The Journal of Veterinary Medical Science

NOTE

Internal Medicine

Congenital anterior staphyloma associated with Peters' anomaly and aphakia in a Holstein calf

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J. Vet. Med. Sci.
79(7): 1151–1154, 2017
doi: 10.1292/jvms.17-0078

Received: 15 February 2017
Accepted: 10 May 2017
Published online in J-STAGE: 22 May 2017

ABSTRACT. A Holstein calf was born with a large protruding right eye and a central corneal opacity. Enucleation was the first choice of treatment. The calf had a good prognosis and was raised for milking purposes. Macroscopically, the enucleated eye was characterized by the protruded cornea, adherence of the iris to the central posterior cornea and aphakia. Microscopically, central corneal thickening and a defect in the endothelium and Descemet's membrane were observed. These data suggest that this represents a case of unilateral anterior segment dysgenesis consistent with congenital corneal staphyloma with Peters' anomaly and aphakia. Neither a mutation of the WFDC1 gene in multiple ocular defects nor any other identifiable cause for ocular anomalies was detected.

KEY WORDS: anterior segment dysgenesis (ASD), aphakia, congenital anterior staphyloma (CAS), Holstein, Peters' anomaly (PA)

There is conflicting information regarding the incidence of congenital ocular disorders in cattle. On the one hand, congenital ocular disorders are reported to occur uncommonly, with multiple abnormalities reported only sporadically [8], while on the other congenital ocular disorders are found to be not unusual, with several types of ocular defects, including microphthalmia, coloboma, and retinal dysplasia, reported [21].

Congenital anterior staphyloma (CAS), also named "congenital corneal staphyloma", is a rare complex ocular malformation syndrome of the anterior segment of the eye, referred to as anterior segment dysgenesis (ASD) [8, 16]. In food-producing animals, a case of unilateral CAS with complete anterior synechiae and a rudimentary lens has been reported in a Holstein-Friesian heifer calf [14]. We reported here a case of unilateral ASD consistent with CAS associated with Peters' anomaly (PA) and aphakia in an otherwise healthy Holstein calf.

An 85-day-old female Holstein calf was presented to Azabu University Veterinary Teaching Hospital, Japan with a corneal opacity of the right eye. Clinical examination revealed a considerably deformed and enlarged eye. Central leukoma was evident and the corneoscleral margin could not be identified (Fig. 1). The eyelids could not completely cover the eye. The left eye was normal.

After physical, clinical, and ophthalmic examinations, the ocular lesion was tentatively diagnosed as keratoconjunctivitis and a course of antibiotics was prescribed. However, as the corneal problem did not respond to antibiotic treatment, about one month later enucleation was selected as the first choice of treatment. Following enucleation, the calf and its left eye have remained healthy to date (about 30 months postoperatively).

The right eyeball was fixed in 10% neutral buffered formalin and then sectioned in the sagittal plane of the eye. Paraffin sections 4-μm thick were prepared from the eye and were stained with hematoxylin and eosin (HE) stain, Azan stain and periodic-acid-Schiff (PAS) reaction.

On the cut surface, the thickened cornea protruded in the shape of a watch glass and the lens was absent. The iris was covered with whitish material on the interior surface and adhered to the central posterior cornea (Fig. 2). The clinical and macroscopic

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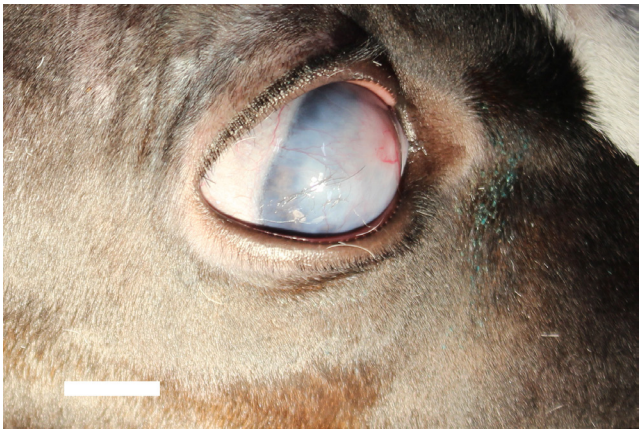

Fig. 1. Over view of a calf with CAS. Protusion of the right eye with leukoma. Scale bar, 1 cm.

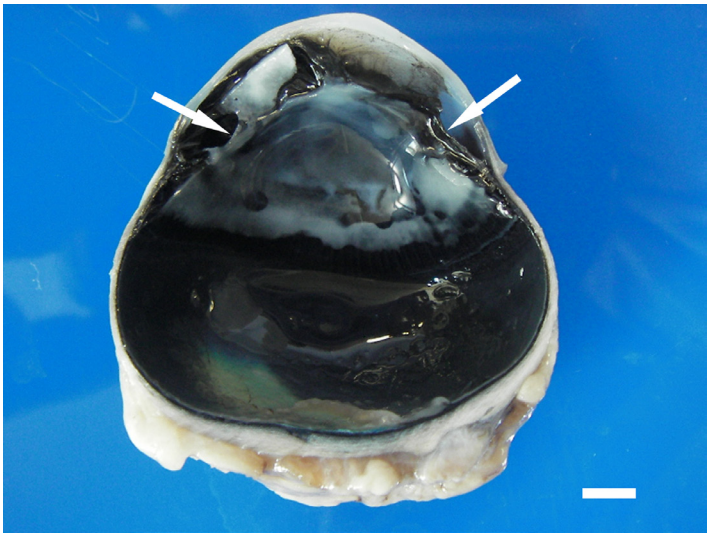

Fig. 2. The cut surface of the right eye fixed with 10% neutral buffered formalin. The anterior ocular segment shows a staphylomatic deformation with watch glass shaped protrusion. The hypoplastic iris is adherent to the central posterior cornea (arrows). Distorted anterior chamber evident. Inner surface of the iris is covered with whitish membrane. The lens is absent. Scale bar, 0.5 cm.

findings corresponded to CAS.

Microscopically, the central cornea was irregularly thickened with vascularized stroma. Irregular sheets of uveal tissue partly covered with faintly eosinophilic materials and coarse collagen fibers adhered to the area around the central part of the cornea and uveal tissue stretched between the posterior central cornea and the iris (Fig. 3). The central anterior chamber was obliterated and peripherally the chamber was shallow (Fig. 4). Descemet's membrane was partly malformed and discontinuous and the corneal endothelial cells had disappeared at the site of the adhesion.

The lens was absent and also PAS-positive lens material was not detected in sclera, cornea, or anterior uvea. The detached retina was hypoplastic and the ganglion cells reduced in number. The optic nerve and optic disk were normal. There were no signs of inflammation of the eye. The macroscopical and microscopical findings in the right eye were identical with those described for PA in human beings.

Blood samples were collected and the following investigations were performed. The WFDC1 gene was sequenced but the frameshift mutation, which has previously been detected in multiple ocular defects (MOD) of Japanese black cattle [1, 20], was not identified. Antigen-specific ELISA and RT-PCR failed to detect bovine viral diarrhea virus (BVDV) in the serum sample. The levels of vitamin A of blood plasma were 80 IU/d*l*.

This case represents a unilateral ASD consistent with CAS associated with PA and aphakia, as confirmed by the pathological examination. ASD resulting from the abnormal development of neural crest cells encompasses a broad range of ocular malformations classified in detail by its characteristics in human ophthalmology [8, 21]. It includes CAS, PA and aphakia, although it is sometimes presents complications [6, 11, 18, 19, 23]. ASD is also well known in animals [2, 7]. However, components of ASD have been rarely reported in cattle [7].

CAS is a rare and severe type of ASD characterized by a cloudy, bulging, vascularized, staphylomatous cornea in humans [8, 9, 16]. Unilateral CAS with complete anterior synechiae and rudimentary lens has been reported in a Holstein-Friesian heifer calf [14].

PA is a rare type of ASD with various severities characterized by central corneal opacity and ring-shaped iridocorneal adhesion caused by the absence of the Descemet's membrane [13]. PA or similar anomalies with PA have been reported in domestic and wild animals [2, 3, 5], although, PA has not yet been reported in cattle.

Congenital lens defects, including aphakia, are rare in cattle [10]. Aphakia may occur through failure of contact between the optic vesicle and the surface ectoderm during the period when the surface ectoderm responds to its inductive influences [2]. This early initiation of aphakia would be associated with ASD [2].

Aphakia is defined as the complete absence of a lens [4], although, in most cases of bovine aphakia, a rudimentary lens, a part of a lens capsule, lens epithelium, or dysplastic lens fibers are present, embedded within the sclera, cornea, or anterior uvea, referred to as "microphakia" [4, 10, 17]. In the present case, rudimentary lens material was not engulfed, although step sections or serial sections throughout the globe were not made as has been done in cases of humans missing lenses entirely [6, 11].

In cattle, most congenital ocular defects have no identifiable cause; others result from environmental, viral, hypovitaminosis A and/or genetic causes [10, 12, 22]. Similarly, in the present case, no possible causes were identified. In the last decade, molecular

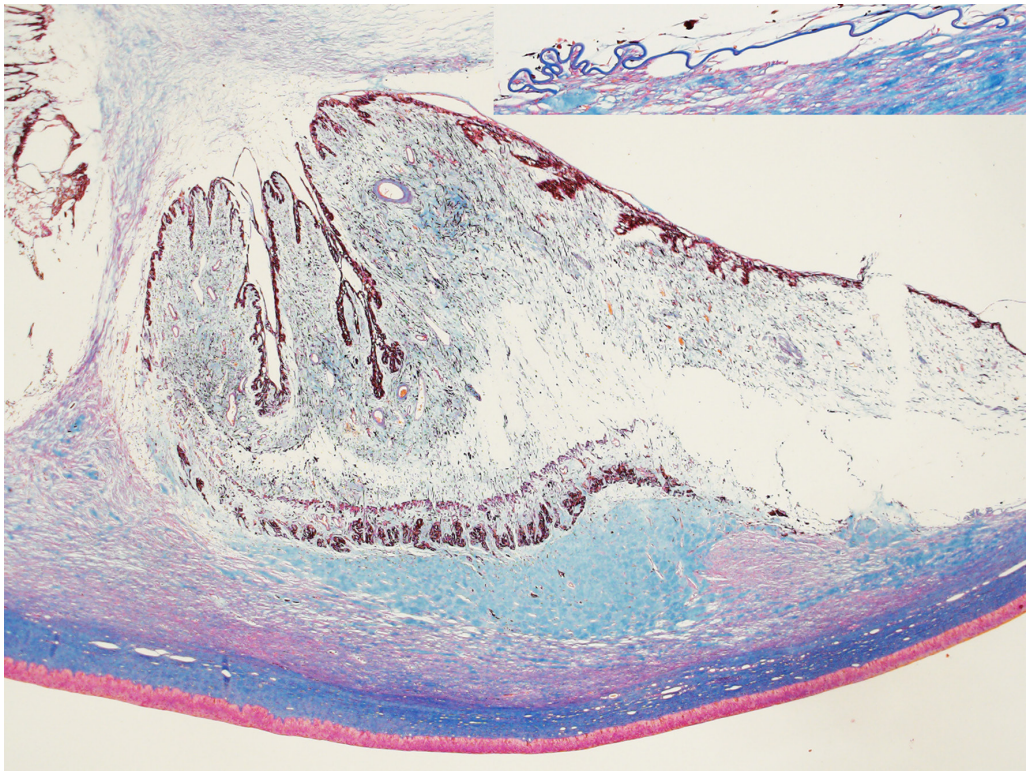

Fig. 3. Irregularly bulged sheets of uveal tissue adhered and stretched between the posterior cornea and the iris. Descemet's membrane and the corneal endothelial cells had disappeared at the site of the adhesion. Azan stain. ×20. Inset: Malformed Descmet's membrane. Azan stain. ×100.

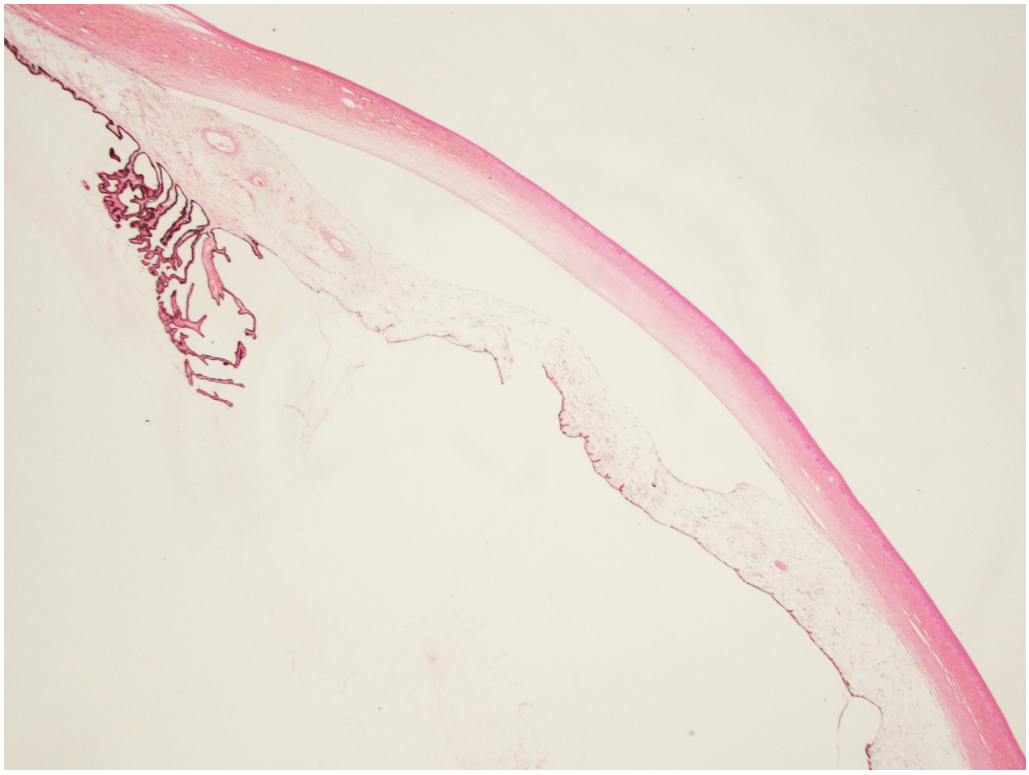

Fig. 4. The hypoplastic iris extending to and adherent to the central posterior cornea. Peripheral shallow anterior chamber. HE. ×12.5.

and developmental genetic research has transformed our understanding of the molecular basis of ASD and the developmental mechanisms underlying these conditions. All of the ASD genes play active roles in ocular development in humans and demonstrate conserved functions across species [15]. Further genetic investigation will be necessary in cases of ASD of food-producing animals.

Clinically, management of human infants with severe CAS is difficult and challenging [21]. CAS seems to carry a hopeless visual prognosis in human beings and the fate of most affected eyes has been enucleation [11]. In calves, enucleation is also necessary if the eye has become so enlarged that the eyelids can no longer protect it [14]. Enucleation was the first choice of treatment for the present case. The calf had good prognosis and was raised for milking purposes.

In conclusion, this is a first report of unilateral ASD consistent with CAS associated with PA and aphakia in cattle. The cause of this rare ocular malformation was unidentified. As the importance of congenital ocular anomalies in large animal practice may be underestimated, further investigations into the etiology of idiopathic ocular malformations of food-producing animals are required.

ACKNOWLEDGMENTS. The authors thank Ms. K. Satoh and Ms. M. Mori for their expert technical assistance. We also thank Dr. Y. Sakoda for antigen-specific ELISA and RT-PCR for BVDV. Lastly, we thank Mr. J. Lynch for English proofreading of the original manuscript.

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