Oculocardiac Reflex in a Dog Caused by a Choroidal Melanoma with Orbital Extension

Andrea Steinmetz, DVM, Kristin Ellenberger, DVM, Imke März, DVM, Eberhard Ludewig, DVM, DECVDI, Gerhard Oechtering, DVM, DECVAA

ABSTRACT

A 7 yr old mixed-breed dog was presented with a choroidal melanoma of the left eye that had penetrated the sclera, producing an orbital mass. Bradycardia was detected on auscultation. The bradycardia resolved after exenteration of the orbit and was therefore presumed to be associated with the oculocardiac reflex. (*J Am Anim Hosp Assoc* 2012; 48:66–70. DOI 10.5326/JAAHA-MS-5685)

Introduction

Bradycardia resulting from an orbital mass has been described in humans.¹ This phenomenon is based on the oculocardiac reflex (OCR) that was first documented by Aschner and Dagnini in 1908.^{2,3} The OCR is most reliably initiated by tension on the medial rectus and inferior oblique muscles. Afferent impulses travel along the ciliary nerves of the globe and the ophthalmic branch of the trigeminal nerve to the mesencephalon. Efferent impulses, provided by the vagus nerve, increase parasympathetic stimulation of the heart, thereby slowing the heart rate.⁴ The purpose of this case report was to describe a oculocardiac reflex in a dog possibly induced by a choroidal melanoma with orbital extension.

Case Report

A 7 yr old male neutered mixed-breed dog weighing 25 kg was referred to the Department of Small Animal Medicine of the Leipzig University, with a complaint of blindness affecting the left eye. The dog had been lethargic for 2 wk prior to presentation. At that time, the dog had a thin body condition (3.5/9). The basal body temperature was 38.3°C. The mucous membranes were pink, and the capillary refill time was approximately 1.5 sec. On

From the Department of Small Animal Medicine (A.S., E.L., G.O.) and Institute of Veterinary Pathology (K.E.), University of Leipzig, Leipzig, Germany; and Department of Veterinary Clinical Sciences, The Royal (Dick) Veterinary College, University of London, Herts, United Kingdom (I.M.).

Correspondence: steinmetz@kleintierklinik.uni-leipzig.de (A.S.)

auscultation over a 5 min period, a heart rate (HR) of 48–60 beats/min was determined.

The left eye was deemed to be blind based on the absence of a menace response, absent dazzle response, and a negative cotton ball test. The palpebral and corneal reflexes were normal. The left direct pupillary light reflex was incomplete as there was no consensual pupillary light reflex to the right eye. No signs of exophthalmos were detected. The left orbital compressibility appeared similar to the right. On slit-lamp biomicroscopic examination^a, the cornea, anterior chamber, iris, and lens were normal. The intraocular pressure (measured using a TonoPen^b) was 9 mm Hg in the left eye. Upon examination of the posterior segment, a nearly complete retinal detachment, without evidence of retinal hemorrhage, was seen. A red-brown discoloration could be seen behind the retina in the dorsomedial quadrant of the left eye (Figure 1). No abnormalities were found on examination of the right eye. Schirmer tear test values in the right and the left eyes were 16 and 17 mm/min, respectively.

During cardiac examination, bradycardia was diagnosed based on a HR of 54 beats/min despite the dog being excited. Auscultation of the heart was otherwise unremarkable. An electrocardiogram (ECG) was performed to rule out sick sinus syndrome,

ECG electrocardiogram; HR heart rate; MRI magnetic resonance imaging; OCR oculocardiac reflex; PO per os



FIGURE 1 Photograph of a near complete retinal detachment without signs of bleeding. Between the 8-o'clock and 12-o'clock position, a reddish mass can be seen through the detached retina.

atrioventricular block, or ventricular escape rhythm. The HR during the ECG was 52–56 beats/min with a regular sinus rhythm. This was interpreted as sinus bradycardia. An atropine response test, performed using 0.03 mg/kg atropine^c IV, resulted in an increase in HR to 116 beats/min and a normal sinus rhythm (**Figure 2**). This finding suggested increased vagal stimulation as the underlying cause of the bradycardia.

Results of a complete blood count, serum biochemistry panel, and routine urinalysis were unremarkable. Lateral and ventrodorsal radiographs of the thorax were interpreted as normal. A B-mode ultrasound examination of the left eye (using a 15 MHz linear probe^d and a horizontal approach) revealed retinal detachment and a subretinal hyperechoic area extending from the ciliary body to the optic nerve (**Figure 3**).

To investigate the extent of the tumor, magnetic resonance imaging (MRI) of the skull was performed^e. Anesthesia was induced with a combination of diazepam^f (0.5 mg/kg) and

levomethadone-fenpipramide^g (0.5 mg/kg) IV and maintained with isoflurane^h in oxygen. Anesthesia was monitored with pulse oximetry, capnography, and an ECG.

MRI consisted of T2-weighted images in transverse and dorsal planes and T1-weighted images in transverse and oblique orientation (along the axis of the optic nerve) before and after the IV administration of gadodiamideⁱ. The T1-weighted oblique images showed a nearly circular area of hyperintensity extending from the optic nerve to the medial aspect of the ciliary body that penetrated the scleral border, but not the orbit itself (**Figure 4**). Increased signal intensity was detected at the same area on T1-weighted images on the transverse scan. Because of the typical appearance of the hyperintensity on T1-weighted scans and the hypointensity on T2-weighted scans, a tentative diagnosis of a penetrating choroidal melanoma was made (**Figure 5**).⁵

Orbital exenteration was performed immediately after diagnostic imaging. Care was taken to remove the globe and as much of the surrounding soft tissue as possible *en bloc*. Examination of the orbit confirmed that macroscopic disease had been removed. The wound was closed in three layers.

During anesthesia, the dog's HR was slow (45–55 beats/min). Atropine was not administered because all other parameters were stable and within acceptable limits. One day postoperatively, the HR was 70–80 beats/min. Postoperatively, the dog was given 4 mg/kg Carprofen^j for 4 days PO q 12 hr and 20 mg/kg amoxicillin trihydrate/clavulanate potassium^k for 10 days PO q 12 hr for pain management and prophylactic antibacterial treatment, respectively.

The globe was submitted for pathologic examination. There was a solid and heavily pigmented mass (1.5 cm in diameter) arising from the choroid. This mass perforated the sclera and displaced the optic nerve dorsally (**Figure 6**). On microscopic



FIGURE 2 An electrocardiogram illustrating a sinus bradycardia of 52 beats/ min (upper line). After administration of 0.03 mg/kg atropine IV, the heart rate increased to 116 beats/min (lower line).



FIGURE 3 *B-mode ultrasound of the left eye using a 15 MHz probe. A very large mass is noted breaking through the scleral wall* (white arrows), *causing the optic nerve to deviate* (red arrow).

examination, a high proportion of heavily pigmented spindle cells were evident. Several tumor cell emboli were seen in episcleral blood vessels adjacent to the tumor, as well as multiple areas of hemorrhage and necrosis. After bleaching the tissue sections, anisokaryosis and 3–6 mitotic figures/high-power field ($40\times$) could be observed (**Figure 7**). A diagnosis of malignant choroidal melanoma was made. The presence of tumor cell emboli in episcleral blood vessels suggested that although every effort had been made to remove the mass with wide margins, there remained significant risk of recurrence or metastasis.

Ten days later, the dog returned for a scheduled follow-up examination. The owners reported an increased activity level compared with the second day postsurgically. Physical examination was unremarkable. The HR was 80 beats/min on physical exam and ECG.

Three months after surgery, the dog presented to the referring veterinary practice because of a mass lesion originating from the left orbit, suggestive of local recurrence. The owners declined further diagnostic investigation and therapy. The dog was euthanized six months later after its condition deteriorated. No postmortem examination was done.



FIGURE 4 Postcontrast magnetic resonance image (MRI; TR 500 msec, TE 20 msec) from an oblique scan (i.e., plane along the axis of the optic nerve) illustrating the extent of the mass.

Discussion

It is likely that the tumor expansion into the dog's orbit evoked a stimulation of the orbital trigeminal nerve roots and stimulated the OCR. The OCR is most reliably initiated via the medial rectus and inferior oblique muscles.⁴ In the present case, an area of hypointensity penetrating the medial scleral border of the eye could be seen in MRI.

Electrical stimulation within discrete sites of the spinal trigeminal complex in anesthetized or decerebrated rabbits results in arterial hypotension (often >50 mm Hg), bradycardia with a HR as low as 60 beats/min, apnea, and gastric hypermotility. Collectively, this is termed the trigeminal depressor response. The trigeminal depressor response represents a vasodepressor response that is, at least in part, anatomically distinct from pathways subserving arterial baroreceptor and somatic vasodepressor reflexes.⁶ Digital pressure on the eyes or nasopharyngeal stimulation with water can evoke reflex bradycardia in anesthetized dogs.⁷ Ophthalmic surgery may cause an OCR in dogs and foals.^{8,9}

It is known that bradycardia can result in humans from an orbital mass or from manipulation of the globe during surgical removal of the mass.^{1,10} When an OCR occurs in humans during surgery, 0.5 mg IV atropine can restore HR and blood pressure and prevent further occurrence of the reflex during the remainder of the operation.¹⁰ OCR-induced bradycardia in anesthetized dogs is reduced by central neural inspiratory activity and by the excitation of pulmonary afferents by inflation of the lungs. In humans,



FIGURE 5 Transverse T2-weighted (TR 4,460 msec, TE 100 msec) MRI showing a mass penetrating the scleral border in the posterior segment. The mass appears hypointense in T2-weighted scans. Left-to-right comparison reveals increased signal change of the diseased left vitreous. Detached and displaced retinal tissue is visible as a star-like hypointense structure in the T2-weighted image.

the OCR is reduced when inspiratory efforts are made against a closed glottis.⁷

The OCR in humans is defined as a reduction in HR of at least 20% and/or the presence of arrhythmias once the nerve tissue



FIGURE 6 Gross appearance of the choroidal melanoma (m) infiltrating (arrowhead) the ciliary body (cb) and penetrating (arrow) the sclera (s). The tumor is associated with retinal detachment (asterisk) and is displacing the optic nerve (n) upward.



FIGURE 7 The canine choroidal melanoma is composed of spindle cells. Note the numerous mitotic figures (arrows). Bleached, hematoxylin and eosin staining, original magnification $\times 40$.

within the orbit is stimulated.¹¹ In one case report, a child with an orbital mass showed nausea, somnolence, and bradycardia.¹ These signs and symptoms were alleviated postoperatively in the child. In the present case, the HR was decreased by >25% by the presumed OCR. The dog showed a HR of 48–60 beats/min before and a HR of 80 beats/minute after surgery.

Other causes for bradycardia in a nonanesthetized dog are administration of drugs that can bradycardia (e.g., β -blockers, calcium channel blockers, digoxin), hypothermia, and hypothyroidism. In this patient, information provided by the owners made administration of drugs extremely unlikely. In addition, the dog had a normal basal body temperature, and serum biochemistry results were within normal limits making an underlying hypothyroidism unlikely.

According to the current World Health Organization's classification of ocular tumors of domestic animals, intraocular melanocytic tumors in dogs are classified as canine anterior uveal melanocytoma, limbal melanocytoma, canine choroidal melanocytoma, and canine diffuse uveal melanosis.¹² The malignant form of choroidal melanoma is described in dogs and has the potential for orbital extension and metastatic disease.¹³⁻¹⁶ In another case report, no signs of recurrence or metastasis were detected by thoracic radiographs, blood tests, or MRI, and that dog was clinically healthy for 23 mo after orbital exenteration of the affected eye.¹⁵ In the present case, a mass lesion originating from the left orbit, suggestive of local recurrence, was detected 3 mo postsurgically. The malignant nature of the tumor and the presence of tumor cell emboli in episcleral blood vessels adjacent to the tumor would explain the recurrence despite the fact that the tumor appeared to be completely excised on gross examination.

Conclusion

Orbital expansion of a choroidal melanoma may cause an OCR.

The authors gratefully acknowledge Professor Ursula Dietrich, Dr. Brady Beale, and Mr. Mickey Tivers for comments on this manuscript.

FOOTNOTES

- ^a SL 14; Kowa company Ltd., Nagoya, Japan
- ^b TonoPen-XL; Medtronic Solan, Jacksonville, FL
- ^c Atropin; B. Braun Melsungen AG, Melsungen, Germany
- ^d Sequoia 512; Siemens, Erlangen, Germany
- ^e Gyroscan5NT; Philips Medical Systems, Hamburg, Germany
- ^f Faustan; Temmler Pharma GmbH, Marburg, Germany
- ^g L-Polamivet; Veterinaria AG, Pfaffikon, Switzerland
- ^h Isofluran; Baxter AG, Wien, Austria
- ¹ Omniscan; Nycomed, Konstanz, Germany
- ^j Rimadyl; Pfizer AG, Berlin, Germany
- ^k Synulox; Pfizer AG, Berlin, Germany

REFERENCES

- Westerling D, Blohmé J, Stigmar G. Orbital mass in a child causing somnolence, nausea and bradycardia. *Can J Anaesth* 1998;45(8): 777–80.
- Aschner B. Ueber einen bisher noch nicht beschriebenen Reflex vom Auge auf Kreislauf und Atmung. *Wien Klin Wochenschr* 1908; 21:1529 [in German].
- Dagnini G. Intorno ad un riflesso provocato in alcuni emiplegici collo stimolo della cornea e colla pressione sul bulbo oculare. *Bull Sci Med* [Bologna] 1908; (8):380–1 [in Italian].
- Rhode J, Grom E, Bajares AC, et al. A study of electrocardiac alterations occuring during operations on the extraocular muscles. *Am J Ophthalmol* 1958;46(3 part 1):367–82.
- 5. Kato K, Nishimura R, Sasaki N, et al. Magnetic resonance imaging of a canine eye with melanoma. *J Vet Med Sci* 2005;67(2):179–82.

- 6. Kumada M, Dampney RA, Reis DJ. The trigeminal depressor response: a novel vasodepressor response originating from the trigeminal system. *Brain Res* 1977;119(2):305–26.
- Gandevia SC, McCloskey DI, Potter EK. Reflex bradycardia occurring in response to diving, nasopharyngeal stimulation and ocular pressure, and its modification by respiration and swallowing. *J Physiol* 1978;276:383–94.
- Clutton RE, Boyd C, Richards DLS, et al. Significance of the oculocardiac reflex during ophthalmic surgery in the dog. J Small Anim Pract 1988;29:573–9.
- Short CE, Rebhun WC. Complications caused by the oculocardiac reflex during anesthesia in a foal. J Am Vet Med Assoc 1980;176(7): 630–1.
- Khan FM, Ankutse MM. Oculocardiac reflex during excision of periorbital tumor—a case report. *Middle East J Anaesthesiol* 1988; 9(4):383–8.
- 11. Mirakhur RK, Jones CJ, Dundee JW, et al. I.m. or i.v. atropine or glycopyrrolate for the prevention of oculocardiac reflex in children undergoing squint surgery. *Br J Anaesth* 1982;54(10): 1059–63.
- Wilcock BP, Dubielzig RR, Render JA. Histological classification of ocular tumors of domestic animals. In: Wilcock BP, Dubielzig RR, Render JA, eds. World Health Organization international histological classification of tumors of domestic animals. Histological classification of ocular and otic tumors of domestic animals. Washington, DC: Armed Forces Institute of Pathology, American Registry of Pathology; 2002:11–25.
- Hyman JA, Koch SA, Wilcock BP. Canine choroidal melanoma with metastases. Vet Ophthalmol 2002;5(2):113–7.
- 14. Lim CC, Cullen CL, Grahn BH. Choroidal melanoma in the right eye with focal retinal detachment. *Can Vet J* 2006;47(1):85–6.
- Miwa Y, Matsunaga S, Kato K, et al. Choroidal melanoma in a dog. J Vet Med Sci 2005;67(8):821–3.
- 16. Allgoewer I, Frieling E, Fritsche J, et al. Das choroidale Melanom beim Hund. *Kleintierpraxis* 2000;45(5):361–9 [in German].