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Sarcoidosis: experience in a Mexican ophthalmological clinic

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Abstract

Background Sarcoidosis is an inflammatory disorder in which patients frequently develop ocular manifestations that precede systemic involvement, sometimes it even presents as an ocular isolated form of the disease. The purpose of this study is to report the ocular and systemic manifestations of sarcoidosis in a series of Mexican patients, as there is a low incidence of the disease in this population.

Methods A retrospective case series of patients with positive classification criteria for sarcoidosis who attended Asociación Para Evitar la Ceguera en México, IAP between 2011 and 2022. Descriptive statistics were used to report the clinical, laboratory, and imaging findings and treatment. Numerical results were presented using median values and first and third quartiles for distribution.

Results Fourteen patients were included in this study, 10 of them had definite ocular sarcoidosis (biopsy-proven), 4 had presumed ocular sarcoidosis. The median age of onset was 52 (34; 67), with a predominance of female patients (71.4%). Ten patients (71.4%) debuted with ocular manifestations. The most common forms of ocular involvement were bilateral anterior uveitis (50%) and panuveitis (28.6%). Median follow-up was 24 (13–49) months.

Conclusions Sarcoidosis is a rare, underdiagnosed condition in Mexico and ocular involvement can be an early manifestation of the disease. Ophthalmologists should be alert to the signs of ocular sarcoidosis and collaborate with a multidisciplinary team to screen for systemic involvement if suspicion is high.

Keywords Ophthalmology, Sarcoidosis, Uveitis, México

Background

Sarcoidosis is an inflammatory disorder of unknown cause, characterized by systemic inflammation and the formation of noncaseating epithelioid cell granulomas, which can affect practically every organ [1]. Its incidence is estimated to be 5.9/100,000 for men and 6.3/100,000

for women in United States, [2] and it is a relatively common cause of uveitis in European patients [3].

Despite this, sarcoidosis in Latin America is rare, and the information on its prevalence, risk, and morbidity in Hispanic patients is limited [4–7]. There are only 28 published cases of sarcoidosis in Mexico and only 5 which report ocular manifestations (Table 1) [4, 8–14].

There is a wide spectrum of systemic manifestations of sarcoidosis that encompass many specialties in medicine. Lungs are the most affected organ in the disease (more than 90% of all cases) [15]. Although these manifestations are mainly non-specific of sarcoidosis, such as dyspnea, cough, and chest pain, lung imaging studies help identify

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Table 1 Sarcoidosis in Mexico 1991–2022

Study	Year	n	Definite with biopsy (WASOG)	Definite Ocular sarcoidosis (IWOS)
Arévalo-López (8)	1991	1	0	0
Estrada-Correa (9)	2006	1	1	0
Fernandez-Sanchez (10)	2012	1	1	0
Carrillo-Pérez (4)	2015	21	21	4 (uveitis)
Peralta-Gómez (11)	2018	1	1	1 (dacryocystitis)
Vega-Cornejo (12)	2019	1	1	0
Almaguer-Morales (13)	2020	1	1	0
Solis (14)	2020	1	1	0
Salazar-Rodríguez	2022	14	10	10
Total		42	37	14

N (number of patients) WASOG (World Association of Sarcoidosis and Other Granulomatous Disorders) [1] IWOS (International Criteria for the Diagnosis of Ocular Sarcoidosis) [21]

specific signs that support the diagnosis. The two main imaging findings in pulmonary sarcoidosis are bilateral hilar lymphadenopathy (BHL) and perilymphatic pulmonary nodules [16].

The second most affected organ in patients with sarcoidosis is the eye. Up to 30–50% of patients with systemic sarcoidosis will show eye involvement, or it can only be confined to the eye. The two main ocular manifestations are keratoconjunctivitis sicca and uveitis. Regarding ocular inflammation, anterior uveitis and panuveitis are the most common form of presentation, although the disease can affect any section of the eye [17–20].

Ocular manifestations are often bilateral. These include orbital and adnexal non-specific manifestations, such as keratoconjunctivitis sicca (dry eye), dacryocystitis, conjunctival granulomas, and less commonly diffuse orbital inflammation, ocular nerve palsy, and scleral granulomas [22].

Specific ocular manifestations support clinical diagnosis and help differentiate sarcoid uveitis from other types of inflammation. These are often accompanied by a sudden onset of pain or loss of visual acuity and include anterior segment signs such as mutton fat keratic precipitates (granulomatous uveitis) iris nodules either at the pupillary margin (Koeppe) or in the stroma (Busacca), Berlin nodules (trabecular meshwork nodules) and anterior tent-shaped synechiae at the iridocorneal angle. There are also intermediate and posterior inflammatory manifestations like snowbanking and snowball vitreous opacities, candle wax vascular shedding (retinal periphlebitis), microaneurysms, and optic disc nodules (granulomas). These manifestations guide the diagnosis of ocular sarcoidosis [1, 19, 21, 23].

Other manifestations include specific syndromes that have ocular and systemic manifestations, which help diagnose sarcoidosis without the need for a confirmatory

biopsy, and include Heerfordt–Waldenström syndrome (uveoparotid fever), a combination of facial palsy, parotid gland enlargement, uveitis, and low/grade fever, and Löfgren syndrome, a combination of fever, BHL, erythema nodosum with migratory arthritis including or without ankle [22].

The aim of this study is to report the ocular manifestations, systemic involvement, management, and outcome of sarcoidosis in a Mexican ophthalmology clinic.

Methods

Medical charts, and records from patients who arrived at the Inflammatory Eye Disease Clinic from 2011 to 2022, in Association Para Evitar la Ceguera en México were retrieved and classified using the revised International Criteria for the Diagnosis of Ocular Sarcoidosis (IWOS) and the Standardization of Uveitis Nomenclature (SUN) classification criteria for ocular sarcoidosis [2, 21, 24]. Patients classified as “presumed sarcoidosis” and “definite sarcoidosis” were included. Initial and final Snellen best-corrected visual acuity (BCVA) were documented.

Furthermore, the clinical evolution of each patient was classified using the SUN nomenclature of clinical status which includes inactive (grade 0 cells on anterior chamber), worsening activity (two-step increase in inflammation of anterior chamber cells or vitreous haze, or increase from 3+ to 4+), improved activity (two-step decrease in the level of inflammation of anterior chamber cells or vitreous haze, or decrease to grade 0), remission (inactive disease for >3 months after discontinuation of treatment) [24].

A rheumatologist performed a systemic evaluation with laboratory and imaging studies. Systemic involvement findings were collected using the updated World Association of Sarcoidosis and Other Granulomatous Disorders (WASOG) tool [1]. Diagnosis was based on the guidelines of the American [25] and British [26] Thoracic Societies. Classic syndromes such as Löfgren (a triad of fever, erythema nodosum, bilateral hilar lymphadenopathy, and associated migratory arthritis, including ankle) and Heerfordt–Waldenström (parotid gland enlargement, facial palsy, anterior uveitis, and fever) were also included.

Laboratory studies included angiotensin-converting enzyme (ACE), which is an enzyme produced by epithelioid cells derived from activated macrophages (characteristic of sarcoidosis) and lysozyme (LYS) is an enzyme produced by giant epithelioid cells, that reflects the presence of granulomas. Both were considered high when they exceeded >120% of the laboratory reference value, blood serum calcium, and lymphocyte count values were collected retrospectively when available. Hypercalcemia was defined as serum calcium >10.2 mequ/L and lymphopenia as <1000 lymphocytes. Also, infectious

diseases were ruled out, including syphilis, with a negative venereal disease research laboratory (VDRL) test and FTA-ABS, and tuberculosis with the tuberculin test (PPD) and/or IGRA test [27]. If a patient presented with a positive PPD test for tuberculosis, a negative IGRA test and a positive biopsy for sarcoidosis could still discard tuberculosis [2].

Pulmonary involvement was defined as the presence of micronodules, atelectasis, hilar lymphadenopathies, or parenchymal changes without predisposing factors. The amount of involvement was categorized using the Scadding test for chest X-rays [16]. Chest computed tomography (CT) was also included when available [28].

Confirmation was achieved with the presence of non-caseating granulomas, Schawman, or asteroid bodies in a tissue biopsy or a classic specific form of sarcoidosis, such as Heerfordt's or Löfgren's syndromes [2, 21].

Results were analyzed using the IBM Statistical Package for the Social Sciences (SPSS) 25.0. Descriptive statistics were used to report the clinical, laboratory, and imaging data. Numerical results were presented using median values and first and third quartiles for distribution.

The study was approved by the Institutional Review Board (IRB) of our hospital and adhered to the tenets of the Declaration of Helsinki.

Results

Fourteen patients with a clinical and/or histological diagnosis of sarcoidosis were identified. The median age was 52 years (27; 67), and 71.4% (n=10) were female. The median follow-up was 24 (13–49) months. Two patients had tattoos and one had a history of smoking. Ten (71.4%) patients were defined as a biopsy-proven definite

diagnosis of ocular sarcoidosis (Table 2), and 4 (28.6%) as a presumed diagnosis by bilateral hilar lymphadenopathy (BHL) and classical ocular signs.

All fourteen patients fulfilled the SUN classification criteria for ocular sarcoidosis (Tables 2 and 3). The most common ocular presentations were anterior uveitis (n=7, 50%), and panuveitis (n=4, 28.6%). Uveitis was granulomatous in 4 (28.6%) patients. Anterior chamber cells were detected in 12 patients (85.6%). Adnexal manifestations included dacryoadenitis (n=2, 14.3%), and conjunctival granuloma (n=1, 7.1%). Only two patients (14.3%) presented clinically relevant keratoconjunctivitis sicca. Six (42.8%) of the biopsy confirmed patients debuted with ocular manifestations, all developed systemic manifestations of sarcoidosis during follow-up. (Table 3).

All patients had systemic involvement; most commonly general symptoms (n=8, 57.1%), and pulmonary manifestations (n=7, 50%) (Tables 2 and 3).

ACE serum levels were available in 10 (71.1%) patients, 6 (60%) had increased levels, with a median concentration of 70.5 (38.6; 89) UI/L. Lysozyme was available in 8 patients (57.1%), showing high levels in 5 cases (62.5%) with a median of 3.81 (5.6; 24) mg/L. PPD was available for 13 patients; one had a positive result, so tuberculosis was discarded by clinical picture, negative IGRA, and a positive skin lesion biopsy for sarcoidosis [2]. Patient biopsies were collected from the skin (n=5, 55%), lacrimal glands (n=2, 22%), bronchi (n=2, 22%), and vitreous body (n=1, 11%).

A chest X-ray was obtained in 9 patients (64.3%) and a CT scan for 13 patients (92.8%). Both studies were available in 8 patients. (Table 3)

Table 2 Characteristics of patients with definite ocular sarcoidosis

	Age	Sex	Ocular	Systemic	Debut	Tests and imaging	Biopsy
1	53	F	Bilateral anterior uveitis (granulomatous) + Dacryoadenitis	Skin granuloma	Ocular	ACE (+) LYS (+) SCAD (3) CT (BHL)	Lachrymal gland
2	70	F	Bilateral anterior uveitis (granulomatous)	Erythema nodosum	Ocular	ACE (-) SCAD (0) CT (pneumonitis)	Skin
3	28	M	Bilateral anterior uveitis (granulomatous)	Löfgren syndrome	Ocular	ACE (+) LYS (+) CT (BHL)	Skin
4	70	F	Bilateral anterior uveitis (non-granulomatous)	Dyspnea, skin plaques, lymphadenopathy	Ocular	ACE (-) LYS (+) PPD (+) SCAD (3) CT (pneumonitis)	Skin
5	56	F	Bilateral panuveitis	Dyspnea	Ocular	ACE (+) LYS (+) SCAD (3) CT (nodules)	Bronchi
6	66	F	Bilateral panuveitis	Arthritis	Ocular	ACE (+) LYS (-) CT (nodules)	Vitreous
7	42	F	Bilateral intermediate uveitis	Heerfordt syndrome	Pulmonary (dyspnea)	SCAD (2) CT (BHL)	Bronchi
8	21	M	Bilateral anterior uveitis (non-granulomatous)	Skin granuloma	Skin	CT (BHL)	Skin
9	24	M	Bilateral anterior uveitis (granulomatous)	Skin granuloma	Skin	-	Skin
10	68	F	Bilateral anterior uveitis (non-granulomatous) + dacryoadenitis	Cough, dyspnea, fever, weight loss	Pulmonary	SCAD (3) CT (BHL)	Lachrymal gland

ACE (angiotensin converting enzyme), ADA (adalimumab), AZA (azathioprine), BHL (bilateral hilar lymphadenopathy), CT (computed tomography), F (female), LYS (lysozyme), M (male), PPD (tuberculin test), SCAD (scudding score on chest x-ray)

Table 3 Patient ocular and systemic manifestations

Ocular signs	n patients (%)	Systemic manifestations	n patients (%)
Anterior uveitis	7 (50%)	Pulmonary	7 (50%)
Mutton fat keratic precipitates	4 (28.6%)	-Dyspnea	7 (50%)
Fine keratic precipitates	7 (50%)	-Chest Pain	6 (42.8%)
Koepe nodules	3 (21.4%)	-Cough	7 (50%)
Bussaca nodules	1 (7.1%)	General	8 (57.1%)
Berlin nodules	1 (7.1%)	-Fever	3 (21.4%)
Intermediate uveitis	1 (7.1%)	-Fatigue	8 (57.1%)
Vitreous haze	5 (35.7%)	-Weight loss	4 (28.6%)
Snowballs	3 (21.4%)	Skin	9 (64.3%)
Snowbanks	1 (7.1%)	-Granulomas	7 (50%)
Posterior uveitis	2 (14.3%)	-Erythema Nodosum	4 (28.6%)
Chorioretinal lesions	5 (14.3%)	-Plaques	3 (21.4%)
Papillitis	2 (14.3%)	-Annular lesions	4 (28.6%)
Candle wax lesions	2 (14.3%)	Neurologic	2 (14.3%)
Periphlebitis	4 (28.6%)	-VII nerve palsy	1 (7.14%)
Panuveitis	4 (28.6%)	-Paresthesia	1 (7.14%)
Imaging signs	n patients (%)	Muscle-Skeletal	8 (57.1%)
Apical changes	2 (14.3%)	-Arthralgia	8 (57.1%)
Volume reduction	6 (42.8%)	Endocrine	3 (21.4%)
Peribronchial thickening	3 (21.4%)	-Parotiditis	3 (21.4%)
Interstitial infiltrates	7 (50%)	Syndromes	2 (21.4%)
Atelectasis	6 (42.8%)	-Löfgren	1 (7.1%)
Perilymphatic nodules	6 (42.8%)	-Heerfordt	1 (7.1%)
Micronodules	6 (42.8%)		
BHL	9 (64.3%)		

*BHL (Bilateral Hilar Lymphadenopathy)

All patients received treatment. (Table 4) Topical 1% prednisolone (64.28%) and oral prednisone (92.8%) were the most common initial treatment. Immunomodulators were prescribed to 12 (85.7%) patients, including azathioprine (n=6, 42.8%), methotrexate (n=6, 42.8%), and adalimumab (n=1, 7.1%); these allowed early removal of corticosteroid therapy in 6 patients (42.8%) with adequate response. These medications were started due to ocular manifestations in eight (57.1%) patients. On their last visit, 10 (71.42%) patients had remission of both systemic and ocular inflammation, 4 (28.6%) patients remained with ocular inflammation, and one as worsening activity of uveitis. Treatment for patients with persistent inflammation consisted of prednisone (n=4, 100%), azathioprine (n=2, 50%), methotrexate (n=3, 75%), and topical steroids (n=2, 50%).

Nine (64.28%) patients with a definite diagnosis had long-term ocular complications (Table 4). At the end of the follow-up, eleven eyes (39.28%) had a visual outcome worse than 20/50, and seventeen eyes (60.7%) had an outcome better than 20/50 (logMAR 0.39).

Discussion

This study describes the clinical characteristics of 14 patients diagnosed with sarcoidosis. This is the largest series of Mexican subjects with ocular sarcoidosis to date, as previous Mexican studies have only reported 5 cases of patients with ocular disease [4, 8–14]. Our institution is a reference center for ocular inflammatory diseases in our country, which allows us to analyze some of the less common diseases in our population, such as sarcoidosis.

In this sample of patients, we found a greater proportion of female patients with either definite (70%) or presumed (75%) sarcoidosis, which is similar to previous international reports (Table 5). Our patients' most common extraocular manifestations are similar to the previous Mexican case series of systemic sarcoidosis [4].

Anterior uveitis was the most common anatomical location, which contrasts with previous international reports of ocular sarcoidosis [19, 20, 29, 30]. (Table 5). Even though keratoconjunctivitis sicca is one of the most common classical presentations in sarcoidosis, only two patients had clinically relevant findings supporting this condition.

All our patients had systemic involvement and activity of the disease compared to previous reports with ranges from 36.6 to 62.6% [17, 19] probably due to the sample size and that our patients had ocular manifestations that led them to seek medical attention. The main clinical signs of systemic involvement were like international reports, involving the skin, musculoskeletal and pulmonary [17, 19].

There are plenty of studies that show an ample group of ocular manifestations as the leading manifestation to diagnose sarcoidosis, ranging from 63 to 100% [19, 20, 30]. Our patients are within that range, finding that 71.4% of patients had ocular activity as the first detectable change in sarcoidosis [31, 32]. For this reason, ophthalmologists should pay attention to early signs of ocular sarcoidosis, as prompt treatment may avoid systemic activity.

Other aspects of patient history, such as tattoos, are associated with cutaneous sarcoidosis, systemic sarcoidosis with uveitis, and isolated sarcoid uveitis [33]. In our study, two patients had permanent tattoos and did not have a reactivation or disease worsening during the follow-up.

The diagnosis of sarcoidosis is often confused with tuberculosis in endemic countries, [27] and Mexico is among the top five countries with the most cases of tuberculosis in America [34]. There is a diagnostic challenge differentiating the uveitic picture caused by both diseases, and an erroneous diagnosis of tuberculosis could be the reason for the low prevalence of sarcoidosis in Mexico.

Table 4 Patients treatment, visual outcome, and ocular complications

Patient	Age	Sex	Treatment	Initial BCVA	Final BCVA	Outcome*, complication
1	53	F	PDN, PRDL, MTX, AZT	20/20 20/20	20/20 20/20	Inactive disease, cataract
2	70	F	PDN, PRDL	20/25 20/20	20/40 20/30	Inactive disease, no complications
3	28	M	PDN, IVMP (3), AZT, PRDL	20/40 20/70	20/20 20/60	Inactive disease, cataract, glaucoma
4	70	F	PDN, MTX, HCQ, PRDL	20/50 20/30	20/20 20/40	Inactive disease, posterior synechiae
5	56	F	PDN, MTX, PRDL	20/30 20/150	20/25 20/25	Inactive disease, cataract
6	66	F	AZT, PDN, PRDL	20/70 20/50	20/60 20/50	Inactive disease, no complications
7	42	F	PDN	20/30 20/30	20/20 20/20	Inactive disease, cataract
8	21	M	PDN, AZT	20/20 20/20	20/20 20/20	Improved activity, posterior synechiae
9	24	M	PDN, MMF, ADA	HM HM	HM HM	Inactive disease, glaucoma, corneal leukoma
10	68	F	MTX, PRDL	20/70 20/30	20/80 20/80	Inactive disease, glaucoma
11	67	F	PDN, MTX, PRDL	20/60 20/200	20/30 20/40	Improved activity, glaucoma
12	35	M	PDN, AZT, PRDL	20/20 20/25	20/30 20/30	Improved activity, cataract
13	47	F	PDN, AZT	20/30 20/30	20/80 20/80	Inactive disease, no complications
14	51	F	PDN, MTX	20/50 20/50	20/200 20/200	Worsening activity, cataract

ADA (adalimumab), AZA (azathioprine), HCQ (hydroxychloroquine), IVMP (intravenous methylprednisolone), MMF (mycophenolate mofetil), MTX (methotrexate), PDN (prednisone), PRDL (topical prednisolone acetate)

We can observe in this study that ocular sarcoidosis can precede systemic manifestations. We must consider sarcoidosis as a differential diagnosis in patients with inflammatory eye diseases, start the diagnostic approach as an ophthalmologist and rely on a multidisciplinary group for proper systemic diagnosis and treatment.

Some of the strengths of the present study are that this is the largest group of sarcoidosis reported in the Mexican population, which can help us identify the disease characteristics, in a tertiary ophthalmology clinic. Furthermore, almost every clinical presentation of sarcoidosis was present in our series; including classic syndromes like Löfgren and Heerfordt, which are rarely mentioned even in international studies (Table 5) [2, 21].

Conclusions

Ocular manifestations, although diverse, can be crucial in the suspicion and diagnosis of systemic sarcoidosis. In our experience, every patient that starts as an isolated form of ocular inflammation later resulted in systemic sarcoidosis. Therefore, ophthalmologists should be attentive to the manifestations of ocular sarcoidosis, and

screen for systemic involvement, along with a multidisciplinary team, when suspicion is high.

Table 5 Ocular Sarcoidosis around the world

Characteristic	International study (Acharya, et al.) (20)	South India (Kalpana, et al.) (27)	Germany (zur Bonsen) (30)	France (Roche-peau et al.) (19)	France (Coulon et al.) (17)	Mexico (APEC)
n	180 (167*)	61	84	83	194	14
Age	49 (39–60)	43 (\pm 16.5)	53 (8–87)	52 (37–62)	52	52 (34; 67)
Female	115 (68.8%)	37(60.7%)	50 (59.5%)	64 (77.1%)	134 (69%)	10 (71.4%)
High ACE (UI/L)	80 (47.9%)	34 (59.6%)	32 (38.4%)	53 (67.1%)	113 (58%)	5 (35.7%)
High LYS (UI/L)		-	-	53 (88.3%)	112 (57%)	5 (35.7%)
Leading ocular manifestation	167 (100%)	-	53 (63%)	62 (75%)	194 (100%)	10 (71.4%)
Bilateral	142 (85%)	42 (68.9%)	62 (73.8%)	63 (75.9%)	151 (77.8%)	13(92.8%)
Löfgren syndrome	-	-	-	-	-	1 (7.1%)
Heerfordt syndrome	-	-	-	-	-	1(7.1%)
Ocular outcome						
< 20/200	-	-	-	2 (2.4%)	21 (11%)	2 (14.3%)
< 20/50	-	-	-	9 (10.8%)	64 (33%)	4 (28.6%)
> 20/50	-	-	-	50 (60.2%)	109 (56%)	8 (57.1%)
Uveitis		61 (100%)	84 (100%)	83 (100%)	194 (100%)	14 (100%)
Anterior	34 (20.3%)	19 (31.1%)	26 (31%)	28 (33.7%)	66 (34%)	7 (50%)
Intermediate	5 (2.9%)	7 (11.5%)	27 (32.1%)	4 (4.8%)	20 (10%)	2 (14.3%)
Posterior	15 (8.9%)	2 (3.3%)	14 (17.6%)	11 (13.2%)	14 (7.5%)	1 (7.1%)
Panuveitis	113 (67.6%)	33 (54.1%)	16 (19%)	40 (48.1%)	94 (48.5%)	4 (28.6%)
IWOS						
Probable	13 (7.2%)	-	27 (32.1%)	-	-	-
Presumed	69 (38.3%)	-	33 (39.3%)	-	49 (25.3%)	4 (28.6%)
Definite	98 (54.4%)	61 (100%)	24 (28.6%)	83 (100%)	145 (74.7%)	10 (71.4%)

- not reported. * Patients analyzed ACE (angiotensin converting enzyme), LYS (lysozyme)

Abbreviations

IWOS	International Criteria for the Diagnosis of Ocular Sarcoidosis
SUN	Standardization of Uveitis Nomenclature
WASOG	World Association of Sarcoidosis and Other Granulomatous Disorders
ACE	Angiotensin Converting Enzyme
LYS	Lysozyme
VDRL	Venereal disease research laboratory
PPD	Tuberculin test
BHL	Bilateral Hilar Lymphadenopathy
SCAD	Scadding score on chest X-ray
CT	Computed Tomography
PDN	Prednisone
MTX	Methotrexate
AZA	Azathioprine
HCQ	Hydroxychloroquine
MMF	Mycophenolate mofetil
ADA	Adalimumab
Bx	Biopsy
Txt	Treatment

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Authors' contributions

ASR collected and analyzed the patient data and was a major contributor to writing the manuscript. DSF Revised and was a major contributor to writing the manuscript. CHT Revised and was a major contributor to writing the manuscript. LECR Drafted the work, revised and was a major contributor to writing the manuscript. All authors read and approved the final manuscript.

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Data Availability

The data that support the findings of this study are available from the corresponding author, LECR, upon reasonable request.

Declarations

Competing interests

The authors declare that they have no competing interests.

Ethics approval and consent to participate

All procedures in this study were in accordance with the ethical standards of the hospital and with the 1964 Helsinki Declaration and its later amendments. This study was approved by the institutional ethics committee "Comité de Ética de la Asociación Para Evitar la Ceguera en Mexico APEC". Informed consent for participation in this study was obtained from all patients.

Consent for publication

Not Applicable (NA)

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