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Review Article

Manifestations and Treatment of Ocular Coccidioidomycosis: A Review of Literature

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Abstract

Purpose of Review: This review aims to summarize the epidemiology, manifestations and treatment of ocular coccidioidomycosis, a rare yet significant fungal infection that can severely impair vision.

Recent Findings: "Recent" is misleading as cases of ocular Coccidioidomycosis are rare and not frequently reported. A comprehensive literature search was performed in PubMed, EMBASE and Medline to identify case reports and retrospective reviews about the ocular manifestations of coccidioidomycosis. We identified 52 articles encompassing 63 case reports and collected data including age, gender, presentation, diagnosis, treatment, outcome and Best Corrected Visual Acuity (BCVA) at presentation and after treatment. Articles reviewed spanned from 1948 through 2022.

Summary: Average patient age was 38.7 years old, 60.3% of patients were male, 31.7% were female and gender was not disclosed 7.9% of cases. 19.0% patients had a disseminated Coccidioides infection and 4.8% of patients were immunocompromised at the time of infection. Clinical presentations of ocular coccidioidomycosis included scleritis, granulomatous lesions of the lid and retina, uveitis and endophthalmitis. 15.9% of patients progressed to enucleation. Climate change is correlated with an increased incidence of Coccidioides infections. Clinicians must maintain a high degree of suspicion for ocular coccidioidomycosis.

Keywords: Coccidioides; Valley Fever; Uveitis; Fungal Infection; Ophthalmology

Abbreviations

BCVA: Best Corrected Visual Acuity; CF: Counting Fingers; HM: Hand Motion; LP: Light Perception; NLP: No Light Perception; SD: Standard Deviation

Introduction

Coccidioidomycosis, commonly known as Valley Fever, is an infection caused by the fungus Coccidioides immitis or Coccidioides posadasii [1]. While most cases of coccidioidomycosis are self-limited, ocular complications are a rare yet serious manifestation of the disease that can lead to permanent vision loss [2]. Unfortunately, ocular coccidioidomycosis is often under-diagnosed and under-treated outside of endemic areas, which can delay appropriate management and result in poor outcomes [1,3]. The ocular manifestations of coccidioidomycosis are diverse and can include scleritis, uveitis, granulomatous lesions of the eyelid and retina and endophthalmitis. Given the severity of these complications, it is crucial to recognize and treat them in a timely and appropriate manner. In this paper, we will review the cases of ocular coccidioidomycosis found in the literature and focus on the medical and surgical treatment options available to manage this rare and challenging condition.

Methods

A comprehensive literature review was conducted on the databases PubMed, Ovid MEDLINE and EMBASE. Keywords included

coccidioidomycosis, valley fever, ocular, orbit, ophthalmology, uveitis, iritis, iridocyclitis, vitritis and chorioretinitis. A representative search strategy is included in supplement 1. Inclusion criteria consisted of peer-reviewed case reports, retrospective/prospective case studies and reviews containing ocular manifestations of coccidioidomycosis. Additional articles not indexed in searched databases were identified from citations of reviewed articles. Title and abstract review yielded 52 articles that met the stated inclusion criteria. The chronicity of coccidioidomycosis infection was determined by the authors of each respective paper. There was no general consensus on the timeframe for acute vs. chronic infection. Visual acuity was recorded only for the affected eye unless otherwise noted.

Best Corrected Visual Acuity (BCVA) for each case was converted into logMAR, with non-numerical BCVA (e.g., Counting Fingers [CF], Hand Motion [HM], Light Perception [LP] and No Light Perception [NLP]) conversion as follows based on published literature: CF - 2.1, HM - 2.4, LP - 2.7, NLP - 3.0 [4,5]. A paired t-test was used to evaluate the difference in mean BCVA at presentation and after treatment in the cases that provided data at both time points.

Results

We identified 52 articles containing 63 case reports of coccidioidomycosis with ocular involvement in the literature. Demographic data are summarized in Table 1. The average patient age was 38.7 years old (SD 18.5, range: 2 weeks - 77 years). 38/63 (60.3%) of patients were male, 20/63 (31.7%) were female and gender was not disclosed in 5 cases (7.9%). Ocular involvement was unilateral in 44/63 cases (69.8%) and bilateral in 19/63 cases (30.2%). Active coccidioidomycosis infection was present in 48/63 patients (76.2%), prior infection in 12/63 patients (19.0%) and no status of systemic infection was given for 3/63 patients (4.8%). 12/63 (19.0%) patients had a disseminated Coccidioides infection. Three patients (4.8%) were immunocompromised at the time of infection. For each case report of ocular coccidioidomycosis, supplement 1 summarizes the age, gender, location, diagnosis, laterality, time from onset of symptoms to presentation, disease dissemination, treatment, patient immune status, BCVA at presentation, BCVA after treatment and length of follow-up.

The BCVA of patients with ocular coccidioidomycosis at presentation and after treatment are plotted in Fig. 1. Among the 18 case reports that provided both initial and post-treatment BCVA values, a paired t-test revealed no significant difference between the mean initial BCVA (1.32 logMAR) and the mean post-treatment BCVA (1.51 logMAR), with a p-value of 0.33.

Table 2 shows the diagnoses associated with ocular coccidioidomycosis and the treatments used by diagnosis. The most common diagnosis was chorioretinitis, with 15 cases (23.8%) of granulomatous chorioretinitis and 12 cases (19.0%) of non-granulomatous chorioretinitis. Other diagnoses include unspecified anterior uveitis (3.2%), granulomatous anterior uveitis (14.3%), non-granulomatous anterior uveitis (1.6%), cutaneous coccidioidomycosis (17.5%), endophthalmitis (6.3%), granulomatous conjunctivitis (1.6%), panuveitis (3.2%), retinitis (1.6%) and scleritis/episcleritis (7.9%). Of medical treatments, 25 patients (39.7%) received IV amphotericin B, 4 (6.3%) received intraocular amphotericin B, 5 (7.9%) received an IV azole, 20 (31.7%) received an oral azole, 1 (1.6%) received an intraocular azole. Surgical treatments included vitrectomy in 3 patients (4.8%), cutaneous surgery in 2 patients (3.2%) and enucleation in 10 patients (15.9%).

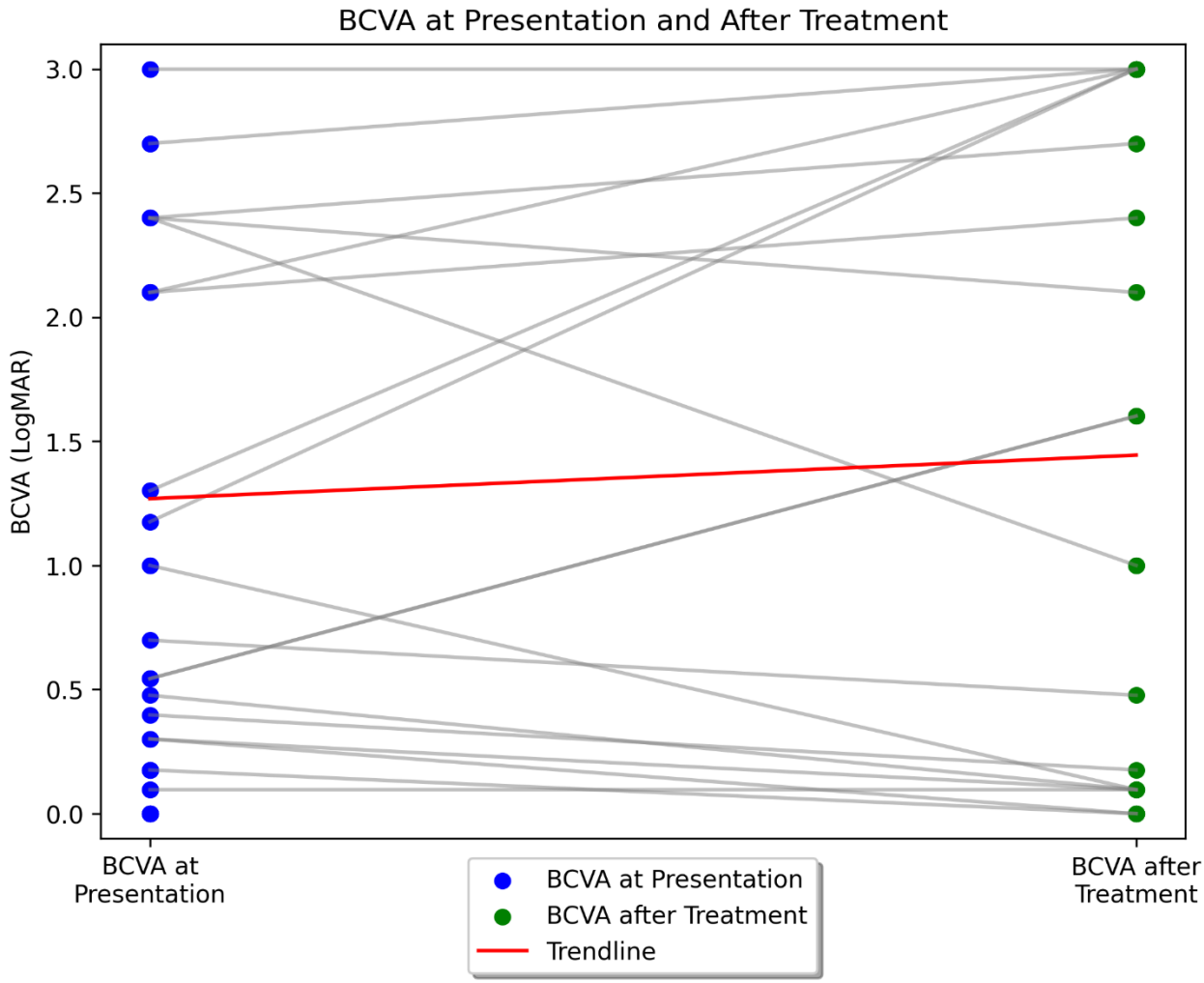

Figure 1: BCVA at presentation and after treatment.

Total Cases	**63**
Age (years)	38.7 ± 18.5 (.038-77)
Male	38 (60.3%)
Female	20 (31.7%)
Unknown Gender	5 (7.9%)
Immunocompromised	3 (4.8%)
Active Disease	48 (76.2%)
Past Disease	12 (19.0%)
Unclear Etiology	3 (4.8%)
Disseminated Disease	12 (19.0%)
Unilateral	44 (69.8%)
Bilateral	19 (30.2%)
BCVA Presentation (logMAR)	0.914 ± 1.609 (0.00-3.00)
BCVA After Treatment (logMAR)	1.609 ± 1.602 (0.00-3.00)

Table 1: Demographics.

Author	Year	Location	Age	Gender	Ocular Diagnosis	Unilateral or Bilateral	Time from onset of symptoms until presentation	Disseminated Disease?	Immuno-compromised?	Successful Treatment	BCVA Presentation	BCVA After Treatment	Length of Follow-up
Alexander[20]	1967	Bakersfield, California	19	F	Chorioretinitis	Unilateral	3 days			IV amphotericin B (total dose 4.3 g), prednisone.	CF	10.5/200	16 weeks
Bell[21]	1972	California	39	M	Granulomatous anterior uveitis	Unilateral	2 years					Enucleation	
Bittencourt[22]	2022	Irvine, CA			Cutaneous	Unilateral				Urgent orbitotomy with incision and drainage of the abscess, followed by oral fluconazole (100 mg/day for 4 months).			
Blumenkranz[23]	1980	San Joaquin Valley, California	57	M	Chorioretinitis	Unilateral	6 weeks			Intrathecal miconazole therapy, 15 mg three times per week, followed by gradually increasing intravenous and intrathecal doses of amphotericin B. Intraventricular therapy with amphotericin B was also used, along with intrathecal administration of miconazole.		20/20	3 months
Blumenkranz	1980	San Joaquin Valley, California	24	M	Granulomatous chorioretinitis	Bilateral	1 week			Amphotericin B therapy IV (total dose 1750 mg).	20/50	20/30	11 months
Blumenkranz[24]	1980	Bakersfield, California	40	M	Chorioretinitis	Unilateral	1 week			Incision and drainage of lid granuloma, intravenous and intrathecal amphotericin and miconazole for meningeal coccidioidomycosis.	20/20		
Blumenkranz	1980	Bakersfield, California	48	M	Granulomatous chorioretinitis	Unilateral	3 months			Intravenous and intrathecal amphotericin was initiated. The patient was subsequently given oral ketoconazole. The herpes was treated with topical idoxuridine, polysporin, and atropine 1%.	20/70		
Boyden[25]	1971	San Joaquin Valley, California	28	M	Chorioretinitis	Bilateral	9 months	Y					
Brown[26]	1957	San Joaquin Valley, California	19	M	Chorioretinitis	Unilateral	3 weeks					20/200	4 months
Brown	1958	Houston, Texas	24	F	Granulomatous anterior uveitis	Unilateral		Y		Topical atropine and cortisone drops plus warm compresses.			
Chandler[27]	1972	Southwestern U.S.	25	M	Granulomatous chorioretinitis	Bilateral	3 weeks	Y	Y	IV amphotericin B.			
Char[28]	2012	Central Valley, California	10	F	Chorioretinitis	Unilateral	1 month			Enucleation.	NLP	Enucleation	
Cheng[29]	2012	Santa Clarita, California	55	M	Endophthalmitis	Unilateral	1 month			Vitrectomy, intravitreal voriconazole, IV voriconazole 4mg/kg q12hr, after discharge oral voriconazole 4mg/kg BID	20/60	20/25	4 months
Coba[30]	2021		50	M	Chorioretinitis	Bilateral		Y		800mg fluconazole daily.			
Conan[31]	1950		30	F	Retinitis	Unilateral		Y		None			
Cunningham[32]	1998	San Joaquin Valley, California	32	M	Granulomatous anterior uveitis	Unilateral	1 month			IV amphotericin B and oral fluconazole (outpatient)	20/200		
Cunningham	1998		31	F	Granulomatous chorioretinitis	Bilateral	5 months			IV and intrathecal amphotericin B for 3 weeks, followed by oral fluconazole		20/20	
Cutler[33]	1978	Southern California	29	M	Granulomatous anterior uveitis	Unilateral	6 months			The patient was treated with intravenous amphotericin B, and an anterior-chamber injection of amphotericin. However, these treatments were unsuccessful in saving the	LP	Enucleation	

										eye, and the patient underwent enucleation.			
Dworak[34]	2016	Patient lived in Chicago and traveled through Southern U.S.	33	M	Cutaneous	Unilateral	3 weeks			Oral itraconazole 200 mg twice a day and topical application of bacitracin/neomycin/polymyxin B ointment three times a day to the affected area for 10 weeks	20/20		
Faulkner[35]	1962	San Joaquin Valley, California	33	F	Cutaneous	Unilateral	1 week			IV amphotericin B for 7 months.	20/20, J1		
Gabriellan[36]	2010	Arizona	46	M	Panuveitis	Bilateral	7 months	Y		Voriconazole 200 mg PO QD	20/40 OD, 20/25 OS	20/25 OU	2 weeks
Glasgow[37]	1987	Logan, Arizona	12	F	Granulomatous chorioretinitis	Bilateral	7 weeks	Y					
Golden[38]	1986	Arizona	2 Weeks		Chorioretinitis	Unilateral	7 weeks			1mg/kg/day amphotericin B, 20 mg total administered	20/20		
Green[39]	1967	Arizona	51	M	Granulomatous chorioretinitis	Bilateral	4 months			Amphotericin B 4.5 g IV, 4.2g intrathecally			
Hwang[40]	2006	California	64	M	Nongranulomatous anterior uveitis	Unilateral	1 week			Prednisolone acetate 1% every hour and cyclopentolate hydrochloride 1% 3 times a day O.S. followed by brimonidine tartrate 0.15% 3 times a day O.S.	20/30		
Irvine[41]	1968	Lancaster, California	73	M	Cutaneous	Unilateral	6 months			IV amphotericin B (1965 mg)			
Jou[42]	1995		36	M	Cutaneous	Unilateral				Amphotericin B 50mg QD for 3 weeks, fluconazole 800mg for maintenance after discharge.	20/20		
Lamer[43]	1982	Bolivia	26	F	Granulomatous chorioretinitis	Unilateral	2 months			Amphotericin B 20-50mg/day for 1 month.	20/70	20/800	1 month
Levitt[44]	1948	British West Africa	20	M	Chorioretinitis	Unilateral	2 weeks			None	20/30		
Lijo-Pavia[45]	1949		28	M	Cutaneous	Unilateral					20/70	20/800	
Ling[18]	2017	Nevada	33	F	Endophthalmitis	Unilateral	5 months			3 intravitreal injections of amphotericin B, IV liposomal amphotericin B, fluconazole, oral Posaconazole, and 7 postop weekly intravitreal injections of amphotericin B, followed by surgical intervention consisting of temporary keratoprosthesis implantation, anterior segment reconstruction, removal of a cyclitic membrane and the crystalline lens, pars plana vitrectomy, pars plana Ahmed drainage device placed in the vitreous cavity, and penetrating keratoplasty. Transscleral cyclophotocoagulation was also performed to control IOP.	HM	20/200	15 months
Lovekin[46]	1951	Arizona	30	F	Granulomatous chorioretinitis	Bilateral	2 weeks						
Luttrull[47]	1995	Southern California	34	M	Granulomatous anterior uveitis	Unilateral	2 days			Oral fluconazole (200 mg) daily and IV amphotericin (systemic) on an increasing dose schedule was started. The iridocyclitis respond well and the vision was 20/20 within one week. after a month, serum creatinine concentration rose to 2.0 mg/dl and IV amphotericin was stopped at a total dose of 600 mg. Oral fluconazole was increased to 800 mg per day afterward (per day). Since then, pt constitutional symptoms improved within 48 hours and within one week choroidal lesion became inactive and a	20/30	20/20	3 months

										small atrophic chorioretinal scar was left.			
Magrath[48]	2010		76	F	Granulomatous chorioretinitis	Bilateral				Some improvement on fluconazole (400mg), then changed to voriconazole which gave her best results.	20/100 OD, 20/40 OS	20/60 OD, 20/20 OS	
Maguire[49]	1994	Southwestern U.S.	65	F	Granulomatous conjunctivitis	Unilateral				Topical amphotericin once every 2 hours and was then stopped after symptoms improved, and patient was kept on fluconazole only (400 mg twice a day).	20/25		
Michelson[50]	1983	Mesa, Arizona	73	M	Granulomatous chorioretinitis	Unilateral	2 months			Patient was started on intrathecal amphotericin B after symptoms worsened but did not mention what happened afterwards.	6/12-2		
Mondino[51]	2007		64	M	Granulomatous anterior uveitis	Unilateral				Oral fluconazole, intravenous amphotericin B, pars plana vitrectomy and lensectomy, initially everything was normal. However, infiltrate reformed in the anterior chamber. Tissue plasminogen activator and intracameral amphotericin B were given, followed by another pars plana vitrectomy. At 1 month after the second vitrectomy, the eye was enucleated for intractable pain.		Enucleation	
Moorthy[3]	1994	Southern California	53	F	Granulomatous anterior uveitis	Unilateral	3 months			Enucleation		Enucleation	
Moorthy	1994	Southern California	45	M	Granulomatous anterior uveitis	Unilateral	3 weeks			Intracameral amphotericin B, and oral fluconazole 400 mg BID.	HM	CF	couple months
Moorthy	1994	Southern California	63	M	Granulomatous anterior uveitis	Unilateral	6 months			Oral itraconazole 200 mg daily.	CF	HM	
Nordstorm[52]	2019	Southern California	64	M	Chorioretinitis	Unilateral						Enucleation	
Nordstorm	2019	Logan, Arizona	12	F	Chorioretinitis	Bilateral		Y					
Nordstorm	2019		27	M	Granulomatous chorioretinitis	Unilateral	At presentation	Y		Intravitreal amphotericin B deoxycholate 5micro g/0.1 ml every 3 days.	LP		
Olavarria[53]	1971	Bakersfield, California	37	M	Granulomatous chorioretinitis	Bilateral	At presentation						
Perry[54]	1960		56	M	Cutaneous	Unilateral				Four months of amphotericin B therapy.			
Pettit[55]	1967	San Fernando Valley, California	41	M	Anterior Uveitis	Unilateral	Several weeks				20/300	Enucleation	
Quinlan[56]	2020	Arizona	40	M	Granulomatous chorioretinitis	Unilateral	1 day			Voriconazole 200 mg			
Reed[57]	2021	Southern California	9	M	Cutaneous	Unilateral	10 days			IV amphotericin liposomal, and systemic fluconazole.			
Reed[19]	2013	Santa Clarita, California	55	M	Endophthalmitis	Unilateral	Diagnosed after 120 days			16 intravitreal antifungal (amphotericin and voriconazole) injections and three vitrectomies, as well as lensectomy and penetrating keratoplasty. Patient was also on 350 mg twice daily of voriconazole and then was transitioned to 800 mg of oral fluconazole daily.	20/200	20/25	13 months
Rixford[58]	1896	San Francisco, California	40	M	Endophthalmitis	Unilateral	6 years			Enucleation		Enucleation	
Shields[59]	2019	Palo Alto, California	34	F	Chorioretinitis	Bilateral		Y		IV fluconazole and amphotericin B and then was	20/20 OU		

										transition to 200 mg of oral fluconazole per day.			
Stone[60]	1993	Seattle Washington, patient grew up in Arizona	26	M	Anterior Uveitis	Unilateral	22 years			None	CF	Enucleation	
Toomey[61]	2019	Southern California	48	F	Panuveitis	Unilateral	3 weeks		Y	Intravenous fluconazole and intravitreal voriconazole.	HM	LP	5 months
Trowbridge[62]	1952	San Joaquin Valley, California	22	F	Cutaneous	Bilateral	1 week						
Trowbridge	1952	San Joaquin Valley, California	52	F	Episcleritis	Bilateral	4 weeks				20/20		
Trowbridge	1952	San Joaquin Valley, California	34	M	Episcleritis	Bilateral	1 month					20/20	1 month
Trowbridge	1952	Fresno, California			Episcleritis	Bilateral	3 days						
Trowbridge	1952	Fresno, California	18	M	Episcleritis	Bilateral	At presentation						
Trowbridge	1952	Fresno, California			Scleritis	Unilateral		Y					
Ugurlu[63]	2005	Arizona	77	F	Cutaneous	Unilateral	2 weeks	Y	Y	Oral fluconazole 400 mg BID and as symptoms improved, deceased to 200 mg BID and then 200 mg QD due to intolerance. Then switched to oral itraconazole.	20/30		
Vasconcelos-Santos[64]	2010	Southern California	64	M	Granulomatous chorioretinitis	Unilateral	18 months			Intravitreal amphotericin B and oral fluconazole. Led to phthisis, later required enucleation.	20/400	Enucleation	
Wood[65]	1967	San Joaquin Valley, California	12	M	Cutaneous	Unilateral	At presentation				20/20		
Zakka[66]	1978	Los Angeles, California	37	M	Granulomatous chorioretinitis	Bilateral	1 week						

Table 2: Summary of ocular coccidioidomycosis case presentations.

Diagnosis	Number of Cases	IV Amphotericin	IV Azole	Oral Azole	Vitrectomy	Intraocular Azole	Intraocular Amphotericin	Cutaneous surgery	Enucleation	Topical Steroids	No Treatment
Anterior Uveitis	2	0	0	0	0	0	0	0	1	0	0
Chorioretinitis	12	5	3	2	0	0	0	1	2	1	2
Cutaneous	11	5	0	4	0	0	0	1	0	0	0
Endophthalmitis	4	1	1	2	2	1	2	0	1	0	0
Granulomatous anterior uveitis	9	5	0	5	1	0	1	0	4	1	2
Granulomatous chorioretinitis	15	9	0	5	0	0	1	0	1	0	1
Granulomatous conjunctivitis	1	0	0	1	0	0	0	0	0	0	0
Non-granulomatous anterior uveitis	1	0	0	0	0	0	0	0	0	1	0
Panuveitis	2	0	1	1	0	1	0	0	0	0	0
Retinitis	1	0	0	0	0	0	0	0	0	0	1

Scleritis/episcleritis	5	0	0	0	0	0	0	0	0	0	0
Total	63	25	5	20	3	2	4	2	9	3	6

Table 3: Summary of presentations and treatments for ocular coccidioidomycosis.

Discussion

Epidemiology of Coccidioidomycosis

Coccidioidomycosis is endemic to the arid and semi-arid regions of the southwestern United States, with California and Arizona accounting for the majority of reported cases in the country [6]. Outside of the United States, Valley Fever also affects parts of Mexico, Central and South America [7,8]. Coccidioidomycosis has two species in North American: C. immitis and C. posadaii. C. immitis is predominantly found in California while C. posadasii is found in other regions of United States. Phenotypically and clinically the two species are identical and can only be distinguished by molecular methods.

The incidence of coccidioidomycosis infections is increasing, with age-adjusted incidence rates increasing nearly 8 times from 2000-2018 in California [9]. The incidence of ocular involvement of Coccidioides infections is unknown, but disseminated coccidioidomycosis is estimated to occur in 0.5-2% of cases [10].

The geographic distribution of the disease may also be expanding in the United States, as more states face drought and extreme weather due to climate change [11]. Temperature is critical in both the mutation and development of the fungi, as it is hypothesized that Coccidioides ssp. thrive in dry and hot seasons by growing in the sterilized top layer of soil without competition from other microorganisms. For example, Washington state recently reported evidence of cases of coccidioidomycosis from strains endemic to the state, where it was not previously known to occur. A new niche for the fungi was already established or is establishing in Washington state. In addition to Washington, the incidence of coccidioidomycosis has been increasing in other Southwestern states such as Utah, New Mexico and Nevada [12-16].

Clinical Presentation and Diagnosis of Ocular Coccidioidomycosis

This study describes 63 case reports of ocular manifestations of coccidioidomycosis. While chorioretinitis was the most common manifestation of ocular coccidiomycosis representing 43% of patient presentations, the fungus can present as a wide variety of pathologies including cutaneous lesions, conjunctivitis, scleritis/episcleritis, uveitis and endophthalmitis. Active infection with the fungus was present in 76.2% of patients, while 19.0% of patients had a history of chronic infection. Therefore, coccidioidomycosis should be considered as a potential etiology for any new inflammatory ocular or orbital lesion in patients with a history of coccidioidomycosis infection or concomitant systemic symptoms indicative of pulmonary or disseminated infection, particularly among individuals residing in or recently visiting endemic regions.

Ocular manifestations of coccidioidomycosis are thought to result from hematogenous spread during disseminated fungal infection. Primary infection typically occurs through inhalation of the fungus, causing an acute pulmonary infection accompanied by fever and malaise that usually resolves spontaneously. However, chronic or disseminated infection may occur, especially in immunocompromised and pregnant patients, leading to spread of the fungus to the skin and bones. Conversely, some patients may present with only ocular symptoms, such as blurriness or inflammation, without any constitutional symptoms. This fact highlights the need to consider ocular coccidioidomycosis in the differential diagnosis of patients with ocular symptoms in an endemic region, even in the absence of other symptoms or signs of disseminated infection. It is especially crucial to consider this diagnosis in patients with a recent acute pulmonary infection, chronic unexplained cough or those who have recently traveled through an endemic area.

Diagnosis of Coccidioidomycosis is difficult as the systemic systems are ambiguous and requires a high degree of suspicion and knowledge from the clinician. General symptoms include cough, fatigue and fever but over half of Coccidioides infections are asymptomatic or minimally symptomatic. Other less common signs and symptoms include night sweats, rash, weight loss and headaches. Skin manifestations should raise suspicion for Coccidioides infection such as erythema nodosum and erythema multiforme.

Laboratory testing is crucial for proper diagnosis and treatment of Coccidioidomycosis. Serological testing includes Enzyme Immunoassay (EIA) for Immunoglobulin (Ig)M and (Ig)G. If the initial EIA is positive, many commercial tests will reflex to immunodiffusion antibody tests. EIA tests are more sensitive but less specific whereas immunodiffusion tests are less sensitive but more specific. Immunodiffusion testing can be quantified and expressed as a titer. Quantifiable data is useful for monitoring treatment response. Limitations of serologic include the development of serum antibodies against Coccidioides tends to trail symptoms by a few weeks. Negative EIA testing does not exclude Coccidioidomycosis and should be re-tested later if suspicion remains high or a diagnosis is not found. A common but frustrating situation arises when the EIA are positive, but the immunodiffusion is negative. Treatment should be based on the clinical picture and degree of suspicion for Coccidioidomycosis. Complement Fixation (CF) is another method to detect the presence of Coccidioidomycosis in fluids other than serum, such as CSF. CF provides a titer result that again is useful for monitoring response to treatment. Microscopic examination of bodily fluids, such as respiratory secretions or aqueous fluid, would also provide diagnostic evidence of Coccidioides infection. Culture of fluids for coccidioidomycosis are notoriously difficult to handle in an outpatient setting and is generally reserved for patients in a hospital setting. Lastly, Polymerase Chain Reaction (PCR) can be used and is highly specific for detection of Coccidioidomycosis.

The prognosis of infection is poor, with 15.9% of patients progressing to enucleation and most patients having decreased visual acuity after treatment. Although there was no significant difference in BCVA at presentation and post treatment, Fig. 1. shows a divergence of outcomes. Nearly all patients who presented with a visual acuity of 20/200 (logMAR 1.0) or better had an improvement in BCVA after treatment. On the other hand, most patients who presented with CF or worse vision remained with non-numerical visual acuity after treatment and many progressed to enucleation.

Treatment of Ocular Coccidioidomycosis

Treatment centers on quelling the proliferation of fungal material and minimizing the inflammatory response. The most common treatment identified in case reports was Amphotericin B, which licensed in the United States in 1959 [17]. Despite poor ocular penetration requiring high doses associated with significant side effects, such as nephrotoxicity, this was the primary treatment of systemic fungal infections until the later development of azole antifungals (Around the 1980s). Currently azoles, such as fluconazole, are now preferred due to excellent penetration into the eye and a more favorable side effect profile. Intraocular injection of antifungals was used less commonly but was the second line therapy for intraocular coccidioidomycosis. Surgical intervention is used sparingly as classic teaching says disruption of the eye leads to seeding of the fungus in an area that was previously unaffected. However, some cases successfully used a combined medical and surgical approach to treat complicated cases, such as endophthalmitis [18,19].

There is no standardized treatment for ocular coccidioidomycosis. The mainstay of treatment for systemic coccidioidomycosis is fluconazole. For treatment resistant or disseminated cases of ocular coccidioidomycosis, Posaconazole, which also has excellent intraocular penetration or Amphotericin B may be required for treatment. 27 patients (42.9%) with intraocular coccidioidomycosis in the review series had parenteral antifungals in addition to intraocular or surgical treatments. Cutaneous, periorbital coccidioidomycosis is treated well with fluconazole (4 patients 6.3%). Intraocular injection of antifungals agents such as voriconazole or amphotericin B are used in treatment resistant cases; 6 patients (9.5%) with intraocular coccidioidomycosis in the review series had intravitreal antifungals.

Surgical intervention for coccidioidomycosis is not performed routinely. Some experts believe coccidioidomycosis affects either the choroid and retina or the aqueous humor, but it is rarely present in both anatomical locations at the time of diagnosis due to the blood retinal barrier. It is theorized that surgical intervention allows for inoculation of fungal particles into all structures of the eye [1]. There are cases of successful combined medical and surgical management to remove foci of suspected coccidioidomycosis or vitrectomy to remove fungal particles.

Conclusion

In this review of 63 case reports on ocular coccidioidomycosis, we documented a range of ocular manifestations from chorioretinitis to endophthalmitis. These findings underscore the complexity of diagnosis and management of ocular coccidioidomycosis and shows the importance of considering coccidioidomycosis in the differential diagnosis for inflammatory ocular or orbital lesions, particularly in patients from or with a history of travel to endemic regions. Notably, despite the

application of treatments ranging from intravitreal antifungals to enucleation, the prognosis remains guarded; there was no significant improvement in BCVA post-treatment, with many patients experiencing persistent or worsening visual impairment. The regional spread of coccidioidomycosis is increasing as our climate continues to become hotter. Suspicion for ocular coccidioidomycosis should remain high in endemic areas and areas surrounding traditional coccidioidomycosis zones.

Key Points

- Coccidioidomycosis area of effect is growing as climate changes increase surface temperature
- High suspicion and knowledge of Coccidioidomycosis ophthalmic pathology is needed to arcuately diagnosis this blinding fungus
- Treatment courses are varied and require frequent observation and adjustment for extended periods of time

Conflict of Interest

The authors declare no potential conflicts of interest with respect to the research, authorship and/or publication of this article.

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