, as can be seen in Figs. 2 and 3, the vascular nerves of capillary veins are similar to those of normal rabbits. Degeneration is never recognized in the fibrous or cytoplasmatic components of the nervous syncytium.

2) Vascular nerves of small blood vessels

In normal rabbits, nerve fibers following small blood vessels are thicker in diameter and more dense in distribution than those following capillaries (Fig. 4, 5, 6, 7 and 8). Sometimes, a few branches of nerve fibers run into the walls of vessels. Therefore, it may be supposed that there are nerve fibers which innervate muscles of small blood vessels.

In diabetes, the nerves of small blood vessels are quite similar to those in normal rabbits. No abnormal conditions are found (Figs. 9, 10, 11 and 12).

3) Vascular nerves of the aorta

In the adventitia of the aorta of normal rabbits, nerve fibers are found which run transversely (Fig. 13) or longitudinally (Fig. 14). Nervous syncytia are abundant, too (Fig. 15). In the media a few nerve fibers run perpendicular (Fig. 16) or parallel (Fig. 17) to the smooth muscle fibers and elastic fibers. The distribution of nerve fibers mentioned above is almost the same as that reported by KIMURA and CHENG (1956).

In diabetes, nerve fibers and syncytia in the wall of the aorta maintain a normal appearance (Figs. 18, 19 and 20).

IV. SUMMARY AND CONSIDERATIONS

In this experiment, the author studied the vascular nerves of Alloxan diabetic rabbits. Heretofore, numerous histological studies on the innervation of blood vessels have been performed by many authors, namely STOEHR jr., BOEKE, JABONERO and others. As for the vascular nerves in normal rabbits, on the whole, results of their studies agree with the findings of the author.

Capillary veins, arterioles and venules are frequently accompanied by fine nerve fibers or nervous syncytia. But these nerves cannot be considered as proper equipment for blood vessels. It seemed that under these circumstances the nervous supply was common to blood vessels and neighbouring tissues.

In the case of small blood vessels which have a smooth muscle layer, a few branches of nerve fibers sometimes run into the vessel wall. Therefore, small blood vessels may be influenced both by their own innervation and by a common nervous supply with other tissues.

In the wall of the aorta, especially in the media, reticular nerves are recognized, as reported by KIMURA and CHENG. On the other hand, nervous syncytia are observed in abundance in the adventitia, though extremely scanty in the media. So it may well be that the wall of the aorta is particularly innervated by its own nervous supply.

The author wished to prove some degeneration of vascular nerves in rabbits afflicted with severe diabetes for 2 to 6 monthes. Contrary to expectations, vascular nerves in diabetes are completely similar to those in normal rabbits. No changes in nerve fibers, such as swelling, severing, atrophy or appearance of granules and vacuoles etc., were ever recognized. In addition, no degenerations of SCHWANN's cells or interstitial cells could be demonstrated. Thus, vascular nerves in diabetic rabbits are not degenerated, at least morphologically.

V. CONCLUSION

The author confirmed that the vasoconstrictor disturbance in diabetes is not based upon morphological changes of vascular nerves.

I am much indebted to Assist.-Prof. Dr. CHUJI KIMURA for his kind guidance throughout this experimental study.

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和文抄録

実験的糖尿病家兎に於ける血管神経末梢の組織学的研究

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糖尿病性壊疽に関する麦谷の実験的研究 (1957年) によれば糖尿病に際しては Raynaud 氏病の場合とは異なり，血管攣縮性が低下し壊疽発生に対しては，むしろ抑制的に作用することが認められた．

著者は2～6ヵ月間罹患し，血糖値が常に250～500 mg/dl の高血糖を持続した重症の Alloxan 糖尿病家兎を用い，その 1) 毛細血管， 2) 血管筋を有する小血管， 3) 大動脈を各々支配する末梢神経を Bielschowsky-炭酸銀法 (Jabonero 氏法) により染色し，正常家兎のそれと比較検討した．その結果，糖尿病家兎の血管支配神経は正常家兎のそれと較べ，支配形式分布密度に差はなく，また神経線維自身にも膨化，断裂，萎縮，顆粒変化，空胞出現等の異常所見を認めなかった．また更に Schwann 氏細胞， interstitielle Zellen 等の細胞成分にも全く変化を見出し得なかった．

即ち糖尿病に際しての血管攣縮性障害は血管神経末梢の形態学的変化を伴わないことを確認した．

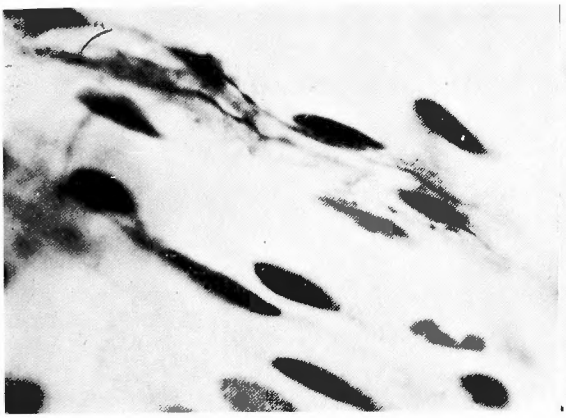

Fig. 1 Nervous syncytium and capillary veins in the ear of a normal rabbit. 95 × 10

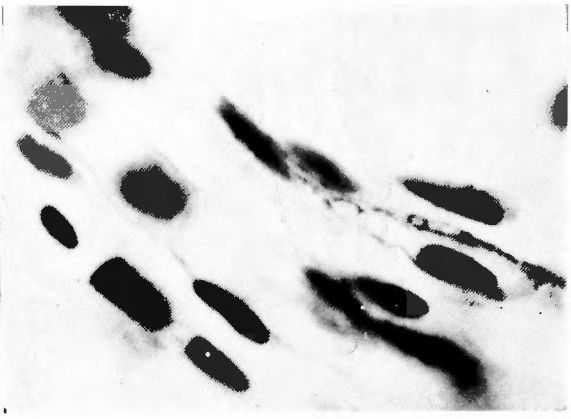

Fig. 2 Nervous syncytium and capillary veins in the ear of diabetic rabbit. (6th month) 95 × 10

Fig. 3 Nervous syncytium and capillary veins in the wall of the colon of diabetic rabbit. (6th month) 95 × 10

Fig. 4 Small artery with fine nerve fibers in the submucous tissue of the colon of a normal rabbit. 95 × 10

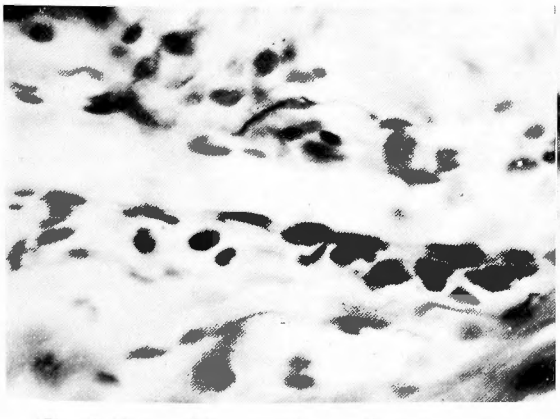

Fig 5 Nerve fibers and small artery in the ear of a normal rabbit. 42 × 10

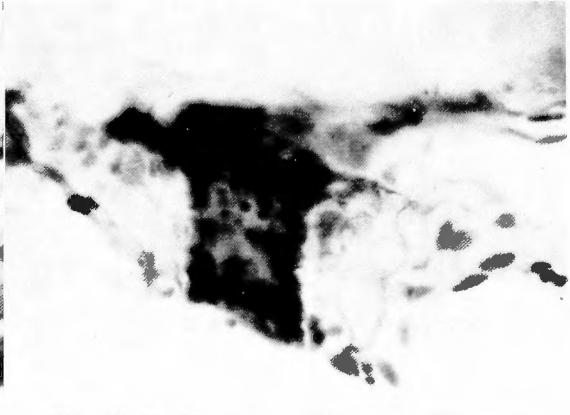

Fig. 6 Small artery with nerve fibers in the submucous tissue of the small intestine of a normal rabbit. 42 × 10

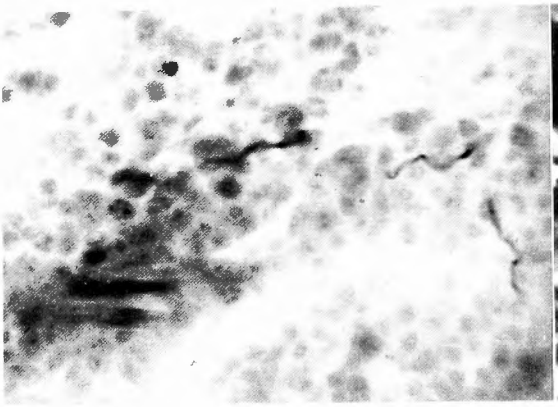

Fig. 7 Small artery with nerve fibers in the medullary zone of the spleen of a normal rabbit. 95×10

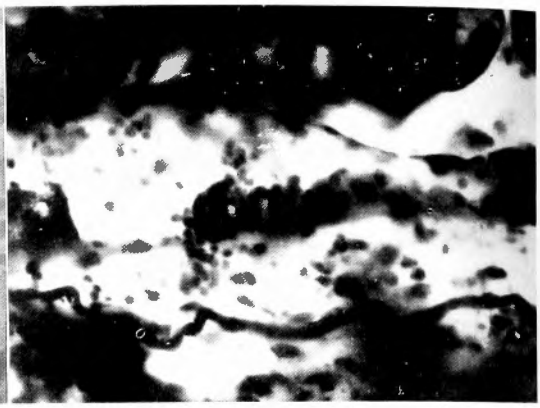

Fig. 8 The vein with nerve fibers in the submucous tissue of the small intestine of a normal rabbit. 42×10

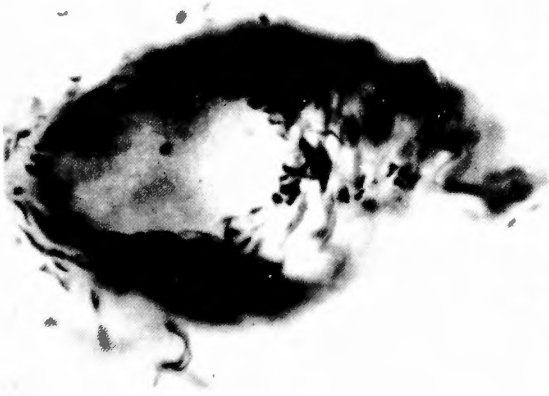

Fig. 9 Small artery and fine nerve fibers in the submucous tissue of the small intestine of diabetic rabbit. (6th month) 42×10

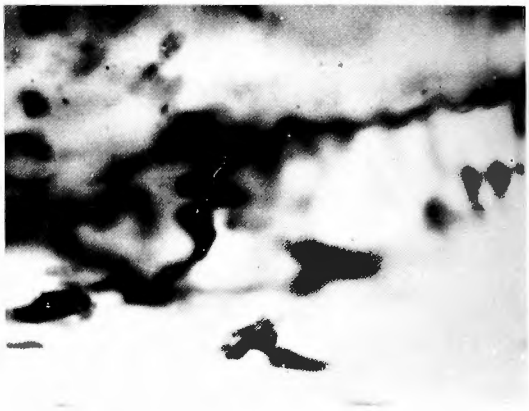

Fig. 10 Small artery and nerve fibers in the liver of diabetic rabbit. (6th month) 95×10

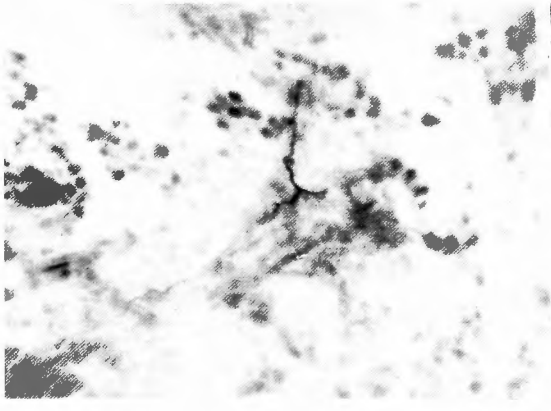

Fig. 11 Small artery and nerve fibers in the medullary zone of the spleen of diabetic rabbit. (6th month) 95×10

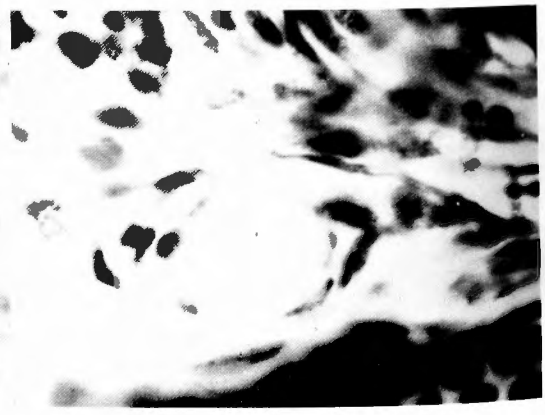

Fig. 12 The vein and nerve fibers in the liver of diabetic rabbit. (2nd month) 95×10

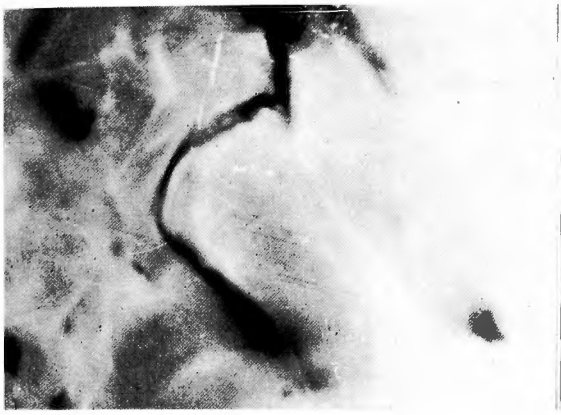

Fig. 13 Nerve fibers in the adventitia of the aorta of a normal rabbit. 95×10

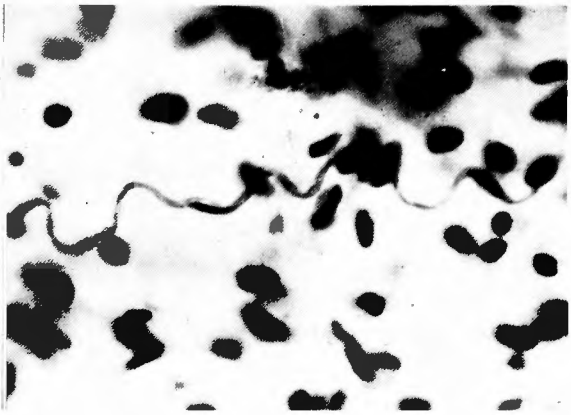

Fig. 14 Nerve fibers in the adventitia of the aorta of a normal rabbit. 42×10

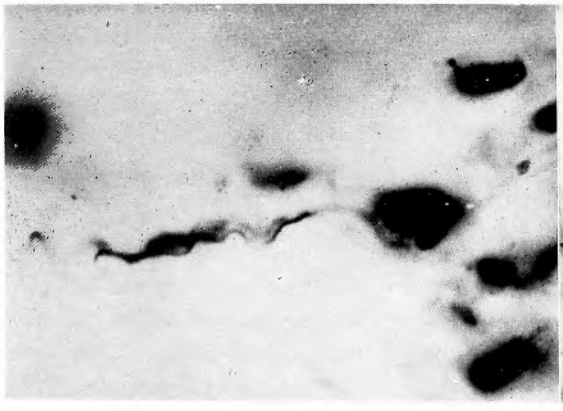

Fig. 15 Nervous syncytium in the adventitia of the aorta of a normal rabbit. 95×10

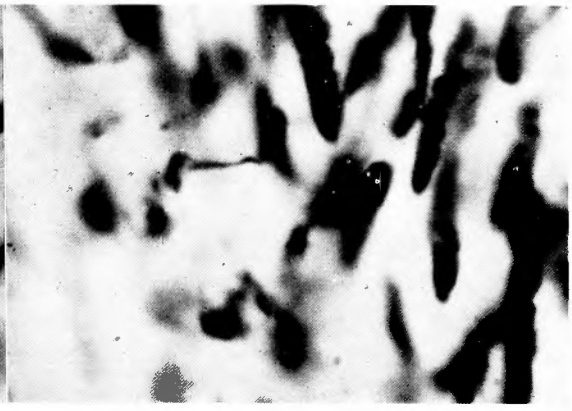

Fig. 16 Nerve fibers in the media of the aorta of a normal rabbit. 95×10

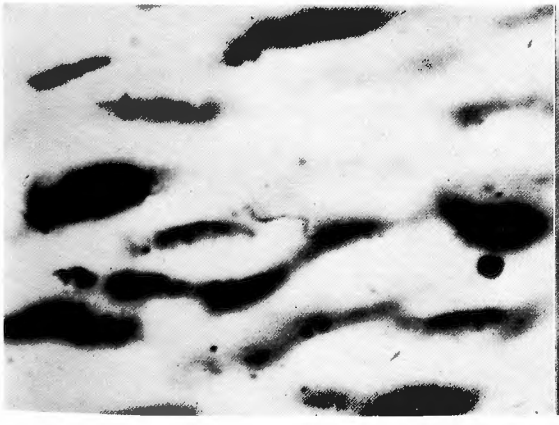

Fig. 17 Nerve fibers in the media of the aorta of a normal rabbit. 95×10

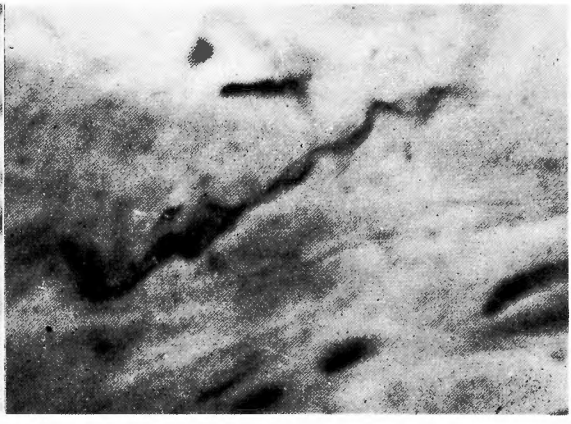

Fig. 18 Nerve fibers in the adventitia of the aorta of diabetic rabbit. (6th month) 95×10

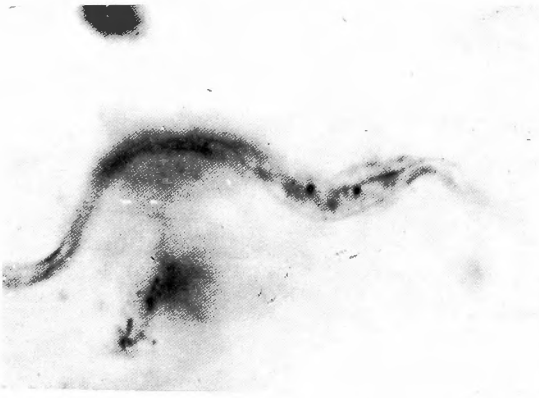

Fig. 19 Nervous syncytium in the advetitia of the aorta of diabetic rabbit. (6th month) 95×10

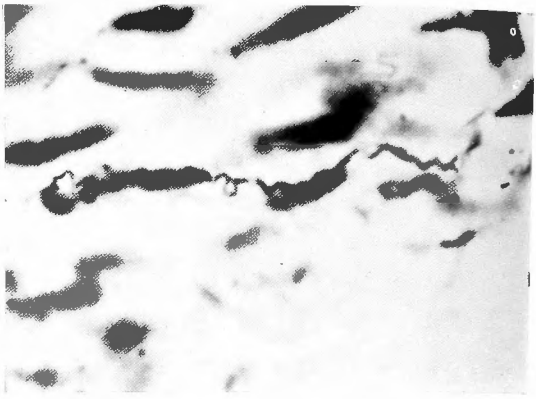

Fig. 20 Nerve fibers in the media of the aorta of diabetic rabbit. (6th month) 95×10