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Case Report

Retinal Degeneration due to Enrofloxacin Intoxication in a Cat

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Abstract: In this case presentation, retinal degeneration due to enrofloxacin intoxication encountered in a domestic short-haired male cat is discussed. History of the patient revealed that he had received 7.8 mg/kg enrofloxacin twice daily for 10 days. Both pupils were dilated. Pupillary light reflexes were negative in both eyes. Direct and indirect ophthalmoscopic examinations showed tapetal hyperreflectivity, and slight attenuation of the retinal blood vessels compared to those of a healthy cat was observed in both retinas. Follow-up information obtained from the owner by telephone 6, 12, and 18 months later revealed that there had been no improvement in the cat's vision, the cat had adapted to blindness, and the pupils remained dilated.

Key Words: Retinal degeneration, enrofloxacin, cat

Bir Kedide Enrofloksasin Toksikasyonuna Bağlı Olarak Gelişen Retina Dejenerasyonu

Özet: Bu olgu sunumunda, kısa tüylü bir evcil kedide enrofloxacin toksikasyonuna bağlı olarak gelişen retina dejenerasyonu değerlendirildi. Hastanın anemnezinde 10 gün boyunca, günde iki kez 7,8 mg/kg enrofloxacini peros aldığı öğrenildi. Hastanın klinik muayenesinde her iki pupillanın dilate olduğu izlendi. Her iki gözde pupillar ışık refleksi negatifti. Direkt ve endirekt oftalmoskobik muayenede, her iki gözde de normal bir kediye göre tapetal hiperrefleksi geliştiği ve retina damarlarının hafif inceldiği belirlendi. Hastanın uzun dönem bilgileri 6, 12 ve 18. ayda telefonla sahibinden alındı. Buna göre hastanın görüşünde bir iyileşme olmadığı, körlüğe adapte olduğu ve her iki puppillanın geniş kaldığı öğrenildi.

Anahtar Sözcükler: Retina dejenerasyonu, enrofloxacin, kedi

Introduction

In small animal practice, intoxications caused by various drugs are encountered occasionally. Among the systemic drugs used in cats, it is known that griseofulvin (1-3), methylnitrosourea-ketamine combination (1,2,4), and fluoroquinolones (1,3,5-8) may cause damage to the retina. Enrofloxacin is a fluoroquinolone derivative antibacterial drug that has been used extensively in small animal practice in recent years (since 1990). However, it has been shown to cause retinal degeneration in cats (1,5,6,8-12). When the drug was first introduced, a general and wide dose interval of 10-20 mg/kg was recommended for cats and dogs. However, after the discovery of the possibility of the active ingredient causing retinal degeneration, the manufacturer reduced the recommended dose for cats to 2.5 mg/kg twice a day (1,5,6).

Initial findings in cats developing retinal degeneration due to enrofloxacin toxicity are loss of vision, blindness, and mydriasis. Fundoscopic findings are tapetal hyperreflectivity and attenuation of the retinal blood vessels (1,3,5,6,8-10,12). Electroretinographic findings obtained from cats with retinal degeneration due to enrofloxacin showed nonrecordable traces (1,3,5,12). In their 2001 study, Gelatt et al. (5) summarised the histopathological retinal appearances of such patients as follows: diffuse degeneration, particularly in the outer nuclear and photoreceptor layers, and hypertrophy of the retinal pigment epithelium.

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Factors thought to influence the possibility of retinal degeneration developing in cats given enrofloxacin are age, hepatic or renal failure, dosage and duration of the drug, and route of administration. On the basis of these factors, in old patients with hepatic or renal failure given enrofloxacin at a high dose for a long period, the risk of retinal degeneration developing rises. Conversely, degeneration may also develop in patients administered low doses for a short period of time. This could indicate that this rarely observed retinal degeneration may develop due to individual predisposition or sensitivity (1,3).

Loss of vision and total blindness are permanent in the vast majority of patients (1,3,5-8). However, improvement of impaired vision was seen when the drug was discontinued in patients diagnosed early and receiving low doses of enrofloxacin (1,3,5,8).

Historical findings are very important in the diagnosis of retinal degeneration. In cats receiving enrofloxacin, sudden development of mydriasis, delayed and diminished pupillary light reflexes, reduction or loss of the menace reflex, and marked loss of vision suggest retinal degeneration due to enrofloxacin intoxication (1,3,5). Other causes of retinal degeneration in cats such as nutritional deficiencies, intraocular inflammatory conditions, systemic hypertension, genetic abnormalities, glaucoma, chorioretinitis, and retinal detachment are conditions that should be considered in the differential diagnosis (1,3,6).

This case is presented in order to bring this topic to the attention of practising small animal veterinarians and to share our findings of the condition, which is also encountered in Turkey.

Case History

A 15-year-old domestic short-haired male cat weighing 3.2 kg was brought to our clinic with dilated pupils and blindness in both eyes. History of the patient revealed that he had suffered an upper respiratory tract infection 20 days previously and had received 50 mg enrofloxacin per day orally (25 mg in the morning and 25 mg in the evening) upon the recommendation of the local veterinary surgeon. It was reported that the initial complaint regressed 1 week after the treatment was started, but that the drug had been administered for a further 3 days and both pupils were noticed to have become dilated during this period. The owner stated that the cat's behaviour inside the house was normal initially and that they had noticed a previously nonexistent green shine in the depth of the eye. Blindness developed in the patient despite enrofloxacin administration being stopped on day 10.

The general condition of the patient was good on clinical examination. The menace test and cotton ball test were used to assess vision. Results of these tests were negative. Both pupils were dilated (Figure). Pupillary light reflexes were negative in both eyes. Therefore, a fundus examination was carried out without the use of mydriatics. Direct and indirect ophthalmoscopic examinations showed tapetal hyperreflectivity (Figure) and slight attenuation in the retinal blood vessels compared to what is found in healthy cats was observed in both retinas. No dysplastic area or pigment abnormality was seen either in the tapetal or in the non-tapetal region. There were no systemic findings in the patient to suggest kidney or liver failure or any other ocular disease such as intraocular inflammation, glaucoma, chorioretinitis, or retinal detachment.

In the light of the historical, clinical, and ophthalmoscopic findings, the patient was diagnosed with retinal degeneration due to enrofloxacin intoxication. The patient's condition was explained to the owner. This person was informed that in some mild cases and when

Figure. Pupillary dilatation and tapetal hyperreflectivity in the case described.

low dose administration is stopped after a short period spontaneous recovery may occur. However, the extremely high dose of the drug and the 10-day administration period caused the prognosis to be poor. It is probably due to the death of the photoreceptors; they cannot regenerate and therefore the patient will remain blind.

Follow-up information obtained from the owner by telephone 6, 12, and 18 months later revealed that there had been no improvement in the cat's vision. The cat had adapted to blindness and the pupils remained dilated.

Results and Discussion

As wide-spectrum antibiotics, fluoroquinolones have been used extensively in recent years in small animal practice. Enrofloxacin is a member of this group of drugs. However, clinical results have revealed that it can have a toxic effect on the retina of cats. The mechanism by which the drug causes retinal degeneration is still unknown (1,3,5-8,11,12). However, pharmacological studies suggest that the blood-brain barrier in cats may be relatively open to the lipophylic portion of enrofloxacin. Therefore, high concentrations of enrofloxacin may accumulate in the central nervous system of cats (11).

Ford et al. (12) observed some behavioural (marked caution, lethargy, and unkempt coat) and neurological abnormalities that included incoordination, tremors, convulsions, blindness, circling, nystagmus, and ptyalism.

In their study comprising 17 cats, Gelatt et al. (5) reported affected cats to be aged between 3 and 16 years. Doses of enrofloxacin administered orally to these patients ranged from 4.6 mg/kg once daily to 27 mg/kg twice daily. The daily dose administered orally to the cat in the present study was 7.8 mg/kg twice daily. When it is considered that the manufacturer reduced its initial recommended daily dose of 11 to 2.5 mg/kg following the discovery of the drug's retinotoxic effects, it is clear that the dose administered to this cat was sufficient to cause a retinatoxic effect. Gelatt et al. (5) observed that, while the blindness and mydriasis noticed by the patient's owner were variable, this condition was more evident between 2-3 days and 12 weeks after drug administration. In our study, the owner had used the drug for 10 days and noticed dilation of the cat's pupils 2-3 days before cessation of administration. Blindness became evident 2 days after the drug was discontinued.

It has been reported that individual predisposition is important in retinal degeneration caused by enrofloxacin (1,8). However, factors such as high dose, long duration, advanced age of the patient, and kidney or liver failure are thought to be causative factors in the development of degenerative changes and their severity (3,4,8). Despite there being no evidence of liver or kidney failure in our patient, it is interesting that the cat was 15 years old.

No findings related to other causes of retinal degeneration such as nutritional deficiencies, systemic hypertension, genetic abnormalities, intraocular inflammatory diseases, glaucoma, chorioretinitis, or retinal detachment were encountered in this case (1,6).

Findings such as bilateral pupillary dilatation, diminished and incomplete pupillary light reflexes, tapetal hyperreflectivity, and attenuation of retinal blood vessels observed in our patient are consistent with data from the literature (1,3,5-8,12). However, findings such as pigment abnormalities (increase in pigmentation or hyperpigmentation) and progressive reduction in the diameter of the optic nerve head observed in some cases by Gelatt et al. (5) were not encountered in this case. In young, healthy cats administered enrofloxacin at a daily oral dose of 50 mg/kg, Ford et al. (10) reported that fundoscopic changes began within 3 days, attenuation of retinal blood vessels was observed between 2 and 4 days, and tapetal hyperreflecivity developed between 5 and 7 days. Our patient had received the drug for 10 days and was examined 10 days after the drug was stopped. Therefore, the onset period of the mentioned changes was not observed.

In some patients with retinal degeneration due to enrofloxacin intoxication, after cessation of the drug an improvement in the loss of vision was observed (5,8,11). In our case, there was total and permanent loss of vision and no improvement was observed according to the cat's owner.

In conclusion, the use of systemic enrofloxacin in cats should not exceed a total daily dose of 2.5 mg/kg, duration of administration should be minimal, the drug should not be used intravenously, and the patient should be monitored with respect to mydriasis and fundoscopic changes throughout the treatment period.

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