Concurrent clinical intraocular findings in horses with depigmented punctate chorioretinal foci

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Abstract
Objective To report concurrent clinical intraocular findings in horses with depigmented punctate chorioretinal foci and to document any correlation with equine recurrent uveitis (ERU).
Procedure Records of 131 horses (241 eyes) examined at the University of Georgia Veterinary Teaching hospital from 2001 to 2010 were reviewed with either clinically normal fundi or depigmented punctate chorioretinal foci in the absence of other fundic pathology. Data collected included patient signalment, concurrent clinical ocular findings and follow-up information. Sex, presence of no other intraocular findings, presence of ERU, presence of cataracts, and presence of vitreal disease were compared between normal and foci groups using chi-squared analysis. Age and length of follow-up time were compared using a student's t-test.
Results Ninety-one horses (167 eyes) with chorioretinal foci and forty horses (74 eyes) with clinically normal ocular fundi were examined. Fifty-eight (64%) horses with chorioretinal foci and 20 (50%) horses with clinically normal fundi had a normal intraocular examination. There was no significant difference in any of the criteria examined between groups.
Conclusions Horses with depigmented punctate chorioretinal foci, in the absence of other fundic pathology, are not more likely to have intraocular disease or ERU than horses with clinically normal ocular fundi. These findings suggest that depigmented punctate fundic foci in horses are not indicative of or associated with ERU.

Key Words: depigmented chorioretinal foci, equine, fundus, ophthalmology, retina

INTRODUCTION
Chorioretinal lesions in horses are typically classified as ‘active’ or ‘inactive’ based on their clinical appearance.¹–³ Active chorioretinal lesions are characterized by retinal hemorrhage, retinal edema, retinal detachment, or cellular infiltrate and may appear raised, hazy, gray, red, or irregular depending on the cause and severity.³,⁴ Inactive chorioretinal lesions may appear as white or depigmented, hyperpigmented, or mottled and are flat with no evidence of cellular infiltrate or hemorrhage.³,⁴ These are often termed chorioretinal scars.³,⁴ Chorioretinal lesions may occur in the tapetal or non-tapetal region and may be focal, multifocal, or diffuse.³ Commonly, inactive chorioretinal lesions are seen in the peripapillary region, typically in the non-tapetal fundus.³,⁴,⁶,⁷

Certain ‘classic’ inactive chorioretinal lesions such as ‘bullet-hole chorioretinitis’ and ‘butterfly lesions’ have been examined histologically. Clinically, ‘bullet-hole chorioretinitis’ is characterized by focal or multifocal circular depigmented chorioretinal foci with a hyperpigmented center, and ‘butterfly lesions’ are characterized by circum papillary mottled hyper- and depigmented scarring radiating nasal and temporal to the optic disk.¹–⁴ Histologically, both lesions demonstrate loss of normal retinal architecture with retinal pigmented epithelial hypertrophy, hyperpigmentation, and depigmentation suggestive of previous episodes of chorioretinitis.⁷

Known systemic causes of chorioretinitis in the horse include adenoviral infection,⁵ equine herpesvirus-1 infection,⁹ Rhodococcus equi infection,¹⁰ and Streptococcus equi var. equi¹¹,¹² among others. West Nile virus affects horses and is a well-documented cause of chorioretinitis in humans.¹³–¹⁵ Experimentally, Leptospira interrogans organisms may cause chorioretinitis¹⁶,¹⁷ and have been implicated in equine recurrent uveitis (ERU).¹⁷–²¹ ERU is known to cause chorioretinitis concurrently with vitritis, panophthalmitis, and/or anterior uveitis.¹⁶,²²–²⁷

Equine recurrent uveitis is a recurrent, bilateral, chronic disease horses and is the most common cause of blindness in
this species.ERU presents a certain diagnostic challenge because of its episodic, chronic nature and intermittent periods of quiescence. A specific diagnosis is made with documentation of repeated intraocular bouts of primary inflammation. The clinician may be suspicious of this disease when multiple intraocular signs of recurrent or chronic uveitis such as keratic precipitates, iris darkening and/or multifocal depigmentation, corpora nigra atrophy, anterior or posterior synechia, cataracts, vitreal degeneration, or chorioretinal scarring are observed without a clearly elucidated underlying cause. There is often a clinical history of periodic photophobia, tearing, blepharospasm, and hyperemia in affected horses. In certain cases, the diagnosis is fairly straightforward; however, an equine patient presented to the veterinary clinician with one or multiple intraocular lesions relatable to ERU may pose a diagnostic challenge. Because ERU is insidious, difficult to treat effectively and often blinding, clinical evidence of its presence should not be ignored, but determining the significance of a potential lesion, such as chorioretinal scarring, may be difficult.

The authors have noted punctate depigmented foci on fundic examination in many horses examined at the University of Georgia Veterinary Teaching Hospital without any other fundic pathologic changes (Figs 1 and 2). It is not known whether these particular foci are, in fact, chorioretinal scars or indicative of inactive chorioretinitis lesions, in the absence of other fundic or intraocular pathology. These foci are not specifically addressed in discussions of the normal equine fundic examination or in descriptions of chorioretinitis. The purpose of this study was to report concurrent clinical ocular findings in horses with depigmented punctate chorioretinal foci and to document whether these foci are found more often in horses diagnosed with ERU than in horses that do not have ERU.

**MATERIALS AND METHODS**

Records of horses receiving a full ophthalmic examination by a board-certified veterinary ophthalmologist at the University of Georgia Veterinary Teaching Hospital between 2001 and 2010 were reviewed. Full ophthalmic examinations included slit-lamp biomicroscopy and indirect and direct ophthalmoscopy. All horses received a local palpebral eyelid block as previously described to facilitate examination and were dilated prior to fundic examination with 1% tropicamide (Alcon Laboratories, Fort Worth, TX, USA). If anterior segment disease precluded posterior segment examination, the affected eyes were not included in the study. Horses were included in the study if they had a normal fundic examination or if they had depigmented punctate chorioretinal foci in the absence of any other fundic...
pathology. Although, the term ‘depigmented’ strictly refers to foci present in the non-tapetal region as the retinal pigmented epithelium is non-pigmented normally in the tapetal region.\(^7,29,31\) These punctate, whitish-gray, flat foci were also observed in the tapetum in our study. Tapetal foci were not observed in any horses without concurrent non-tapetal foci. For purposes of this study, the foci are referred to as depigmented regardless of location in the fundus. Horses were excluded if they had large choriotinal scars, ‘bullet-hole choriotinitis,’ ‘butterfly lesions,’ optic nerve head pathology, or any other fundic abnormalities on initial ophthalmic examination. Because neonatal septicemia and certain infectious diseases more likely to be contracted by foals are known causes of choriotinitis,\(^8,10\) all foals younger than 6 months were excluded to attempt to prevent this as a confounding variable. Horses systematically ill for any reason or horses with colic treated medically were also excluded. Horses that were otherwise healthy and had recently undergone colic surgery were not excluded if the cause of colic was known and not because of underlying infectious systemic disease.

The concurrent clinical ocular examination findings and all follow-up information as well as the signalment of the horses fitting the inclusion criteria were recorded. Sex, presence of no other intraocular findings, presence of ERU, presence of cataracts, presence of vitreal disease, and length of follow-up were compared between normal and foci groups by chi-squared analysis. Horses were determined to have ERU if they had recurrent (defined as ≥2) bouts of periodic uveitis with no clearly identifiable underlying cause, intraocular pathology relatable to ERU such as iris darkening and/or depigmentation, corpora nigra atrophy, synechia, cataracts, glaucoma,\(^33\) and vitreal degeneration or vitritis and a history of periodic tearing and blepharospasm. Age and length of follow-up time were compared between groups by student’s \(t\)-tests. The folded form \(F\) statistic was used to test whether variances were equal between groups. If unequal, the Satterwaite’s approximation for degrees of freedom for the student’s \(t\)-test was used. All hypothesis tests were two sided, and \(P < 0.05\) was considered significant.

RESULTS

One hundred and thirty-one horses (247 eyes) fit the inclusion criteria and were divided into two groups based on fundic examination. Ninety-one horses (167 eyes) had depigmented punctate choriotinal foci present. Of these, 15 horses had choriotinal foci in one eye and a normal fundus in the contralateral eye. For statistical purposes, these horses were included in the foci group. Forty horses (74 eyes) with clinically normal ocular fundi were examined. Those horses in which the fundus could only be visualized in one eye, leaving the foci status of the remaining eye unknown, were initially excluded from the statistical comparison. It was determined that their inclusion did not alter the statistical outcome for any of the comparisons; therefore, they are reported as part of the normal group.

Sixty-four percent (58/91) of horses with choriotinal foci and 50% (20/40) of horses without choriotinal foci had an otherwise normal intraocular examination (Fig. 3). The sex, average age, and length of follow-up time between horses with foci and horses without foci were not significantly different. The average age of horses with choriotinal foci was 11.9 years (range 0.5–28 years), and the average age of horses with ophthalmologically normal fundus was 9.6 years (range 1–25 years). The average length of follow-up time was 10.0 months (range 0–96 months) in horses with foci and 4.5 months (range 0–59 months) in horses without foci. Presence of ERU (horses with foci 14.2% \([n = 13]\), horses without foci 15.0% \([n = 6]\)\), presence of cataracts (horses with foci 28.6% \([n = 26]\), horses without foci 40.0% \([n = 16]\)\), and presence of vitreal disease (horses with foci 18.7% \([n = 17]\), horses without foci 17.5% \([n = 7]\)\) were not significantly different between groups (Fig. 3). All of the horses in both groups had no obvious clinical visual deficits in any eye able to be funduscopically evaluated.

Follow-up was available for eleven (27.5%) horses with clinically normal fundi. None of these horses had any change to their fundic appearance during the follow-up period. Follow-up was available for 50 (54.9%) horses with choriotinal foci. Of these, 43 (86.0%) horses did not have any change to the number or appearance of the choriotinal foci over the follow-up period (range 2–96 months). One horse with clinically normal fundi in both eyes on presentation developed depigmented choriotinal foci in one eye by the 27-month recheck. The contralateral eye could not be evaluated because of corneal edema. This horse was included in the foci group as foci developed on follow-up examination. Six horses (12.0%) with depigmented choriotinal foci had changes to their fundic appearance during the follow-up period (range 9–55 months). Four of these horses had ERU and developed large choriotinal scars, butterfly lesions, or retinal detachments over time. In all cases, these fundic changes occurred simultaneously with the progression of
concurrent intraocular disease. Of the two horses without ERU that had changes in the appearance of the fundus over time, one horse developed lesions consistent with a classic ‘bullet-hole’ appearance in both eyes 24 months after first documentation of foci with no apparent concurrent intraocular disease. The other horse had a normal fundic exam in one eye and foci present in the contralateral eye without any change in the fundic appearance until thirty months after initial presentation. At the 30-month recheck, foci were present in both eyes with no change in appearance of these foci over the next 7 months. Fifty-five months after initial presentation, larger depigmented regions were present in both eyes, consistent with described chorioretinal scars.3,4,29

DISCUSSION

To the author’s knowledge, this is the first report describing focal or multifocal depigmented punctate chorioretinal foci in horses. In our study, these foci were most often seen in the peripapillary non-tapetal region (Figs 1 and 2); however, some foci were noted extending to the peripheral non-tapetal fundus (Fig. 2) and occasionally were documented in the tapetal region. The nature of these foci makes them difficult to observe clinically in the tapetum as they are whitish-gray and punctate. Whether they occur more frequently in the tapetum and are not being detected clinically because of the reflective nature of the equine tapetum7,31 and lack of contrast because of the normal stars of Winslow7,31 is unknown. These foci were noted in color-dilute horses with subalbinotic fundi as well as in fully pigmented horses in our study.

The purpose of this study was to describe concurrent intraocular findings in horses with depigmented punctate chorioretinal foci and to determine whether these foci were found more commonly in horses with ERU. Because of the retrospective nature of this paper, there are inherent limitations present in this study. These include inherent variation in medical records, lack of standardization of the study groups, lack of histologic description of the foci, unknown history of possible infectious causes of chorioretinitis, and inability to determine the effect of topical or systemic medications given during the study period. Efforts were made to exclude any horses with a history of previous or current systemic disease as many different types of systemic disease may cause chorioretinal lesions. Although previous infectious disease causing chorioretinal foci in the horses in our study cannot be ruled out, the age, sex, and systemic state were similar for both groups, making this less likely. Our study population may not be representative of the overall equine population as they were presented to the University of Georgia Ophthalmology Service for examination, and certain bias is thus inherently present for horses with ocular disease. Attempts were made to minimize such bias with the addition of a control group consisting of horses with a normal fundus. In addition, using horses examined by a board-certified veterinary ophthalmologist ensured that only horses with carefully described depigmented punctate chorioretinal foci were included, thus ensuring that horses with ambiguous fundic lesions or chorioretinal scarring were excluded.

It is not known whether these foci represent a variation of normal or are indicative of previous chorioretinal disease or insult. Recently, fluorescein angiography has been described in normal horses34 and may be used clinically to further evaluate horses with depigmented chorioretinal foci. Fluorescein angiography has been used diagnostically in dogs35 and humans36,37 with active chorioretinitis, although equine fluorangiographic pathology has not been described. Histopathologic descriptions of these foci would greatly contribute to our understanding of pathophysiology and the significance of these foci. It is interesting to note that 86% of the horses with chorioretinal foci available for follow-up did not have any change in the appearance of the foci, regardless of the diagnosis of ERU. In addition, horses with ERU and a normal clinical fundic appearance at presentation did not develop foci even in the face of progression of intraocular disease at follow-up examination. These findings, along with the lack of any statistical correlation between the presence of foci and ERU, suggest that depigmented punctate chorioretinal foci are not related to or indicative of ERU. Other causes of chorioretinitis cannot be ruled out without histopathology, and it is not known whether these punctate foci indeed represent chorioretinitis. Although it is possible for these foci to progress, only two horses (4.0%) in our study had progression of these foci to larger scars or classic ‘bullet-hole’ appearance without concurrent intraocular changes. This study suggests that even if they are chorioretinitis lesions, they are not progressive in the majority of cases.

In our study, no visual disturbances were noted in any of the patients examined, and all horses responded to crude vision testing (e.g. menace test, maze test, behavior consistent with presence of vision). Inactive chorioretinal lesions have not been documented to cause visual disturbances in horses. It has been suggested that if any multifocal chorioretinal lesions or ‘bullet-hole’ lesions exceed twenty or if they are located in the area centralis, they may cause visual deficits; however, this is not well documented.2,3 Visual deficits, therefore, cannot be reliably used to determine whether lesions are indicative of chorioretinitis and would not be helpful in determining whether these foci are pathologic.

Finally, it is possible that some horses with punctate chorioretinal foci did have ERU that was not detected or diagnosed clinically as some of the horses were not available for follow-up or had short follow-up times. Because ERU is insidious, a diagnosis is made after serial examination or rigorous historical descriptions of specific clinical signs. When groups were evaluated for any lesion relatable to ERU (e.g. cataract, vitreal disease), there were no significant differences between groups, supporting the assertion that horses with depigmented chorioretinal foci are not more likely to have ERU. Horses with depigmented punctate chorioretinal

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foci in the absence of other fundic abnormalities are not more likely to have cataracts, vitreal disease, or ERU than horses that have clinically normal fundi. Additionally, in horses with chorioretinal foci available for follow-up, there was no progression or change in appearance of the foci in the majority of horses. This study suggests that the presence of these foci in horses is not indicative or suggestive of ERU. Further work is needed to determine whether these foci represent a pathologic change.

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REFERENCES