Cataract in Kniest Dysplasia: Clinicopathologic Correlation

Kniest dysplasia is a variant of the spondyloepiphysseal dysplasias caused by an abnormal synthesis of collagen type II. In 1952, Kniest reported the first specific description of a variety of chondrodystrophy that he termed an *atypical chondrodys trophy*, which came to be known as *Kniest dysplasia.*

A patient with Kniest dysplasia usually is seen with characteristic round faces, midfacial flatness, and proptosis. Radiologic findings are pathognomic and differentiate this syndrome from other bone dysplasias and dwarfism. Histologically the syndrome is characterized by abnormal cartilage with large chondrocytes embedded in loosely woven matrix that contains many empty spaces and gives rise to the name *Swiss cheese cartilage syndrome.* The chondrocytes have dilated cisternae of endoplasmic reticulum. Abnormal organization of type II collagen has been found to be due to a gene mutation.

Kniest dysplasia is associated with multiple ocular abnormalities. Myopia, vitreous liquefaction and synechiae, vitreous condensation, traction at the vitreous base, areas of white without pressure at the retinal periphery, and extensive perivascular lattice degeneration are common findings. Cataracts tend to develop at an early age and are firm in consistency. We report the ultrastructural features of the lens capsule in a patient with Kniest dysplasia.

Report of a Case. A 4-year-old white girl was examined at the retina service with a 6-month history of decreased vision in the left eye. Results of examination showed that her best-corrected visual acuity was 20/60 OD (~5.00 diopters sphere) and light perception OS. Horizontal and vertical corneal diameters were 12.5 mm and 11.9 mm OD and 12.4 mm and 11.9 mm OS, respectively. Slitlamp examination of the right eye showed a deep anterior chamber and clear lens. The left eye had a shallow anterior chamber, elongated ciliary processes, and a dense white cataract centrally, with the capsule showing a corrugated (wrinkled) surface. The iris vessels were engorged, and a fine network of neovascularization, resembling the vessels of the tunica vasculosa lentis, was present on the anterior lens surface. Dense posterior synechiae were noted. Intraocular pressures were 14 mm Hg OD and 5 mm Hg OS.

Fundus examination results of the right eye showed prominent vitreous veins, liquefaction, synechiae, and a partial posterior vitreous detachment. Disc pallor was present, with a cup-disc ratio of 0.3. The peripheral retina had areas of lattice, extensive microcystoid degeneration, and long oral bays. The fundus of the left eye was not visible because of the white cataract. Ultrasonography of the right eye showed evidence of vitreous degeneration with sparse echodes in the posterior third of the vitreous. The left eye had total closed funnel retinal detachment.

Systemic examination findings showed abnormal growth with flexion contractures, delayed motor development, hearing loss, muscle atrophy, and normal intelligence. Radiographs showed vertebral defects, short tubular bones with epiphyseal irregularities, and metaphyseal enlargement of the femurs producing a typical “dumbbell-shaped” appearance, along with platyspondyly, vertebral spurs, and clefts in the vertebrae. Photographs showed that the patient had been born with short limbs and a hypoplastic midface, and she developed lumbar lordosis resulting in a typical “about to dive” posture. She had a dishlike facies with button nose and prominent eyes.

Pars plana vitrectomy with lensectomy was performed in the left eye. The central anterior and posterior capsules were dissected with scissors and placed in 2.5% glutaraldehyde for electron microscopy. The vitreous base demonstrated retracted vitreous with severe anterior loop traction, heavy deposits of pigments, and dense vitreous veins and strands. Schlierenlike subretinal fluid was drained through a supranasal hole. Giant retinal macrocytods made flattening of the thinned, foreshortened, cystic retina difficult. The retina remained flat and attached for a month, after which it redetached and eye became phthisical.

Histopathologic examination of the lens capsule disclosed thickened anterior and posterior capsules and metaplastic lens epithelium. Transmission electron microscopy of the anterior capsule confirmed the aforementioned findings and additionally demonstrated loss of normal architecture of the lens epithelium. The metaplastic epithelial cells were surrounded by fine fibrillar and amorphous extracellular matrix material, as well as basement membrane material (Figure 1 and Figure 2). The aberrant epithelial cells were elongated and spindle shaped and had swollen mitochondria and dilated cisternae of endoplasmic reticulum (Figure 2 and Figure 3). Fine fibrillar collagen and dystrophic calcification were also apparent (Figure 3).

The posterior capsule tissue showed aberrant lens epithelial cells that had probably migrated into the posterior subcapsular plaque (Figure 4). These cells with electron-dense granules had cystic mitochondria and dilated endoplasmic reticulum (Figure 5) similar to the anterior subcapsular region. These cells were also surrounded by fine fibrillar collagen.
Comment. Congenital severe myopia, vitreoretinal degeneration, and retinal detachment are known ocular abnormalities associated with Kniest dysplasia. Previous studies showed a predominant defect in the type II collagen major fibril, which is a major constituent of the vitreous. It has also been postulated that collagen type IIA has an important role in the maturation and maintenance of the retina. The predisposition for retinal detachment in these patients may be due to improper maturation of collagen type IIA.

Early development of cataracts has been believed to be related to the pathogenesis of the disease. The cataracts are unusually hard for the age and require phacoemulsification rather than aspiration, as was evident in our patient. The mechanism of cataract development in these patients has not been established.
Electron microscopy of the anterior and posterior capsule of the lens showed aberrant epithelial cells with dilated endoplasmic reticulum, formation of collagenous fibrous tissue, and dystrophic calcification. These findings are reminiscent of the changes seen in cartilage. The histopathologic changes in the lens indicate that it is involved in Kniest dysplasia either primarily or secondarily. Formation of abnormal subcapsular collagen plaques beneath the capsules together with dystrophic calcification may be responsible for the abnormally hard cataracts. The cataract could also develop as a posterior capsular opacity and progress to a total cataract. Another possible mechanism for cataract development could be abnormal lens fiber formation due to the metaplastic lens epithelial cells. Dilated endoplasmic reticulum in cartilage chondrocytes and lens epithelial cells may be indicative of synthesis of abnormal protein and extracellular matrix material. Although changes in Kniest dysplasia appear to be developmental, unilateral cases of cataract and retinal detachment have been reported.3

Our observation supports the theory that the underlying defect causing cataracts is primarily a collagen synthesis defect. Production of abnormal glycosaminoglycans probably has a minimal role in the pathogenesis of the ocular defects. Our findings bear great similarity to the histopathologic features described in Lowe syndrome.7,8 The abnormalities noted in Kniest dysplasia could be developmental, and a periodic comprehensive ophthalmic evaluation of the patient is warranted.

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Polymorphous Low-Grade Adenocarcinoma of the Lacrimal Gland

Malignancies constitute half of all epithelial tumors of the lacrimal gland, with the majority being adenoid cystic carcinoma. Adenocarcinomas are much less common and generally demonstrate a poor prognosis. However, the recent application of histological subtyping to this group is leading to a better characterization of what appears to be a heterogeneous collection. We present a rare case of polymorphous low-grade adenocarcinoma (PLA) of the lacrimal gland and discuss the clinical manifestation and prognosis in the context of similar tumors arising within the salivary glands.

Report of a Case. A 67-year-old man was initially seen with painless right upper eyelid swelling and conjunctival hyperemia across a 2-day period. The patient had been previously asymptomatic, and old photographs were not available for review. Examination revealed him to be afebrile with a visual acuity of 6/12 OD and 6/9 OS, 6 mm of proptosis, 3-mm inferior globe displacement, temporal conjunctival hyperemia, and a tender mass in the superotemporal orbit. Extraocular movements were limited in lateral and up gazes. The erythrocyte sedimentation rate was 61 mm/h and white blood cell count, 13,200/µL (13.2 × 109/L). Computed tomography findings showed an ill-defined mass in the lacrimal gland with a central radiolucency, rim enhancement, and no bony changes (Figure 1).

The mass was surgically explored via a skin-crease incision and appeared to consist of an abscess containing yellow-green viscous material. A culture yielded no growth, but biopsy findings of the cavity wall revealed adenocarcinoma thought to represent a primary lacrimal neoplasm rather than metastasis because the tumor expressed both cytokeratin (CAM 5.2) and S100 protein immunoreactivity. This immunoprofile, while not diagnostic, is typical of salivary gland tumors including PLA.

The patient underwent thorough systemic evaluation, including computed tomography of the chest, abdomen, and head. All investigation results were normal, and a lid-sparing exenteration, including the biopsy track, was performed.

Results. Histopathologic results revealed PLA of the lacrimal gland (Figure 2). The tumor cells were cytologically bland, showing mild nuclear pleomorphism, and no mitoses were identified. However, there was extensive infiltration of the adjacent tissue, and the tumor displayed a variety of architectural patterns, including cribriform, tubular, and fascicular areas along with solid cell nests. Some necrosis was seen centrally, and infiltration of the extraocular muscle was present.

Figure 1. Axial computed tomographic scan shows a mass in the right lacrimal gland with a central radiolucent area.