Ophthalmic examination of heterotopic bone formation in guinea pig: A case report

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Abstract

Two different types of ophthalmic optical coherence tomography (OCT) imaging were used to evaluate ocular health in a guinea pig suspected of having heterotopic bone formation (HBF). Captured images facilitated diagnosis of HBF. This case report provides reference OCT images of HBF in the guinea pig.

Key Clinical Message

The application of advanced ophthalmic imaging techniques facilitates the diagnosis of heterotopic bone formation in a guinea pig. These devices can provide additional important clinical insight into the functional implications of this pathology.

INTRODUCTION

Heterotopic bone formation (HBF) or osseous metaplasia/choristoma describes the abnormal growth of bone in muscle and soft tissues.[1] Although ocular HBF has been reported across a range of species, it is most often reported in the guinea pig (*Cavia porcellus*),[2–5] with one study, by Williams and Sullivan, reporting a prevalence figure for HBF in the ciliary body of 8 in 1000 guinea pigs.[5] Such bony tissue outgrowths appear to also originate in the ciliary body, becoming more visible when or if they grow into the iridocorneal angle. Associated discomfort and/or visual problems are generally believed to be unlikely, unless the entire circumference of the iridocorneal angle is affected.

While intraocular osseous metaplasia can develop secondary to penetrating trauma, intraocular infections, and intraocular inflammation, its precise etiology is unknown. However, one hypothesis has linked this condition to the accumulation of high levels of ascorbic acid (vitamin C) in the ciliary body and aqueous humor.[5] Although deficiencies in vitamin C are known to cause signs of scurvy and other health problems in guinea pigs, over-supplementation may lead to high concentrations of this essential nutrient in the ciliary body and promote localized mineralization and bone formation.

Optical coherence tomography (OCT)[6] has become the standard of care in ophthalmology, providing real-time, high resolution structural information for use in diagnosing disease and helping to understand disease pathogenesis.[7,8] However, the application of OCT imaging in the evaluation of HBF in guinea pig has not been reported to-date.

The primary purpose of this case report is to establish reference OCT ophthalmic findings for HBF in guinea pig.

MATERIALS AND METHODS

A 3.8-year-old male guinea pig (1.4 kg; Elm Hill pigmented strain [Elm Hill Labs, Chelmsford, MA, USA]) underwent a comprehensive ophthalmic examination after being suspected of having HBF by one of the campus veterinarians (co-author KJ). This animal was housed in an approved facility under a 12 h on/12 h off light cycle, with an average floor luminance of approximately 160 to 180 lux, and had free access to water and vitamin C-supplemented food; it also received fresh fruit and vegetables three times a week as dietary enrichment. All animal care and procedures outlined in this report conformed to the ARVO Statement for the Use of Animals in Ophthalmic and Vision Research. Experimental protocols were also approved by the Animal Care and Use Committee of the University of California, Berkeley, USA.

The examination included slit lamp biomicroscopy, gonioscopy, optical biometry (Lenstar LS900; Haag-Streit AG, Koeniz, Switzerland), rebound tonometry (iCare; Tonolab, Helsinki, Finland), anterior segment OCT (AS-OCT; Visante, Carl Zeiss Meditec, Inc., Dublin, CA, USA), and posterior segment spectral domain OCT (SD-OCT; Bioptigen Envisu R-Series, Morrisville, NC, USA). Cross-sectional ocular images, including of the HBF with AS-OCT and of the optic nerve head with SD-OCT, were captured for later analysis. From the latter images, overall retinal and nerve fiber layer thicknesses were estimated at one location, approximately 700 um nasally with respect to the center of the optic nerve head.

All procedures were performed on the animal subject while awake, with the exception of SD-OCT imaging and gonioscopy, for which the subject was anesthetized with a ketamine/xylazine cocktail (27/0.6 mg/kg body weight). A topical anesthetic (0.5% proparacaine hydrochloride ophthalmic solution, Sandoz Inc) was also instilled prior to gonioscopy, which made use of a custom-designed 5.5 mm four mirror gonioprism lens (Ocular Instruments, Inc, Bellevue, WA, USA).

RESULTS

Slit lamp biomicroscopy revealed vascularized white masses in the anterior chambers of both eyes, sandwiched between the posterior corneal (endothelium) and anterior iris surfaces, adjacent to the limbus both nasally and temporally in the right eye, and superiorly and temporally in the left eye (Figure 1a-f). AS-OCT and gonioscopy confirmed the location of these white lesions in the space between the cornea and iris (Figure 1g-j). Results from tonometry and optical biometry are summarized in Table 1. The IOP of the right eye was found to be slightly higher than that of the left eye, and its axial length was also longer. However, SD-OCT imaging showed no obvious differences in the appearance of the optic nerve heads of right and left eyes (Figure 2a & b), and both overall retinal and nerve fiber layer thickness in the sampled regions were similar for the two eyes (see Table 1).

DISCUSSION

Diagnosis of HBF is usually made on clinical appearance alone.[2–5] While there is no known treatment for the condition, intervention is typically not necessary as affected eyes generally remain healthy and the animals remain comfortable. For the same reasons, histopathologic confirmation of the diagnosis is rarely done.

In the case reported here, the two eyes were differentially affected, both in terms of location and extensity of the lesions. Both AS-OCT and gonioscopy proved valuable in assessing the location of the lesions, which were confirmed to lie in the region of the iridocorneal angle, adjacent to the corneal endothelium rather than within the cornea.[8]

While the overall prognosis for HBF appears to be good, it would seem prudent to continue with periodic ocular examinations of affected animals to include monitoring of IOP. To-date, an association with secondary glaucoma, the byproduct of accumulation of bone in the iridocorneal angle, has not been definitively established.[5,9] For example, glaucoma was not recognized clinically in a recent large study of guinea pigs,[5] although a possible association between HBF and glaucoma has been raised based on postmortem findings in another study, which unfortunately lacked IOP data.[9]

The subject of the current study offers provocative evidence in support of a link between HBF and secondary glaucoma in that the right eye recorded a higher IOP, by 5 mmHg, compared to that of the left eye. Moreover, the right eye was also slightly longer than the left eye, raising the possibility of pressure-induced accelerated

scleral creep, as also noted in human babies with congenital glaucoma.[10] However, it is important to note that the IOPs of both eyes of this guinea pig subject were still within normal reference limits.[11] The latter finding may also explain why there were no obvious differences between the two eyes, in either the appearance of the optic nerve heads or thicknesses of nearby retina and nerve fiber layer, as evaluated by SD-OCT. Nonetheless, as HBF is considered a progressive condition,[12] longer term monitoring may reveal changes over time, in both IOP and optic nerve head morphology.

Two different types of ophthalmic OCT imaging instruments were used to examine the eyes of this animal, with each having their own merits. AS-OCT allowed visualization of the lesions, yielding high quality cross-sectional images of the anterior ocular segment without the need for corneal anesthesia as required with gonioscopy. However, it should be acknowledged that there are substantial differences in instrument costs, with gonioscopy being more affordable, despite the need for custom designing a gonio lens for use on the guinea pig eye. SD-OCT imaging was also undertaken in the examination of this subject, offering potential early insight into the functional implications of any increase in IOP, with additional value when direct visual function testing is not possible.

In conclusion, advanced ophthalmic imaging techniques have utility in the diagnosis and monitoring of HBF in the guinea pig, with the potential to offer new insights into its pathophysiology and disease progression.

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ABBREVIATIONS

AS-OCT; anterior segment optical coherence tomography

HBF; heterotopic bone formation

SD-OCT; spectral domain optical coherence tomography

IOP; intraocular pressure

AUTHOR CONTRIBUTIONS

SG planed and wrote the manuscript. QZ and JT collected the data. KJ and CW contributed to the interpretation of data, and critically revised the manuscript. All authors approved of the final manuscript version.

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