


Intravitreal Clindamycin as First-Line Therapy for Toxoplasmic Retinochoroiditis: A Case Series

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Purpose: To report a case series of four ocular toxoplasmosis patients who received intravitreal clindamycin as first-line treatment.

Materials and Methods: Retrospective interventional case series.

Results: Four (two females and two males) patients were diagnosed with active primary toxoplasmic retinochoroiditis based on their clinical presentation. All patients received intravitreal clindamycin 1mg/0.1mL as first-line therapy (two injections with 1-week interval). Oral corticosteroid 1mg/kg/day was also given in a tapering fashion over 4–6 weeks. A remarkable response was seen in all cases with improved visual acuity, sharpening of the lesion borders, and resolution of inflammation within 4–6 weeks. No recurrence or reactivation was noted until 2 years follow-up.

Conclusion: Intravitreal clindamycin, combined with oral corticosteroids, can be considered an effective and safe first-line therapy for active toxoplasmic retinochoroiditis. It provides the patient a more convenience, safer systemic side effect profile, increased availability, and fewer follow-up visits and hematologic investigations.

Keywords: toxoplasmosis, toxoplasmic retinochoroiditis, intravitreal clindamycin, uveitis, vitritis

Introduction

Ocular toxoplasmosis is the most common cause of posterior uveitis in immunocompetent patients.¹ Focal retinitis adjacent to a pigmented chorioretinal scar, with overlying vitritis, is the frequent ocular presentation.² Though the disease is commonly self-limited, the vision may be affected due to optic nerve or macular involvement and/or severe vitritis.^{2,3} Hence, early and adequate treatment is usually indicated for such lesions to avoid profound visual impairment. The conventional systemic medications include sulfadiazine, pyrimethamine with folinic acid, clindamycin, and trimethoprim-sulfamethoxazole double-strength (TMP-SMZ DS). Other antimicrobials, such as azithromycin and atovaquone, have also been used effectively.^{2–4} However, some patients are intolerant, allergic, or have infections resistant to systemic therapy.^{1,4} Intravitreal injections can deliver a high concentration of drug to the intraocular tissues, bypassing the ocular barriers, thereby acting directly on the target site.³ Intravitreal clindamycin alone or in combination with dexamethasone had been previously reported as an alternative treatment for ocular toxoplasmosis.^{2,3,5–13} However, the use of intravitreal clindamycin alone as the first-line therapy for toxoplasmic retinochoroiditis is not commonly practised. We report our experience with intravitreal clindamycin as first-line treatment in four patients of toxoplasmic retinochoroiditis.

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Case Series

This retrospective consecutive interventional case series included patients who received intravitreal clindamycin, 1mg/0.1mL, as first-line therapy for active toxoplasmic retinochoroiditis at Centre for Sight eye hospital, New Delhi, India, between January 2018 and December 2018. Written informed consent was obtained from all the patients/legal guardians according to the tenets of the Declaration of Helsinki. Ethical approval was waived by the institutional ethics committee of Centre for Sight, given the retrospective nature of the case series that limits itself to collecting clinical data with no personal identifiers of the patient being captured from the records. The confidentiality of patients was maintained throughout all stages of the data analysis.

The toxoplasmic retinochoroiditis diagnosis was based on at least 1 of the following clinical findings: (a) optic nerve or macular involvement or threat thereof by an adjacent lesion, (b) a lesion adjacent to large retinal vessels, and (c) severe vitreous inflammation ($\geq 2+$ vitreous cells), in the absence of other identifiable causes, as well as positive serum titers of antibody (immunoglobulin [Ig] G or M) to *Toxoplasma gondii*. The degree of vitreous inflammation was determined on a scale from 0 to 4 as described by Kimura et al.¹⁴ A clinically significant response to the treatment was defined as Snellen visual acuity change of ≥ 2 lines or a final visual acuity of 6/6, sharpening of the lesion border with or without hyperpigmentation, and resolution of vitreous inflammation at the end of 6 weeks. A decrease of vitreous cells to the level of 0 or trace after treatment was considered to be vitreous inflammation resolution.

Table 1 summarizes the patient data.

Case 1

A 40-year-old woman was diagnosed with ocular toxoplasmosis based on her presentation with a corrected distance

visual acuity (CDVA) of counting fingers (CF) at 1 metre, 2+ vitreous cells, and an active juxtamacular retinitis (Figure 1A) in the right eye (RE). There was no history of consumption of raw meat or contact with animals. The examination of the left eye (LE) was within normal limits with a CDVA of 6/6. Intraocular pressure (IOP) was normal in both eyes. Spectral-domain optical coherence tomography (SD-OCT) of RE revealed macular edema with intra- and sub-retinal fluid, and vitreous hyperreflectivity (Figure 1C). She was treated with intravitreal clindamycin 1mg/0.1mL (two injections with 1-week interval) administered under sterile conditions. Oral corticosteroid 1mg/kg/day was also initiated with gradual tapering over 6 weeks. One month later, CDVA improved to 6/9 with a quiescent lesion free of inflammation and macular edema reduced. At 2 months, CDVA was 6/6 with an inactive lesion and complete resolution of macular edema (Figure 1B and D). No recurrence of the disease was noted until 2 years follow-up.

Case 2

A 57-year-old woman presented with a CDVA of CF at $\frac{1}{2}$ metre, 3+ vitreous cells, and focal juxtamacular retinochoroiditis (Figure 2A) in the RE. She did not give any specific exposure history like consumption of undercooked meat, ingestion of contaminated water, or contact with animals. IOP was normal in both eyes. RE SD-OCT showed elevation of the neurosensory retina and retinal pigment epithelium (RPE) with the presence of intra- and sub-retinal fluid (Figure 2C). LE examination was unremarkable. IgG antibody titres to *Toxoplasma gondii* were elevated, and a diagnosis of ocular toxoplasmosis was made. She received intravitreal clindamycin 1mg/0.1mL twice with an interval of one week and oral corticosteroid 1mg/kg/day in a descending regime over 6 weeks. CDVA improved to 6/24 at 1 month with the sharpening of the

Table 1 Summary of Patient Data

Age (Years)/ Sex	Baseline Visual Acuity	Time Taken to Lesion Inactivity After the First Injection of Intravitreal Clindamycin	Final Visual Acuity	Number of Injections	Total Follow-Up
40/ female	CF 1 m	6 weeks	6/6	2	2 years
57/ female	CF $\frac{1}{2}$ m	6 weeks	6/12	2	2 years
12/ male	6/18	4 weeks	6/6	2	2 years
22/ male	6/9	2 weeks	6/6	2	2 years

Abbreviation: CF, counting fingers.

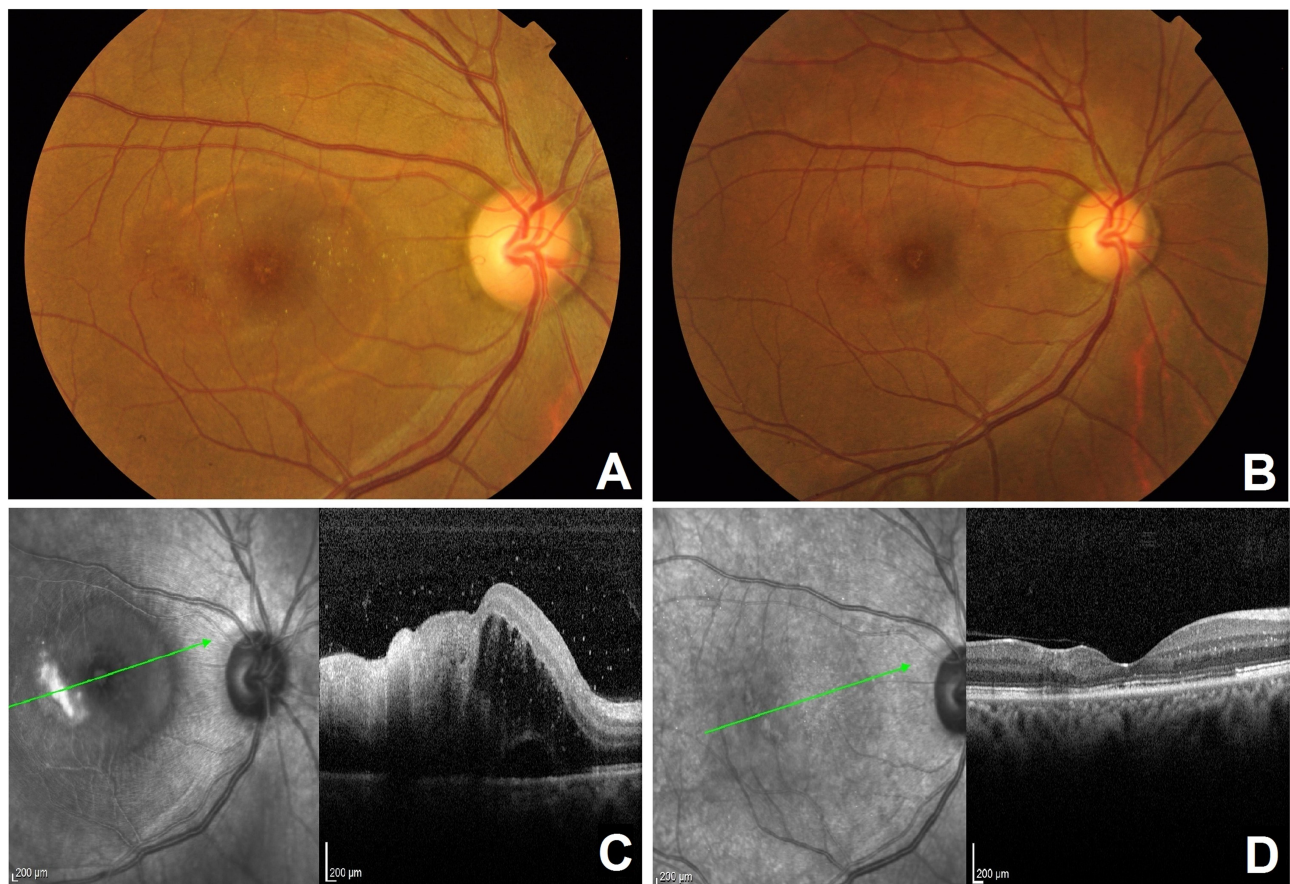


Figure 1 (A) Fundus photograph showing active juxtamacular retinitis before treatment, (B) inactive lesion after treatment with intravitreal clindamycin, (C) spectral-domain optical coherence tomography showing hyperreflective spots in the vitreous, macular edema with intra- and sub-retinal fluid before treatment, hyperreflectivity of the neurosensory retina can be noted in the temporal aspect precluding the individualization of the different layers, (D) normal retinal thickness and foveal contour after treatment.

borders of retinochoroidal lesion. At 2 months, CDVA was 6/12, vitreous inflammation resolved, and the lesion remained quiescent with some evidence of outer retinal and RPE atrophy (Figure 2B and D). No reactivation of the lesion was noted up to 2 years follow-up.

Case 3

A 12-year-old boy was diagnosed with active toxoplasmosis based on his presentation with a CDVA of 6/18, 2+ vitreous cells, and focal juxtamacular retinitis (Figure 3A) in the RE. There was no history of consumption of undercooked meat or contact with animals. The examination of LE was unremarkable with normal IOP in both eyes. SD-OCT of RE revealed macular edema with increased retinal thickness, sub-retinal fluid, and vitreous hyperreflectivity (Figure 3C). He was treated with two injections of intravitreal clindamycin 1mg/0.1mL and oral corticosteroid 1mg/kg/day in a tapering regime over 4 weeks. One month later, CDVA improved to 6/6 with the sharpening of the

lesion borders, resolution of vitritis and macular edema (Figure 3B and D). He remained free of inflammation with a CDVA of 6/6 at 3 months. No recurrence was observed for 2 years until the last follow-up.

Case 4

A 22-year-old male presented with a CDVA of 6/9, 2+ vitreous cells, and an active juxtapapillary retinitis (Figure 4A) in the RE. He had no history of consuming undercooked meat, ingesting contaminated water, or contact with animals. The examination of LE was normal, with a CDVA of 6/6. A positive titre of IgG antibody to *Toxoplasma gondii* confirmed the diagnosis of ocular toxoplasmosis. He was administered intravitreal clindamycin 1mg/0.1mL twice and given oral corticosteroid 1mg/kg/day in a tapering fashion over 4 weeks. CDVA improved to 6/6 at 1 month with a quiescent toxoplasmic lesion free of inflammation (Figure 4B). The disease remained

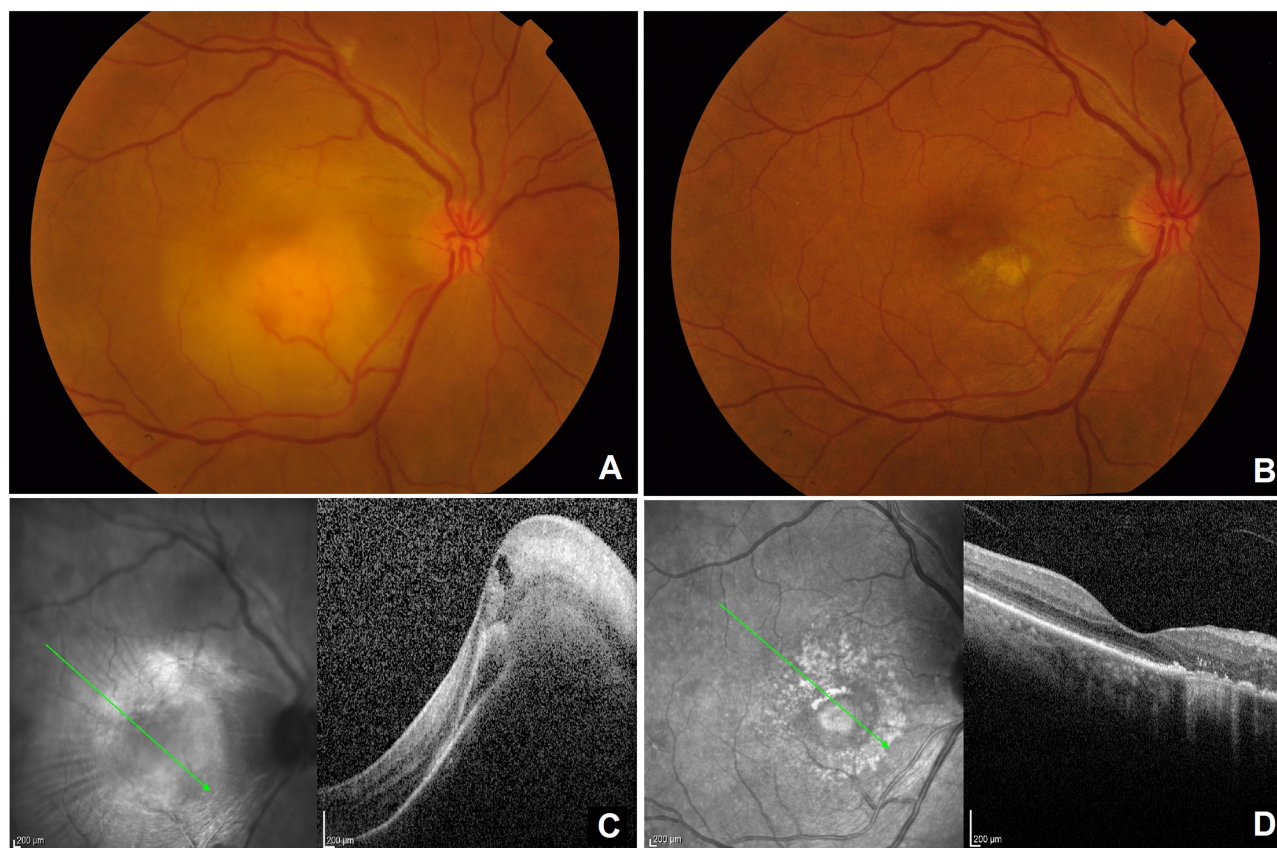


Figure 2 (A) Fundus photograph showing active juxtamacular toxoplasmic retinochoroiditis before treatment, (B) sharpening of lesion borders after treatment with intravitreal clindamycin, (C) spectral-domain optical coherence tomography showing elevation of the neurosensory retina and retinal pigment epithelium with the presence of intra- and sub-retinal fluid before treatment, hyperreflectivity of the neurosensory retina can be noted in the inferior nasal aspect precluding the individualization of the different layers, (D) normal foveal contour with evidence of retinal pigment epithelial and outer retinal atrophy after treatment.

inactive at 3 months, maintaining a CDVA of 6/6. No reactivation was seen till 2 years follow-up.

Discussion

Many of the traditional systemic anti-toxoplasmosis medications used may have side effects that compromise patient care. Pyrimethamine has been shown to produce leukopenia and thrombocytopenia in 26% of patients.¹⁵ Sulpha-containing medications such as sulfadiazine and TMP-SMZ DS may cause skin rashes in >10% of patients.^{1,2} Oral clindamycin may generate vomits and/or diarrhoea due to the risk of pseudomembranous colitis.^{1,2,5} Two alternative treatment options that avoid these systemic side effects include local treatment with alternate day subconjunctival clindamycin injections for 1 month or the intravitreal injection of clindamycin.^{2,3,5,6,15}

Our patients received intravitreal clindamycin as first-line therapy due to its direct action on the target site at high concentration and lack of systemic side effects. It is believed that 1mg of intravitreal clindamycin allows concentrations of 1.6µg/mL for 40 hours, a level exceeding the 50% inhibitory

concentration for toxoplasma.⁵ Also, no retinal toxicity has been reported yet with intravitreal clindamycin.^{2,3,5-9} All our patients improved without recurrence following two injections of intravitreal clindamycin despite continuing on a tapering dose of systemic prednisolone without antibiotic cover. This could be due to the high concentration of clindamycin available to the retina and choroid when the treatment was given via intravitreal route and the possible superior potential of clindamycin to treat the encysted form of toxoplasma.

Previous studies have compared the use of intravitreal clindamycin and dexamethasone against classic oral treatment, demonstrating similar effectiveness with both treatment modalities.⁷⁻⁹ An intravitreal dose of 1mg/0.1mL clindamycin at weekly intervals and up to four injections had been administered by most of the authors.^{2,3,5-7,9} In our series, all patients received two intravitreal injections with a 1-week interval and responded well. There is no consensus on the best mode of corticosteroid administration in ocular toxoplasmosis cases. We believe that oral administration provides better results as intravitreal administration exhibits short

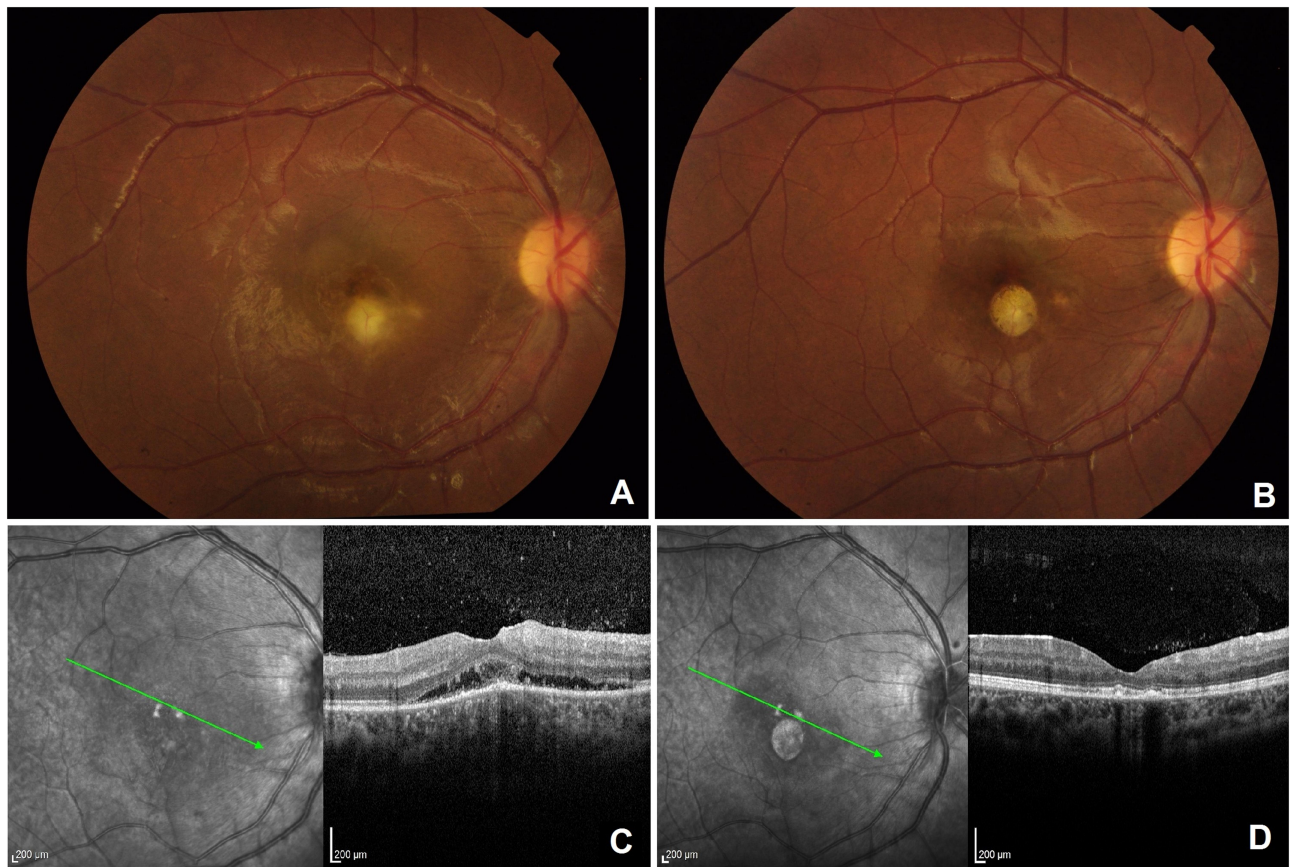


Figure 3 (A) Fundus photograph showing active juxtamacular focal retinitis before treatment, (B) sharpening of lesion borders after treatment with intravitreal clindamycin, (C) spectral-domain optical coherence tomography showing increased retinal thickness, subretinal fluid, and vitreous hyperreflectivity before treatment (D) normal retinal thickness and foveal contour after treatment.

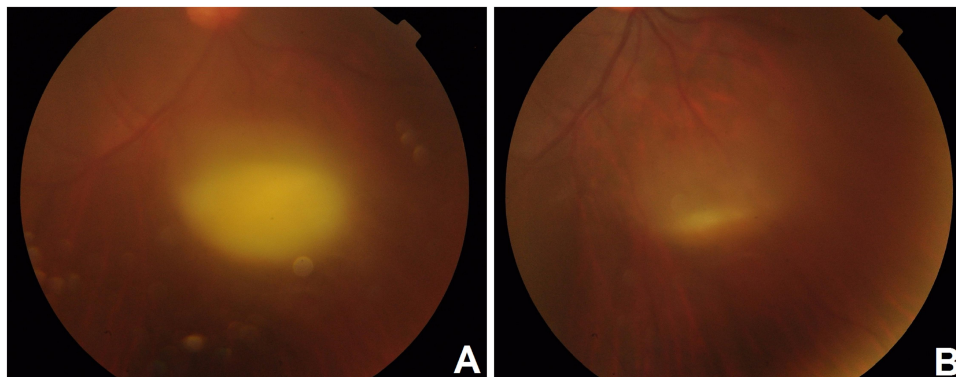


Figure 4 (A) Fundus photograph showing active juxtapapillary retinitis before treatment, (B) quiescent lesion after treatment with intravitreal clindamycin.

mean life. Some authors believe that co-administration of intravitreal steroids may interfere with the effectiveness of intravitreal clindamycin.^{2,7} Also, reactivation of the disease has been reported with intravitreal and periocular steroids.^{16–18} All patients in this series received oral steroids in a tapering regime for 4–6 weeks and no recurrence was noted until 2 years follow-up.

The risk of recurrence of ocular toxoplasmosis during the first few years after an active episode is found to be significantly greater in patients with a primary lesion, which then decreases with increasing disease-free intervals.^{19–21} Therefore, patients should be followed up more often in the first year after suffering from an active lesion of ocular toxoplasmosis. The age of the patient also seems to influence

the risk of recurrence, which is controversially discussed in the literature. However, recent studies suggest that elderly individuals are more likely to have a higher risk of recurrence.^{19,20} Our case series included patients of all age groups ranging from 12 to 57 years with a primary active lesion and were followed up regularly up to 2 years. None of our patients had a recurrence at 2 years of follow-up, similar to the report by Lasava et al.⁸ However, studies by Soheilian et al, Baharivand et al, and Kishore et al showed episodes of recurrence with intravitreal clindamycin and dexamethasone.^{7,9,10} It is important to note that the risk of recurrence is additionally affected by other host-specific and parasite-specific factors such as immune status, cytokine profile, the genotype of the patient, and strain of the parasite.^{20,22}

Possible complications of intravitreal injections include inadvertent retinal damage and retinal detachment, infectious endophthalmitis, and damage to the posterior capsule of the lens. However, these risks can be avoided by following the guidelines for the intravitreal injection of drugs and sterilization procedures.²³ Only one case report described a hypersensitivity reaction following intravitreal clindamycin in a patient with ocular toxoplasmosis.²⁴ In our patients, injections were well tolerated without any associated complications during or after the procedure.

Sobrin et al initially reported the efficacy of intravitreal clindamycin in the treatment of toxoplasmic retinochoroiditis. Their study included six patients treated with intravitreal clindamycin (1.0 mg/0.1 mL) because of intolerance to systemic therapy or disease progression despite oral antimicrobial treatment. Four patients underwent concomitant pars plana vitrectomy at the time of injection. They concluded that intravitreal clindamycin was associated with control of toxoplasmosis and resolution of vitreous inflammation.²

Wong et al described a patient with ocular toxoplasmosis with an atypical presentation managed successfully with intravitreal clindamycin because of intolerance to oral therapy. After two injections of intravitreal clindamycin and oral prednisolone without concomitant systemic antibiotics, this patient continued to improve without recurrence.⁵ Tabuenca Del Barrio et al reported using intravitreal clindamycin and oral steroids in a case of bilateral ocular toxoplasmosis in a sulfamide allergic patient with unilateral activation. They concluded that weekly intravitreal clindamycin treatment is a suitable therapeutic alternative in severe ocular toxoplasmosis and/or in patients with a contraindication to classical

treatment.⁶ Hosseini et al explained a case of toxoplasmic chorioretinitis resistant to standard oral treatment that responded dramatically to intravitreal clindamycin.³

In contrast to the published literature, our patients had no contraindication to standard oral therapy and received intravitreal clindamycin as first-line therapy. The lesion became inactive, the visual acuity improved, and the vitritis resolved within 4–6 weeks in all four patients. Three out of four patients had a final CDVA of 6/6. One patient's CDVA was limited to 6/12 due to the development of RPE and outer retinal atrophy. Moreover, no recurrence or reactivation of the lesion was noted till 2 years follow-up.

This case series demonstrates that intravitreal clindamycin, together with oral corticosteroids, suppose an effective and safe first-line strategy for patients with toxoplasmic retinochoroiditis due to better patient compliance, improved systemic safety profile, enhanced availability at the target site, and lesser follow-up visits and hematologic investigations. It could be a better choice of treatment for pregnant and pediatric patients. However, further prospective clinical studies are needed to validate the efficacy of intravitreal clindamycin as a first-line treatment.

Data Sharing Statement

The data are available within the manuscript.

Ethics Approval and Informed Consent

Written informed consent was obtained from all the patients/legal guardians for the publication of the case details and any accompanying images. Ethical approval was waived by the institutional ethics committee of Centre for Sight, given the retrospective nature of the case series that limits itself to collecting clinical data with no personal identifiers of the patient being captured from the records.

Consent for Publication

Written informed consent was obtained from the patients (Cases 1, 2, 4) and legal guardian (Case 3) for the publication of the case details and any accompanying images. This report does not contain any personal identifying information.

Author Contributions

All authors contributed to data analysis, drafting or revising the article, have agreed on the journal to which the article will

be submitted, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

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Disclosure

The authors report no conflicts of interest for this work.

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