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Corneal Myxoma

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Background: Myxomas are rare benign tumors that can be found most frequently in the heart. We report the clinical and histological findings in a very rare case of corneal myxoma, which is only the sixth case in the literature.

Case: A whitish elevated tumor of the anterior cornea developed in the left eye cornea of a 46-year-old man 2 years after luxation of the patient's lens into the anterior chamber and subsequent endothelial decompensation. The tumor covered the entire surface of the cornea except for the outer limbal periphery at Schwalbe's line.

Observations: Histologically, the hypocellular tumor was characterized by scattered spindle- and stellate-shaped cells with wavy, randomly oriented collagen fibers in a myxomatous ground substance staining positively for acid mucopolysaccharides. Bowman's layer was absent. Immunohistochemically, the tumor cells were positive for vimentin. Ultrastructurally, the tumor cells had features characteristic of keratocytes with no basement membrane, much rough endoplasmic reticulum and vacuoles containing mucoid-like material.

Conclusions: The ultrastructural observations support the hypothesis of a cellular origin of the myxoma from keratocytes. The tumor growth was most probably stimulated by chronic endothelial failure and bullous keratopathy. **Jpn J Ophthalmol 2002;46:193–197** © 2002 Japanese Ophthalmological Society

Key Words: Bowman's layer, bullous keratopathy, cornea, myxoma.

Introduction

Myxomas are rare benign tumors that resemble primitive mesenchyma or the loose, mucoid tissue in the umbilical cord, the so-called Wharton's jelly. They can be found most frequently in the left atrium of the heart but also in skeletal muscle, bone, the urogenital system, and skin.[1]

In ophthalmology, myxomas have been described in the lids, orbit, and conjunctiva.[2] In the cornea, 5 cases have been reported so far in the literature (Table 1).[3–7] This is the second immunohistochemical[7] and the third electron-microscopic study[5,7] of corneal myxoma. The present case reveals the pathogenetic factors and possible cellular origin of corneal myxoma.

Case Report

A 48-year-old man from Dresden, Germany, had sustained a perforating scleral wound by glass splinters in the left eye at the age of 12 (in 1963). One year later, an encircling band operation had to be performed for secondary retinal detachment. In 1966, the left eye had gone blind because of nonhealed retinal detachment and the encircling band was removed because of the patient's pain. In 1994, severe bullous keratopathy developed due to endothelial failure caused by the luxation of the patient's lens into the anterior chamber of the left eye. Therefore, the lens was removed through a 7-mm corneal tunnel incision. Postoperatively, bullous keratopathy persisted and deterioration continued. Corneal neovascularization developed. In 1996, two years after the beginning of bullous keratopathy, an elevated "keloid"-like lesion started to grow over the cornea from the paracentral-nasal area. In 1999, the superficial, 1.5-mm thick,

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Table 1. Summary of Previous Reports on Corneal Myxoma

Authors	Age	Sex	Cause
Mitvalsky	26	Female	Keratitis with staphyloma
Léger et al	26	Female	Keratoconus
Bussy	66	Male	Corneal ulcer
Pérez-Grossmann et al	53	Male	Corneal ulcer
Lo et al	44	Female	Primary tumor

smooth tumor which had spread like a cap over the entire surface of the cornea except for the outer limbal periphery (Figure 1), was carefully peeled off from the underlying corneal stroma in the university eye hospital in Dresden using a hockey-knife and a forceps, similar to the removal of a pterygium. There was no tissue connection towards the conjunctiva. The cornea underneath appeared scarred (Figure 1). No recurrence of the lesion has occurred so far.

Materials and Methods

The excised whitish, nontranslucent tumor measured 9 × 8 × 1.5 mm in diameter and was bisected. The cut surface had a glistening appearance. There were no cysts, hemorrhages nor areas of necrosis. One half of the specimen was fixed in 10% neutral-buffered formaldehyde for light microscopy and the other half in 2.5% glutaraldehyde for electron microscopy. For light microscopy, the tissue was embedded routinely in paraffin, and 4-μm-thick sections were stained with hematoxylin-eosin, periodic acid Schiff, Prussian blue, Alcian blue with and without hyaluronidase digestion (at pH 2.5), colloidal iron, Masson trichrome, Congo-red, von Kossa and Verhoeff-van Gieson. For immunohistochemical study, the 4-μm sections were mounted on polylysine-coated slides. Immunohistochemical analysis was performed with the strepto-avidin-biotinylated immunoperoxidase method using diaminobenzidine as the chromogen. Commercially available monoclonal antibodies against vimentin, cytokeratin, desmin, α-smooth muscle actin, and α-1-antitrypsin were used. For electron microscopy, the glutaraldehyde-fixed tissue was postfixed in 1% osmium tetroxide, embedded in epoxy resin, and contrasted with uranyl acetate and lead citrate.

Results

Histological Findings

The tumor was covered by a flattened two-layered corneal epithelium with marked edema of the basal epithelial cells. No goblet cells were present. The tumor was composed of scattered spindle- and stellate-shaped cells embedded in a loose myxoid mucopolysaccharide matrix (Figures 2–4). Almost no mitoses were present. The interspersed collagen fibers were wavy and randomly oriented within the stroma (Figures 3, 4). They were relatively short and appeared to be thickened compared to normal corneal collagen fibers. No Bowman's layer was present, neither under the epithelium nor at the interface towards the normal cornea. At two locations, there were small needle-like fragments, which might be remnants of a calcified Bowman's layer (Figure 5). A few small blood vessels were present at the margins of the lesion. A

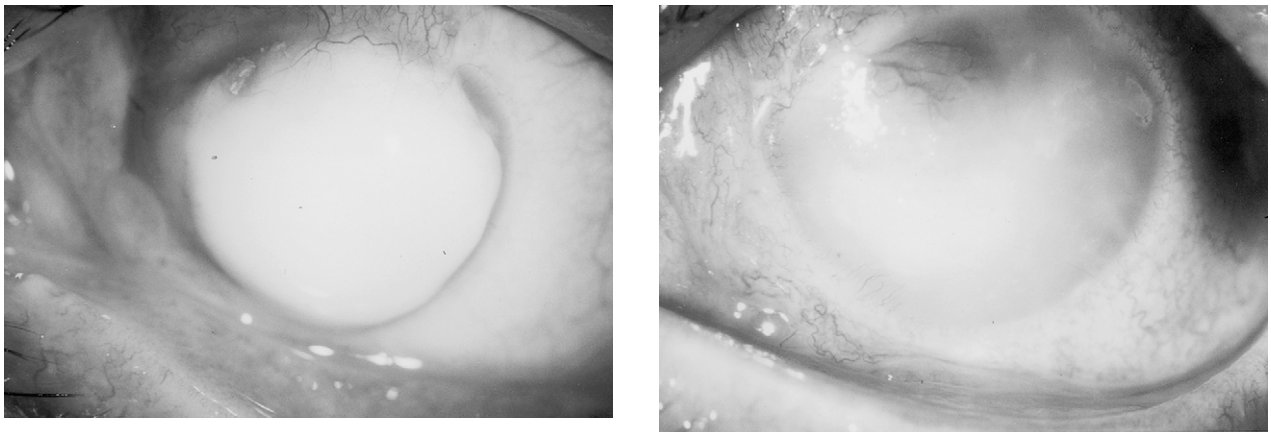

Figure 1. (Left) the corneal myxoma covers the entire corneal surface sparing only the limbal region at Schwalbe's line in the 46-year-old male patient. (Right) superficial scarring and moderate neovascularization in the underlying cornea after removal of the myxoma.

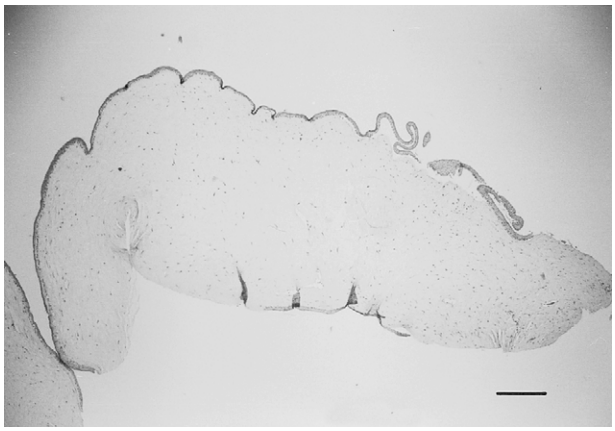

Figure 2. Overview of myxoid, hypocellular lesion covered by corneal epithelium. Hematoxylin-eosin stain. Bar = 250 μm.

few macrophages and polymorphonuclear leukocytes could be found, especially near the blood vessels. A relatively sharp transition zone towards the underlying normal-appearing corneal stroma was present at the base of the lesion (Figure 3). No capsule was present.

Histochemical Findings

The extracellular myxoid matrix was stained strongly positive for acid mucopolysaccharides (ie, glycosaminoglycans) using the colloidal iron stain. In Alcian blue staining, the matrix stained positively only without hyaluronidase treatment, demonstrating hyaluronidase-sensitive acid mucopolysaccharides. Von Kossa staining revealed two needle-like calcifications at the margins of the lesion (Figure 5). The Congo-red stain for amyloid was negative.

Figure 3. Sharp transition zone between myxoma and underlying normal corneal stroma. Periodic acid Schiff stain. Bar = 50 μm.

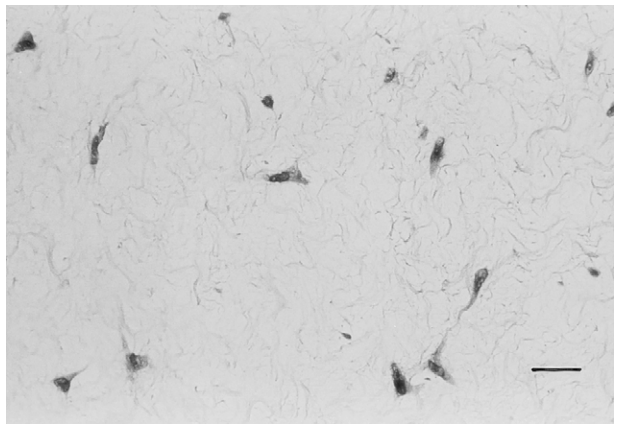

Figure 4. Scattered spindle- and stellate-shaped cells and wavy, randomly oriented collagen fibers interspersed within a myxoid matrix. Absence of Bowman's layer under the epithelium. Periodic acid Schiff stain. Bar = 25 μm.

Immunohistochemical Findings

All tumor cells were strongly positive for vimentin (Table 2, Figure 6).

The tumor cells did not react positively with cytokeratin, desmin, α-smooth muscle actin or α-1-antitrypsin antibodies. The flattened corneal epithelium reacted positively with cytokeratin antibodies. The basal epithelial cells reacted positively with anti-vimentin as well.

Electron Microscopy

Examination disclosed flattened and elongated outer epithelial cells and basal epithelium with severe intra- and intercellular edema. A loose meshwork of thickened collagen fibrils (ie, 66 nm fiber diameter compared to 22.5–35 nm in normal corneal collagen

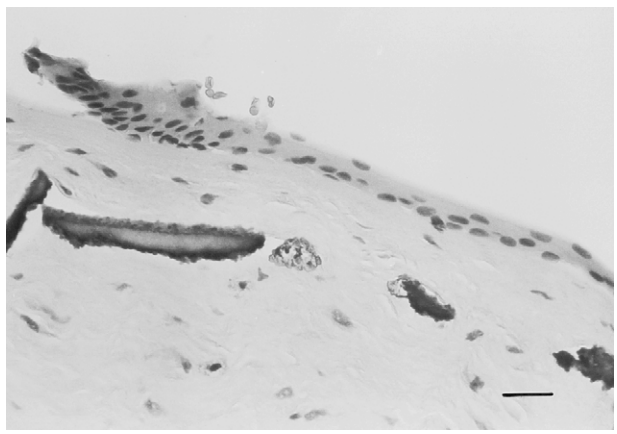

Figure 5. Needle-like calcifications under the epithelium. Von Kossa stain. Bar = 25 μm.

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Table 2. Immunohistochemical Analysis of the Cells

Antibody	Immunoreactivity
α-1-Antitrypsin	–
α-Smooth muscle actin	–
Cytokeratin	–
Desmin	–
Vimentin	+

fibers) was enmeshed in abundant fibrillo-granular material. Spindle- and stellate-shaped cells with much rough endoplasmic reticulum and no basement membrane (fibrocytes) were present in the matrix (Figure 7). Some contained 1–2 μm slightly osmophilic oval inclusions containing the mucinous ground substance (Figure 8) which was obviously produced by these cells. A few macrophages and polymorphonuclear leukocytes were also identified.

Discussion

In all but one of the previously reported cases of corneal myxoma, a prior affection of the cornea, such as keratitis, corneal ulcer, or advanced keratoconus with destruction of Bowman's layer, was observed (Table 1). The common pathogenetic feature of all the cases is chronic corneal edema.

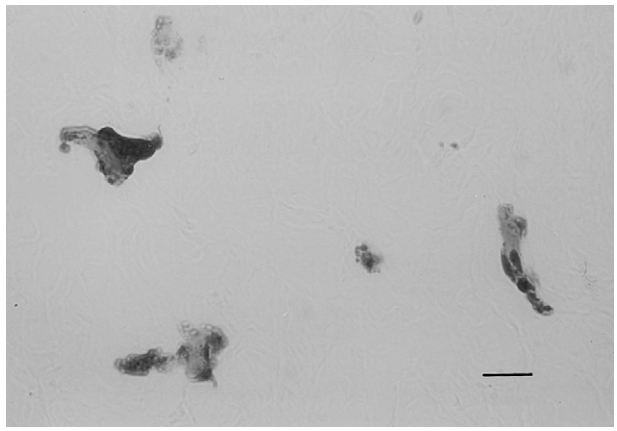

Figure 6. Tumor cells are strongly positive for vimentin. Immunostain, oil immersion. Bar = 10 μm.

Also in our case, endothelial decompensation caused by luxation of the lens into the anterior chamber and consecutive chronic corneal edema with destruction of Bowman's layer were the probable pathophysiologic factors leading to myxoma. Accordingly, the myxoma developed in the whole corneal surface except for the limbal region at Schwalbe's line where the endothelium ends and trabecular cells contribute to the clarity of the cornea.

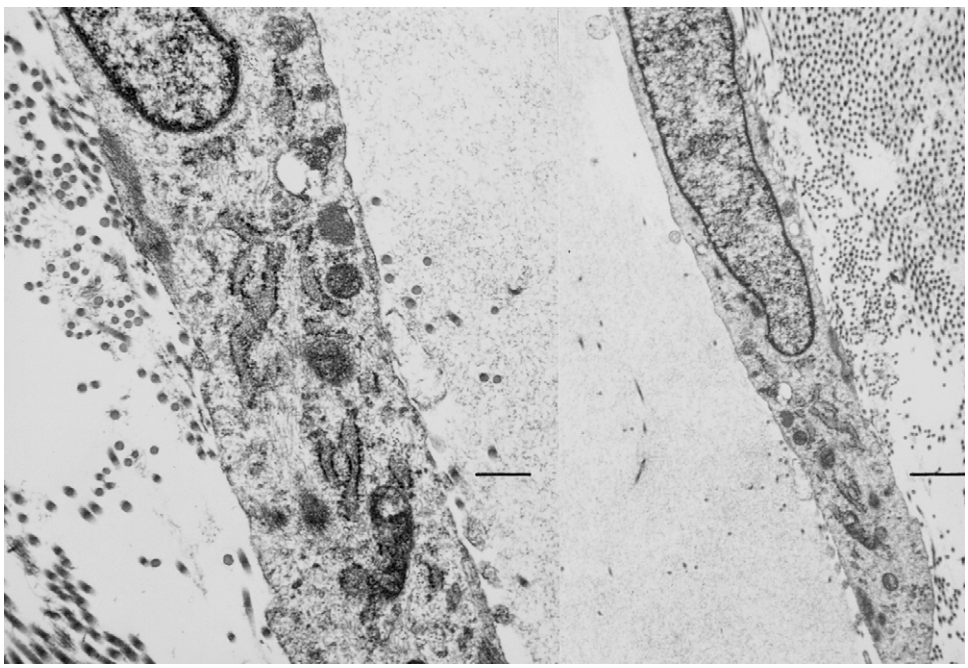

Figure 7. (Right) Electron micrograph demonstrating fibrocyte and 66 nm-thick collagen fibers interspersed in fine-granular myxoid substance. Uranyl acetate/lead citrate. Bar = 1.2 μm. (Left) Higher magnification of fibrocyte revealing dilated rough endoplasmic reticulum. Uranyl acetate/lead citrate stain. Bar = 0.5 μm.

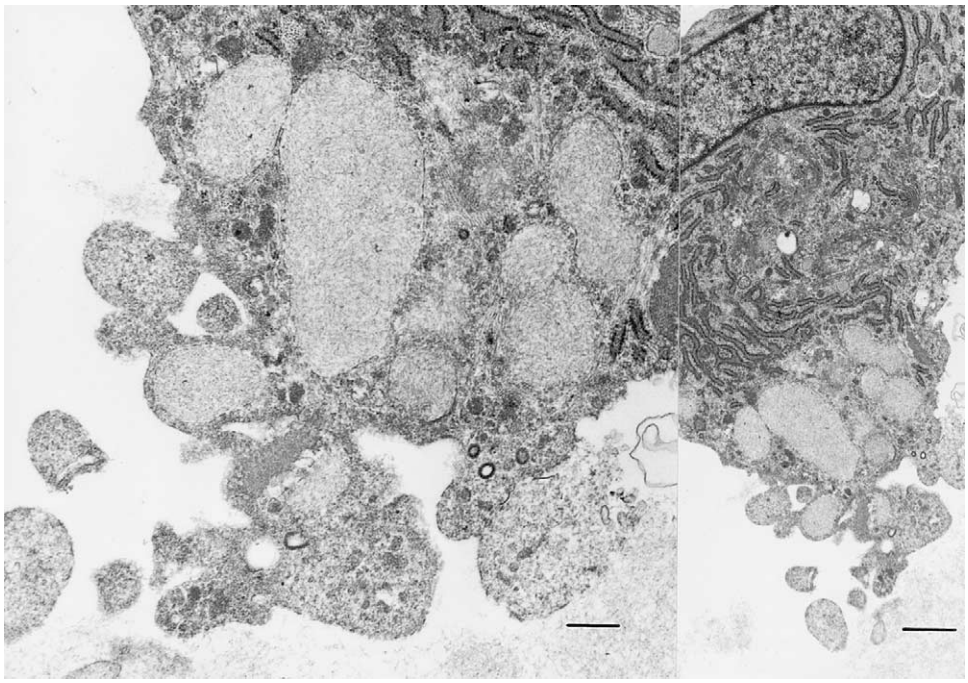

Figure 8. Osmophilic inclusions of tumor cells with material resembling the myxomatous ground substance. Uranyl acetate/lead citrate stain. (Left) Bar = 0.5 μm. (Right) Bar = 1.2 μm.

Only in the case report by Lo et al no prior ocular disease was noted in the patient. Therefore, their case may be primary myxoma as has been observed in myxomas of the conjunctiva or other organs.[1,2] However, also in that case Bowman's layer was histologically absent, suggesting a previous condition,[5] and electron microscopy revealed that the myxoma cells were altered fibrocytes (ie, keratocytes) rather than pluripotential embryonic mesenchymal cells, suggesting a primary myxoma. Also in our case, the myxoma cells were identified as keratocytes with much rough endoplasmic reticulum and intracellular vacuoles containing the myxoid ground substance (Figures 7, 8).

In all the cases reported, the lesion formed anteriorly directly under the epithelium and not in the deep corneal stroma. Therefore, in addition to chronic corneal edema, the destruction of Bowman's layer may be an important factor for the formation of corneal myxoma.[2–7] In our case, Bowman's layer was absent except for two possible calcified fragments of Bowman's layer.

Clinically, several diseases may resemble the appearance of corneal myxoma. The clinical differential diagnosis comprises Salzmann's nodular degeneration, corneal keloid,[8] corneal squamous cell carcinoma,[9] amyloid deposition, pannus, acute hydrops in keratoconus, limbal dermoid, or fibrous histiocytoma. Clinically, the diagnosis may therefore be difficult. This may be one of the reasons why corneal myxoma has been reported so rarely. Histologically, however, the lesion can be clearly defined and differentiated from other lesions due to its unique and characteristic features.

References

1. Bulkley BH, Hutchins GM. Atrial myxomas: a 50-year review. Am Heart J 1979;97:639–43.
2. Horie Y, Ikawa S, Okamoto I, Nagata M, Tamai A. Myxoma of the conjunctiva: a case report and a review of the literature. Jpn J Ophthalmol 1995;39:77–82.
3. Mitvalsky J. Sur les myxomes de la corneé Arch d'Ophtalmol 1894;14:480–7.
4. Bussy L. Le myxome de la corneé Arch d'Ophtalmol 1925; 42:33–8.
5. Lo GG, Biswas J, Rao NA, Font RL. Corneal myxoma. Case report and review of the literature. Cornea 1990;9:174–8.
6. Pérez-Grossmann RA, Mesias LA, Contreras F, Spencer WH. Solitary corneal myxoma. Cornea 1997;16:498–500.
7. Léger F, Sawan B, Mortemousque B, Williamson W, Vital C. Corneal myxoma associated with keratoconus and Down's syndrome. Cornea 2000;19:561–3.
8. Risco JM, Huaman A, Antonios SR. A case of corneal keloid: clinical, surgical, pathological, and ultrastructural characteristics. Br J Ophthalmol 1994;78:568–71.
9. Cameron JA, Hidayat AA. Squamous cell carcinoma of the cornea. Am J Ophthalmol 1991;111:571–4.