The stromal lesion in lattice dystrophy of the cornea

A light and electron microscopic study

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The corneal stromal lesions of a case of lattice dystrophy that fulfilled all the clinical and histopathologic criteria of this disease were examined by light and electron microscopy. The lesions were found to consist of two distinct parts: (1) a nonbirefringent mass of disoriented filaments of approximately one-third the diameter of normal stromal collagen fibrils and (2) a second, birefringent part containing modified stromal lamellas with highly oriented fibrils of normal diameter but increased density. These observations suggest that the normal collagen fibril separates into filaments of smaller diameter ("fibrillary degeneration").

The stromal lesions of lattice dystrophy have been characterized histopathologically by Jones and Zimmerman as focal areas of hyaline degeneration of the corneal collagen. These workers called attention to the usefulness in histopathologic diagnosis of certain characteristics of the lesions, one of which is their increased birefringence when examined with polarized light. Lesions of macular and granular dystrophy exhibit diminished birefringence. More recently, Wolter and Henderson have revived the idea that the lesions in lattice dystrophy represent degenerated and hyalinized corneal nerves.

We have recently had the opportunity to study by light and electron microscopy two corneal buttons from a patient with lattice dystrophy. This study has provided additional information concerning the specific stromal lesions of lattice dystrophy.

Materials and methods

The specimen used for electron microscopy consisted of a full-thickness corneal button approximately 7 mm in diameter, removed from the right eye and fixed promptly during a penetrating keratoplasty for lattice dystrophy. The corneal button was fixed for 50 minutes in Dalton's solution, dehydrated through ascending concentrations of alcohol, and embedded in Epon as described elsewhere. All sections for electron microscopy were treated with 1 per cent uranyl acetate in 50 per cent ethanol for 30 minutes. Sections 1.0 to 1.5 μ thick were also obtained from this right corneal button for light microscopy.

A similar corneal button previously removed from the left eye of the same patient was fixed in formalin, embedded in paraffin, sectioned in
Fig. 1. Paraffin section of the left corneal button stained with hematoxylin and eosin. The dense eosinophilic lesions within the corneal stroma are easily recognized when the preparation is examined with ordinary illumination (1A), but they are even more apparent when examined with polarized light (1B). Compare the lesion indicated by the arrow in 1A with the same lesion as seen by polarized light in 1B. Note that only a part of this lesion is birefringent. The same lesion is shown in greater magnification in Fig. 2. (×115.) (AFIP Neg. Nos. 63-4651 and 63-4653.)
Fig. 2. Higher magnification of the lesion indicated by the arrows in Fig. 1. Fig. 2A, The lesion with ordinary illumination. Fig. 2B, The same lesion under polarized light showing that only parts of the lesion are birefringent. (Hematoxylin and eosin. ×750.) (AFIP Neg. Nos. 63-4651 and 63-4653.)
Fig. 3. For legend see page 361.
Fig. 5. A smaller lesion of lattice dystrophy clearly showing the filamentous portion in the center of the micrograph. Normal lamellas can be seen cut obliquely and longitudinally at COL. These normal fibrils are seen in cross section at X. Normal collagen fibrils cut transversely and longitudinally blend with the filamentous portion of the lesion at its periphery. An area containing an admixture of abnormal filaments and fibrils of normal diameter is seen at AD. A fragment of cell cytoplasm is seen at CL. COR, corneal lamella of increased density. (×14,300.)
Fig. 3. Electron micrograph of a lesion of lattice dystrophy within the corneal stroma. The disoriented mass of delicate filaments can be seen at A. Normal corneal collagen can be seen at COL. Above the latter zone is a broad band of collagen fibrils, some of which are more dense (free arrows) than those in the more normal areas below. Normal diameter collagen fibrils cut in cross section (X) and longitudinally (L) are seen interspersed with the abnormal filamentous material seen at A. Fragments of cells are seen at CL, and CL. The area around CL is better seen in the enlargement (Fig. 4). (x13,000.)

Fig. 4. Higher magnification of area CL from Fig. 3, to show the delicate filamentous composition of this portion of the lesion. These filaments (approximately 100 Å in diameter) are seen cut in oblique and cross section in area A and in longitudinal section in area B. Collagen fibrils7 of apparently normal size (approximately 300 Å in diameter) and density are seen at COL, interspersed through the abnormal filamentous portion of the lesion. Occasional fibrils of normal diameter are still present deep within the filamentous mass (arrows). (x40,800.)

Fig. 6. Higher magnification of the extreme lower left part of the filamentous portion of the lesion shown in Fig. 5. The area of fine, randomly oriented filaments is clearly seen. A few fibrils of normal dimension can be seen in this area (arrow). More normal stromal fibrils cut obliquely and in cross section are seen at COL. (x46,000.)
Fig. 7. For legend see opposite page.
Fig. 8. Portion of a stromal lesion to show cross sections of both lucent (N) and dense (AB) fibrils of normal diameter near the edge of the mass of disoriented filaments (A). The lucent fibrils of more normal stroma are clearly seen in both longitudinal and cross section in the upper right portion of the micrograph. (×36,250.) The inset shows the two forms of fibrils of normal diameter at higher magnification. The more lucent fibrils are considered normal, the dense fibrils (arrows) abnormal. (×80,000.)

Fig. 7. Higher magnification of the extreme right part of the filamentous portion of the lesion shown in Fig. 5. Collagen fibrils of normal diameter (arrows) blend with the fine filaments of the area (FIL). The fine filaments are randomly oriented, unlike the fibrils of normal diameter of the corneal stroma. (×46,000.)
the conventional manner for light microscopy, and the sections stained and studied to confirm the clinical diagnosis of lattice dystrophy according to the histopathologic criteria of Jones and Zimmerman.1, 2

The patient was a 34-year-old woman whose father, sister, paternal uncle, and cousin exhibited the same corneal disease. Her own visual disturbance was first noted at age 15. Slit-lamp examination showed nodular and lattice opacities through the full thickness of the cornea. The peripheral 2 to 3 mm. of cornea was clear in both eyes.

Results
The results are recorded in the legends of the micrographs. Micron markers indicate 1 μ unless otherwise designated.

Discussion

Light (Fig. 1) and electron microscopic examination of the right cornea showed numerous lesions throughout the stroma. The typical lesion was found to consist of two distinct parts. One part (Figs. 3 and 5) was seen by electron microscopy to be a mass of delicate filaments (approximately 80 to 100 A in diameter) showing no special orientation (Figs. 6 and 7). Suitable sections show some of these filaments in cross, oblique (Fig. 4, A), and longitudinal (Fig. 4, B) sections. The presence of these long, delicate filaments together with an intermingling of a number of fibrils of normal diameter and low density (Fig. 3, the lamella above the normal area indicated by COL) suggests that the lesions develop as a result of a breakdown of the larger fibril, which separates into its laterally aggregated constituent filaments (“fibrillary degeneration”).

The second part consists of highly oriented fibrils of normal diameter but greater density (Fig. 3, the lamella above the normal area indicated by COL). This difference in density of the fibrils is clearly seen in both longitudinal (Fig. 3, free arrows) and cross section (Fig. 4, arrows; Fig 8, AB and inset).

These observations suggest a transition from the fibril of normal diameter and low density, through the fibril of normal diameter and low density, through the fibril of normal diameter and high density, and finally to a separation of the fibril into the delicate component filaments having approximately one-third the normal diameter. This idea is supported by the presence of mixtures of cross-sectioned fibrils of normal lucency with those of increased density within and at the periphery of a collection of delicate filaments (Fig. 8).

The separation of fibrils of normal diameter into the more delicate fibrils of smaller diameter might be explained, in part, on the basis of a change in or loss of a binding polysaccharide. This possibility is compatible with the characteristic loss of stainable mucopolysaccharide in these lesions when examined by light microscopy.2

In addition, there is the possibility that aggregation of these areas of fibrillary degeneration, increasing in mass, may serve to further compress adjacent stromal fibrils and so increase their density.

Nothing was found during the investigations to suggest the presence of nerve tissue in these lesions.

The presence of these two distinct parts, one of disoriented filaments and another of oriented fibrils of greater density, suggested that only certain parts of the lesion should be birefringent. These observations, therefore, led to a re-examination of the stromal lesions by light microscopy (Figs. 1 and 2), with particular attention to the criterion of the increased birefringence of the lesion. That portion of the lesions consisting of a highly disoriented mass of delicate filaments did not seem likely to possess the property of birefringence. This consideration was borne out on re-examination of the lesions by light microscopy. Examination with polarized light revealed only certain portions of the lesions to be birefringent (Fig. 2). The electron microscopic investigation showed that this birefringent zone apparently corresponded to the lamellas containing the oriented fibrils exhibiting increased density. These dense lamellas were then interpreted as the basis for the increased birefringence previously described in the lesions of lattice
dystrophy. These birefringent portions may be seen completely enveloping a non-birefringent portion or may appear to be interwoven through the nonbirefringent mass, depending upon the plane of section of a particular lesion.

REFERENCES