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CASE REPORT

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Reversible blindness after erroneous prescription of closantel: A case report

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Abstract

A 20-year-old girl was referred with vision loss upon closantel use. Plasma exchange and high-dose corticosteroid pulse therapy were administered. A 2.5-year follow-up showed improved vision and increased layer thickness of the peripheral nerve fiber. Early treatment with plasma exchange and high-dose corticosteroid therapy can be beneficial to reverse closantel toxicity.

KEYWORDS

blindness, closantel, toxicity

1 | INTRODUCTION

Halogenated salicylanilides are well-known for their anti-parasitic effects. The most famous medicine in this category is closantel, which is used worldwide against *Haemonchus* spp. and *Fasciola* spp. infestations in sheep and cattle.[1,2]

Animal studies indicate that the oral bioavailability of closantel in sheep and cattle is about 50% and that the maximum plasma concentrations (Cmax) are reached 24–48 h after administration with extensive binding to plasma albumin (>97%). Moreover, the elimination half-life is from 7 days to 3 weeks depending on the animal.[3,4] Closantel poisoning is usually accompanied by neurotoxicity, ophthalmic toxicity, and hepatotoxicity in animals. There is no specific antidote for this poisoning, and information about its effects on humans is scarce.[5]

This study reports a rare case of blindness after wrong administration of closantel to treat *Fasciola hepatica* infection in a young girl, who successfully managed with drug discontinuation, plasmapheresis, and corticosteroids.

2 | CASE PRESENTATION

A 20-year-old girl with the primary complaints of bilateral blurred vision and decreased color vision, progressing from 3 days earlier, was admitted to the emergency department on August 16, 2018. She had a history of *Fasciola hepatica* from 20 days earlier. Although her specialist had

prescribed triclabendazole, the pharmacist mistakenly gave her closantel as an alternative. She took 500 mg of closantel twice daily for 3 days. On the second day of closantel administration (3 grams totally), she was unable to see fine details and lost vision sharpness bilaterally. On the third day, her problem progressed to blurred vision followed by color blindness. Her visual acuity was 20/800 in the first examination of both eyes, and the Ishihara test confirmed her total color blindness. Visual acuity had worsened such that it became limited to hand motion in both eyes within 24 h.

There was no systemic illness and her physical examination was normal, including central nervous system and abdominal examination. On primary eye examination, the intraocular pressure of the right eye and the left eye was 12 and 13, respectively; and refraction was +0.5 in both eyes. In slit-lamp examination, the cornea and lens as well as media were clear. Fundus examination showed a normal macula appearance. She had a bilateral pale disc, a sluggish pupillary reaction to light, and a negative RAPD (relative afferent pupillary defect).

In the Humphrey visual field test, she showed a complete visual field defect in the central 24-degree vision. Optical coherence tomography (OCT) and retinal nerve fiber layer (RNFL) thickness in the temporal-superior-nasal-inferior-temporal (TSNIT) map revealed a thinning neural area of both eyes and a temporal fiber thinning in the right eye (Figure 1). Inferonasal and superonasal fiber had a good condition in both eyes. However, the superotemporal and inferotemporal peripapillary fiber of the right eye had prominent thinning. Together, RNFL thinning was dominant in the right eye. Inferior to superior hemispheric asymmetry in the RNFL thickness and ganglion cell layer thickness was not significant. Fundus autofluorescence was normal. Fluorescein angiography of both eyes had no defects in the vascular filling.

Plasmapheresis was performed immediately in an emergency department, and the course of treatment consisted of five sessions of apheresis. She also underwent corticosteroid pulse therapy with methylprednisolone (1,000 mg once daily for three consecutive days). At discharge, after 14 days of treatment, she could see the shape of people or objects, and notice their movement. In the course of the 5-month follow-up, optic atrophy was seen and her visual field gradually improved with the defect being confined to central 10 degrees. The vision

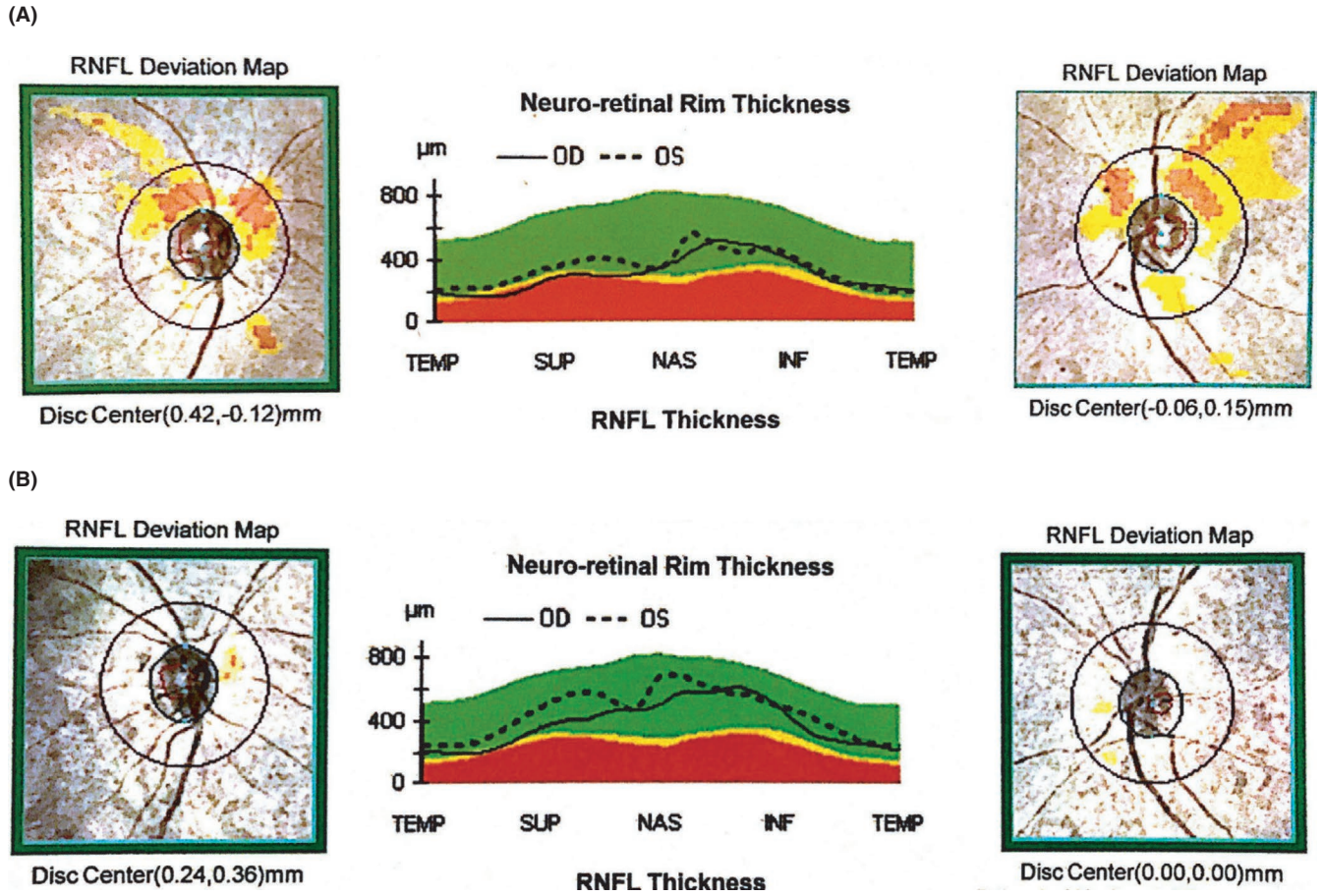

FIGURE 1 OCT findings: (A) showing the thinning of external and internal layers of retinae at baseline. (B) improvement in superior and inferior arcuate fibers in the thickness analysis of the peripapillary nerve fiber layer after a 2.5-year follow-up

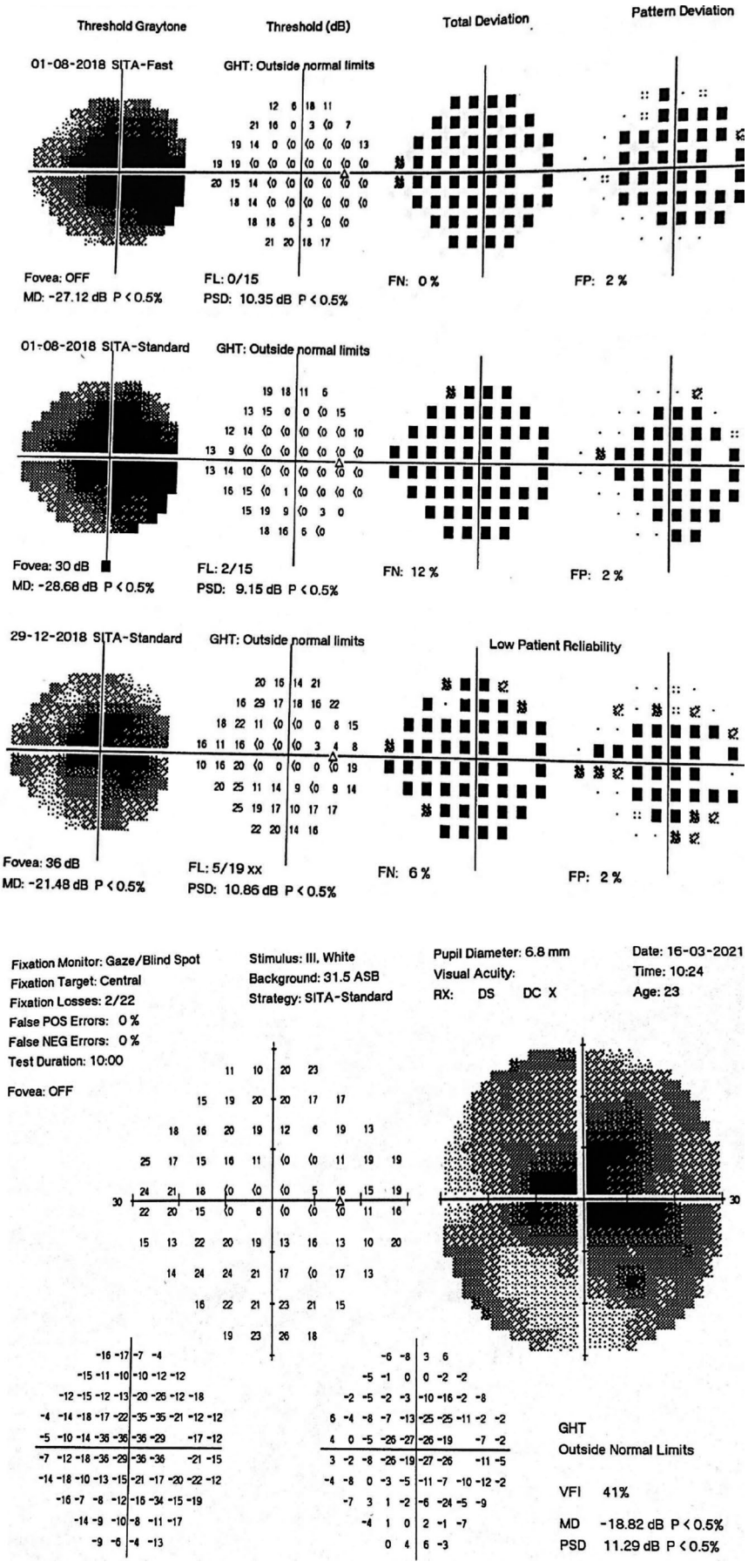

FIGURE 2 Improvement on visual field apparent in the visual field test (right eye)

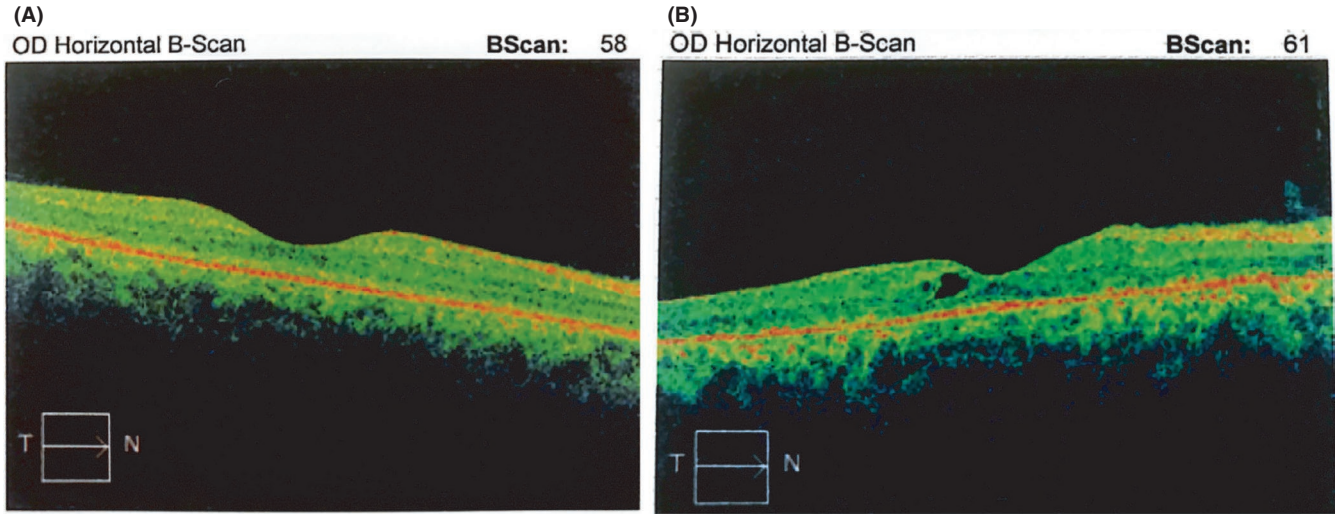

FIGURE 3 Macula OCT at baseline (A) and after a 2.5-year follow-up (B): Macular area was more involved in objective data in macular OCT in early and long-term follow-ups. Intra-retinal cystic changes due to outer retinal layer atrophy were noticed

enhanced from hand motion to 20/200. After 18 months of follow-up, her vision improved to 20/30. Furthermore, after a 2.5-year follow-up, her vision maintained the same 20/30 acuity and the peripheral nerve fiber layer showed the highest improvement in superior and inferior arcuate fibers in the thickness analysis of the peripapillary nerve fiber layer, a finding that was compatible with the subjective data of visual field improvement (Figures 1 and 2).

3 | DISCUSSION

Ocular studies in animals following closantel intoxication have shown edema in the intracanalicular portion of the optic nerve, causing demyelinated axons, fibrosis of the optic nerve, and retinal degeneration, which in turn result in mydriasis, loss of pupillary reflexes, and bilateral blindness.[6,7] Besides, retina injury leads to the thinning of photoreceptive cells.[5] Recent findings of closantel toxicity have shown that the toxic effects on retinae ganglion cells may harm the central visual acuity and optic nerve.[8] According to our findings from RNFL and macula analysis (Figure 3), it seems that the process of repairing damages to peripheral layers occurs faster than that of damages to the central layers, which may explain the reduction of the central visual field (Figure 2).

Wrong prescriptions of closantel for 11 Lithuanian women were the first human-documented closantel exposure, with temporarily visual acuity loss after closantel exposure.[9] After 22 years, the vision loss of five of them was partially reversed without significant recovery over time.[10] According to our information, the use of plasmapheresis in one case and systemic corticosteroid in another one showed significant recovery of the vision.[5,11] However, the literature also reports complete vision loss because of closantel poisoning.[12]

Systemic corticosteroids were used in two case reports of closantel poisoning, with different results.[5,12] It seems that the time of treatment onset has a key role. Moreover, a recent case report of reversible blindness upon accidental use of closantel highlighted that immediate management with corticosteroids can have beneficial effects on visual function.[13] Although the exact mechanism of closantel toxicity is not well understood, considering the possible effects of inflammatory mediators, it is reasonable to conclude that the early use of high dose of corticosteroids can minimize the toxic effects of inflammation.[5]

Corticosteroid and vitamin B12 have been routinely prescribed for some poisoning cases.[5,12,14] Furthermore, given the pharmacokinetic property and the high protein binding of closantel,[11,15] plasmapheresis was used for two cases.

In our case, look-alike sound-alike (LASA) problem seems the main cause of closantel's wrong prescription. Due to the potential effects of this medication error on patient visual acuity, it is vital to implement some preventive strategies in this regard. The pre-treatment OCT scan of the macula showed a generalized and uniform reduction in neural thickness of both eyes. Her blindness was fairly treated with plasmapheresis and corticosteroid pulse, and her vision improved significantly after an 18-month follow-up. Vision improvement of both eyes may suggest that early initiation of plasma exchange and corticosteroid pulse therapy can reverse the destructive effects of closantel on retina ganglion cells over time. Moreover, regarding pharmacokinetic

characteristics (low volume distribution and high protein binding), plasma exchange can be an effective method to be used alongside corticosteroid therapy to eliminate the toxic effects of closantel.

4 | CONCLUSION

This is a case report of successful treatment of closantel-induced blindness. Early treatment with plasmapheresis and systemic corticosteroid can be considered an effective intervention to reverse the toxic effects of closantel. Besides, it seems reasonable to provide education on the use of veterinary products and to relabel this drug as forbidden for humans, given the lack of a definite antidote for it and the possibility of irreversible blindness.

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CONFLICT OF INTEREST

The authors declare that they have no competing interests.

AUTHOR CONTRIBUTIONS

HCH, RJ, and MGH carried out diagnostic management. EK and MGH contributed in writing of manuscript and organizing patients' files. MGH revised the manuscript. All authors read and approved the final manuscript.

CONSENT

Written informed consent for publication of their clinical details and/or clinical images was obtained from the patient/parent/guardian/relative of the patient. A copy of the consent form is available for review by the Editor of this journal.

DATA AVAILABILITY STATEMENT

The data of the study are available from the corresponding author upon rational request.

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