DBAマウス自然発生舌病変の電顕的変化

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Ultrastructure of Spontaneous Degenerative Lesions in the Tongue of DBA Mice

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DBA mice have been reported to have spontaneous calcification in the heart [1, 2, 9] as well as many other soft tissues [3, 4, 7, 11]. The calcified lesions in the tongue are grossly polypoid or slightly elevated in *Dorsum linguae* near *Margo linguae* [8] and most frequently encountered at 6 weeks of age [5]. The lesions were described to appear in the superficial longitudinal muscles with marked inflammation. The purpose of this study is to elucidate the ultrastructure of altered lingual myocytes and to compare its morphological feature with that of cardiac ones in the same strain of mice [6, 12].

Thirty four male DBA/2NCrj (DBA) mice (5, 10, 10 and 9 mice at 3, 4, 6 and 8 weeks of age, respectively) and 16 male C57BL/6Crj (C57BL) mice (every 4 mice at 3, 4, 6 and 8 weeks of age) were examined. C57BL mice, inbred mice without tongue lesions [8], were served as controls. Small pieces from both dorsolateral sides in the middle portion of the tongue were fixed in 4% glutaraldehyde, post-fixed in 1% osmium tetroxide and processed for transmission electron microscopy. When gross lesions were recognized, pieces from both the lesion and the adjacent intact part were processed in the same way.

Macroscopically, 4(1), 8(2), 9(9) and 5(4) DBA mice at 3, 4, 6 and 8 weeks of age, respectively, had tongue lesions (number in each parenthesis indicates the number of mice with one or two large polypoid tongue lesions over than 5 mm-dimater).

Ultrastructurally, the saccular matrices of sarcoplasmic reticula and mitochondrial membranes of some microscopically normal myocytes increased their electron density (Fig. 1a). On the other hand, dilatation of sarcoplasmic reticulum, swelling of mitochondria and streaming of Z-bands were reported as the earliest changes in cardiac myocytes of DBA mice [6]. These alterations were also observed in tongue myocytes of mice of both strains (Figs. 1b, 2) although the number of them in C57BL mice were much less than that in DBA mice. Therefore, at least in the case of tongue myocytes, they may just as well be considered to be one of the mechanical artifact or reversible changes. The findings shown in Fig. 1a might suggest excess workload of myocytes beyond the physiological conditions although whether they are specific for tongue myocytes or not is unknown.

Disorganized sarcomeres, disintegrated myofibrils and inter-myofibrillar edema in myocytes were seen in more advanced cases showing depletion of glycogen granules, and fragmentation, partial separation and sparcity of myofibrils (Fig. 2a). Some sarcomeres with wavy-deranged myofibrils and streaming of Z-bands were intermingled with normal ones (Fig. 2b). Similar figures indicating focal degeneration of myofibrils

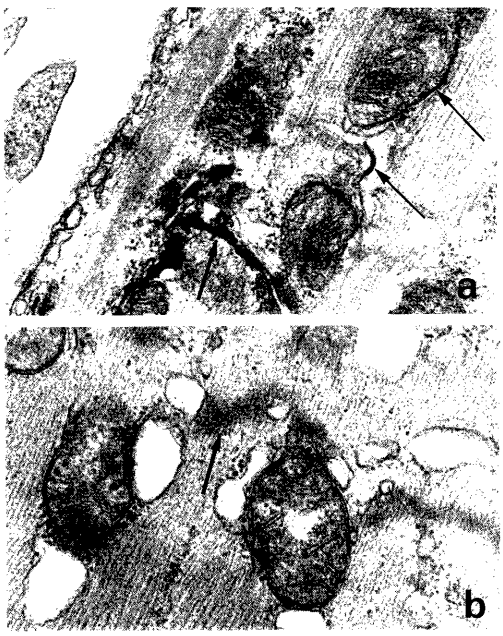

Fig. 1. 1. 4-week-old DBA mouse. (a) Increased electron density of matrices of sarcoplasmic reticula (thick arrow) and mitochondrial membranes (thin arrows). x27,000. (b) Dilatated sarcoplasmic reticula and moderate streaming of Z-bands (arrow). ×35,000.

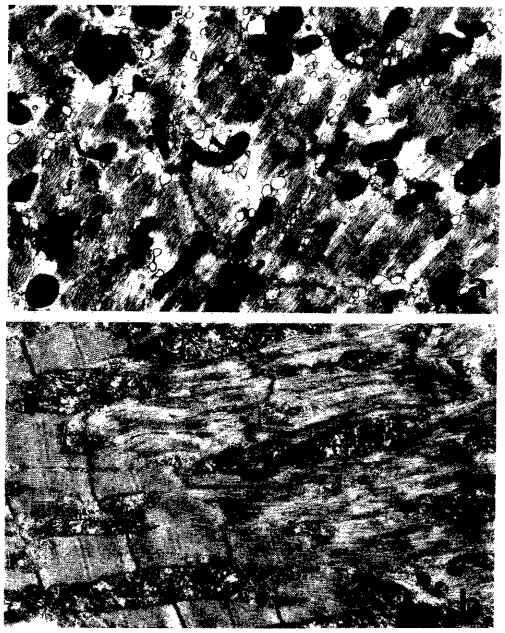

Fig. 2. (a) Myocyte with dilatated sarcoplasmic reticula and intermyofibrillar edema in a 6-week-old DBA mouse. ×7,000. (b) Sarcomeres of wavy-deranged myofibrils and streaming of Z-bands (upper right) and moderately swollen mitochondria in a 4-week-old DBA mouse. ×7,000.

within a myocytes were also reported in the cardiomyopathy of KK mice [10] and they are considered to be one of the degenerating process of myofibrils. Supercontraction of myofibrils with fusion of Z-bands which formed contraction bands was also observed as reported in the cardiac calcification of DBA mice [6]. Such myofibrillar degeneration in myocytes generally accompanied the alteration of mitochondria and/or sarcoplasmic reticulum.

Lysis of myofibrils and loss of normal binding patterns were observed in more severely damaged myocytes. Most of these cells had degenerative mitochondria containing electron dense amorphous materials and remnants of cristae, which occasionally showed needle or radiating-spicular shape (Fig. 3). In the most advanced cases, the whole myocytes increased electron density (Fig. 4) and finally the large uniformly mineralized masses were formed. Necrotic cells and mineralized masses were surrounded by several macrophages as recognized by light microscopy. Small remnants of mineralized material were sometimes engulfed by macrophages and the cytoplasm of some macrophages was

Fig. 3. Myofibrillar lysis and degenerative mitochondria in a myocyte of a 4-week-old DBA mouse. ×4,000. Insert: Higher magnification of degenerated mitochondria. ×17,000.

Fig. 4. Increased electron density of the whole sarcoplasm in a myocyte of a 6-week-old DBA mouse. The outline of mitochondria is recognizable. ×5,400

filled with electron dense mineralized materials. Thus it was suggested that necrosis of macrophages bearing mineralized masses, in addition to clustering of mineralized myocytes, might take part in expansion and enlargement of calcified lesion.

In case of cardiac myocytes, some mitochondria were shown to be wholly occupied with mineral deposits without lysis of myofibrils, suggesting that the elevated uptake of calcium possibly leads to myofibrilar calcification [6]. However, this type of change was not detected in the tongue myocytes.

Ultrastructural findings in this study indicate that tongue lesions in DBA mice may be initiated by necrosis of myocytes and followed by subsequent dystrophic calcification. And, the above-mentioned ultrastructural findings of the tongue lesion were independent on the age of mice.

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要　　約

DBA マウス自然発生舌病変の電顕的変化（短報）：板垣慎一・前田尚之[1]・町田一彦・土井邦雄・光岡知足（東京大学農学部実験動物学教室，[1]三共（株）生物研究所）——3～8週齢 DBA/2NCrj マウスの自然発生舌病変を電顕的に観察した．筋小胞体内およびミトコンドリア膜の電子密度の上昇，ついで筋線維の断裂・粗鬆化を伴った不整筋節，さらに重度の例では，筋線維の融解，筋細胞全域にわたる mineralization がみられ，本病変は細胞壊死につづく異栄養性石灰沈着によることが示唆された．