Ocular abnormalities in the myopathic hamster (UM-X7.1 strain)

J. H. Thakar, D. H. Percy,** and K. P. Strickland**

Eyes from cardiomyopathic hamsters (UM-X7.1 strain) were examined histologically for evidence of ocular defects. Changes observed included microphthalmia, scleral ectasia, scleral rupture, keratoconus, retinal detachment, retinal dysplasia, retinal fragmentation, retinal thinning, fibrosis of iris and ciliary body, ectopia lentis, and cataract formation. Lesions characteristic of cardiomyopathic hamsters were observed in the myocardium and skeletal muscle. This strain may be a suitable animal model to study the pathogenesis of ocular changes seen in certain congenital connective tissue disorders in man.

Key words: Cardiomyopathic hamster, animal model, microphthalmia, scleral ectasia, retinal dysplasia, ectopia lentis, cataract formation.

In the strains BI0 14.6 and UM-X7.1 of Syrian hamster, there is a hereditary polymyopathy characterized by primary cardiomyopathy and muscular dystrophy.[1-3] Both of these strains are considered to be appropriate animal models of the Duchenne type of human muscular dystrophy.[1-3] Muscular dystrophy in these polymyopathic hamsters is transmitted by an autosomal recessive gene, and histological evidence of skeletal muscle lesions may be observed in animals as young as 20 days old.[2] In the UM-X7.1 strain, lesions in skeletal and cardiac muscle are present in virtually all mature animals.[2, 3] Death is usually due to terminal congestive heart failure.[2] In this animal model, abnormalities of membrane-bound enzymes have been observed.[4] Of particular interest are the elevated calcium levels in serum, skeletal, and cardiac muscles.[5, 6] The purpose of this communication is to describe concurrent ocular changes observed in animals of the UM-X7.1 strain.

From the *Departments of Biochemistry, and **Bacteriology and Immunology, The University of Western Ontario, London, Canada.

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Reprint requests: Dr. J. H. Thakar, Health Sciences Centre, The University of Western Ontario, London, Ontario, N6A 5C1 Canada.

Materials and methods

Animals of the UM-X7.1 strain were obtained from Dr. G. Jasmin, University of Montreal, Montreal, P. Q., and then bred locally. Both animals with clinically detectable abnormal eyes and those with normal eyes were killed at various ages for macroscopic and microscopic evaluation. Tissues from nonaffected BI0 hamsters (Trenton Experimental Laboratory, Bar Harbor, Maine) were used as controls. Animals were killed by chloroform inhalation, fixed by immersion in Bouin's fluid or 3 percent glutaraldehyde, embedded in paraffin, sectioned at 5 μ, and stained with hematoxylin and eosin (H & E). Halved, meridional sections of both eyes, quadriceps muscle, and heart were routinely examined. Lesions were graded accord-

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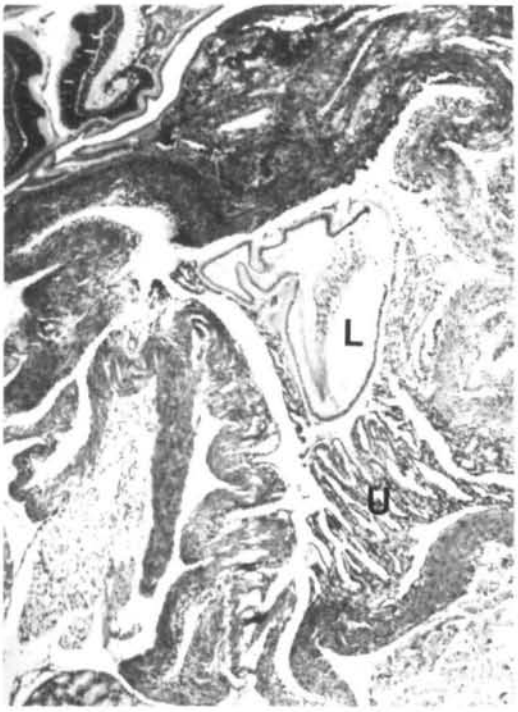

Fig. 1. Hamster 3759 examined at 3 months of age. There is marked microphthalmia with irregular contours of sclera and lens *(L)*. Primordial uveal tract *(U)* is thrown into folds and adherent to lens. Retina is at upper left. (H & E; ×30.)

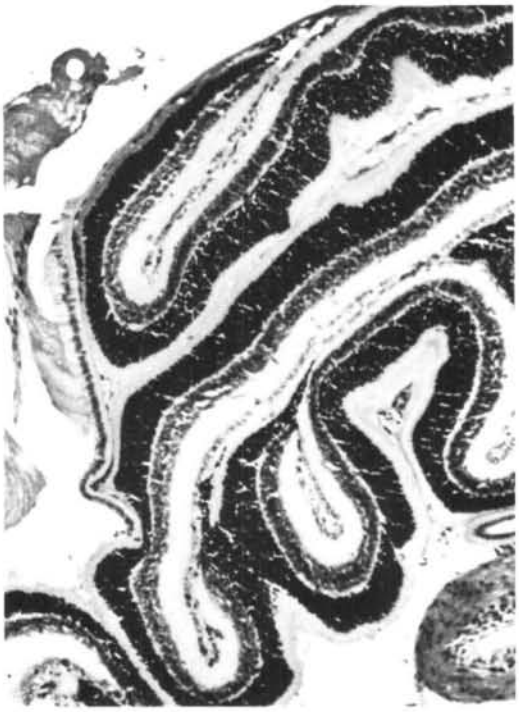

Fig. 2. Higher magnification of retina shown in Fig. 1. Although there are multiple undulations, most layers, including the inner and outer nuclear layers, are clearly delineated. Identifiable lens epithelium and fibers are present at the left. (H & E; ×82.5.)

Table I. Incidence of ocular lesions in the UM-X7.1 hamster

Age at examination (days)	*No. of animals affected/ no. of animals examined*	*Sclera & cornea**	*Uveal tract**	*Retina**	*Lens**	*Microphthalmia**
1-34	4/11	4/22	2/22	4/22	4/22	2/22
35-56	0/5	0/10	0/10	0/10	0/10	0/10
70-112	4/9	5/18	4/18	6/18	2/13	1/18
180-245	7/8	11/16	5/16	8/16	6/12	1/16

*No. of eyes with lesions/no. of eyes examined.

ing to the size, distribution, and intensity of the affected areas.

Results

Clinical and macroscopic findings. Some clinically affected animals were reported to exhibit intermittent ptosis with a tendency to recur and regress over a period of several weeks. Frequently, only one eye was involved. Macroscopically, a few affected eyes were irregular in shape and markedly reduced in size. In some instances, irregularities in the corneal or scleral contours were demonstrable on gross examination, but frequently ocular abnormalities were only evident microscopically.

Microscopic findings. In general, abnormal eyes were most numerous in older animals (Table I). Unilateral microphthalmia was observed in four hamsters. Scleral outlines were irregular and undulating, with no evidence of normal globe formation (Fig. 1). The uveal tract was poorly developed, with incomplete adherence to the adjacent sclera. Portions interpreted to

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Fig. 3. Animal 3715-3, age 6 months, with scleral ectasia. Note marked reduction in width of sclera progressing from normal sclera (lower center) to thin undulating areas. There is a corresponding reduction in width of the adjacent retina. (H & E; ×82.5.)

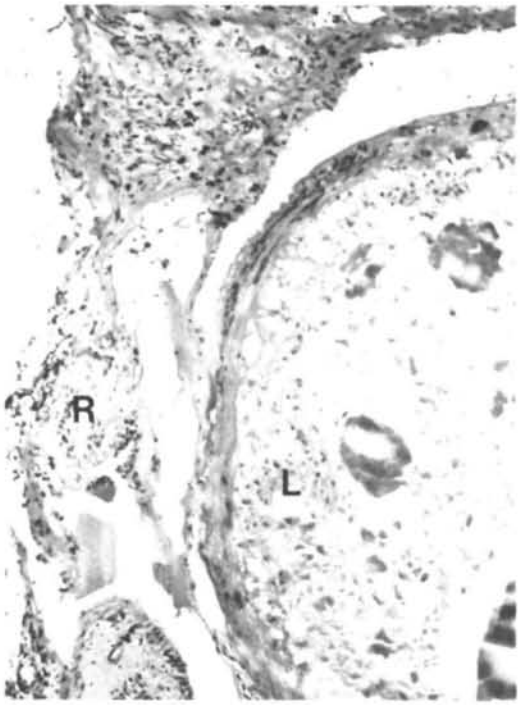

Fig. 4. Eye from No. 3715-2 at 6 months of age. Rupture of sclera (upper left) with fibrosis and pigment deposition in damaged tissue. Note distortion and fragmentation of retina *(R)*. Lens *(L)* has a thickened capsule, with numerous bladder cells in subcapsular region. (H & E; ×82.5.)

be primordial iris and ciliary body were composed of a folded layer lined by cuboidal epithelial cells present in close apposition to the lens (Fig. 1). In one animal, the retina was located outside the confines of the sclera (Figs. 1 and 2). The lens was reduced in size and lined by a relatively normal layer of epithelial cells and had contours that followed the outlines of the adjacent sclera (Fig. 1).

Scleral ectasia was a frequent finding. The sclera was markedly reduced in width in affected areas, with undulations and eversion of the scleral contours. Changes in the retina included thinning and obliteration of identifiable nuclear layers (Fig. 3). In a few eyes, there were apparent focal scleral disruption and rupture, with retraction of the severed ends, collapse of the globe, and herniation and degeneration of pigment epithelium and neural retina. Clefts between the retina and sclera appeared to contain vitreous material. Degenerative retinal changes observed in affected eyes included retinal detachment, dysplasia, infolding, thinning, cystoid degeneration, and separation of affected portions (Figs. 4 to 6). Thinning and obliteration of the layers of the retina, when present, were always in association with obvious scleral abnormalities. In a few eyes, there was concurrent proliferation of pigment epithelial cells, with fibrosis and obliteration of the normal achitecture.

Keratoconus and irregularities in the filtration angle were occasionally observed. Marked thickening of the iris stroma and fibrosis and mineralization of the iris root and trabecular meshwork were especially striking in single eyes from two animals examined at 6 months of age (Fig. 7). In these animals, there were also marked

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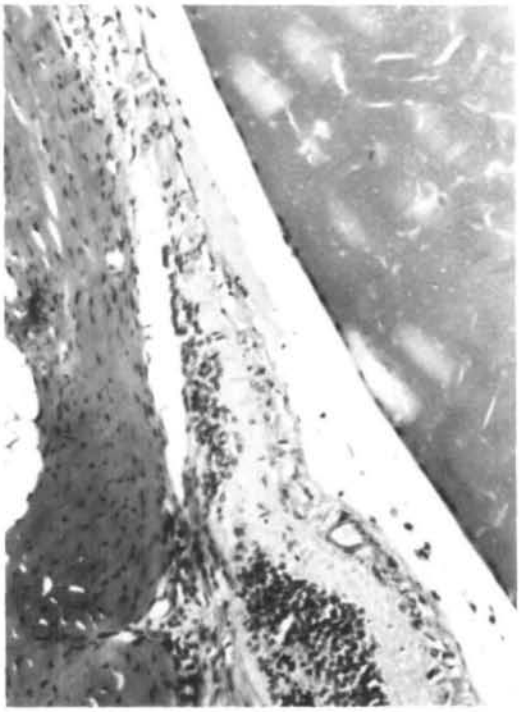

Fig. 5. Animal 3737B examined at 6 months of age. Progressive reduction in width of retina with loss of identifiable layers. Lens is at right. (H & E; ×82.5.)

Fig. 6. Higher magnification of Fig. 5, illustrating extensive retinal degeneration. Large clefts are evident, with absence of normal retinal architecture. Sclera is at left. Note subcapsular cataractous change in adjacent lens. (H & E; ×208.)

changes in other regions of the same eye. However, in some eyes with scleral deformities, the iris, ciliary body, and filtration angle appeared to be histologically normal. In one animal (No. 3740) there was malformation of the iris, with proliferation of pigment cells suggestive of melanoma of the iris.

The lens was sometimes displaced into the vitreous cavity and separated from the ciliary process. Lenticular changes included spherophakia, thickening and irregularities of the lens capsule, proliferation and migration of epithelial cells with "bladder cell" formation, fragmentation of lens fibers, and liquefaction of lens material (Figs. 4 and 6).

Myocardial lesions similar to those previously described[8] were evident in virtually all animals examined at 6 weeks of age or older. The degree of involvement of skeletal muscle varied from degeneration of isolated myofibers to large areas involving an entire segment of muscle. In reactive myofibers, poles of the nuclei were frequently aligned in close proximity along the sarcolemmal sheath (Fig. 8).

Discussion

Knapp and Polivanov[7] and Robinson[8] reported on anophthalmic hamsters, and Yoon[9] described anophthalmia in progeny resulting from the cross-mating of two inbred lines, BI0 72.79 and BI0 4.24. A variety of eye defects have been associated with certain connective tissue diseases. Keratoconus and ectopia lentis have been observed in the myopathic hamsters in this study and also occur in Marfan's syndrome in man.[10, 11] Spherophakia and ectopia lentis have been observed in the Weill-Marchesani syndrome,[11] and defects observed in the eye of patients with Ehlers-Danlos syndrome have included keratoconus and ectopic lens.[11] Ocular tonometry was not performed on our animals to determine

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Fig. 7. Animal 3737-A examined at 6 months of age. Note marked thickening and fibrosis of iris and ciliary body. The abnormal ciliary body is adherent to the lens capsule *(L)*. (H & E; ×82.5.)

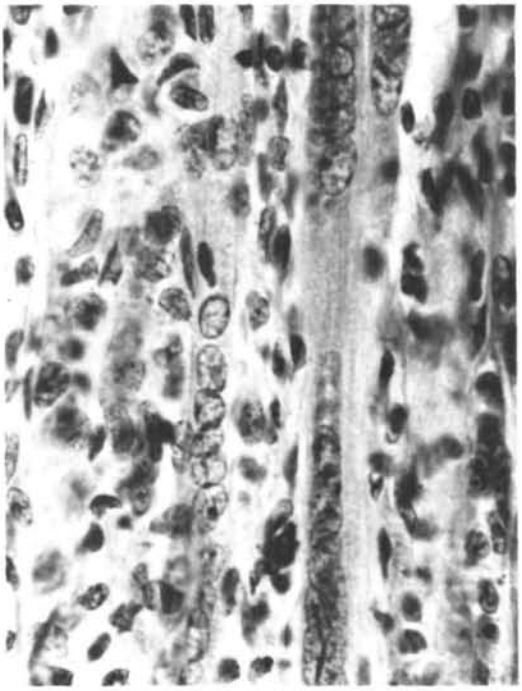

Fig. 8. Quadriceps muscle from hamster 3759. There is marked degeneration of sarcoplasm, with hypercellularity and proliferation of sarcolemmal nuclei. (H & E; ×160.)

whether intraocular pressures were normal, but changes in the sclera, cornea, and retina might be secondary to glaucoma. Infantile glaucoma has occasionally been observed in patients with Marfan's syndrome and Weill-Marchesani syndrome.[12]

At present, the exact nature of the abnormalities and the sequence of events have not been determined. However, with the exception of eyes with severe microphthalmia, the retinal changes may be secondary to events such as detachment from pigment epithelium, scleral ectasia, and scleral rupture. The UM-X7.1 strain represents a possible animal model to study the pathogenesis of ocular changes that may have application to certain congenital connective tissue disorders in man. Abnormalities observed in the heart and skeletal muscle are attributed to a "membrane defect,"[4, 5] which may also play a role in the ocular changes. Additional studies are in progress.

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