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ULTRASTRUCTURE OF NECROBIOSIS LIPOIDICA DIABETICORUM

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Abstract. The skin of 5 patients suffering from Necrobiosis lipoidica diabeticorum was studied by electron microscopy. The necrobiotic areas contained rather compact collagen fibril bundles while no or few elastic fibres could be demonstrated. The collagen fibrils varied in diameter and showed bent, curled and disarranged fibrils with normal axial periodicity. Numerous mucopolysaccharide filaments, thickened vascular walls, and disintegrated elastic fibres were found outside the necrobiotic areas. The infiltrating cells were histiocytes, giant cells, and occasionally mast cells and fibroblasts. The histiocytes and giant cells contained numerous lysosomes and mitochondria. Some held fat droplets without enclosing membranes in their cytoplasm. The mast cells contained large mature granules.

By light microscopy, the corium of necrobiosis lipoidica diabeticorum shows thickening of vascular walls, homogenisation of collagen fibres and a lack of elastic fibres. Palisade-arranged cell infiltrates are histiocytes and giant cells. Hitherto, ultrastructural observations of these changes have been lacking in the available literature.

MATERIAL AND METHODS

Five patients suffering from necrobiosis lipoidica diabeticorum were studied. Three were females, 17, 27, and 33 years of age, while two were males, aged 35 and 70 years. Two had a family history of diabetes. One patient showed a high level of blood sugar, while the rest had a slightly lowered sugar tolerance. Skin biopsies were removed from dark-red coloured plaques as well as areas adjacent to the plaques.

The tissues were fixed in a 6% glutaraldehyde solution (pH 7.2) with 7.5% sucrose. After osmification, the specimens were embedded in Epon 812. Ultrathin sections were cut from skin areas showing necrobiotic changes, cell infiltration and normal fibrous structures. After staining with uranyl acetate and lead citrate, the sections were studied under a Siemens electron microscope (Elmiskop IA) at 80 kV with a double condensor system.

OBSERVATIONS

The fibrous components showed three different patterns. 1) Transformed elastic fibres intermingled with normal collagen fibrils (Fig. 1). These changes were found adjacent to necrobiotic areas. 2) Anomalies of collagen fibrils and lack of elastic fibres in necrobiotic areas. Here and there, scarce elastic fibrils could be seen (Fig. 2). 3) Transitional patterns. Round particles containing fine filamentous material were seen in the interfibrous spaces of patterns 1 and 3. Cell infiltrates were seen in the areas showing patterns 2 and 3. Thickened vascular walls (Figs. 7 and 8) appeared in pattern 1, while few vessels could be seen in pattern 2. The dermo-epidermal junction showed no remarkable changes.

The pathological elastic fibres showed dense, grainy material in their matrix. Elastic fibrils were now and then seen in the marginal parts of the matrix (Fig. 1). Neither calcium deposits nor myelin-figures were found. In pattern 2, collagen fibrils showed thicknesses varying from 25 to 220 nm with a regular banding of 55 nm and rounded cut surfaces. Such fibrils were arranged in parallel, forming compact bundles. Bent, curled and disarranged fibrils were gathered in certain areas (Figs. 2 and 3). Neither twisted nor branched fibrils could be seen. Parallel filaments with segments of about 110 nm were found close to the cell infiltrates. In pattern 1, small vessels were surrounded by a thick layer of thin collagen fibrils and amorphous material simulating basal lamina (Fig. 8).

In larger vessels, the smooth muscle cells were encircled by a thickened basal lamina, and dense meshy basal lamina material was located below the endothelial cells. The collagen fibrils between the smooth muscle cells were irregularly thick (Fig. 7). No definite changes were found in the individual endothelial cells, pericytes or smooth muscle cells. The infiltrating cells were mainly histiocytes and giant cells with a few fibroblasts and mast cells. The histiocytes and giant cells contained numerous lysosomes, mitochondria and ribosomes as well as

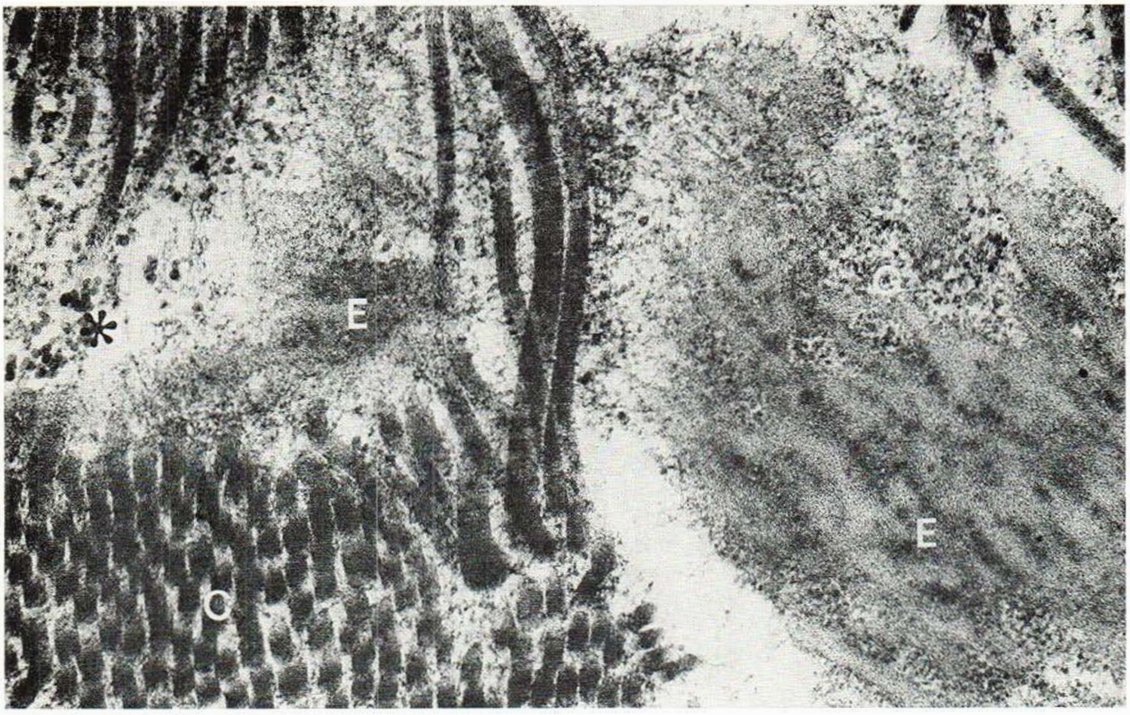

Fig. 1. Dermal fibres apart from cell infiltrates. Collagen fibrils (*C*) are normal, while elastic fibres (*E*) show a granular matrix (*G*). Dense particles with fine filaments representing acid mucopolysaccharides appear in the interfibrous spaces (asterisk). × 50 000.

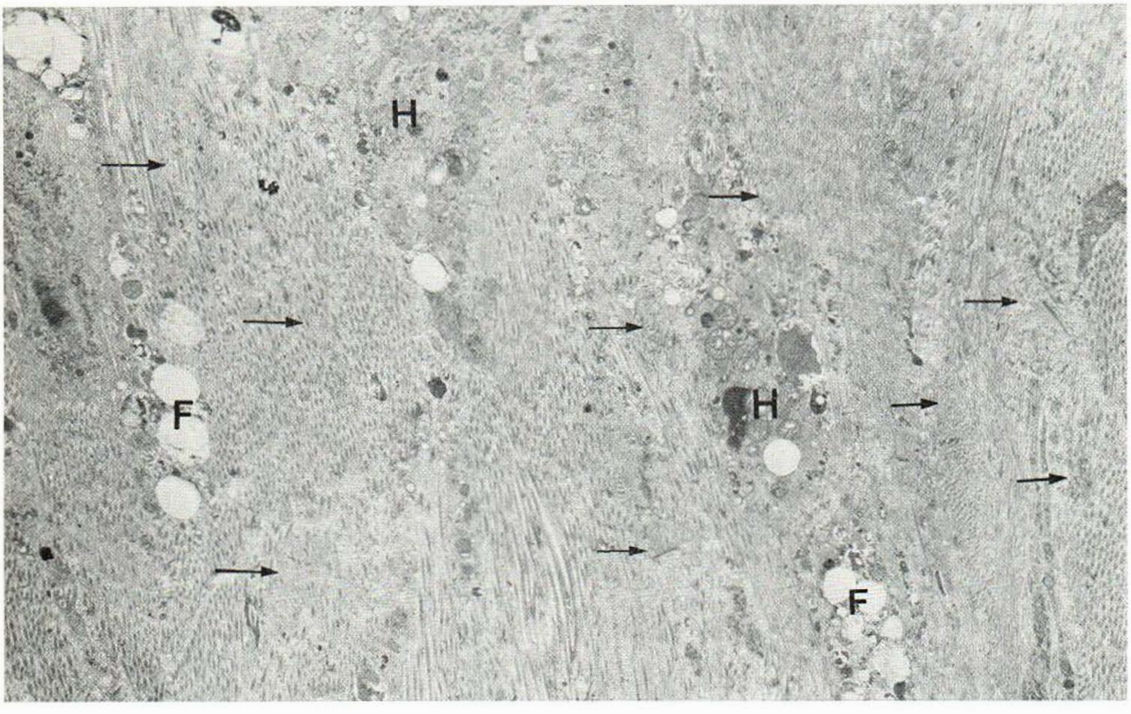

Fig. 2. Necrobiotic area with cell infiltrate. Collagen fibrils appear in compact bundles. The individual fibrils are of varying thickness and show disarray in several areas (*arrows*). Histiocytes (*H*) contain fat droplets (*F*). Details are seen in Fig. 3. × 5 000.

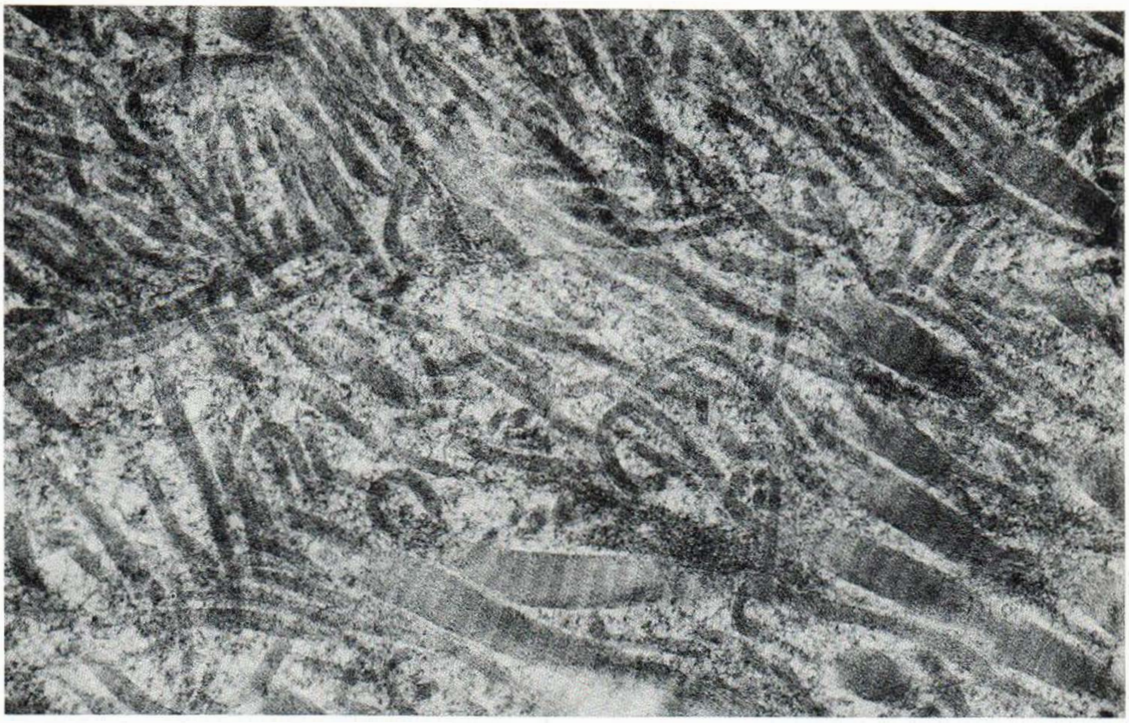

Fig. 3. Disarranged collagen fibrils of varying diameter. Notice the bent and curled types. The axial periodicity is normal. × 50 000.

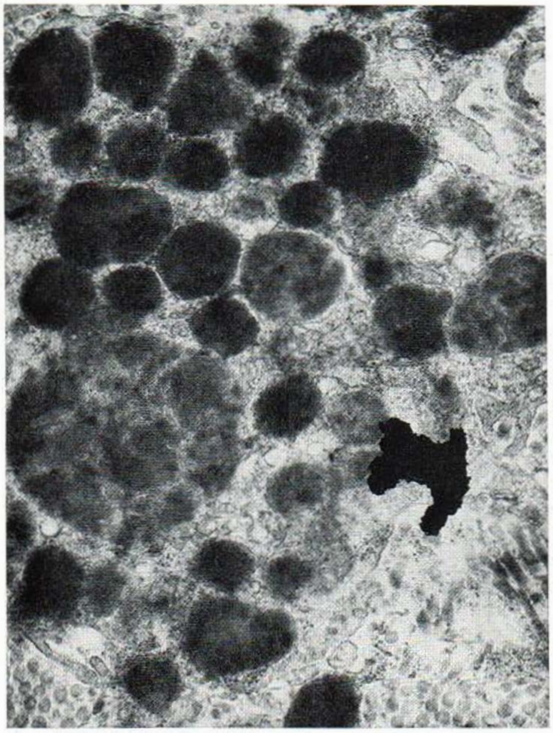

Fig. 4. Mast cell containing large, mature granules. × 20 000.

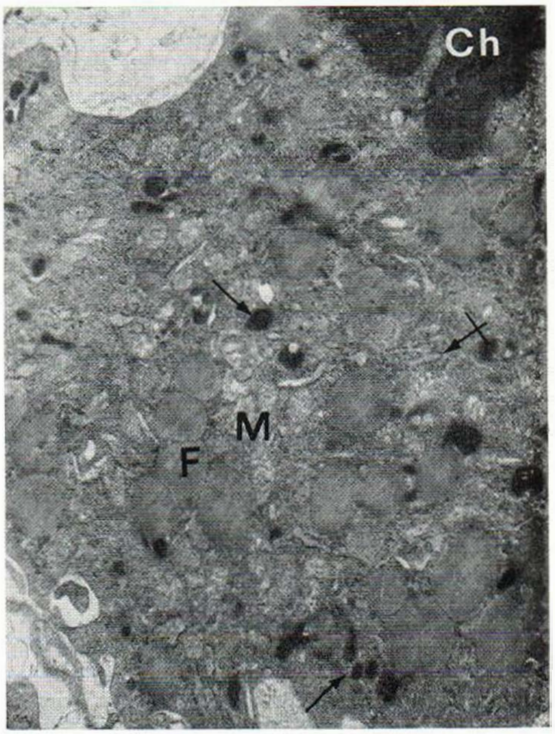

Fig. 5. A histiocyte in mitosis contains numerous small lysosomes (*arrows*), mitochondria (*M*) and reticula (arrow with cross). Fat droplets are not enclosed by a membrane (*F*). Chromosome (*Ch*). × 14 000.

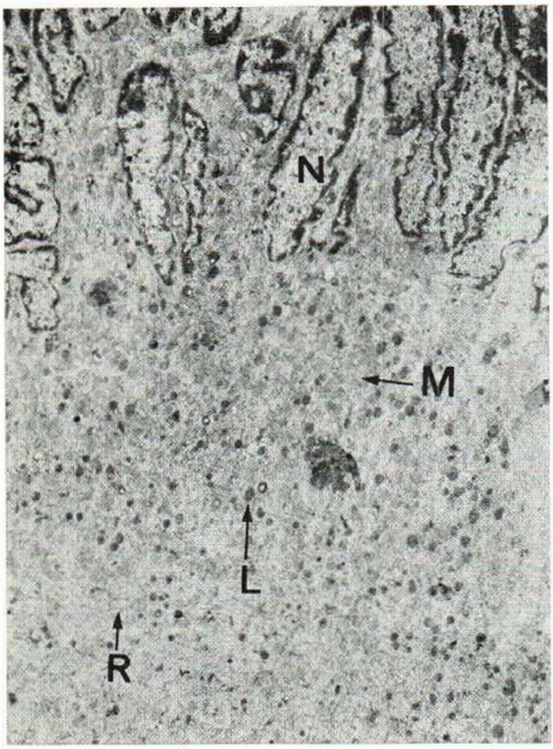

Fig. 6. A giant cell showing large numbers of lysosomes (*L*), mitochondria (*M*), and granular endoplasmic reticulum (*R*). Multiple nuclei (*N*) are seen in the upper area. × 4 000.

endoplasmic reticulum (Figs. 5 and 6). Some contained numerous fat droplets without an enclosing membrane (Fig. 5). The mast cells contained large mature granules (Fig. 4), while some extracellular granules were the only remnants of disintegrated cells.

DISCUSSION

A granular matrix with fine filamentous material has previously been described in marginal zones of elastic fibres of the skin in diabetics. The changes were varying in severity with clinical symptoms (1). Although most of our patients showed no manifest diabetic symptoms, the findings of pathological elastic fibres were identical with those of this study. The fine filamentous material around diabetic elastic fibres described by Caulfield (1) seems to represent both elastic fibrils and acid mucopolysaccharide filaments. Elastic fibres in aged skin show granular material resembling the present findings (3), though the granules were coarser in diabetic skin. The absence of calcium deposits and myelin figures represents a departure from the findings in pseudoxanthoma elasticum skin and light-exposed skin (2, 3). In sclerotic areas of both diffuse and localized scleroderma, elastic fibres and fibrils were not lacking (4, 6).

The present findings suggest that the elastic fibres disintegrate in necrobiotic areas. The individual collagen fibrils had not degenerated in necrobiotic areas, but composed thick compact and disarranged bundles. The changes resemble those in localized scleroderma. However, in contrast to this disease, no branched fibrils were seen in necrobiosis lipoidica. Collagen fibrils of varying thickness were always in orderly arrangement in sclerotic areas of diffuse scleroderma (4). Shagreen patches of the tuberous sclerosis syndrome contain curled fibrils, here and there with whisk-like endings, occurring in normal collagen bundles (5). These phenomena differed from those of the present study. Basal lamina material precipitates around the vessels in

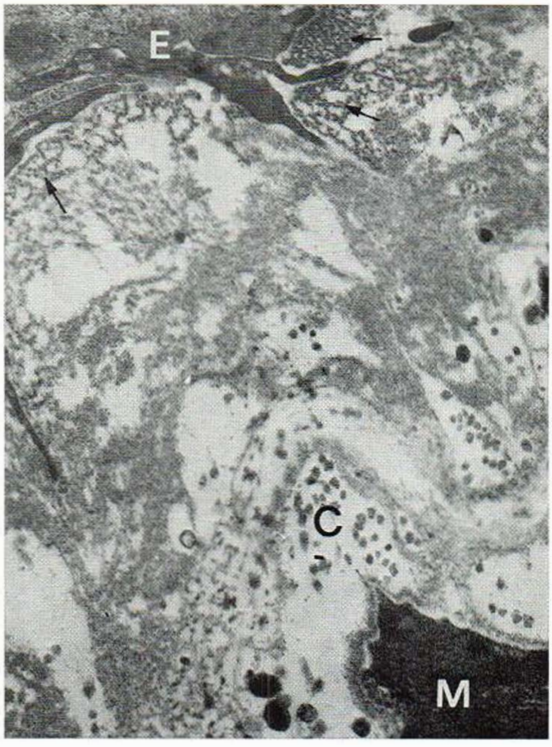

Fig. 7. Vascular wall with smooth muscle cell. The basal lamina below the endothelial cells shows a meshy structure (*arrows*), while the basal lamina around a smooth muscle cell (*M*) is thickened. Collagen fibrils (*C*). Endothelial cell (*E*). × 20 000.

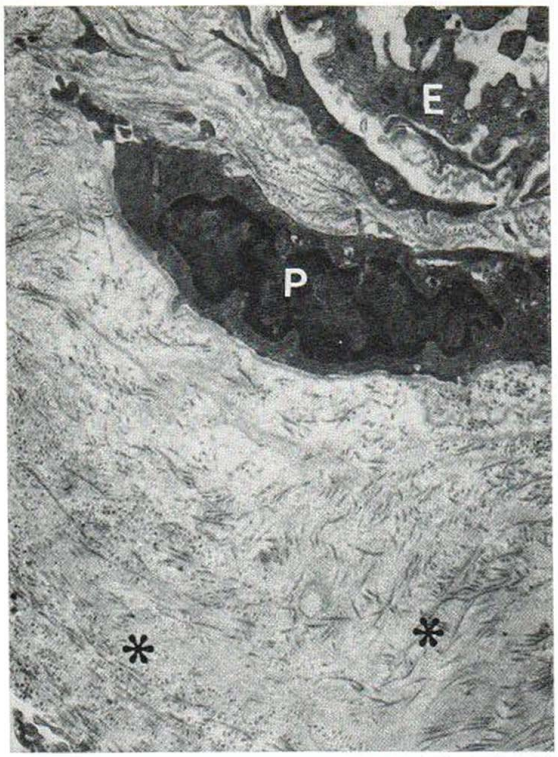

Fig. 8. A small vessel with a pericyte (*P*). Basal lamina material and thin collagen fibrils are located in a thick layer around the vessel (asterisks). Endothelial cell (*E*). × 10 000.

diabetic skin; the longer the duration of the diabetes, the thicker the precipitate (7). The exact time of onset of diabetes in our patients is unknown. The changes reported are identical with those reported by Otto et al. (7). Fat droplets without an enclosing membrane seen in both histiocytes and giant cells of necrobiosis lipoidica suggest a metabolic disturbance, not phagocytosis.

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