Animal Model of Closed Angle Glaucoma in Albino Mutant Quails

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The intraocular pressure of imperfect albino mutant quails with a sex-linked recessive gene was measured by using a cannulating method, and morphological changes of the iridocorneal angle were observed with a gonioprism. Albino mutant quails were characterized by an elevated intraocular pressure and lens enlargement at 6 mo after hatching. Initially the iridocorneal angle opened and eventually closed. The usefulness of the closed angle glaucoma as an animal model system for human diseases was discussed.


Animal models have provided valuable information for understanding human eye diseases. Spontaneous buphthalmos or glaucoma model in animals has been reported in rabbits and dogs.1–5 An imperfect albino mutant quail with a sex-linked recessive gene exhibits interesting ocular diseases, such as eye enlargement, retinal ganglion cell degeneration, cupping of the optic disc, and cataract.6–8 The histopathological findings in the retina of albino mutant quails are similar to those in animals with experimentally induced or spontaneous glaucoma. Previously,7 we did not consider the albino mutant quails as an avian glaucoma, because we had not measured their intraocular pressure.

In this study, we measured intraocular pressure by means of manometry and observed the morphological changes of the iridocorneal angle in albino mutant quail eyes at early, moderate, and advanced stages of avian glaucoma to elucidate the primary defect responsible for the development of the disease and its pathogenesis.

Materials and Methods

Imperfect albino mutant quails (Coturnix coturnix japonica, gene symbol al) were used at 3 (n = 25), 6 (n = 25), and 12 (n = 15) mo of age, and normal wild type quails at 3 (n = 15), 6 (n = 15) and 12 (n = 5) mo of age. The quails become mature at 2 mo after hatching. Animals were kept, from the time of hatching, under continuous 20-W incandescent bulbs for 4 wk. The animals were then exposed to a diurnal schedule, usually 16 hr of light per day. Animals were fed a normal quail diet and water ad libitum.

The animals were anesthetized with sodium pentobarbital (2.5 mg/100 g i.p.), and their eyes were examined with a slit-lamp biomicroscope and Koeppe type gonioprism modified for small animal eyes. To measure intraocular pressure, the quails were anesthetized with sodium pentobarbital, and the head was immobilized by ear bars which were inserted into the external auditory meati. The eyes were cannulated with 27 G needles connected via short lengths of polyethylene tubing (outer diameter 1 mm) to Statham pressure transducer (Nihon Koden; Tokyo, Japan). The entire system was filled with heparin solution. Entry through the cornea into the anterior chamber was made from the temporal side of the eye, in order to minimize irritation of the nictitating membrane. Care was taken to prevent aqueous humor loss and not to strike the iris. Continuous recording was done with an ink writing oscillograph.

After the intraocular pressure was measured, the animals were killed by cervical dislocation. The one third of the eyeball including the lens was carefully removed, and normal wild type quails at 3 (n = 15), 6 (n = 15) and 12 (n = 5) mo of age. The quails become mature at 2 mo after hatching. Animals were kept, from the time of hatch-
pillarae in avian eyes is composed of striated muscle rather than smooth muscle. There were many pigment granules in the pigment epithelium, choroid, ciliary processes, ora serrata, and iris in normal quails. In al mutant quails, there were few pigment granules in the pigment epithelium and choroid, while some pigment granules could be observed in the ciliary processes, ora serrata and iris. Therefore, al mutant quails have a ruby eye color instead of brown. The corneas in al mutant quails were flatter than those in normal quails at 3 mo of age (Figs. 1A–B). At 12 mo of age the corneas in some al mutant quails protruded forward and were milk white. The cornea of normal quails had not changed at 12 mo.

**Intraocular Pressure (IOP)**

Figure 2 shows the IOP of normal and al mutant quails determined by the cannulating method. The mean IOP of the normal quails at 3 and 6 mo of age was 16.3 mm ± 1.4 mm Hg and 17.3 mm ± 1.7 mm Hg. The mean IOP of al mutant quails at 3 mo of age was 19.6 mm ± 1.6 mm Hg. At this age, there was no significant difference between the mean IOP of normal and al mutant quails. However, the mean IOP (25.2 mm ± 2.2 mm Hg) of al mutant quails at 6 mo of age was significantly higher than the mean IOP of normal quails. Some al mutant quails showed markedly elevated IOP (over 35 mm Hg) at 12 mo.

**Lens Dimensions**

The mean lens dimensions of normal quails at 3 or 12 mo of age were 4.2 × 4.1 × 2.7 mm. No anomalous appearances were observed in normal quail lenses at 3 or 12 mo after hatching. The mean lens dimensions (4.4 × 4.3 × 3.1 mm) of al mutant quails at 3 mo of age were slightly larger than those of normal quails. At 6 mo of age, many lenses had become opaque, and the mean lens dimensions (4.7 × 4.5 × 3.5 mm) of the al mutant quails were larger than those of the normal quails (Fig. 3). The lens was particularly enlarged in the antero-posterior direction. The mean lens dimensions of al mutant quails were 4.8 × 4.7 × 3.5 mm at 12 mo of age. The whole lens was opaque, and lens atrophy was observed in severe cases at this age group.

The lens weight at 3 mo of age was 23.6 mg ± 1.6 mg in normal quails and 24.8 mg ± 2.2 mg in al mutant quails. At 6 mo of age, the lens of the al mutant quails (33.2 mg ± 3.5 mg) was heavier than that of the normal quails (23.8 mg ± 1.4 mg).

**Iridocorneal Angle**

No differences were detected in the iridocorneal angles between the 3- and 6-mo-old normal quails. The angles in normal quails were open (Fig. 4A). At 3 mo of age, when glaucoma was in the early stage, the iridocorneal angles in most al mutant quails opened (Fig. 4B). The corneal curvature in al mutant quails was flat compared with that in normal quails (Figs. 1A and 1B). Although the iridocorneal angles in al mutant quails at 3 mo of age were open, the anterior chambers were shallow. At 6 mo of age, the iridocorneal angles in 13 of the 20 eyes of the al mutant quails were closed (Fig. 4C). At 6 mo of age, when glaucoma was in an advanced stage, the whole iris was attached to the posterior cornea. This suggests anterior synechia. Under this condition, the pupil was not reflexed by light. At 12 mo of age, the iridocorneal angles in most al mutant quails were usually closed, and many congested vessels
largement, shallowed anterior chamber, reduced corneal curvature, closed iridocorneal angles and elevated IOP. Anterior synechia eventually develops in the late stage of light-induced avian glaucoma. Lauber and McGinnis reported that eye enlargement does not de-

were present on the anterior surface of the iris. Corneal edema and a fixed pupil were also observed.

**Discussion**

Lauber was the first to find sex-linked albinism in the Japanese quail. He crossed the F1 offsprings with each other, and found that most albino quails died within 3 to 4 days after hatching and that the albino gene itself was semi-lethal. However, avian species are easily killed by inbreeding. Nakamura and Kaneko also found a spontaneous sex-linked recessive albino mutation in a Japanese quail. The female albino quail was mated with unrelated normal quails, and then F1 males were mated with their mother and sisters. However, the mating was unsuccessful. Most of the albino quail chicks died. Subsequently, they mated F1 males with unrelated female normal quails and paid special attention to the suitable temperature for broodings. In that case, the viability and hatchability of the albino quails have markedly increased.

Accurate measurement of IOP in the glaucomatous animals is essential. We measured IOP by means of manometry following cannulation. A noninvasive method of IOP measurement would be valuable. However, common instruments for measurement of IOP (Schiotz tonometer, Winters; Hamburg, West Germany, applanation tonometer of Goldmann, Haagstreich; Bern, Switzerland, or pneumatic applanation tonometer) could not be used in the present study, because quail corneas were too small. IOP in avian species has been reported by several investigators. The mean IOP values for normal quails were similar to those for domestic fowl reported by Sears and Seaman and Himelfarb. Because the al mutant quails at 6 mo of age had showed significantly higher IOP, they were considered to have avian glaucoma.

Chickens reared from hatching in continuous incandescent light have been reported to develop eye en-
velop in Japanese quails reared under continuous light, but that corneal curvature is reduced and corneal diameter small in the quails.16 We used normal quails which were kept from the time of hatching, under continuous 20-W incandescent bulbs for 4 wk. Therefore, the normal quails may not serve as a baseline control. However, neither eye enlargement nor degeneration of retinal ganglion cells has been observed in normal quails.14 In al mutant quails, we had found eye enlargement, retinal ganglion cell loss and cupping of the optic disc. In the present study, we detected reduced corneal curvature and elevated IOP in al mutant quails. If the corneal curvature of al mutant quails was compared with that of normal quails kept under truly diurnal conditions, the differences in corneal curvature might have been greater.

In the postnatal growing period, some animals have a regulatory mechanism which directs the growth of the eye toward emmetropia.17 In al mutant quails, a low corneal refraction due to reduced corneal curvature might give rise to elongation of the eye in order to improve the visual image. However, eye dimensions of al mutant quails at 3 mo of age were similar to those of normal quails. The quails are mature at 2 mo after hatching. The eye enlargement of al mutant quails was observed during 6–12 mo after hatching. Therefore, eye enlargement in al mutant quails is not due to the elongation of the eye to improve the visual image. Albinism in humans is often associated with myopia. The al mutant quails have weak eyes and are photophobic. It appears that al mutant quail eyes are useful only for near vision, on the basis of behavioral observation.

Gonioscopic examination of al mutant quail eyes indicated an open iridocorneal angle at 3 mo of age, an early stage of glaucoma. In moderate and advanced glaucomatous stages at 6 mo of age, the iridocorneal angles of al mutant quail eyes were closed due to anterior synchia. This suggests that al mutant quails are closed angle type of glaucoma. Closed iridocorneal angle in al mutant quails may be associated with reduced corneal curvature and lens enlargement. Smith et al suggested that reduced corneal curvature and narrowed iridocorneal angle were related to the angle-closure glaucoma that later developed,13 but Frankelson et al reported that iridectomies performed on newly hatched chicks that were subsequently reared under continuous light failed to alter the course of development of the characteristic glaucoma.18 Therefore, Lauber et al concluded that increased inflow may be the primary lesion in light induced avian glaucoma, but not impaired aqueous outflow facility.14 The IOP of al mutant quails at 3 mo of age was slightly higher than that of normal quails at the same age, although eye enlargement could not be detected in al mutant quails. Eye enlargement could be observed in al mutant quails at 6 mo of age.17 In this age group, elevated IOP and lens enlargement were discernible. Narrowed iridocorneal angle due to reduced corneal curvature and lens enlargement may cause an obstacle of drainage in the aqueous humor. In human senile cataract, an intumescent cataract pushes the iris forwards forcing the anterior chamber to become shallow and block the iridocorneal angle.19 Although lens enlargement was not reported in light-induced avian glaucoma, it may play an important role in the pathogenesis of albino avian glaucoma. However, studies on aqueous flow, iridectomy, and extraction of lens must be performed in the future to elucidate the pathogenesis of this albino avian glaucoma.

Spontaneous buphthalmos or glaucoma as an animal model has been reported in rabbits and dogs. Recessive buphthalmos in the rabbits was linked to a semilethal trait accompanied by other congenital malformations.1 Spontaneous glaucoma has been investigated in three breeds of dogs: American cocker spaniel, basset hound, and the beagle.20,21 It appeared that beagle glaucoma was a simple autosomal inheritance. It takes over 12 mo before the dogs suffer from glaucoma. The al mutant quails described here are an imperfect albino mutation with a sex-linked recessive gene. The al mutant quails as a glaucoma model exhibit a predictable clinical course over a period of at least 3 to 6 mo after hatching and show no congenital anomalies except for the pigmentation. It is easy to maintain and to handle al mutant quails in a laboratory. Although the primary pathologic event is still obscure, albino avian glaucoma in experimental animals presents a unique opportunity in the study of the etiology and pathogenesis of the disease. The ocular changes, such as lens enlargement, lens opacity, or reduced corneal curvature, in al mutant quails may be associated with the recessive albino gene itself, or be a secondary effect caused by illumination or other environmental factors.

Key words: avian glaucoma, animal model, albino quails, closed iridocorneal angle, elevated intraocular pressure, lens enlargement

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