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Case report

## Sequential multimodal imaging of isolated necrotic full-thickness macular hole secondary to toxoplasma retinochoroiditis



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### ABSTRACT

**Purpose:** To describe the sequential multimodal imaging features of an isolated necrotic macular hole secondary to *Toxoplasma retinochoroiditis*.

**Observation:** A 23-year-old male was referred for surgical management of an idiopathic macular hole following sudden decrease in vision in his right eye. Right eye examination showed best-corrected visual acuity of 20/200, mild anterior segment inflammation, and a full thickness non operculated macular hole (MH) with ill-defined ragged margins and surrounding strip of pallid edema. Further multimodal imaging including optical coherence tomography (OCT), fundus autofluorescence (FAF), fluorescein angiography (FFA), and OCT-angiography confirmed the atypical configuration and inflammatory nature of MH. Serological tests showed elevated level of *Toxoplasma gondii*-specific antibodies. A diagnosis of necrotic isolated full-thickness MH secondary to toxoplasma retinochoroiditis was made. Patient was treated medically with anti-toxoplasma medication for 6 months. Sequential multimodal imaging highlighted the healing process of necrotic MH with vision improving to 20/80 at 6 months after presentation.

**Conclusion and importance:** A high level of suspicion and multimodal imaging plays an important role in accurate etiological diagnosis and management of atypical macular hole as in our case. Sequential multimodal imaging may provide an insight into the pathogenesis and healing pattern of such lesion.

### 1. Introduction

Ocular toxoplasmosis, caused by the parasite *Toxoplasma gondii*, is the most common cause of infectious posterior uveitis in immunocompetent individuals worldwide.<sup>1,2</sup> The typical and most common presentation of ocular toxoplasmosis is recurrent episodes of unilateral focal necrotizing retinochoroiditis accompanied by vitritis, frequently associated with an adjacent pigmented retinochoroidal scar.<sup>2,3</sup> *Toxoplasma retinochoroiditis* is frequently associated with the vitreoretinal complications such as epiretinal membrane, cystoid macular edema, vitreoretinal traction, choroidal neovascularization and retinal detachment.<sup>2</sup> However, formation of macular hole secondary to toxoplasma retinochoroiditis has been rarely reported in literature.<sup>1-5</sup>

We report a case of toxoplasma retinochoroiditis associated with macular hole and the process of healing following treatment with multimodal imaging.

### 2. Case report

A 23-year-old male was referred to our vitreoretinal services for surgical management of an idiopathic macular hole in his right eye. There was a history of sudden decrease in vision in the right eye for three weeks. There was no history of ocular trauma or any previous ocular complaints.

On examination, his best-corrected visual acuity (BCVA) was 20/200 in the right eye and 20/20 in the left eye. A slit-lamp examination of the right eye revealed 1+ cells and 1+ flare in anterior chamber, and 1+ cells in anterior vitreous face. Fundus examination revealed a full thickness non-operculated macular hole (MH) with ill-defined ragged margins and surrounding strip of pallid edema [Fig. 1A]. Rest of the fundus including periphery was normal. There was no evidence of posterior hyaloid detachment. The left eye examination was normal. Optical coherence tomography (OCT) of the right eye showed a full thickness MH with a loosely overhanging intact internal limiting

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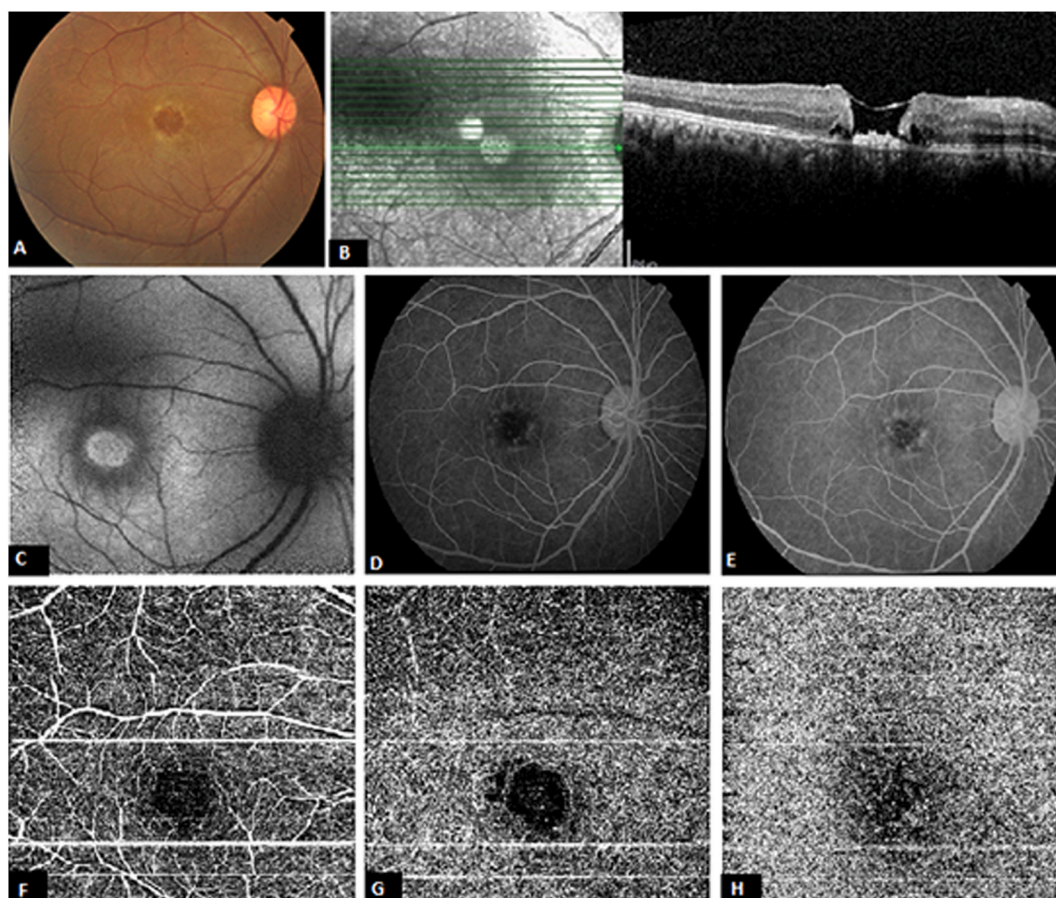
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membrane (ILM) and hyper-reflective material deposit at the base [Fig. 1B]. Due to the absence of classical configuration of MH in the OCT along with the presence of anterior segment inflammation and vitritis in a young patient without any history of ocular trauma, we suspected an inflammatory etiology of MH.

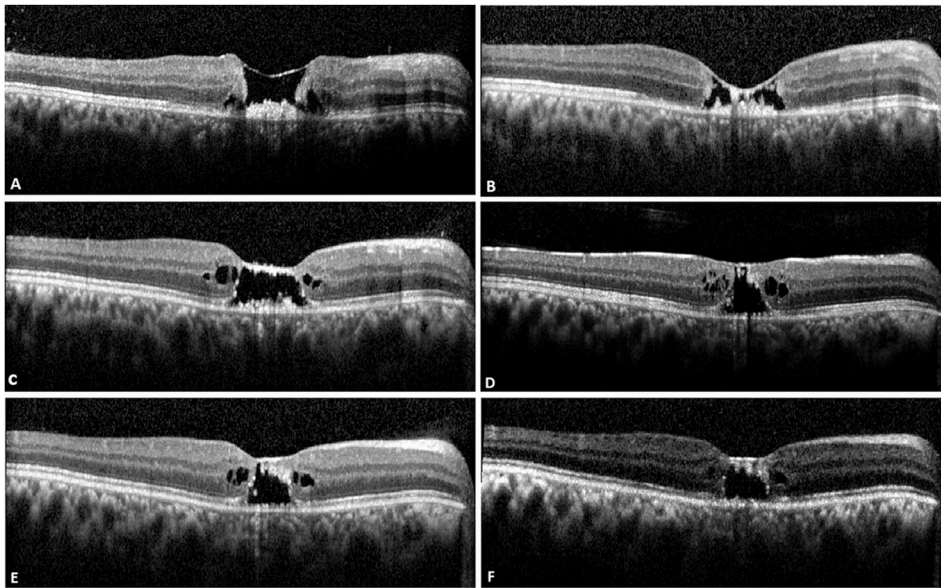
Fundus Autofluorescence (FAF) of the right eye showed a central hyper-autofluorescence corresponding to the area of clinically observed MH and a surrounding halo of hypo-autofluorescence corresponding to the retinal edema, which in turn was encompassed by another ring of hyper-autofluorescence. The outer ring of hyper-autofluorescence suggested that the inflammatory pathology extended well beyond the clinically observed lesion [Fig. 1C]. Fluorescence angiography (FFA) showed central blocked fluorescence caused by the central necrotic deposit, enlargement of foveal avascular zone in early phase, and leakage due to perifoveal edema in the subsequent phases resulting in multiple hyper-fluorescent satellite lesions suggestive of inflammatory activity [Fig. 1D and E]. OCT-angiography (OCTA) of the right eye revealed an enlargement of foveal avascular zone (FAZ) with the areas of capillary dropouts at the level of superficial and deep capillary plexus suggesting an ischemic insult [Fig. 1F and G]. OCTA image at choriocapillaris layer showed low flow suggesting sub foveal choroidal hypoperfusion [Fig. 1H].

The inflammatory work-up included routine blood tests and serological tests for *Toxoplasma gondii* (*T. gondii*), Human

immunodeficiency virus and *Treponema pallidum*. The serology results were positive for *T. gondii*-specific immunoglobulin M antibody, done by ELISA kit, (2.7 S/Co, cut off value 1.3 S/Co) and immunoglobulin G antibody (8.5 S/Co, cut off value 1.2 S/Co) and the titres were elevated. Serological tests for Human immunodeficiency virus and *Treponema pallidum* were negative and all other tests including CBC and CD4 count (912 cells/mm<sup>3</sup>) were normal. Therefore, a diagnosis of necrotic isolated full-thickness MH secondary to toxoplasma retinochoroiditis was made in the right eye. Patient was started on oral Prednisolone (40mg/day) along with empirical oral treatment with anti-toxoplasmosis drugs -sulphamethoxazole (800 mg)/trimethoprim (160 mg) twice a day. Oral steroid was gradually tapered off, but anti-toxoplasmosis drugs were continued for 6 months. Serial OCT showed gradual disappearance of the necrotic debris, regeneration of photoreceptors, appearance and disappearance of intraretinal cystoid spaces, gradual reduction in the size of the MH and finally its conversion to residual outer lamellar hole at 6 months [Fig. 2]. Sequential autofluorescence images during follow-up visits correlated with changes of reducing inflammation with healing and scarring [Fig. 3]. During serial follow-ups, the intraocular inflammation subsided gradually with a final BCVA of 20/80 at 6 months after presentation. No surgical intervention was considered.



**Fig. 1.** Multimodal imaging of the right eye at presentation: Fundus photo showing macular hole with ragged margins and surrounding pallid retinal edema (appearing as whitish edge) [A]; OCT showing full thickness macular hole with hyperreflective necrotic debris at the base, loss of photoreceptors extending beyond margin of macular hole, overlying loose intact internal limiting membrane, and the presence of few inflammatory cells in the pre-retinal hyaloid [B]; Fundus Autofluorescence showing central hyper-autofluorescence with a surrounding halo of hypo-autofluorescence and outer ring hyper-autofluorescence suggesting extent of inflammatory pathology beyond clinically observed macular hole [C]; FFA showing enlarged foveal avascular zone with perifoveal capillary dropouts in early phase [D], and leakage from retinal edema resulting in multiple spots of hyper-fluorescence along the edge of macular hole in the late phase [E]; OCT angiography showing enlargement of foveal avascular zone with perifoveal capillary dropouts at the level of superficial and deep capillary plexus suggestive of macular ischemia [F,G respectively]; OCT angiography showing low flow at the level of choriocapillaris suggestive of sub-macular choroidal hypoperfusion [H].



**Fig. 2.** Sequential OCT images: At presentation as described in Fig. 1B [A]; at 2 weeks, showing basal necrotic debris, rounding of macular hole edge, obvious loss of photoreceptors beyond configuration of hole, and sagging of internal limiting membrane [B]; at 1 month, showing reduction in necrotic debris, regeneration of photoreceptor layer, and taut internal limiting membrane due to appearance of intraretinal cystoid spaces [C]; at 2 months, showing complete clearance of basal necrotic debris and reduction in the size of macular hole due to migration of retinal cells under internal limiting membrane [D]; at 3 months, showing gradual closure of macular hole with further growth of retinal cells under internal limiting membrane [E]; at final visit (6 months), showing reduction in cystoid edema, conversion of full-thickness macular hole to outer lamellar hole due to gliosis of inner retina along with significant regeneration of photoreceptor layer [F].

### 3. Discussion

In literature, there are very limited case reports and series describing MH formation as a complication of toxoplasma retinochoroiditis.<sup>1-5</sup> Toxoplasma infection is often highest in the area that have hot and humid climates, and lower altitudes because the oocysts survive better in these types of environment. Many studies have reported higher incidence of Toxoplasma in Southern India,<sup>6</sup> the region of our report. Although there was no history of exposure to water contamination or close contact with cats, we attributed Toxoplasmosis as the cause of necrotic MH based on clinical and multimodal imaging features, results of the inflammatory work-up as well as response to the anti-toxoplasma regimen. The main mechanism implicated in the pathogenesis of MH formation is either an antero-posterior or a tangential vitreoretinal traction.<sup>4,7</sup> The antero-posterior traction is caused by posterior vitreous detachment induced by associated inflammation of vitreous, while tangential traction could be caused by an epiretinal membrane or an adjacent retinochoroidal scar.

The absence of vitreomacular traction and epiretinal membrane with the presence of loosely overhanging intact ILM seen in OCT, and the absence of an operculum ruled out any antero-posterior or tangential traction in our case. The additional findings seen in this case included the presence of surrounding pallid retinal edema with an ill-defined ragged margin of MH seen on clinical examination, the thinned out edge of hole with hyper-reflective necrotic debris at the base of MH in OCT. Though we are not sure about the exact pathogenic changes in our case, we hypothesize two possible mechanisms as ischemic necrosis or necrosis due to intracellular replication of the parasite itself. Other findings like choroidal vascular hypoperfusion in ICGA and macular hypoperfusion seen as enlarged FAZ with capillary dropouts in FFA and OCTA were suggestive of ischemic retinal necrosis being the main pathological insult causing development of MH in this case.

The only case with similar presentation with toxoplasmosis induced necrotic MH with intact ILM and basal debris has been reported by Babu et al.<sup>5</sup> However, their case presented with fovea involving retinochoroiditis which gradually evolved into MH.

Histopathological changes of focal retinochoroiditis of ocular toxoplasmosis is characterised by local leukemic infiltration, ischemic coagulative retinal necrosis and granulomatous inflammation of underlying choroid causing choriocapillitis.<sup>8</sup> These changes in a macula involving lesion may cause foveal hypoperfusion leading to development of MH as seen in our case. Similar necrotic macular defect has been

described in a case measles associated subacute sclerosing panencephalitis.<sup>9</sup>

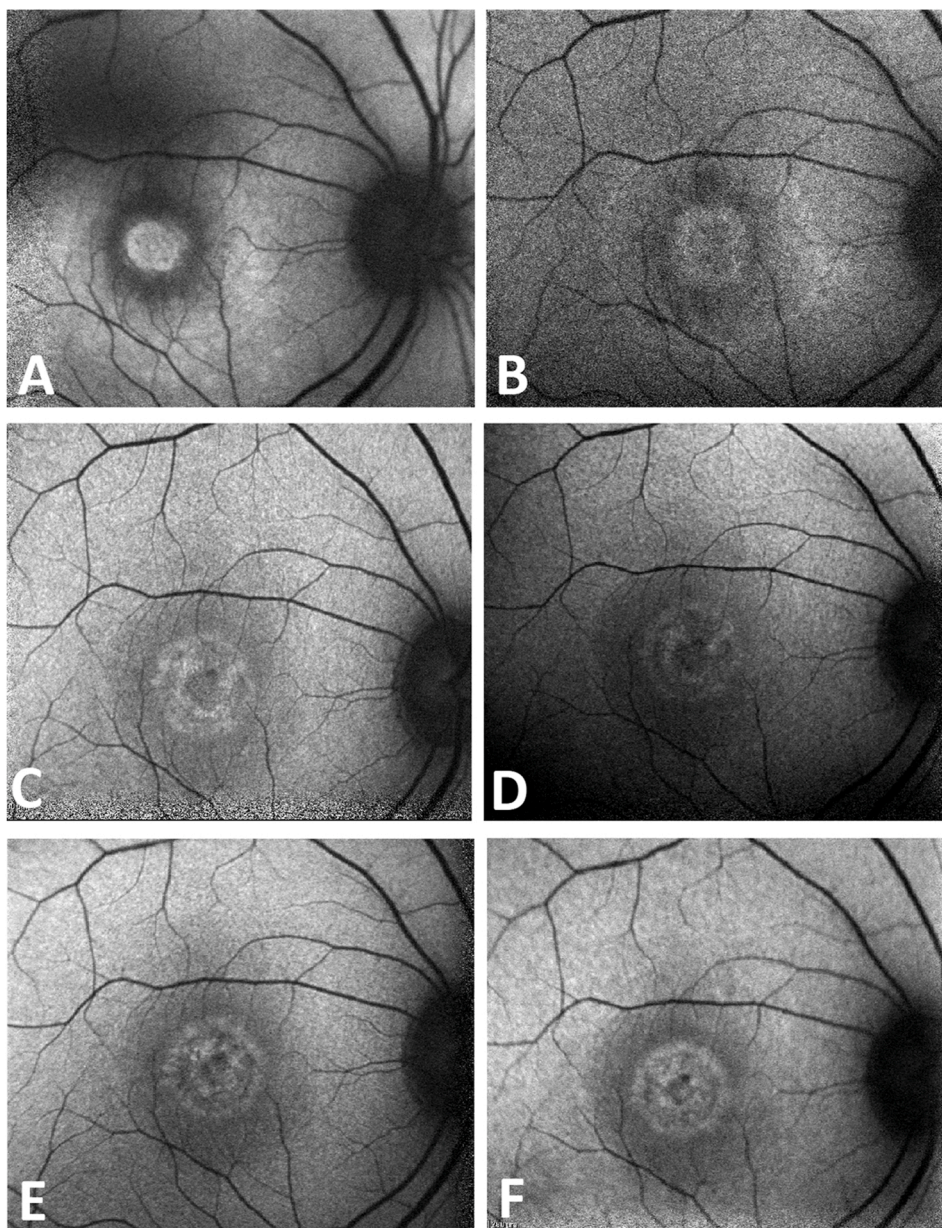
Posterior uveitis induced MH are reportedly more difficult to close via conventional surgical interventions compared with idiopathic MH.<sup>10</sup> It has been hypothesized that chronic inflammation in combination with recurrent cystoid edema and choroidal ischemia in the macula creates atrophied retinal epithelium that makes MH less amenable to closure. However, as most of the reported MH secondary to toxoplasma chorioretinitis result from vitreoretinal traction, surgical interventions have been attempted for them.<sup>2,4,7</sup> Sousa et al. presented a series of 11 patient with toxoplasma retinochoroiditis associated tractional MH with good functional and anatomical improvement.<sup>2</sup> On the contrary, Bonin et al. reported a case series of 3 patients with spontaneous closure of inflammatory macular hole following medical therapy.<sup>11</sup> They postulated that treating the inflammation can relieve the intraretinal constraints like cystoid edema or epimacular tractions, and produce spontaneous healing of the macular hole. Similarly, spontaneous MH closure was noted in our case following medical management of toxoplasma inflammation. Serial multimodal imaging demonstrated the gradual disappearance of inflammatory changes, clearing of necrotic debris, and gliotic changes with retinal cellular remodelling leading to conversion of full-thickness MH to outer lamellar hole in response to the medical therapy.

The surgical interventions including vitrectomy and internal limiting membrane peeling should be contemplated cautiously in such cases. Brasnon et al. recommended that surgical intervention should not be pursued until conservative strategies have proved ineffective.<sup>11</sup> The surgery should be reserved for the cases having evidence of antero-posterior or tangential vitreoretinal traction in absence of active inflammation. Though the MH closure was incomplete in our case, the surgical intervention was not contemplated in view of limited visual prognosis and the absence of any vitreomacular traction or cuff of subretinal fluid on OCT.

### 4. Conclusions

To conclude, ophthalmologists must suspect atypical causes like inflammation for the development of MH in a young patient with the presence of anterior chamber cells or vitreous cells and the absence of posterior vitreous detachment. This case of toxoplasma retinochoroiditis had unique presentation as an isolated non-tractional necrotic MH, sequential multimodal imaging of which provided an insight into the





**Fig. 3.** Sequential autofluorescence images: At presentation as described in Fig. 1C [A]; at 2 weeks, showing decrease in the central and outer ring of hyperfluorescence due to decrease in retinal inflammation [B]; at 1 month, 2 month, 3 month and 6 month, showing doughnut-shaped stippled hyperautofluorescence with centripetally expanding surrounding hypoautofluorescence due to scarring and healing processes [C,D,E,F respectively].

pathogenesis and healing pattern following the medical treatment. Early treatment of active retinitis should be the first line of management and surgical intervention should be reserved for an inactive persistent MH despite medical therapy.

#### **Patient consent**

An informed consent has been obtained from the patient for using his clinical details and images for publication purpose.

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#### **Authorship**

All authors attest that they meet the current ICMJE criteria for authorship.

#### **Declaration of competing interest**

Authors have no conflict of interest.

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