

Ivermectin toxicity induced retinopathy management

C. Niranjana*¹, Palukuri Venkata Kalyani², C. Jayanthi³ and M. Shiju Simon³

Department of Veterinary Surgery and Radiology, Madras Veterinary College,
Tamil Nadu Veterinary and Animal Sciences University, Chennai-600007

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Abstract

A two-year-old male Chippiparai dog (14 kg) was presented with blindness after treatment with ivermectin (10 mg/kg for 10 days, PO) for alopecia by the pet parent. Ophthalmic examination revealed no menace response, no pupillary light reflexes (PLR) and mydriasis. Fundus examination revealed retinopathy with circular to vermiform blackish pigmentation at the tapetal and non-tapetal border bilaterally. Intraocular pressure and other structures were normal, as were hematology and biochemistry. After stopping ivermectin and administering prednisolone (1 mg/kg, IM) and hydroxocobalamin (total dose of 1000µg, IM), PLR returned in 3 days, with complete vision recovery in 5 days. Early diagnosis with detailed fundus examination and treatment was useful in recovery of vision in this dog.

Keywords: Retinopathy, Ivermectin toxicity, hydroxocobalamin, prednisolone, dog

Introduction

A two-year-old, brown, male Chippiparai weighing 14 kg was presented to the Small Animal Ophthalmology Unit of Madras Veterinary College, with a history of blindness for the past six days displaying signs like bumping into objects and having a cautious gait as reported by the pet parent. The animal had undergone treatment with ivermectin @ 10 mg/kg BW, PO daily for the last 10 days for

multifocal alopecia on the dorsal and lateral aspects of the body extending from the neck to the rump. Ivermectin is usually used to treat infestation of ectoparasites on the skin in Chippiparai, usually without any complications provided the dosage is correct (Arul, 2023).

Case History and Observation

Maze test that was conducted on day one of the animal being presented revealed that the animal was indeed not able to visualize obstacles in front of him and proceeded to bump into them while being beckoned to walk in a particular direction with audio cues. Ophthalmic examinations revealed that the menace reflex, dazzle response, pupillary light reflex were all negative for both the eyes (OD and OS) on day one. The cornea was transparent and the sclera did not show any abnormalities. Bilateral mydriasis could be observed very prominently (Fig 1).

Schirmer tear test and fluorescein dye tests were normal. Intraocular pressure (IOP) was measured with a tonopen, and found to be 14 mm Hg for both the eyes. Ophthalmic examination was done using an indirect ophthalmoscope along with a 20D lens that was placed close to the eye (Fig.2). Fundus images and videos were obtained via smartphone-based indirect ophthalmoscopy, using an iPhone XR in conjunction with a 40-diopter condensing lens (Kanemaki *et al.*, 2017). Acquisition was technically challenging given the patient's neurological signs of ivermectin toxicosis, which compromised positioning and cooperation during imaging, and the dog required manual

*Corresponding author Email: niranjana_bvm@yahoo.com

¹Assistant Professor,

²Undergraduate student of B.V.Sc & AH

³Assistant Professor, Department of Clinics

restraint to obtain diagnostic images. Fundus examination revealed that the tapetal border was disrupted and vermiform and circular blackish lesions along with abnormal pigmentation was observed (Fig 3 and 4).

To assess systemic health and rule out differentials, hematological and biochemical evaluations were performed. Hematology revealed a hemoglobin of 16.1 g/dL, packed cell volume (PCV) of 46.2%, platelet counts reaching 2,080,000/cm³ and a total leukocyte count of 13,400/cm³; blood parasite examination was negative. Serum biochemistry revealed elevated alanine aminotransferase (ALT) at 119.0 IU/L, along with normal glucose (87 mg/dL) and elevated phosphorus (5.29 mg/dL) relative to expected reference intervals. Other parameters, including cholesterol (129 mg/dL), total proteins (8.50 g/dL), albumin (2.90 g/dL), alkaline phosphatase (ALP; 25.0 IU/L), gamma-glutamyl transferase (GGT; 9.0 IU/L), blood urea nitrogen (BUN; 9.64 mg/dL), creatinine (0.91 mg/dL), and calcium (10.11 mg/dL), were within normal reference ranges for the species.

While the combination of clinical history, fundoscopic findings, and systemic workup strongly supports the diagnosis, it must be acknowledged that electroretinography (ERG), the gold-standard objective test for assessing retinal photoreceptor function was not performed in this case. The absence of ERG data constitutes a limitation of this study in quantitatively confirming the extent and nature of retinal dysfunction.

Treatment and Discussion

Stabilization of the animal was done on day one with fluid therapy using Ringer's lactate and the treatment for reversing the effects of ivermectin toxicity was started by administering prednisolone at 1 mg/kg body weight, IM and hydroxocobalamin at total dose of 1000µg, IM. Alternate day treatment was continued and four

doses in total of this protocol was administered. Dermatological examination on day one with skin scraping procedures resulted negative for any mite infestation.

On day 3 of the animal's treatment, general observation before administering of the drugs revealed that while the menace response was still negative, dazzle response and PLR were sluggish and by day five of the treatment (two doses of the protocol being given), all the reflexes including menace were positive.

The diagnosis of ivermectin-induced retinopathy was justified based on the history of recent ivermectin exposure in conjunction with these characteristic bilateral retinal pigmentary and tapetal changes. Importantly, retinal damage was differentiated from neurological or optic nerve involvement primarily through the direct fundoscopic visualization of these structural retinal lesions. In cases of purely neurological blindness (e.g., central cortical lesions) or optic neuritis/neuropathy, the fundus typically appears normal or may show optic disc swelling, hyperemia, or subsequent pallor; in this case, the pathology was clearly localized to the retinal pigment epithelium and tapetum, with no observable abnormalities of the optic nerve head. The normal intraocular pressure and clear ocular media further ruled out glaucoma and anterior segment pathologies as primary causes of the blindness.

Ivermectin is a broad spectrum antiparasitic drug commonly used for dogs in cases of dermatological issues to eliminate most suspected ectoparasites at the dose rate of 50-300 µg/kg PO or SC (Lovell, 1990 and Fergus Allerton, 2020). Ivermectin is an agonist of invertebrate-specific, glutamate-activated, inhibitory chloride channels; it causes flaccid paralysis and subsequent death in nematodes and mites. Ivermectin's toxic effect in mammals is due to the similarity of these invertebrate-

specific channels to vertebrate aminobutyric acid (GABAA)-gated chloride channels that inhibit interneurons in the central nervous system

Hydroxocobalamin is a precursor of methylcobalamin and adenosylcobalamin, which are the active forms of vitamin B12. The methylcobalamin component in hydroxocobalamin plays a role in the development of the nervous system during childhood and hematopoiesis. Adenosylcobalamin is involved with the metabolism of carbohydrates, amino acids, and fatty acids and is thus, involved in myelin formation (Thakkar and Billa, 2015). Welsey Chan *et al.*, 2018 reported that cobalamin scavenges superoxide and is neuroprotective for neuronal cells of RGCs after axonal injury *in vivo*. Cobalamin has a significant role in maintaining cellular reduction-oxidation status, and support the hypothesis that vitamin B12 deficiency optic neuropathy results from a misplaced signal for cell death because of unconstrained superoxide generation (Thompson and Marrs, 2012). Prednisolone was administered as adjunctive anti-inflammatory therapy to reduce ivermectin-associated cerebral/vasogenic edema, consistent with prior reports of corticosteroid use in macrocyclic lactone toxicosis (Yas-Natan *et al.*, 2003; Merola and Eubig, 2018).

Summary

A case of blindness due to ivermectin toxicity. Visual recovery occurred after withdrawal of ivermectin and supportive treatment.

References

- Arul, N., Arumugam, A. P., Padmanaban, V., Narayanan, D. and Karuppaiah, R. (2023). Successful Management of Concurrent Scabies and Dermatophytosis in a Chippiparai Pup. *Small Animal Advances*, **2**(2): 29–32.
- Fergus Allerton. (2020). In.: Small Animal Formulary, BSAVA. Pp.: 216.
- Lovell, R. (1990). Ivermectin and piperazine toxicosis in dogs and cats. *Veterinary Clinics of North America: Small Animal Practice*, **20**:453
- Kanemaki N, Inaniwa M, Terakado K, Kawarai S, Ichikawa Y. (2017) Fundus photography with a smartphone in indirect ophthalmoscopy in dogs and cats. *Veterinary Ophthalmology*, **4**:280–284.
- Merola V.M. and Eubig P.A. (2018). Toxicology of Avermectins and Milbemycins (Macrocyclic Lactones) and the Role of P-Glycoprotein in Dogs and Cats. *Veterinary Clinics of North America: Small Animal Practice*, **48**:991–1012
- Thakkar, K and G Billa. (2015). Treatment of vitamin B12 deficiency-methylcobalamine? Cyancobalamine? Hydroxocobalamin?-clearing the confusion. *European Journal of Clinical Nutrition*, **69**(1): 1-2.
- Thompson, J.P., and Marrs, T.C. (2012). Hydroxocobalamin in cyanide poisoning. *Clinical Toxicology*, (Phila), **50**(10): 875-85
- Welsey Chan, Almasieh, M., Catrinescu, M.M. and Levin, L.A. (2018). Cobalamin-Associated Superoxide Scavenging in Neuronal Cells Is a Potential Mechanism for Vitamin B12-Deprivation Optic Neuropathy. *The American Journal of Pathology*, **188**(1):160-172.
- Yas-Natan, M. Shamir, S. Kleinbart, I. Aroch (2003). Doramectin toxicity in a collie. *Veterinary Record*, **153**: 718-20.



Fig.1 Bilateral mydriasis on presentation



Fig. 2 Smartphone-based indirect ophthalmoscopy

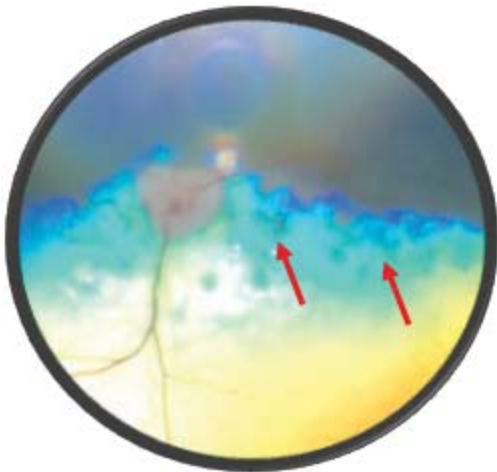


Fig. 3. Fundus image of right eye revealing blackish lesions

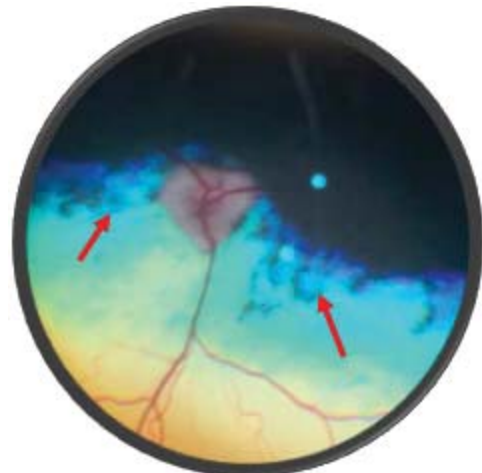


Fig. 4 Fundus image of left eye revealing disrupted tapetal border and vermiform blackish lesions