Macular Colobomata: Comparison of Clinical and Optical Coherence Tomography Features With Serologic Results

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• PURPOSE: To assess the correlation between the morphologic features and serology in eyes with macular colobomata (MC).
• DESIGN: Retrospective comparative case series.
• METHODS: Setting: Institutional. Study Population: Patients presenting with MC to the retina clinic over a period of 2 years (January 2016 to December 2017). Interventional/Observational Procedure: Color fundus and swept-source optical coherence tomography (SSOCT) features were reviewed and assessed in 3 groups based on the serum IgG results: positive for *Toxoplasma*, positive for cytomegalovirus (CMV), and serology negative. Main Outcome Measure: Morphologic features on clinical and OCT-based examination.
• RESULTS: A total of 49 eyes of 27 patients were recruited. The mean age was 24.8 ± 14.9 years (range 7-60 years). While the lesion size, the presence of satellite lesions, choroidal excavation, and choroidal lacunae (large choroidal vessels) on SSOCT differed significantly among the groups, pigmentation, retinal fibrosis, shape, retinal vessel pattern, and choroidal vessel visibility did not vary significantly. The lesions in CMV serology–positive cases were mostly solitary (n = 8/8), large (n = 5/8) and deeply excavated (n = 8/8). The lesions in *Toxoplasma* serology–positive cases were mostly flat to shallow (n = 18/26), medium-sized (n = 19/26), and either a solitary lesion (n = 17/26) or multiple satellite lesions (n = 9/26). The lesions in serology-negative cases were mostly small to medium (n = 13/15), solitary (n = 15/15), deeply excavated lesions (n = 11/15) with choroidal lacunae (n = 8/15).
• CONCLUSIONS: The clinical and SSOCT features such as the lesion size, the presence of satellite lesions, choroidal excavation, and choroidal lacunae can provide a clue toward the etiology of macular colobomata. (Am J Ophthalmol 2019;200:47–56. © 2019 Elsevier Inc. All rights reserved.)

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RETINOCHOROIDAL COLOBOMATA OR THE TYPICAL uveal colobomata is an uncommon ocular malformation, reported to occur at a rate of 0.048% (1 in 2077 live births) in the general population.[1] This is thought to be owing to an anomalous closure of the fetal fissure. A distinct type of coloboma is macular colobomata, which is even more uncommon. Because of their central nature, the patients often present with poor vision and nystagmus (in case of congenital or early acquired lesions). Their etiology remains an enigma and they are believed to result from either congenital developmental abnormality or inflammation owing to intrauterine or postnatal infection.[2–5] Congenital macular colobomata form as a result of faulty differentiation of the arcuate bundles along the horizontal raphe during retinal development.[2,5,6] On the other hand, postinflammatory macular scars are often a result of ocular toxoplasmosis or cytomegalovirus (CMV) infection.[2,3,5,7] Ocular toxoplasmosis is often secondary to congenital infection and tends to occur during the chronic phase of the disease.[8–10] It sometimes follows acquired infection associated with the ingestion of undercooked meat or water contaminated with cysts of *Toxoplasma gondii*. Congenital CMV infection can also manifest with chorioretinitis lesions and macular scarring.[11] In addition, retinal dystrophies may be associated with macular scarring/coloboma. These include Leber congenital amaurosis, progressive cone-rod dystrophy, and North Carolina macular dystrophy.[3,5,12]

Assessing the serologic status of the patient and family history may be of great help in differentiating the etiology of these cases. Though fundus and optical coherence tomography (OCT) features of these entities have been defined and differentiated in the past, they are often indecisive.[6,7,13,14] Therefore, we performed this study to determine if the morphologic characteristics of macular coloboma vary with the serology results.

METHODS

THIS IS A RETROSPECTIVE STUDY OF CONSECUTIVE patients with macular coloboma, who attended the retina clinic over last 2 years (January 1, 2016 to December 31, 2017) at a tertiary eye care center in North India. The study adhered to the tenets of the Declaration of Helsinki and to

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the institutional research guidelines. A review of the database of the retina clinic was performed to identify the cases. Exclusion criteria included the presence of active chorioretinitis, presence of features suggestive of an inherited retinal dystrophy, unavailability of retinal imaging data, preverbal children, and patients in whom serology was not performed or was positive for both *Toxoplasma* and CMV.

Detailed ophthalmic, family, personal, and systemic history of *Toxoplasma* and CMV infection was obtained. All patients had undergone a complete ophthalmic examination including best-corrected visual acuity (BCVA) assessment (Snellen chart), anterior segment examination using slit lamp, and dilated fundus examination. The macular lesions were imaged using color fundus photographs and swept-source optical coherence tomography (SSOCT; Triton; Topcon Inc, Oakland, New Jersey, USA). The clinical features of macular coloboma in terms of the size of the lesion (as compared to the size of the optic disc), shape, location, retinal pigment epithelium (RPE) changes, and overlying fibrosis, if any, were noted. SSOCT imaging protocol included 12 equidistant radial line scans through the lesion. The various scans were analyzed for the presence of retinal thinning, retinal cysts, RPE atrophy/proliferation, choroidal atrophy, excavation, choroidal lacunae, and scleral backscatter.

Based on size, lesion were classified into small (≤1 disc diameter [DD]), medium (1-3 DD), and large (>3 DD) lesions. Based on the pigmentation within the lesions, the lesions were categorized into no/minimally, moderately (<50% of area pigmented), and heavily (>50% of area pigmented) pigmented. Shapes defined were circular/round, oval, irregular, and ill-defined. The excavation was subcategorized as none/flat, shallow (<50% of choroidal thickness), and deep (>50% of choroidal thickness). Choroidal vessel visibility was subdivided into not visible, just or barely visible, and prominently visible vessels.

Electrochemiluminescence immunoassay (ECLIA) was performed and results were available for TORCH serology for all recruited cases (IgM, IgG for *Toxoplasma* and CMV). IgM and IgG were considered negative if <1 and positive if ≥1.

Data entry was performed and analyzed using SPSS 20 software (IBM Corp, Armonk, New York, USA). The qualitative/quantitative data were expressed as frequency as well as percentages. Morphologic changes on clinical and OCT-based examination were analyzed if different among eyes with different serologic results. Visual acuity and age were compared between the groups with Kruskal-Wallis test. Categorical data were subjected to Pearson χ^2 test or Fisher exact test to compare the features between the groups.

RESULTS

A TOTAL OF 49 EYES WITH MACULAR COLOBOMA OF 27 PATIENTS (5 unilateral, 22 bilateral cases) were recruited for this study. Family history including parental consanguinity was noncontributory in all cases. None of the patients had a history of seizures or central nervous system problems. Two patients with positive CMV serology had a sensorineural hearing loss. None of the patients had any ocular or systemic abnormality suggestive of inherited retinal dystrophy.

The mean age of patients was 24.8 ± 14.9 years (range 7-60 years). The male and female subjects constituted 51.8% and 48.1% of the patients, respectively. The mean logMAR BCVA was 0.78 ± 0.38 (range 0-1.48). The detailed characteristics of the patients and macular colobomata are included in Table 1.

Serology was positive in 69.4% (34/49) of the eyes. Out of 34 eyes, *Toxoplasma* serology was positive in 26 eyes (12 bilateral and 2 unilateral cases) and CMV was positive in 8 eyes (3 bilateral and 2 unilateral cases). In patients with unilateral macular coloboma (n = 5), 2 patients were positive for *Toxoplasma*, 2 were positive for CMV, and 1 was negative for both. Age was statistically different between these groups ($P = .045$), with *Toxoplasma*-positive patients being younger than the rest.

Small-, medium-, and large-size lesions (Figure 1) constituted 22.4% (11/49), 59.2% (29/49), and 18.4% (9/49) of eyes, respectively. The majority of eyes (81.6%, 40/49) had a singular macular lesion, while the remaining 9 eyes (18.4%) had multiple satellite lesions (Figure 1, Middle left). A total of 93.8% (46/49) of eyes had lesion involving the fovea, while the remaining 3 eyes had extrafoveal lesions (Figure 1, Bottom right). The majority of eyes (46/49, 93.8%) had pigmented lesions, out of which 36.9% (17/46) had profound pigmentation (Figure 1, Top right, Middle left). The other clinical features were as follows: fibrosis within the lesion (Figure 1, Bottom left), 40.8% (20/49); retinal vessel continuity over the lesion (Figure 1, Bottom left), 59.2% (29/49); choroidal vessel visibility through the lesion (Figure 1, Middle right), 57.1% (28/49); temporal disc drag (Figure 1, Bottom right), 16.3% (8/49); scleral show (Figure 1, Top left, Middle right), 44.9% (22/49); and surrounding retinal pigmentary changes (Figure 1, Top right), 20.4% (10/49). The lesions had different shapes, including well-defined and round (33%), well-defined and oval (31%), irregular but well-defined (16%), and ill-defined lesions (20%).

On SSOCT, choroidal excavation (Figure 2), intraretinal cystic changes (Figure 2, Bottom left), generalized retinal thinning, choroidal thinning, and choroidal lacunae were visible in 81.6% (40/49), 28.6% (14/49), 69.4% (34/49), 83.7% (41/49), and 32.3% (16/49) of eyes, respectively. Increased hyper-reflectivity from

TABLE 1. Clinical and Optical Coherence Tomography–Based Characteristics in Macular Colobomatous Lesions Grouped on the Basis of Serologic Results

Feature	Serology Negative	*Toxoplasma* IgG Positive	CMV IgG Positive	Total	*P* Value
Number of eyes	15	26	8	49	-
Age (y), median (min-max)	24 (19-60)	17 (7-58)	18 (14-29)	20 (7-60)	.045[a]
CDVA, mean ± SD/median (min-max)	0.82 ± 0.27/0.78 (0.3-1.48)	0.74 ± 0.38/0.6 (0.18-1.48)	0.85 ± 0.52/1 (0-1.48)	0.78 ± 0.38/0.78 (0-1.48)	.56[a]
Size					.007[b]
Small	6	5	0	11	
Medium	7	19	3	29	
Large	2	2	5	9	
Satellite lesion					.008[b]
No	15	17	8	40	
Yes	0	9	0	9	
Location					.73[b]
Foveal	14	25	7	46	
Extrafoveal	1	1	1	3	
Pigmentation					.18[b]
None	2	1	0	3	
Some	11	13	5	29	
Profound	2	12	3	17	
Fibrosis					.066[b]
Absent	10	12	7	29	
Present	5	14	1	20	
Shape					.81[b]
Round	6	9	1	16	
Oval	4	7	4	15	
Irregular	3	4	1	8	
Ill-defined	2	6	2	10	
Retinal vessels					.62[b]
Discontinuous	7	11	2	20	
Continuous	8	15	6	29	
Excavation					.003[b]
Flat	3	6	0	9	
Shallow	1	12	0	13	
Deep	11	8	8	27	
Choroidal vessels					.87[b]
Not visible	7	12	2	21	
Visible	4	7	3	14	
Prominent	4	7	3	14	
Disc drag					.23[b]
Absent	13	23	5	41	
Present	2	3	3	8	
Intraretinal cyst					.68[b]
Absent	13	17	5	35	
Present	2	9	3	14	
Retinal layers					.94[b]
Intact inner layers	3	9	3	15	
Atrophic	12	17	5	34	
Retinal pigment epithelium changes					.13[b]
Atrophic	7	9	4	20	
Hypertrophic	8	17	4	29	
Choroidal thinning					.075[b]
None	1	7	0	8	
Some	4	9	3	16	
Profound	10	10	5	25	

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TABLE 1. Clinical and Optical Coherence Tomography–Based Characteristics in Macular Colobomatous Lesions Grouped on the Basis of Serologic Results (*Continued*)

Feature	Serology Negative	*Toxoplasma* IgG Positive	CMV IgG Positive	Total	*P* Value
Retinal pigmentation					.99[b]
Absent	12	20	7	39	
Present	3	6	1	10	
Choroidal lacunae					.035[b]
Absent	7	21	5	33	
Present	8	5	3	16	
Scleral show					.001[b]
Absent	7	20	0	27	
Present	8	6	8	22	

CDVA = corrected distance visual acuity; CMV = cytomegalovirus.
[a]Kruskal-Wallis test.
[b]Fisher exact test.

thickened RPE layer was visible in 59.1% (29/49) of eyes, while in the remaining, RPE layer was absent or discontinuous.

The morphologic changes on clinical and OCT-based examination were further analyzed if they were significantly different among eyes with different serologic results. Most of the features, such as CDVA, location, pigmentation within and outside lesion, fibrosis, shape, retinal vessel pattern, choroidal vessel visibility, disc drag, intraretinal cysts, retinochoroidal thinning, and RPE changes, were not significantly different between the groups. However, features like lesion size, the presence of satellite lesion, the presence of excavation, choroidal lacunae, and scleral show were statistically significant in differentiating between the types (Fisher exact *P* value = .007, .008, .003, .035, and .001, respectively). The positive and negative predictive values of each discrimination trait/characteristic are given in Table 2.

All eyes of patients with CMV-positive serology had medium-to-large lesions (3 medium, 5 large) (Figure 3, Top left). Most of the *Toxoplasma* lesions were of medium size (73.1%, 19/26) (Figure 3, Bottom left), while most of the serology-negative lesions were small-to-medium (small 40%, medium 46.7%) (Figure 3, Middle left). On subgroup analysis, size differentiated significantly between CMV-positive eyes and the rest of the eyes (vs *Toxoplasma*-positive *P* value = .006; vs serology-negative *P* value = .021), while it failed to differentiate significantly between serology-negative and *Toxoplasma*-positive eyes (*P* value = .20). All 9 eyes with satellite lesions belonged to the *Toxoplasma* group.

The majority of serology-negative eyes (73.3%, 11/15) and all 8 CMV-positive eyes had deep excavated lesions (Figure 3, Top right, Middle right), whereas *Toxoplasma*-positive eyes had mostly flat to shallow excavation (only 32% [8/25] of eyes had deep lesion) (Figure 3, Bottom right). On subgroup analysis, excavation differentiated significantly between *Toxoplasma*-positive eyes and the rest of the eyes (vs CMV-positive *P* value = .004; vs serology-negative *P* value = .023), while it failed to differentiate significantly between serology-negative and CMV-positive eyes (*P* value = .36).

Choroidal lacunae were visible in 53.3%, 13.6%, and 37.5% of seronegative (Figure 3, Middle right), *Toxoplasma*-positive, and CMV-positive eyes, respectively. On subgroup analysis, choroidal lacunae differentiated significantly between serology-negative and *Toxoplasma*-positive eyes (*P* value = .025), while it failed to differentiate significantly between CMV-positive eyes and the rest of the eyes (vs *Toxoplasma*-positive *P* value = .30; vs serology-negative *P* value = .67).

The scleral show was noted in 53.3%, 23.1%, and 100% of seronegative, *Toxoplasma*-positive, and CMV-positive eyes, respectively. On subgroup analysis, it differentiated significantly between *Toxoplasma*-positive eyes and the rest of the eyes (vs CMV positive *P* value < .005; vs serology-negative *P* value = .049), while it just failed to differentiate significantly between serology-negative and CMV-positive eyes (*P* value = .052).

Owing to a small number of patients with unilateral macular coloboma, laterality could not be compared statistically between the groups.

DISCUSSION

CONGENITAL MACULAR COLOBOMATA ARE ATYPICAL, AS they occur in an area different from the area of the embryonic cleft.[15] Congenital macular coloboma and its simulations have long been a topic of controversy, starting from the etiology to the pathogenesis and clinical features. The reasons behind grouping such abnormalities of the macular region under the congenital category include absence of a

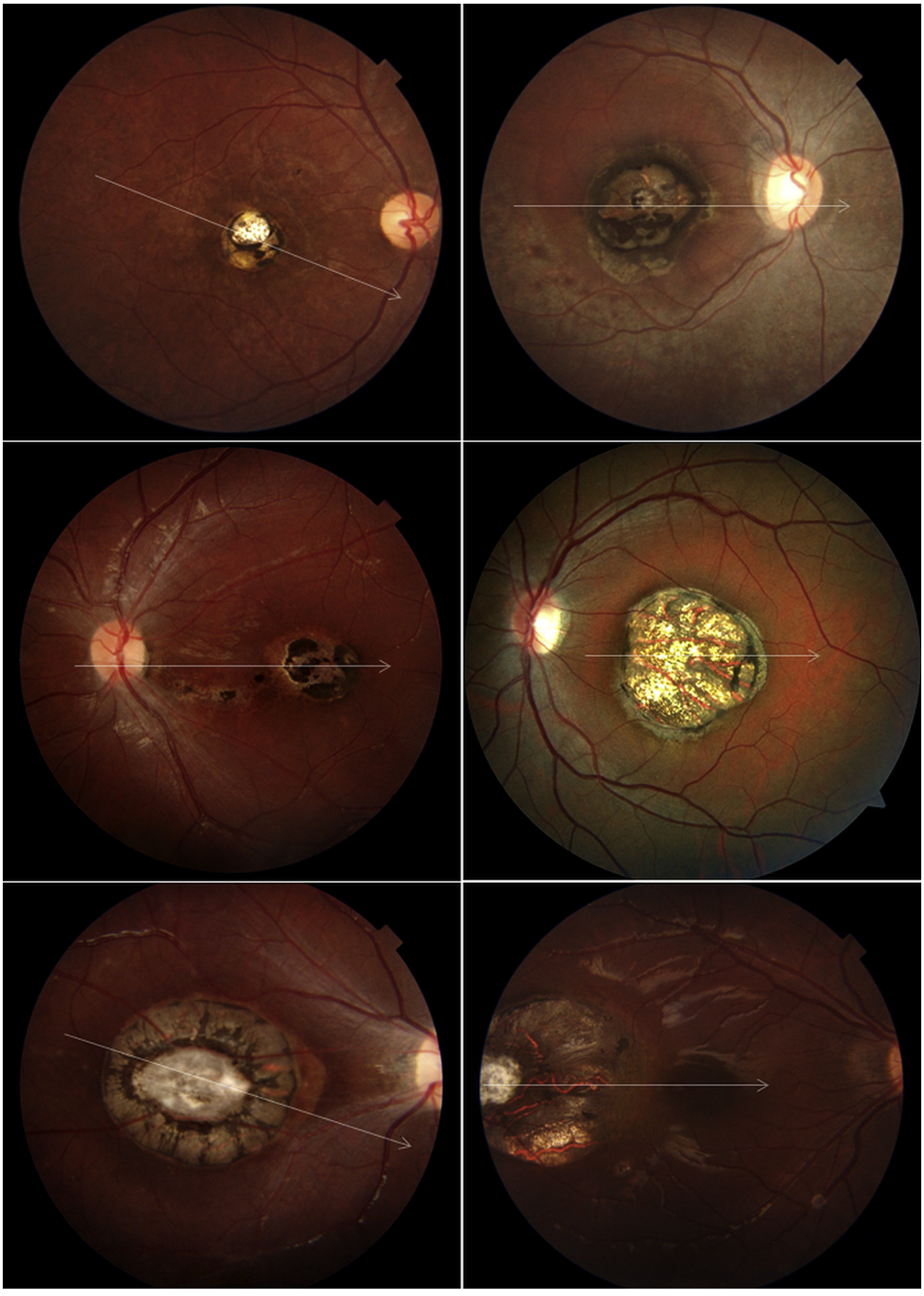

FIGURE 1. Varied clinical fundus presentations of macular coloboma: (Top left) The right eye of a 23-year-old man with serology negative for both *Toxoplasma* and cytomegalovirus (CMV). A solitary small, moderately pigmented excavated lesion with an underlying scleral show is noted. (Top right) The right eye of a 23-year-old man with serology negative for both *Toxoplasma* and CMV. A solitary medium-sized foveal profoundly pigmented excavated lesion with surrounding retinal pigmentary changes is noted (more prominent outside the inferotemporal arcade). (Middle left) The left eye of a 13-year-old man with serology positive for *Toxoplasma*. A profoundly pigmented medium-sized, relatively flat lesion at the fovea is noted with adjacent multiple small satellite lesions. (Middle right) The left eye of a 38-year-old man with serology negative for both *Toxoplasma* and CMV. A medium-sized foveal minimally pigmented and excavated lesion with prominently visible large choroidal vessels and sclera is seen. (Bottom left) A 7-year-old girl with serology positive for *Toxoplasma*. The macular lesion in the right eye is a single mildly pigmented and excavated lesion with retinal vessels continuing through the lesion. A central area of retinal fibrosis is also noted. (Bottom right) The right eye of a 13-year-old girl with serology positive for CMV. A large extrafoveal mildly pigmented and excavated lesion with prominent large choroidal vessels and associated temporal disc drag is seen.

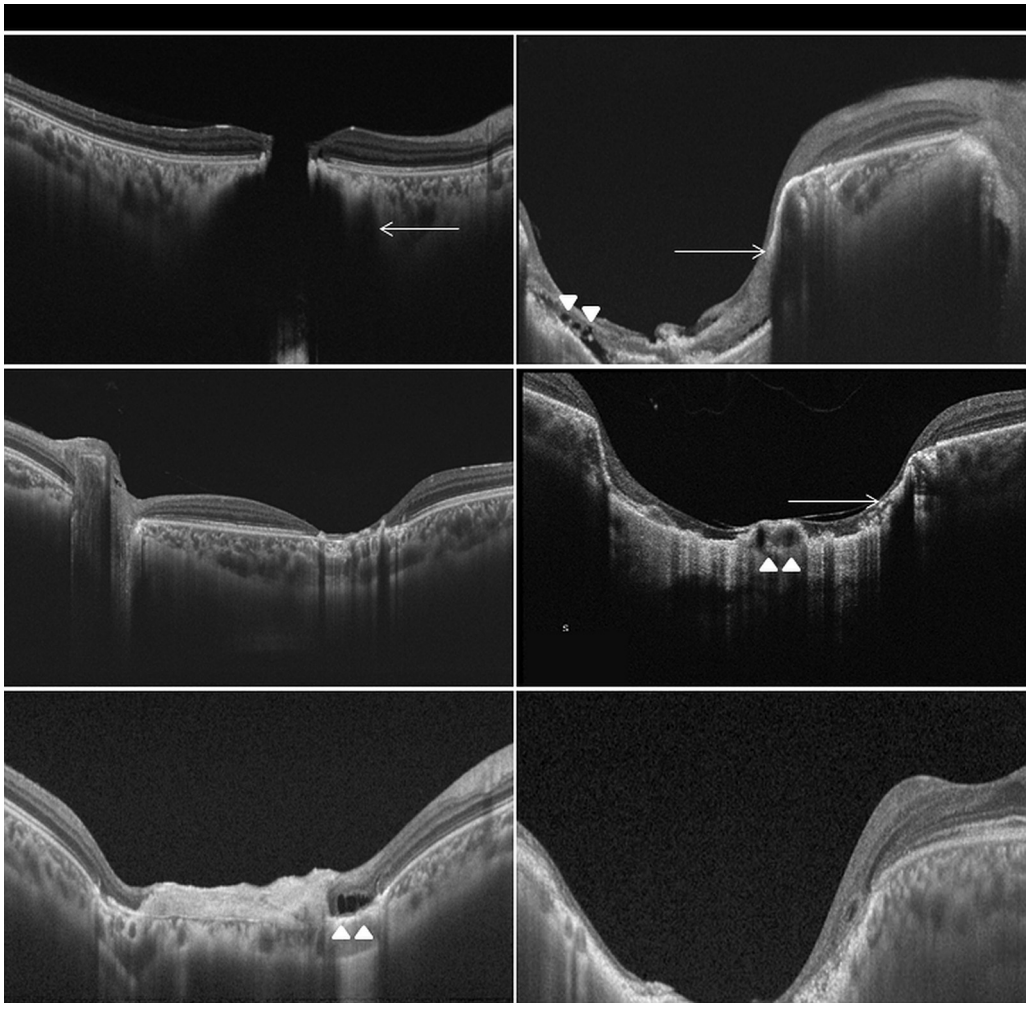

FIGURE 2. Radial optical coherence tomography (OCT) line scan along the white axis shown in respective color fundus photographs in Figure 1. (Top left) OCT shows a sharply defined deep macular retinochoroidal excavation with overhanging retinal layers. Immediately adjacent to it, choroidal lacuna can be visualized (white arrow). (Top right and Middle right) Deep excavated lesions with disrupted retinal pigment epithelium (RPE) layer (white arrow) and choroid and continuous dysplastic retinal layers with cavitations (white arrowheads). (Middle left) A relatively flat macular lesion with severe retinal thinning and hyperreflective RPE layer. (Bottom left) A relatively shallow macular excavation with a central area of retinal hyperreflectivity corroborating with the glial tissue seen in Figure 1, Bottom left. Outer retinal cavitations (white arrowheads) are visible just adjacent to the central fibrotic area. (Bottom right) A large deeply excavated lesion temporal to the fovea, with severe retinochoroidal atrophy.

certain history of onset, stationary nature throughout the life, and young age at diagnosis in all such cases.[16]

Based on the ophthalmoscopic appearance, Ida Mann classified congenital macular colobomatous lesions into 3 types: common pigmented nonectatic lesions, which arise late in gestation owing to irritative insult (seventh to eighth month); nonpigmented ectatic lesions occurring because of a destructive insult during the fifth to sixth month of gestation when retinal vessels are forming; and rare lesions with abnormal vessels, where insult occurs prior to the third month of gestation.[16] However, in clinical practice, most of the cases are intermediate and the classification fails to identify the etiology of the lesion.

Various etiopathologic theories have been put forward to account for these lesions.[16–18] First, there may be a failure of normal development of the eye different from the choroidal cleft closure defects. There may be a possible primary localized abnormality of differentiation of the cells of the wall of optic cup (ie, the neuroectoderm), or there may be a primary mesoderm (choroidal) abnormality with secondary failure of the development of ectoderm.[16] Second, the development may be initially normal to start with but later gets affected by any pathologic process, such as infection in intrauterine life or soon after birth and retinal degenerations later in life.

An abnormality of the developmental mechanism has been proposed in cases with positive family history,

TABLE 2. Predictive Values of Different Characteristics/Traits in Macular Colobomatous Lesions Grouped on the Basis of Serologic Results

Serial No.	Feature			Serology Negative	Toxoplasma IgG Positive	CMV IgG Positive
1	Size	Small	PPV	54.5%	45.4%	0%
			NPV	76.3%	44.7%	78.9%
		Medium	PPV	24.1%	65.5%	10.3%
			NPV	60%	65%	75%
		Large	PPV	22.2%	22.2%	55.5%
			NPV	67.5%	40%	92.5%
2	Satellite lesion		PPV	0%	100%	0%
			NPV	62.5%	57.5%	80%
3	Excavation	Flat	PPV	33.3%	66.7%	0%
			NPV	68.4%	50%	80%
		Shallow	PPV	92.3%	3.3%	0%
			NPV	61.1%	61.1%	77.7%
		Deep	PPV	40.7%	29.6%	29.6%
			NPV	81.8%	18.2%	100%
4	Choroidal lacunae		PPV	50%	31.3%	18.8%
			NPV	78.8%	36.4%	84.8%
5	Scleral show		PPV	36.4%	27.3%	36.4%
			NPV	74%	25.9%	100%

CMV = cytomegalovirus; NPV = negative predictive value; PPV = positive predictive value.

systemic abnormalities, and bilateral symmetric excavated/punched-out lesions with sharp borders.[17] Unilateral lesions with definitive inheritance have been reported as well.[19] Dominantly inherited cases mostly occur alone, while an autosomal-recessive inheritance is seen in association with retinitis pigmentosa, Leber amaurosis, and idiopathic infantile hypercalciuria. Pigmentary changes of the retina, as seen in tapetoretinal degeneration and Leber congenital amaurosis, again point to a noninfective developmental abnormality.[20–22] Dominant foveal dystrophy of North Carolina, progressive cone dystrophy, and central areolar choroidal dystrophy are among other simulators of congenital macular coloboma but tend to have other symptoms, such as photophobia and color vision difficulties.[23–26]

Existing literature suggests that unilateral macular scars with or without pigmentation in the absence of positive family history are secondary to chorioretinitis, especially owing to toxoplasmosis, cytomegalovirus, and, rarely, larval toxocariasis.[11,27,28] The earlier the infection occurs in gestation, the more resemblance is to the developmental defects. Reported pathologic features in postinflammatory scars secondary to these infections include a destruction of the choriocapillaris, prominent scar tissue, proliferation of pigment epithelium, and disorganization of retinal layers.[16,17] Clinically the presence of pigmentation and fibrosis within the lesion and the absence of excavation have been known to be relative but not absolute factors in favor of postinflammatory scars when compared to developmental defects.[17]

Literature shows that serologic results can help in clinching the diagnosis in such situations. Ocular toxoplasmosis (OT) can be the result of a congenital maternal-to-fetal transmission and infection or acquired disease owing to acute infection after birth, or otherwise a reactivation of latent disease.[8,27] Though the diagnosis of OT can be confirmed only based on the detection of *Toxoplasma* DNA (polymerase chain reaction) in aqueous/vitreous samples,[29] early and specific treatment against *Toxoplasma* following serologic diagnosis has been shown to limit the size of the scars. Acquiring the aqueous/vitreous samples is an invasive procedure. Routinely serum IgM/IgG levels are being performed at most places and can be of supporting value in the diagnosis of OT. CMV has also been reported to cause macular colobomatous lesions.[11,28]

We performed this study to answer certain controversies that revolve around the topic. We classified serology-negative eyes into the developmental group to include all noninfective malformations or hereditary disorders. The rest of the eyes were divided into *Toxoplasma*-positive and CMV-positive eyes.

Firstly, do clinical features vary between these groups, and which one is characteristic? We found that the previously reported features, such as pigmentation within and outside the lesion, fibrosis, shape, retinal vessel pattern, choroidal vessel visibility, and disc drag, did not vary significantly among the groups. Only lesion size, the presence of satellite lesion, and scleral show were significant factors. CMV lesions were solitary and large, with a significant scleral show. A significant scleral show was seen in all CMV-positive cases. *Toxoplasma*-positive lesions were

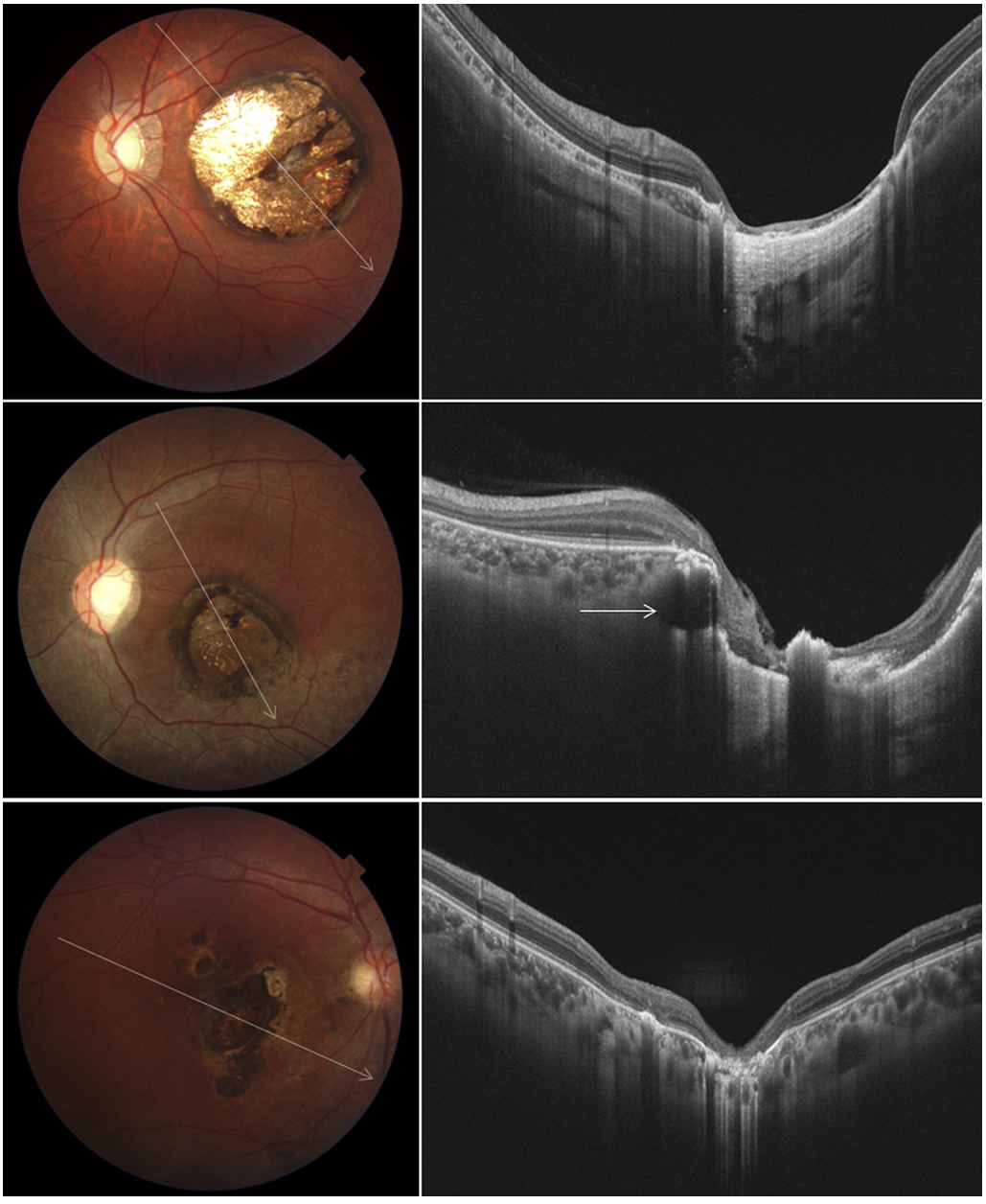

FIGURE 3. Characteristic color fundus photographs and optical coherence tomography line scans of macular coloboma with different serologic results. (Top left and Top right) A 30-year-old woman with serology positive for cytomegalovirus (CMV) had a large, deeply excavated, relatively nonpigmented macular lesion with prominent visible choroidal vessels, scleral show, and severe retinal atrophy. (Middle left and Middle right) A 29-year-old woman with serology negative for both CMV and *Toxoplasma* had a medium-sized, deeply excavated, moderately pigmented lesion with prominent large choroidal lacuna (white arrow). (Bottom left and Bottom right) A 20-year-old man with serology positive for *Toxoplasma* had a medium-sized, ill-defined, foveal pigmented, relatively flat lesion with adjacent multiple small pigmented satellite lesions.

either solitary or with satellite lesion, were medium in size, and had lack of scleral show. Satellite lesions occurred only in *Toxoplasma*-positive cases. Serology-negative eyes had small-to-medium solitary lesions, but the scleral show was distributed equally.

Secondly, there is a vast amount of literature on OCT features of *Toxoplasma* scars where the diagnosis was clinical and serology-based. But we failed to observe any significance in parameters such as the presence of intraretinal cysts, retinochoroidal thinning, and RPE changes. Excavation has previously been reported as a relative feature to differentiate among these eyes, but we found it to be very significant. All CMV eyes and the majority of serology-negative eyes had deep excavation leading to

severe choroidal thinning, while the majority of *Toxoplasma*-positive eyes had flat or shallow excavation. A new observation made was of large hyporeflective spaces in the choroid, referred to as "choroidal lacunae," which may reflect abnormally large choroidal vessels. Most such lesions were noted in serology-negative eyes in which we believe an early insult in gestation severely affected the choriocapillaris and inner Sattler layers, leaving behind abnormally large Haller vessels.

The study carries some limitations. First, ocular fluid was not used for serologic diagnosis. Second, family history was ascertained only from the patients/parents and the remaining family members were not examined, by which approach we may have misdiagnosed inherited cases of macular coloboma. Third, genetic and electrophysiologic tests were not performed in cases with retinal pigmentary changes to rule out retinochoroidal dystrophies. Fourth, *Toxoplasma* and, more often, CMV may cause subclinical systemic infection.[30] So whether mere seropositivity should be considered indicative of OT/ocular CMV infection if macular scars exist in these eyes is inconclusive.

To conclude, although most previously reported morphologic features failed in differentiating between the etiologies of macular coloboma, some features, such as size of the lesion, presence of satellite lesion, excavation, scleral show, and choroidal lacunae, can help guide in reaching a diagnosis so that appropriate counseling of the patients/parents regarding recurrence of disease, follow-up, and family screening can be advised.

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