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**REVIEW** **Open Access**

# Subretinal abscess: causative pathogens, clinical features and management

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**Abstract**

**Purpose:** To review the literature on endogenous subretinal abscess (SRA).

**Methods:** We searched in the literature for the terms 'subretinal abscess', 'chorio-retinal abscess' and 'choroidal abscess'.

**Results:** A total of 122 patients were identified, of whom 20 patients (22 eyes) had no identified systemic infective foci (group 1) and 102 (120 eyes) had systemic infective foci (group 2). The mean age for group 1 was 44.6 years (range 2 weeks-82 years) and for group 2 was 43.2 years (range 1–89 years). The responsible pathogen was identified in 90% and 95% of cases, respectively. In group 1 the most frequent causative agents were *Aspergillus* and *Nocardia*, while in group 2 were *Nocardia*, *Mycobacterium Tuberculosis* and *Klebsiella*. In both groups the most common symptoms were reduced vision (70% and 72.5%, respectively), pain (65% and 29.4%, respectively) and redness (35% and 17.6%, respectively). For group 1 there was no difference between mean initial and final visual acuity (1.7 logMAR, range 0–3 logMAR), while for group 2 mean initial and final visual acuities were 0.8 logMAR and 0.6 logMAR, respectively. Final visual acuity was significantly better in group 2 ($p = 0.003$). Anterior segment inflammation was seen in 77.3% of cases of group 1 and 66.7% of cases of group 2. In both groups the abscess most common locations were posterior pole (45.4% and 32.5%, respectively) and temporal periphery (13.6% and 13.3%, respectively). Clinical features included hemorrhages (76.5% and 76.3%, respectively) and subretinal fluid (75% in both groups). Diabetes mellitus (20% and 25.5%) and immunosuppressive drug intake (35% and 23.5%) were the main predisposing factors for SRA. Combination of systemic and intravitreal antibiotics/antifungals and vitrectomy was the main therapeutic strategy for both groups. Systemic treatment alone was used mainly for cases of tubercular etiology. The timing of vitrectomy differed between the two groups, as it more commonly followed the use of systemic and intravitreal antibiotics in the forms associated with systemic infective foci. Additional abscess drainage or intralesional antibiotics were performed in 23.8% of cases.

**Conclusion:** At present no guideline exists for the treatment of subretinal abscess. Systemic broad-spectrum antibiotic treatment is of primary importance and should be used in all cases unless contraindicated. Combination of systemic and local treatment is the most frequently adopted strategy.

**Keywords:** Subretinal abscess, Endogenous endophthalmitis, Therapeutic strategy, Systemic antibiotics

## Introduction

Subretinal abscess (SRA) is a rare and sight-threatening manifestation of endogenous endophthalmitis, where a pathogen reaches the choroid via the bloodstream from another site of the body and crosses the blood-retinal barrier, invading the retina and potentially the vitreous cavity [1]. In 1983, Wilmarth was the first to describe a case of SRA associated with endogenous endophthalmitis

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caused by *Aspergillus fumigatus* in an intravenous (IV) drug user [2]. Subsequently, several cases of SRA [3–5], intraretinal abscess [6], septic retinal cyst [7], choroidal or chorio-retinal abscess [8, 9] were reported, but the distinction between these entities remains unclear. Given the rarity, there are no data on the incidence of SRA. In the British Ophthalmological Surveillance Unit (BOSU) study on 62 cases of endogenous endophthalmitis, SRA was the second most common retinal finding (6.5%) after retinitis (31%) and followed by Roth's spots (4.8%) [10]. Predisposing conditions of SRA are the same of endogenous endophthalmitis [1], including diabetes, immunosuppression, extraocular foci of infection, sepsis [4], IV drug use, blood malignancies and autoimmune diseases. The etiology is most frequently bacterial, the commonest being *Nocardia* followed by *Pseudomonas Aeruginosa*, *Streptococcus Viridans* and *Klebsiella Pneumoniae*. *Aspergillus* is the most frequent fungal agent [3]. Rarely the etiology is protozoan [11] or mixed [12]. The visual prognosis of SRA is often very poor due to the aggressive course despite treatment, with the most severe cases complicated by subretinal pseudo-hypopyon [11] and exudative or rhegmatogenous retinal detachment, requiring enucleation or evisceration if not timely treated.

We reviewed all cases of SRA with and without systemic infective foci published between 1967 and 2021, focusing on epidemiology, causative pathogen and method of identification, symptoms and signs at presentation, systemic predisposing factors and treatment approach.

## Methods

We identified published studies from Pubmed (National Library of Medicine), EMBASE (Embase.com) and Scopus (Elsevier) from inception to January 2021. The publication period ranges between September 1967 and January 2021.

There were no language restrictions. To ensure appropriate study inclusion, the search terms were 'subretinal abscess', 'chorio-retinal abscess' and 'choroidal abscess'. The titles and abstracts were screened and full-texts were obtained for inclusion and data collection. A total of 105 articles were preliminarily enrolled and after a full-text review a total of 96 articles were chosen for inclusion, with 122 patients in total. For the rarity of the condition all chosen articles were case reports (84) and case series (12), and were considered of sufficient quality for inclusion if documented: 1) presenting clinical features, responsible pathogen and method of identification; 2) treatment strategies; 3) final outcomes. Articles lacking detailed information and cases of exogenous SRA developing after ocular surgery or ocular trauma were excluded. For the purpose of our study SRA cases without identified systemic infective foci (group 1) and with systemic infective foci (group 2) were analyzed separately. Snellen visual acuity (VA) was converted to logarithm of minimal angle of resolution (logMAR) and was analyzed as a continuous variable. Continuous variables (e.g. VA) were compared using an unpaired t-test. A loss of 0.3 logMAR of VA or more from baseline was considered a worsening, while a gain of 0.3 logMAR or more was considered an improvement.

## Results

### Group 1: SRA without identified systemic infective foci

#### *Demographics*

Our literature search identified 20 patients (22 eyes) with a mean age at presentation of 44.6 years (range 2 weeks-82 years). There were 11 males and 9 females. The majority of reports were from the United States (10 patients) and India (5 patients). Mean follow-up duration was 9.8 (median 6.5 , range 0.3–48 ) months.

General health was reported as unremarkable in 5 patients (25%), whereas 7 patients (35%) were on systemic steroids and/or immunosuppressive drugs, 4 (20%) were type 2 diabetic, 2 (10%) had a history of IV drug use and 2 (10%) were human immunodeficiency virus (HIV) positive. In all patients an active systemic infective process was not identified, but one suffered with gastro-enteritis 2 weeks before the onset of ocular symptoms, one had an urinary tract infection a month before and one had fevers of unknown origin during a recent exotic travel.

#### *Clinical features at presentation*

At presentation SRA was isolated, without vitreous involvement, in 4 patients (4 eyes) and associated with endophthalmitis in 16 patients (18 eyes). There was no difference in laterality (9 right eyes, 9 left eyes, 2 bilateral). The three most frequent symptoms were reduced vision (14 patients, 70%), pain (13 patients, 65%) and redness (7 patients, 35%). Mean symptom duration, specified for 17 patients, was 18.1 (median 7, range 1–180) days.

VA at presentation, available for 21 eyes, was 20/40 or better in 7/22 eyes (31.8%), and 14 eyes (63.6%) had a VA of 20/200 or worse. In one eye (4.6%) of a newborn baby the initial VA was not specified.

No difference was observed between initial and final VA, as the mean VA at presentation was 1.7 logMAR (median 1.9 logMAR, range: 0–3 logMAR) and the mean final VA, available for 17 eyes, was 1.7 logMAR (median 1.9 logMAR, range: 0–3 logMAR). Four eyes were enucleated.

Anterior segment involvement was observed in 17 eyes (77.3%), and signs consisted in cellularity in the anterior chamber (15 eyes), conjunctival injection (10 eyes)

and hypopyon (6 eyes). In one case the anterior segment description was missing.

The most frequent location of SRA was the posterior pole (10 eyes, 45.5%), followed by the temporal periphery (3 eyes, 13.6%). Where described, hemorrhages were associated with SRA in 13 out of 17 eyes (76.5%), and subretinal fluid in 9 out of 12 eyes (75%).

#### *Causative pathogens and methods of identification*

Causative agents were identified in 18/20 patients (90%), and the most frequent were *Aspergillus* (*Fumigatus*, *Nidulans*, *Terreus* and *Flavus* species) and *Nocardia*, detected in 4 and 3 patients, respectively. Given the absence of a systemic infective focus, pathogen identification was from ocular samples, the commonest being SRA (8 eyes from 8 patients), followed by vitreous (7 eyes from 7 patients). In the 3 patients (3 eyes) with isolated SRA where the vitreous analysis was performed it did not allow the pathogen identification, while of the 16 patients (18 eyes) with SRA associated with vitritis the pathogen was isolated from SRA drainage or biopsy in 7 eyes (7 patients) and from vitreous in 7 eyes (7 patients). In the 8 eyes (8 patients) where the vitreous culture failed in yielding a growth the pathogen was identified by direct drainage of the SRA.

Clinical features, pathogen and method of identification of SRA without systemic foci are summarized in Table 1.

#### *Therapeutic approaches*

The most common therapeutic strategy was the combination of systemic and intravitreal antibiotics or antifungals followed by vitrectomy (13 patients, 13 eyes; 65%). In the majority of these patients (9 patients, 9 eyes, 69.2%) vitrectomy was a second line treatment performed for progression despite systemic and intravitreal antibiotics/antifungals, and in 4 patients (4 eyes, 30.8%) was first line strategy with the dual purpose of diagnosis and treatment. Additional SRA drainage was performed in 5 patients (5 eyes) and intralesional antibiotics or antifungals were administered in 3 patients (3 eyes). In one case (one eye) enucleation was performed due to failure of these treatments.

Vitrectomy and SRA drainage without systemic treatment was adopted only in one eye of a case caused by *Aspergillus* where intravitreal agents were not deemed necessary for minimal vitreous involvement [13].

Systemic treatment and vitrectomy without intravitreal antibiotics was performed in 2 cases (2 eyes).

Of the 17 patients undergoing vitrectomy, in 8 it was first line treatment while in the remainder 9 it was performed as second line treatment.

Systemic treatment was the only treatment strategy in one eye of a case of Tubercular etiology [14].

Enucleation was the first line treatment for 2 paediatric cases (2 eyes) where retinoblastoma could not be clinically excluded [15] and for one case (one eye) refusing other treatments where the SRA progressed to panophthalmitis [16]. Systemic and intravitreal agents were the strategy adopted for the eye of a patient with bilateral involvement by *Candida* where the fellow eye underwent vitrectomy [17] and in one case of bilateral SRA caused by *Nocardia* and *Mycobacterium TB* where the fellow eye underwent vitrectomy [18].

Steroids were used in four cases of bacterial etiology: one receiving intravitreal dexamethasone at the end of vitrectomy [19] and three receiving oral steroids, of whom one was also on systemic anti-tubercular treatment. Intravitreal dexamethasone was given in a diabetic patient with SRA caused by *S. aureus* where the final VA improved.

#### *Responses to treatment, secondary complications and their treatment*

Of the 17 eyes where the final VA was available, in 3 eyes (17.6%) VA was 20/40 or better, in 2 eyes (11.8%) was between 20/40 and 20/200, and in 12 eyes (70.6%) was 20/200 or worse.

Comparing initial and final VA, in 6 eyes (35.3%) VA improved, in 8 eyes (47.1%) remained stable and in 3 eyes (17.6%) worsened. VA was not specified for one eye and 4 eyes were enucleated.

In 8/13 cases multiple surgeries were necessary either because the lesion expanded despite previous vitrectomy or for development of complications such as retinal detachment or retinal traction. One case caused by *Aspergillus Fumigatus*, progressed despite the initial treatment with systemic and intravitreal amphotericin, vitrectomy and lensectomy, rendering enucleation necessary [2]. In 2 paediatric cases enucleation was performed as retinoblastoma could not be ruled out.

Baseline and final VA, treatment interventions and final outcomes of SRA without systemic foci are summarized in Table 2.

### Group 2: SRA with identified systemic infective foci

#### *Demographics*

One hundred and two patients (120 eyes) were identified. There were 69 males and 33 females, with a mean age of 43.2 (median 44; range 1–89) years specified for 101 patients. The mean duration of follow-up, available for 96 patients, was 8.3 (median 6, range 0.2–48) months.

Twenty-three (22.5%) patients were healthy, 26 patients (25.5%) had diabetes mellitus, 24 (23.5%) were on

**Table 1** Summary of study details, clinical features, pathogen and method of identification of SRA without systemic foci

| S/N | Study | Year | Country | N of patients | Laterality | Sex | Age | Type of SRA | Co-morbidities | Causative pathogen | Method of identification |
|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Wilmarth, Annal Ophthal | 1983 | USA | 1 | RE | M | 27 | SRA + EE | IV drug and amphetamins use | *Aspergillus Fumigatus* | vitreous, cotton wool balls |
| 2 | Halperin, Arch Ophthal | 1988 | USA | 1 | RE | M | 40 | SRA + EE | IV drug use | *Aspergillus Flavus* | SRA |
| 3 | Shields, Retina | 1995 | USA | 2 | LE | F | 6 | SRA + EE | none | not isolated | – |
| | | | | | LE | F | 2 weeks | SRA + EE | none | not isolated | – |
| 4 | Garg, Retina | 2006 | USA | 1 | RE | F | 52 | SRA + EE | DM | *Moraxella* spp. | vitreous |
| 5 | Huynh, Ret Cas Brief Rep | 2008 | USA | 1 | BE | F | 62 | SRA + EE<br>SRA + EE | auto-immune haemolitic anaemia | *Candida A.* | SRA |
| 6 | Kanuraki, Int Ophthalmol | 2010 | Japan | 1 | RE | F | 51 | SRA | cirrhosis, liver transplant | *Candida A.* | epiretinal proliferative tissue |
| 7 | Anderson, Ret Cas Brief Rep | 2012 | USA | 1 | LE | M | 40 | SRA | none | *Acanthamoeba* | SRA |
| 8 | Matthews, Indian J Ophthalmol | 2013 | UK | 1 | RE | M | 67 | SRA + EE | rheumatoid arthritis | not specified fungus (phaeohyphomycosis) | SRA |
| 9 | Panigrahi, Indian J Ophthalmol | 2014 | India | 1 | RE | M | 50 | SRA + EE | healthy | *Aspergillus Terreus* | vitreous |
| 10 | Silva, Retina | 2015 | USA | 2 | RE | M | 46 | SRA + EE | HIV | *Nocardia Asteroides* | SRA |
| | | | | | LE | F | 69 | SRA | Wegener granulomatosis | *Nocardia Asteroides* | enucleated eye |
| 11 | Cheng, Ret Cas Brief Rep | 2016 | Australia | 1 | LE | M | 82 | SRA + EE | DM | *E. coli* | SRA |
| 12 | Xu, BMC Ophthalmol | 2018 | China | 1 | RE | M | 61 | SRA + EE | DM, peptic ulcer | *Klebsiella P.* | vitreous |
| 13 | Joseph, Indian J Ophthalmol | 2018 | India | 1 | RE | M | 36 | SRA + EE | HIV | *Cryptococcus Neoformans* | vitreous |
| 14 | Majumder, Ocul Immun Inflamm | 2018 | India | 1 | BE | M | 25 | SRA (RE)<br>SRA + EE (LE) | glomerolusclerosis | *Nocardia Arthritidis*, *Mycobacterium TB* | SRA |
| 15 | Verma, Ocul Immun Inflamm | 2020 | India | 1 | LE | M | 45 | SRA + EE | none | *Citrobacter* | vitreous |
| 16 | Nair, Indian J Ophthalmol | 2020 | India | 1 | LE | F | 14 | SRA + EE | none | *Mycobacterium TB* | acqueous |
| 17 | Mata-Moret, Europ J Ophthalmol | 2020 | Spain | 1 | LE | F | 42 | SRA + EE | asthma | *Aspergillus Nidulans* | vitreous |
| 18 | Yang, Ret Cas Brief Rep | 2021 | USA | 1 | LE | F | 77 | SRA + EE | DM | *S. aureus* | SRA |

*S/N* Study number, *RE* Right eye, *LE* Left eye, *BE* Both eyes, *M* Male, *F* Female, *SRA* Subretinal abscess, *EE* Endogenous endophthalmitis, *IV* Intravenous, *DM* Diabetes mellitus

**Table 2** Summary of initial and final visual acuity, treatment interventions and final outcomes of SRA without systemic foci

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 1 | Wilmarth, Annal Ophthal | *Aspergillus Fumigatus* | 1.9 | – | - intravenous amphotericin<br>- intravitreal amphotericin<br>- vitrectomy + lensectomy<br>- enucleation | enucleated |
| 2 | Halperin, Arch Ophthal | *Aspergillu Flavus* | 1.9 | 1.9 | vitrectomy + SRA drainage | same VA |
| 3 | Shields, Retina | not isolated | 2.7 | – | enucleation | enucleated |
| | | not isolated | N/A | – | enucleation | enucleated |
| 4 | Garg, Retina | *Moraxella* spp | 2.3 | 0.6 | - vitrectomy + lensectomy<br>- intravitreal vancomycin and ceftazidime<br>- intravenous vancomycin, ceftazidime and ceftriaxone | better VA |
| 5 | Huynh, Ret Cas Brief Rep | *Candida A.* | 0.3; 0.3 | 0; 0 | - LE vitrectomy + SRA drainage oral voriconazole<br>- RE 2 intravitreal amphotericin<br>- LE 2$^{nd}$ vitrectomy | BE better VA |
| 6 | Kanuraki, Int Ophthalmol | *Candida A.* | 0 | 2.3 | - Systemic acetylspiramycin and levofloxacin<br>- vitrectomy + cataract + SRA drainage + silicone oil + intralesional fluconazole and imipenem<br>- vitrectomy + silicone oil + antifungals<br>- vitrectomy + scleral encircling + membrane removal + silicone oil + antifungals<br>- intravitreal amphotericin<br>- intravenous fluconazole | worse VA |
| 7 | Anderson, Ret Cas Brief Rep | *Acanthamoeba* | 1.3 | 1.3 | - systemic ceftriaxone, metronidazole, and fluconazole<br>- vitrectomy + intravitreal vancomyin, ceftazidime and amphotericin<br>- 2$^{nd}$ vitrectomy + SRA drainage<br>- systemic amphotericin, fluconazole, sulfamethoxazole, trimethoprim, rifampin | same VA |
| 8 | Matthews, Indian J Ophthalmol | phaeohyphomycosis | 0.2 | 1.5 | - topical prednisolone and cyclopentolate<br>- pyrimethamine + sulfadiazine + clindamycin<br>- vitrectomy<br>- SRA biopsy + silicone oil<br>- oral voriconazole<br>- 2$^{nd}$, 3$^{rd}$ and 4$^{th}$ vitrectomy<br>- intravitreal amphotericin | worse VA |
| 9 | Panigrahi, Indian J Ophthalmol | *Aspergillus Terreus* | 2.7 | 2.7 | - vitrectomy + intravitreal vancomicin, ceftazidime, voriconazole<br>- 6 x intravitreal voriconazole<br>- 2$^{nd}$ vitrectomy + endolaser + silicone oil<br>- oral voriconazole | same VA |

**Table 2** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 10 | Silva, Retina | *Nocardia Asteroides* | 1.9 | 1.9 | - intravitreal ganciclovir<br>- oral acyclovir, azithromycin and valganciclovir | same VA |
| | | *Nocardia Asteroides* | 0.3 | – | - 1st vitrectomy<br>- 2nd vitrectomy + retinotomy + SRA biopsy + silicone oil<br>- oral TMP-SMX<br>- 2 x intravitreal amikacin<br>- enucleation | enucleated |
| 11 | Cheng, Ret Cas Brief Rep | *E. coli* | 2.3 | 2.3 | - intravitreal vancomycin, ceftazidime, foscarnet and voriconazole<br>- intravenous ceftriaxone and flucloxacillin<br>- vitrectomy + AC washout + silicone oil<br>- 2nd vitrectomy + chorio-retinal biopsy<br>- oral ciprofloxacin and amoxicillin | same VA |
| 12 | Xu, BMC Ophthalmol | *Klebsiella P* | 2.7 | 2.3 | - intravitreal vancomycin and ceftazidime<br>- topical levofloxacin, prednisolone 1% and atropine<br>- intravenous cefoperazone<br>- vitrectomy + phaco | better VA |
| 13 | Joseph, Indian J Ophthalmol | *Cryptococcus Neoformans* | 3.0 | 3.0 | - vitrectomy + intravitreal ganciclovir<br>- intravitreal amphotericin<br>- oral valganciclovir<br>- systemic amphotericin | same VA |
| 14 | Majumder, Ocul Immun Inflamm | *Nocardia Arthritidis*, *Mycobacterium Tubercolosis* | 0.1; 1.9 | 0.3; 1.9 | - oral ATT and steroid<br>- LE vitrectomy + silicone oil<br>- RE intravitreal imipenem<br>- intravenous cefotaxime and amikacin | RE worse and LE better VA |
| 15 | Verma, Ocul Immun Inflamm | *Citrobacter* | 2.3 | 1.0 | - intravenous vancomicin and ceftriaxone<br>- topical antibiotics, steroids and cyclopentolate<br>- intravitreal vancomicin and ceftazidime<br>- 1st vitrectomy + intralesional piperacillin and tazobactam + silicone oil<br>- systemic prednisolone<br>- oral antibiotic ciprofloxacin<br>- 2nd vitrectomy + phaco + buckle + silicone oil | better VA |
| 16 | Nair, Indian J Ophthalmol | *Mycobacterium Tubercolosis* | 0 | N/A | - oral ATT and steroids | – |
| 17 | Mata-Moret, Europ J Ophthalmol | *Aspergillus Nidulans* | 2.3 | 3.0 | - oral voriconazole<br>- 7 x intravitreal voriconazole<br>- 1st vitrectomy + intravitreal foscarnet<br>- 2nd vitrectomy + SRA drainage + subretinal voriconazole<br>- 3rd vitrectomy + SRA aspiration + lensectomy + endolaser | worse VA |

**Table 2** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 18 | Yang, Ret Cas Brief Rep | *S. aureus* | 2.7 | 1.9 | - intravenous vancomycin and ceftazidime<br>- intravitreal vancomycin, ceftazidime and dexamethasone<br>- 1st vitrectomy<br>- 2nd vitrectomy+SRA drainage<br>- 3rd vitrectomy + silicone oil<br>- topical prednisolone and moxifloxacin | better VA |

*S/N* Study number, *RE* Right eye, *LE* Left eye, *BE* Both eyes, *M* Male, *F* Female, *N/A* Not available, *ATT* Anti-tubercular treatment

immunosuppressive medications or oral steroids, and 3 (2.9%) were HIV-positive. The most common infective focus was the respiratory system (25 patients) followed by disseminated infection (16 patients) and soft tissue infection (13 patients).

#### *Clinical features at presentation*

SRA was isolated in 13 patients (14 eyes), associated with endophthalmitis in 84 patients (100 eyes), and not better described in 5 patients (6 eyes). There were 30 right eyes, 40 left eyes, 18 bilateral and 14 eyes unilateral with unspecified laterality.

The three most frequent symptoms were reduced vision (74 patients, 72.5%), sudden in 8 patients and gradual in 66 patients, pain (30 patients, 29.4%) and redness (18 patients, 17.6%), followed by floaters (9 patients, 8.8%) and photophobia (5 patients, 4.9%).

Mean symptom duration, specified for 67 patients, was 16.3 days (median 3 days, range 0–365 days).

The mean visual acuity at presentation, available for 105 eyes, was 1.0 (median 1, range: 0–3) logMAR, and the mean final visual acuity, available for 99 eyes, was 0.6 (median 0, range: 0–3 ) logMAR.

VA at presentation, available for 105 eyes, was 20/40 or better in 15 eyes (14.3%), between 20/40 and 20/200 in 25 eyes (23.8%), and 20/200 or worse in 65 eyes (61.9%).

Anterior segment involvement was observed in 76 eyes from 68 patients (66.7%), with the most frequent signs being anterior chamber cells (63 eyes), conjunctival hyperemia/chemosis (33 eyes) and flare (23 eyes).

The most frequently observed location of SRA was the posterior pole (39 eyes, 32.5%) followed by the temporal periphery (16 eyes, 13.3%). Hemorrhages were present in 58/76 eyes (76.3%), and subretinal fluid in 33/44 eyes (75%).

#### *Causative pathogens and methods of identification*

The causative pathogen was identified in 97 patients (95%) and not identified in 5 patients.

*Nocardia* was the most frequent pathogen - detected in 24 patients (23.5%) - followed by *Mycobacterium Tuberculosis* (18 patients, 17.6%), *Klebsiella* (18 patients, 17.6%) and *S. aureus* (14 patients, 13.7%). *Mycobacterium Tuberculosis* and *Nocardia* spp. were the two main responsible agents of respiratory infections (14 and 5 patients, respectively) and systemic infections (3 and 14 patients, respectively).

Pathogens were identified from ocular tissues in 42 patients (43.3%) and from extra-ocular tissues in 49 patients (50.5%), of whom 27 from blood cultures. In six patients *Mycobacterium Tuberculosis* was not isolated but tubercular disease was diagnosed based on the typical pulmonary findings on chest X-ray or CT and a positive Mantoux test and/or QuantiFERON-TB gold.

The vitreous was the main ocular source for pathogen identification (20 patients, 47.6%, 20 eyes), followed by SRA (14 patients, 33.3%, 14 eyes) and aqueous (7 patients, 16.7%, 7 eyes).

In all cases of isolated SRA (13 patients, 14 eyes) the pathogen was identified, but ocular sampling was performed only in 7/13 (53.8%), with a yielding rate for vitreous of 20% (1/5 patients) and for SRA of 100% (3/3 patients).

In cases of SRA and endophthalmitis (84 patients, 100 eyes), vitreous sampling was performed in 50 cases and the pathogen yielding rate for vitreous was 38% (19 cases), while SRA biopsy allowed pathogen identification in 20% of cases (10 cases).

*Nocardia* was by far the most common pathogen in immunosuppressed patients (18/24 patients), *Klebsiella* and *S. aureus* were the main causative agents in diabetic patients, detected in 9/26 cases and 7/26 cases, respectively; *Mycobacterium Tuberculosis* was the most common pathogen in healthy subjects (12/23 patients).

Clinical features, pathogen and method of identification of SRA with systemic foci are summarized in Table 3.

#### *Therapeutic approaches*

The combination of systemic and intravitreal antibiotics/antifungals with vitrectomy was the most common therapeutic approach, performed in 28 patients (27.5%), with additional drainage of SRA and/or intralesional antibiotics or antifungals performed in most of cases (21 patients and 1 patient, respectively).

Vitrectomy was the first line strategy in 6 patients, all caused by *Klebsiella* or *Nocardia*, while for the remainder (33 patients) it was performed as second line treatment for failure of other treatment modalities. In 10 cases multiple surgeries were necessary to address SRA progression or complications (retinal detachment or tractional complications).

Combined systemic and intravitreal antibiotics were the second most common treatment strategy (20 patients). In a limited number of cases (3 cases) only vitrectomy and intravitreal antibiotics were adopted. Intravitreal dexamethasone was used in 9 eyes, of whom 7 eyes had SRA caused by *Klebsiella*, one eye caused by *Mycobacterium TB* and in one eye the pathogen was not isolated. Of these, in 6 eyes the VA improved, in one eye the VA remained the same, in one eye VA not specified and in one eye evisceration was necessary.

Systemic treatment without other treatment modalities was used in 18 patients, of whom 6 had TB, 5 had *S. aureus*-related and 4 had *Nocardia*-related infections.

Combined systemic and topical antibiotics or steroids were adopted in 18 cases, the majority of whom (13/18) had TB.

In one SRA case caused by *Klebsiella* treatment consisted only in intravitreal antibiotics, and one case caused by *Nocardia* received systemic treatment and intravitreal anti-VEGF.

In 13 cases enucleation (7 cases), evisceration (4) or exenteration (2 cases) were performed due to failure of other treatments.

#### *Responses to treatment, secondary complications and their treatment*

Of the 99 eyes where the final VA was available, in 29 eyes (29.3%) was 20/40 or better, in 30 eyes (30.3%) was between 20/40 and 20/200, and in 40 eyes (40.4%) was 20/200 or worse. Comparing initial and final VA of 89 eyes, in 49 eyes (55.1%) VA improved, in 23 eyes (25.8%) remained stable and in 17 eyes (19.1%) worsened. Final VA was not specified in 9 eyes. Six eyes were enucleated, 5 were eviscerated and 1 was exenterated.

In 10 cases multiple surgeries were necessary either because the lesion expanded despite the previous surgery or for development of complications such as retinal detachment or retinal traction. Twelve cases were non responsive to treatment and therefore enucleation, evisceration or exenteration were necessary, and the most common pathogens associated with these were *Nocardia* (one evisceration and two enucleations) and *Pseudomonas* (one evisceration and two enucleations).

Baseline and final VA, treatment interventions and final outcomes of SRA with systemic foci are summarized in Table 4.

## Discussion

Our review of the literature showed that *Nocardia* was the most frequent causative pathogen of SRA associated with systemic infective foci, while for SRA in absence of systemic foci *Aspergillus* was seen with a higher frequency. In absolute numbers *Nocardia* was the most frequent causative agent.

In SRA without systemic infective foci the pathogen was more commonly isolated from SRA if there was no vitreous involvement, while for forms with vitreous involvement a similar yielding rate from vitreous and from SRA was observed. By contrast, in presence of a systemic infective focus the pathogen was isolated mainly from extra-ocular sites, and when ocular sampling was performed in cases of SRA with no vitreous involvement the observed yielding rate for vitreous was 20% and for SRA was 100%. In the forms with vitritis where ocular sampling was done the vitreous was the commonest ocular site of pathogen identification. However, failure of vitreous sampling in isolating the pathogen has been described by many authors, who were subsequently able to isolate it by direct drainage of the lesion [11, 19]. Despite vitritis being observed with a similar frequency in both groups (81.8% versus 83%) the vitreous yielding rate was higher in the forms without systemic infective foci (43.8% versus 35.7%).

The most common systemic predisposing conditions of SRA were immunosuppression and diabetes mellitus, the former being more frequent in SRA without systemic foci (35% of patients) and the latter being more frequent in SRA associated with infective foci (25.5% of patients). Isolated SRA was more frequently observed in cases without systemic infection (18.2% of eyes versus 10.8% of eyes of group 2). A higher frequency of bilateral involvement was observed in the forms with systemic foci, where it was detected in 17.6% of patients (30% of eyes) compared to 10% of patients (18.2% of eyes) without systemic foci.

Reduced vision was observed with a similar frequency in both groups (70% and 72.5%). Baseline visual acuity did not show a significant difference between the groups, but final visual acuity was better in the group associated with systemic foci ($p = 0.003$).

*Pseudomonas*, *Nocardia* and *Aspergillus* were the microorganisms related to a worse prognosis requiring

**Table 3** Summary of study details, clinical features, pathogen and method of identification of SRA with systemic foci

| S/N | Study | Year | Country | N of patients | Laterality | Sex | Age | Type of SRA | Co-morbidities | Systemic infective process | Causative pathogen | Method of identification |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 1 | Manor, Ophthalmologica | 1965 | Israel | 1 | LE | F | 49 | Pre-papillary abscess + EE | mitralic valve stenosis | bacterial endophthalmitis | not isolated | – |
| 2 | Davidson, Trans Am Ac Ophthalmol | 1967 | USA | 1 | LE | M | 46 | SRA + EE | liver gallstones | lung infection | *Nocardia Asteroides* | enucleated eye |
| 3 | Fleming, Can J Ophthalmol | 1972 | USA | 1 | BE | M | 10 months | SRA (vitreous not described) | congenital small bowel atresia, deficit of growth | UTI, lung abscess | *Candida A.* | blood<br>lung |
| 4 | Naidoff, Am J Ophthalmol | 1975 | USA | 1 | LE | M | 26 | SRA + EE | renal transplant | pneumonia, brain abscess | *Aspergillus Fumigatus* | lung<br>vitreous |
| 5 | Hiss, Ophthalmology | 1988 | USA | 1 | RE | M | 63 | SRA + EE | DM, HBP, angina, chronic renal failure, anemia, polyarteritis nodosa | meningitis, pneumonia, sepsis | *Criptococcus Neoformans* | SRA<br>cerebro-spinal fluid |
| 6 | Mamalis, Ann Ophthalmol | 1988 | USA | 1 | LE | M | 44 | SRA + EE | cardiac transplant | nocardiosis with testicular abscess | *Nocardia Asteroides* | testis |
| 7 | Gregor, Retina | 1989 | USA | 1 | RE | M | 46 | SRA | cardiac transplant | nocardiosis with brain abscess | *Nocardia Asteroides* | SRA |
| 8 | Coll, Retina | 1994 | USA | 1 | RE | M | 44 | choroidal abscess | DM, heroin use | endocarditis, toe cellulitis | *S. aureus* | blood<br>toe |
| 9 | Webber, British J Ophthalmol | 1995 | UK | 1 | RE | M | 23 | SRA + EE | lung transplant | systemic | *Pseudomonas A.* | sputum<br>SRA |
| 10 | Biswas, Retina | 1995 | India | 2 | RE | F | 42 | SRA + EE | sarcoidosis | lung TB | *Mycobacterium TB* | vitreous |
| | | | | | RE | F | 58 | SRA + EE | DM | systemic TB | *Mycobacterium TB* | acqueous |
| 11 | Jolly, Arch Ophthalmol | 1996 | Canada | 1 | RE | F | 40 | SRA + EE | renal transplant | systemic | *Nocardia Asteroides* | lung |
| 12 | Yarng, Ophthal Surg Las Im | 1997 | Taiwan | 1 | LE | M | 39 | SRA + EE | none | liver abscess | *Klebsiella P.* | blood<br>liver<br>vitreous |
| 13 | Rimpel, British J Ophthalmol | 1999 | USA | 1 | LE | M | 56 | SRA | multiple myeloma | endocharditis, brain septic emboli | *Streptococcus Viridans* | blood<br>vitreous |
| 14 | Lakosha, Retina | 2000 | Canada | 1 | RE | M | 41 | SRA | chronic myeloid leukemia | subcutaneous abscess | *Nocardia Farcinica* | subcutaneous abscess |
| 15 | Harris, Am J Ophthalmol | 2000 | USA | 1 | RE | M | 32 | SRA + EE | beta-thalassemia major | liver and kidney abscess | *Klebsiella P.* | liver<br>blood |

**Table 3** (continued)

| S/N | Study | Year | Country | N of patients | Laterality | Sex | Age | Type of SRA | Co-morbidities | Systemic infective process | Causative pathogen | Method of identification |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 16 | Costen, Eye | 2001 | UK | 1 | BE | F | 68 | SRA + EE | none | meningitis, sepsis | *Streptococcus Pyogenes* | blood |
| 17 | Yao, Eur J Pediatr | 2001 | Taiwan | 1 | LE | F | 14 | SRA + EE | beta-thalassemia major | pneumonia, mastoiditis | *Klebsiella P.* | external auricular canal |
| 18 | Yoon, Retina | 2003 | Korea | 2 | Unilateral, side NA | M | 41 | SRA + EE | DM | liver abscess | *Klebsiella P.* | vitreous, blood, liver |
| | | | | | BE | M | 47 | SRA + EE | DM | liver abscess | *Klebsiella P.* | blood, liver |
| 19 | Bozbeyoglu, Retina | 2004 | Turkey | 1 | LE | M | 46 | choroidal abscess (vitreous not described) | renal transplant | nocardiosis with brain and lung abscess | *Nocardia Asteroides* | SRA<br>blood |
| 20 | Shah, Indian J Ophthalmol | 2004 | India | 1 | BE | F | 23 | SRA + EE | none | genito-urinary tract | *Candida A.* | vitreous<br>vagina |
| 21 | Wjjesekera, Eye | 2004 | UK | 1 | LE | M | 75 | SRA + EE | post TB bronchiectasis | chronic brochial colonization | *Pseudomonas A.* | SRA |
| 22 | Motley, Retina | 2005 | USA | 1 | LE | M | 25 | choroidal abscess + EE | cystic fibrosis | lung infection on cystic fibrosis reacutization | *Pseudomonas A.* | SRA<br>vitreous<br>sputum |
| 23 | Yu, Am J Neurorad | 2005 | Canda | 1 | LE | F | 41 | SRA + EE | bone marrow transplant | systemic | *Nocardia Asteroides* | skin |
| 24 | Rafiei, Europ J Ophthalmol | 2005 | USA | 1 | LE | M | 61 | SRA + EE | idiopathic thrombocytopenia purpura | systemic | *Nocardia Asteroides* | bronchus<br>skin |
| 25 | Dodds, Ocul Imm Inflamm | 2006 | Argentina | 1 | LE | F | 26 | SRA + EE | SLE | lung, brain, cerebellum abscesses | *Nocardia Farcinica* | SRA |
| 26 | Yang, Ophthalmol | 2007 | Taiwan | 1 | Unilateral, side NA | M | 48 | SRA + EE | DM | liver abscess | *Klebsiella P.* | blood<br>liver |
| 27 | Contreras, Ret Cas Brief Rep | 2007 | Spain | 1 | BE | M | 24 | SRA + EE | acute myeloid leukemia, graft versus host disease | sepsis | *Candida A.* | blood<br>central catheter |
| 28 | Christoforidis, Ret Cas Brief Rep | 2007 | USA | 1 | RE | F | 56 | SRA + EE | DM, nephrolithiasis, peptic ulcer | kidney abscess | *Klebsiella P.* | blood<br>vitreous |
| 29 | Li, Int Ophthalmol | 2008 | China | 1 | RE | M | 75 | choroidal abscess + EE | bronchiectasis | pneumonia | *Pseudomonas A.* | enucleated eye<br>sputum |
| 30 | Jones, Eye | 2010 | UK | 1 | LE | F | 32 | SRA | bone marrow transplant (aplastic anemia) | brain, lung liver abscesses | *Nocardia Asteroides* | lymph node<br>lung |

**Table 3** (continued)

| S/N | Study | Year | Country | N of patients | Laterality | Sex | Age | Type of SRA | Co-morbidities | Systemic infective process | Causative pathogen | Method of identification |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 31 | Trigui, Int Ophthalmol | 2011 | Tunisia | 1 | LE | M | 27 | SRA + EE | DM | sepsis | *S. aureus* | skin |
| 32 | Eschle-Meniconi, Surv Ophthalmol | 2011 | Switzerland | 1 | LE | M | 78 | SRA + EE | prostate ca, Hodgkin lymphoma | brain multiple abscesses, UTI | *Nocardia Asteroides* | SRA |
| 33 | Gupta, Ret Cas Brief Rep | 2012 | USA | 1 | LE | M | 89 | chorio-retinal abscess + EE | colon ca, prostate ca, HBP | soft tissue | *Pseudomonas A.* | conjunctiva blood |
| 34 | Peeler, J Neuro-ophthalmol | 2013 | USA | 2 | BE | M | 16 | SRA + EE | none | sepsis with CNS infacrtions | *S. aureus* | blood, skin, pericardial fluid, hip |
| | | | | | RE | F | 62 | SRA + EE | necrotizing pancreatitis | entero-cutaneous fistula, brain abscess | *Bacillus* | blood |
| 35 | Eisenberg, Ret Cas Brief Rep | 2014 | USA | 1 | RE | M | 40 | SRA | acute myeloid leukemia | systemic | *Nocardia Asteroides* | skin |
| 36 | Arai, Clin Ophthalmol | 2014 | Japan | 1 | BE | M | 64 | SRA (vitreous not described) | rheumatoid arthritis, rectal ca, pericarditis | pneumonia | *Candida A.* | exenteratio |
| 37 | Siu, BMJ Cas Rep | 2015 | China | 1 | LE | M | 43 | SRA | DM | liver abscess | *Klebsiella P.* | blood |
| 38 | Shetty, Indian J Ophthalmol | 2015 | India | 1 | LE | F | 33 | SRA | none | lung TB | *Mycobacterium TB* | a |
| 39 | Silva, Retina | 2015 | USA | 3 | RE | M | 45 | SRA | acute lymphoblastic leukemia | pneumonia | *Nocardia Cyriacigeorgica* | SRA |
| | | | | | LE | F | 51 | SRA + EE | SLE | systemic | *Nocardia Farcinica* | SRA |
| | | | | | LE | F | 21 | SRA | IgA nephropathy | lung abscess | *Nocardia Farcinica* | SRA |
| 40 | Won Jin, Optom Vis Sci | 2015 | Korea | 1 | BE | M | 59 | SRA + EE | none | prostate abscess | *Klebsiella P.* | vitreous |
| 41 | Richards, Clin Exp Ophthalmol | 2015 | Australia | 1 | BE | M | 80 | SRA + EE | DM, previous syphilis, hepatitis B | liver and cerebral abscesses | *Nocardia Beijingensis* | SRA |
| 42 | Tsai, BMC Ophthalmol | 2015 | Taiwan | 1 | LE | M | 56 | SRA + EE | DM | liver and subdural abscess | not isolated | |
| 43 | Kamath, BMK | 2016 | India | 1 | RE | M | 28 | SRA + EE | TB, DM | muscle abscess | *Mycobacterium TB* | muscle |
| 44 | Schlaenm Ret Cas Brief Rep | 2016 | Argentina | 1 | RE | M | 47 | SRA + EE | acute myeloid leukemia | sepsis | *Fusarium Solani* | vitreous |
| 45 | Venkatesh, Int J Ret Vitr | 2016 | India | 1 | LE | F | 30 | SRA + EE | none | cellulitis | not isolated | – |

**Table 3** (continued)

| S/N | Study | Year | Country | N of patients | Laterality | Sex | Age | Type of SRA | Co-morbidities | Systemic infective process | Causative pathogen | Method of identification |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 46 | Soria, Cas Rep Ophthalmol | 2016 | Argentina | 1 | LE | M | 24 | SRA (vitreous not described) | none | miliary TB | *Mycobacterium TB* | lymph node |
| 47 | Martel, J Fran Ophtalmol | 2017 | France | 1 | LE | M | 60 | SRA + EE | DM | liver and UTI | *Klebsiella P.* | blood urine |
| 48 | Ganesh, Indian J Ophthalmol | 2017 | India | 1 | BE | M | 37 | SRA + EE | none | lung TB | *Mycobacterium TB* | vitreous |
| 49 | Kimura, Cas Rep Ophthal | 2017 | Japan | 1 | BE | M | 62 | SRA + EE | hepatitis, liver abscess, spondylosis, disseminated intravascular coagulation | | *Klebsiella P.* | liver abscess blood |
| 50 | Boonsopon, J Med Cas Rep | 2017 | Thailand | 1 | RE | F | 29 | SRA + EE | HIV | lung TB | *Mycobacterium TB* | conjunctiva |
| 51 | Pittenger, BMJ | 2017 | USA | 1 | RE | M | 32 | SRA (vitreous not described) | IV drug use | endocharditis | *S. aureus* | blood |
| 52 | Fortun, Ophthal Surg Las | 2017 | USA | 7 | RE | F | 14 | SRA | healthy | myositis, ostemyelitis | *S. aureus* (all) | blood |
| | | | | | BE | M | 32 | SRA + EE | HIV | cellulitis | | skin |
| | | | | | LE | M | 47 | SRA + EE | DM | cellulitis, osteomyelitis | | toe |
| | | | | | RE | M | 78 | SRA + EE | DM | cellulitis | | sacral abscess |
| | | | | | BE | F | 62 | SRA + EE | breast ca | sepsis | | blood |
| | | | | | BE | M | 64 | SRA + EE | DM | ostemyelitis | | finger |
| | | | | | BE | F | 51 | SRA + EE | DM | paraspinal abscess, | | blood |
| 53 | Oduard, Clin Exp Ophthalmol | 2017 | Australia | 2 | RE | M | 58 | SRA + EE | DM, HBP, hypercholesterolemia | hepatic abscess | *Klebsiella P.* | blood, liver |
| | | | | | BE | M | 51 | SRA + EE | hypercholesterolemia | hepatic abscess | *Klebsiella P.* | liver, urine |
| 54 | Pappuru, Int Ophthalmol | 2017 | India | 1 | LE | F | 26 | SRA | none | lung TB | *Mycobacterium TB* | a |
| 55 | Bendhe, J Ophthal Inflamm Infect | 2017 | India | 1 | LE | M | 74 | SRA + EE | DM | UTI, septicemia | *Roseomonas mucosa* | SRA |

**Table 3** (continued)

| S/N | Study | Year | Country | N of patients | Laterality | Sex | Age | Type of SRA | Co-morbidities | Systemic infective process | Causative pathogen | Method of identification |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 56 | Dutta-Majumder, Ocul Imm Inflamm | 2018 | India | 12 | Unilateral, side NA | F | 25 | SRA + EE | healthy | TB | *Mycobacterium TB* (all) | acqueous |
| | | | | | Unilateral, side NA | M | 14 | SRA + EE | lung TB | lung TB | | acqueous |
| | | | | | Unilateral, side NA | M | 45 | SRA + EE | healthy | TB | | acqueous, vitreous |
| | | | | | Unilateral, side NA | M | 22 | SRA + EE | lung TB | lung TB | | a |
| | | | | | Unilateral, side NA | M | 23 | SRA + EE | lung TB | lung TB | | a |
| | | | | | Unilateral, side NA | M | 15 | SRA + EE | healthy | lung TB | | acqueous |
| | | | | | Unilateral, side NA | F | 26 | SRA + EE | lung TB | lung TB | | vitreous |
| | | | | | Unilateral, side NA | F | 17 | SRA + EE | lung TB | lung TB | | vitreous |
| | | | | | Unilateral, side NA | F | 19 | SRA + EE | healthy | TB | | acqueous |
| | | | | | Unilateral, side NA | M | 29 | SRA + EE | healthy | TB | | acqueous, vitreous |
| | | | | | Unilateral, side NA | M | 62 | SRA + EE | healthy | lung TB | | a |
| | | | | | Unilateral, side NA | F | 60 | SRA + EE | healthy | lung TB | | a |
| 57 | Harvey, BMJ Cas rep | 2018 | UK | 1 | LE | M | 26 | SRA + EE | DM | sepsis, muscle abscess | *S. aureus* | blood |
| 58 | Prajapati, BMJ Cas Rep | 2018 | UK | 1 | RE | M | – | SRA + EE | HIV | glomerulonephritis, sepsis | *S. aureus* | blood |
| 59 | Zafar, BMC Res Not | 2018 | Pakistan | 1 | RE | F | 32 | SRA + EE | none | vaginal infection | *Candida A.* | vitreous |
| 60 | Chawla, Middle East Afr J Ophthalmol | 2018 | India | 1 | BE | M | 47 | SRA + EE | none | lung TB | *Mycobacterium TB* | cervical lymph node |

**Table 3** (continued)

| S/N | Study | Year | Country | N of patients | Laterality | Sex | Age | Type of SRA | Co-morbidities | Systemic infective process | Causative pathogen | Method of identification |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 61 | Puri, Am J Ophthalmol | 2018 | USA | 1 | RE | F | 49 | SRA + EE | bullous pemphigoid | systemic | *Nocardia Farcinica* | brain |
| 62 | Xu, BMC Ophthalmol | 2018 | China | 1 | LE | M | 58 | SRA + EE | DM, nephrotic syndrome | pneumonia with lung abscess | *Nocardia* | blood sputum |
| 63 | Tran, Clin Exp Ophthal | 2019 | Australia | 1 | LE | M | 37 | SRA + EE | Hodgkin's Lymphoma | systemic | *Nocardia Farcinica* | brain |
| 64 | Scavelli, Am J Cas Rep | 2019 | USA | 1 | LE | F | 25 | SRA + EE | SLE | systemic | *Nocardia Farcinica* | blood |
| 65 | Manoharam, JRSM Open | 2019 | UK | 1 | LE | M | 41 | SRA + EE | chronic pancreatitis, vitamin D deficiency | splenic abscess, sepsis | *Proteus Mirabilis*, *Enterococcus Faecium*, *E. coli* | blood |
| 66 | Mohd-Ilham, Cureus | 2019 | Malaysia | 1 | RE | F | 39 | SRA + EE | DM, recurrent UTI | Pyelonephritis, sepsis | *Klebsiella P.* | blood |
| 67 | Angermann, Ocul Imm Inflamm | 2019 | Austria | 1 | LE | M | 56 | SRA + EE | brain astrocytoma | systemic | *Nocardia Cyriacigeorgica* | vitreous SRA |
| 68 | Dogra, Ocul Imm Inflamm | 2020 | India | 1 | LE | M | 48 | SRA + EE | hepatitis C, liver cirrhosis | UTI | *Klebsiella P.* | urine vitreous |
| 69 | Yiesiltas, Ocular Imm Inflamm | 2020 | Turkey | 1 | LE | M | 40 | SRA + EE | none | onychomycosis | *Candida A.* | vitreous |
| 70 | Shen, Retina | 2020 | Canada | 1 | RE | M | 28 | SRA (vitreous not described) | IV drug use | Endocarditis, lung septic emboli, MRSA bacteremia | *Klebsiella P.* | blood |
| 71 | Hojjatie, J Ophthalmic Inflamm Infect | 2020 | USA | 1 | RE | M | 64 | SRA + EE | liver transplant | pneumonia | *Nocardia Farcinica* | BAL |
| 72 | Vamsidhar, J R Coll Physicians Edinb | 2020 | India | 1 | BE | M | 31 | SRA (vitreous not described) | none | systemic | *S. aureus* | blood muscle |
| 73 | Lim, Case Rep Ophthalmol Med | 2020 | Korea | 2 | LE | F | 50 | SRA + EE | DM | liver abscess | *Klebsiella P.* | blood, liver |
| | | | | | RE | F | 62 | SRA + EE | DM | liver abscess | not isolated | – |
| 74 | Nair, Indian J Ophthalmol | 2020 | India | 1 | RE | M | 25 | SRA + EE | none | systemic | *Mycobacterium TB* | lung |
| 75 | Kapoor, Indian J Ophthalmol | 2020 | India | 1 | LE | F | 80 | SRA + EE | DM, HBP | perinephric abscess | not isolated | – |

**Table 3** (continued)

| S/N | Study | Year | Country | N of patients | Laterality | Sex | Age | Type of SRA | Co-morbidities | Systemic infective process | Causative pathogen | Method of identification |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 76 | Malik, BMJ Cas Rep | 2020 | Pakistan | 1 | RE | M | 50 | SRA + EE | demyelinating polyneuropathy | systemic | *Nocardia* | blood<br>BAL |
| 77 | Fan, Ret Cas Brief Rep | 2020 | USA | 1 | LE | M | 46 | SRA + EE | none | liver and splenic abscess | *Klebsiella P.* | vitreous |
| 78 | Cunha, Ret Cas Brief Rep | 2021 | Portugal | 1 | LE | M | 50 | SRA | lung silicosis | systemic | *Nocardia Abscessus* | bronchus |

*S/N* Study number, *RE* Right eye, *LE* Left eye, *BE* Both eyes, *M* Male, *F* Female, *SRA* Subretinal abscess, *EE* Endogenous endophthalmitis, *IV* Intravenous, *DM* Diabetes mellitus, *UTI* Urinary tract infection, *HBP* High blood pressure, *TB* Tuberculosis, *SLE* Systemic lupus erythematosus, *ca* Cancer, *CNS* Central nervous system

[a] Diagnosis based on typical imaging findings and positive Q-gold test

**Table 4** Summary of initial and final visual acuity, treatment interventions and final outcomes of SRA with systemic foci

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 1 | Manor, Ophthalmologica | not isolated | 1.0 | 0 | - systemic antibiotics (not specified)<br>- retrobulbar depomedrol | better VA |
| 2 | Davidson, Trans Am Ac Ophthalmol | *Nocardia Asteroides* | N/A | – | - systemic steroids<br>- topical steroids<br>- enucleation | enucleated |
| 3 | Fleming, Can J Ophthalmol | *Candida Albicans* | N/A | – | systemic antibiotics (not specified) | N/A |
| 4 | Naidoff, Am J Ophthalmol | *Aspergillus Fumigatus* | 2.7 | – | - intravenous amphotericin<br>- intravitreal amphotericin<br>- topical steroid<br>- enucleation | enucleated |
| 5 | Hiss, Ophthalmology | *Criptococcus Neoformans* | 0.5 | 2.7 | - intravitreal amphotericin<br>- intravenous amphotericin<br>- oral 5-fluorocytosine<br>- scleral buckling | worse VA |
| 6 | Mamalis, Ann Ophthalmol | *Nocardia Asteroides* | 1.4 | 2.3 | intravenous salfadiazine and sulfisoxazole | worse VA |
| 7 | Gregor, Retina | *Nocardia Asteroides* | 1.9 | 0.3 | - intravenous amphotericin<br>- oral 5 fluorocytosine<br>- intravenous thrimetoprim-sulfametoxazole | better VA |
| 8 | Coll, Retina | *S. aureus* | 1.9 | 1.3 | intravenous antibiotics for endocarditis (oxacillin and gentamicin) | better VA |
| 9 | Webber, British J Ophthalmol | *Pseudomonas A.* | 2.3 | 2.3 | - systemic amphotericin and ganciclovir<br>- 1$^{st}$ vitrectomy<br>- SRA drainage + intravitreal amikacin, vancomycin and amphotericin B<br>- intravitreal colomycin<br>- intravenous imipenem<br>- 2$^{nd}$ vitrectomy + lensectomy + silicone oil + encircling | same VA |
| 10 | Biswas, Retina | *Mycobacterium TB*<br>*Mycobacterium TB* | 0.5<br>2.3 | –<br>0.6 | - oral prednisolone<br>- topical steroids<br>- periocular hydrocortisone<br>- 1$^{st}$ vitrectomy + lensectomy<br>- intravitreal cefazolin, gentamicin and dexamethasone<br>- 2$^{nd}$ vitrectomy<br>- ATT<br>- evisceration<br>- ATT<br>- topical steroid + atropine | eviscerated<br>better VA |
| 11 | Jolly, Arch Ophthalmol | *Nocardia Asteroides* | N/A | N/A | intravenous trimethoprim-sulfamethoxazole and amikacin | N/A |

**Table 4** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 12 | Yarng, Ophthal Surg Las Im | *Klebsiella P.* | 2.3 | 1.6 | - intravenous cefonicid, gentamicin, amikacin and cefazolin<br>- intravitreal cefazolin and amikacin × 6<br>- 6 x intravitreal dexamethasone<br>- vitrectomy + silicone oil + lensectomy + SRA drainage + buckle | better VA |
| 13 | Rimpel, British J Ophthalmol | *Streptococcus Viridans* | 2.7 | – | - intravenous vancomycin and ceftazidime<br>- 3 x intravitreal vancomycin<br>- evisceratio | eviscerated |
| 14 | Lakosha, Retina | *Nocardia Farcinica* | 0 | 2.3 | trimethoprim-sulfametoxazole | worse VA |
| 15 | Harris, Am J Ophthalmol | *Klebsiella P.* | 0.2 | 0.2 | - ampicillin, gentamicin, and metronidazole, then piperacillin-tazobactam, gentamicin, then ceftriaxone,<br>gentamicin, and metronidazole<br>- intravitreal amikacin and vancomycin<br>- vitrectomy + SRA removal + amikacin + lensectomy<br>- topical prednisolone and ciprofloxacin<br>- oral prednisone<br>- 2$^{nd}$ vitrectomy + endolaser | same VA |
| 16 | Costen, Eye | *Streptococcus Pyogenes* | 0.3; 0.5 | 0.2; 0.2 | - intravenous ceftriazone, amoxicillin, benzylpenicillin, cephradine - oral chloramphenicol, clindamycin, ciprofloxacin | BE better VA |
| 17 | Yao, Eur J Pediatr | *Klebsiella P.* | N/A | 1.9 | - AC irrigation + vitrectomy + intravitreal vancomicyn and amikacin + intravitreal dexamethasone<br>- intravenous ceftriaxone<br>- 2$^{nd}$ vitrectomy + SRA drainage<br>- 3$^{rd}$ vitrectomy + buckle + silicone oil | N/A |
| 18 | Yoon, Retina | *Klebsiella P.* | 2.3 | 1.9 | - intravitreal amikacin and ceftazidime<br>- 1$^{st}$ vitrectomy + SRA drainage<br>- 2$^{nd}$ vitrectomy +silicone oil | better VA |
| | | *Klebsiella P.* | 0.4; 0.7 | 1.5; 1.4 | - BE intravitreal vancomycin and amikacin<br>- vitrectomy + SRA drainage | BE worse VA |

**Table 4** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 19 | Bozbeyoglu, Retina | *Nocardia Asteroides* | 0.3 | 2.3 | - intravenous amphotericin, cefotaxime, amikacin, trimethoprim–sulfamethoxazole<br>- intravitreal amphotericin | worse VA |
| 20 | Shah, Indian J Ophthalmol | *Candida A.* | 1.9; 1.9 | 0.8; 0.8 | - BE intravitreal amphotericin<br>- oral itraconazole<br>- topical natamycin | BE better VA |
| 21 | Wjjesekera, Eye | *Pseudomonas A.* | 0 | – | - dexamethasone drops<br>- isoniazid and pyridoxine<br>- intravitreal amikacin and vancomycin<br>- vitrectomy + intravitreal amikacin and vancomycin<br>- oral steroids and oral ciprofloxacin<br>- evisceratio | eviscerated |
| 22 | Motley, Retina | *Pseudomonas A.* | 0.5 | – | - topical prednisolone and ketorolac<br>- vitrectomy + intravitreal vancomycin, ceftazidime, and amphotericin<br>- intravenous ceftazidime and tobramycin<br>- 2 x intravitreal and subconjunctival ceftazidime, tobramycin and vancomycin<br>- 2$^{nd}$ vitrectomy + trans-scleral drainage + silicon oil<br>- 3$^{rd}$ vitrectomy + SRA endoresection + silicone oil<br>- enucleation | enucleated |
| 23 | Yu, Am J Neurorad | *Nocardia Asteroides* | 2.3 | – | - antiviral therapy (not specified)<br>- vitrectomy<br>- enucleation | enucleated |
| 24 | Rafiei, Europ J Ophthalmol | *Nocardia Asteroides* | 1.9 | 2.3 | - systemic cotrimoxazole, linezolid, ciprofloxacin<br>- topical cycloplegic and steroids | worse VA |
| 25 | Dodds, Ocul Imm Inflamm | *Nocardia Farcinica* | 1.9 | – | - intravenous ceftriaxone, clyndamicin, and fluconazole. Then intravenous trimethoprim -sulfamethoxazole<br>- intravitreal amikacin<br>- vitrectomy + SRA aspiration<br>- oral ciprofloxacin | N/A |
| 26 | Yang, Ophthalmol | *Klebsiella P.* | N/A | 1.0 | - intravenous cephalosporin and aminoglycoside<br>- intravitreal antibiotics | N/A |
| 27 | Contreras, Ret Cas Brief Rep | *Candida A.* | 0.4; 1.9 | 0.1; 0.7 | intravenous caspofungin | BE better VA |

**Table 4** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 28 | Christoforidis, Ret Cas Brief Rep | *Klebsiella P.* | 2.3 | 0.4 | - intravitreal vancomycin, ceftazidime and dexamethasone<br>- oral prednisone<br>- topical atropine, prednisolone<br>- vitrectomy + intravitreal vancomycin and ceftazidime<br>- intravitreal ceftriaxone<br>- 2$^{nd}$ vitrectomy + SRA drainage + intravitreal ceftazidime<br>- 3$^{rd}$ vitrectomy + scleral buckle | better VA |
| 29 | Li, Int Ophthalmol | *Pseudomonas A.* | 2.3 | – | - intravenous ticarcillin and clavulanate, gentamicin<br>- topical levofloxacin<br>- enucleation | enucleated |
| 30 | Jones, Eye | *Nocardia Asteroides* | 2.3 | 1.6 | - intravitreal amikacin and vancomycin<br>- systemic cotrimoxazole, linezolid and ciprofloxacin | better VA |
| 31 | Trigui, Int Ophthalmol | *S. aureus* | 0.7 | 0 | - intravenous ceftriaxone | better VA |
| 32 | Eschle-Meniconi, Surv Ophthalmol | *Nocardia Asteroides* | 2.3 | 0.1 | - intravenous ceftriaxone, clarithromycin and trimethoprim-sulfamethaxozole<br>- vitrectomy + retinectomy + SRA aspiration + silicone oil | better VA |
| 33 | Gupta, Ret Cas Brief Rep | *Pseudomonas A.* | 2.3 | 1.9 | - topical ciprofloxacin and gentamicin, then topical ceftazidime and tobramycin<br>- oral cephalexin<br>- intravenous piperacillin–tazobactam, vancomycin and tobramycin | better VA |
| 34 | Peeler, J Neuro-ophthalmol | *S. aureus* | 2.3; 0 | 1; 0 | - intravenous rifampin, nafcillin, and gentamicin<br>- intravitreal vancomycin × 2 and ceftazidime | RE: better; LE: same |
| | | *Bacillus* | 1.9 | 2.3 | - intravenous vancomycin, cefepime, metronidazole, voriconazole, levofloxacin<br>- intravitreal vancomycin × 2 and ceftazidime × 2<br>- topical moxifloxacin, prednisolone, atropin | worse VA |
| 35 | Eisenberg, Ret Cas Brief Rep | *Nocardia Asteroides* | 0.7 | 0.3 | - intravitreal vancomycin and × 2 amikacin-<br>- systemic vancomycin, sulfamethoxazole/trimethoprim and meropenem | better VA |

**Table 4** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 36 | Arai, Clin Ophthalmol | *Candida A.* | 0; 1.4 | 1.7; – | - intravenous acetylspiramycin + valganciclovir<br>- LE vitrectomy<br>- imipenem/cilastatin, amikacin and levofloxacin<br>- LE intravitreal ceftazidime, vancomycin and voriconazole<br>- LE exenteratio<br>- systemic fosofluconazole<br>- RE 3 x intravitreal ceftazidime, vancomycin and voriconazole<br>- RE vitrectomy + phaco + silicone oil | RE: worse VA; LE eviscerated |
| 37 | Siu, BMJ Cas Rep | *Klebsiella P.* | 0 | 1 | - intravenous piperacillin/tazobactam, amoxicillin/clavulanate, ceftriazone<br>- oral ciprofloxacin<br>- intravitreal amikacin and ceftazidime<br>- 1st vitrectomy + SRA + silicone oil + intravitreal vancomycin and ceftazidime<br>- encircling band + 2nd vitrectomy + silicone oil + phaco | worse VA |
| 38 | Shetty, Indian J Ophthalmol | *Mycobacterium TB* | 0.2 | 0.9 | - IV methyl prednisolone, then oral prednisolone<br>- ATT + oral steroids | worse VA |
| 39 | Silva, Retina | *Nocardia Cyriacigeorgica* | 0 | 0.1 | - vitrectomy + retinotomy + SRA biopsy<br>- systemic TMP-SMX and intravenous ertapenem<br>- × 4 intravitreal amikacin | worse VA |
| | | *Nocardia Farcinica* | 1.4 | 2.3 | - 1st vitrectomy + lensectomy + SRA biopsy + intravitreal Vancomycin, amikacin, amphotericin<br>- systemic thrimetoprim.-sulfamethoxazole + oral ciprofloxacin and amikacin<br>- 2nd vitrectomy + silicone oil | worse VA |
| | | *Nocardia Farcinica* | 0.7 | – | - pyrimethamine, sulfonamide, and folinic acid<br>- vitrectomy + SRA biopsy<br>- intravenous TMP-SMX, ceftriaxone and amikacin<br>- × 3 intravitreal amikacin<br>- enucleation | enucleated |

**Table 4** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 40 | Won Jin, Optom Vis Sci | *Klebsiella P.* | 0.7; 1.2 | 0; 3 | - intravenous acyclovir, ceftazidime + oral prednisolone<br>- LE vitrectomy + intravitreal vancomycin and ceftazidime<br>- intravenous Ceftazidime<br>- RE intravitreal vancomycin and ceftazidime<br>- oral levofloxacin<br>- intravitreal ceftazidime × 3 RE and ×1 LE | RE: better VA; LE: worse VA |
| 41 | Richards, Clin Exp Ophthalmol | *Nocardia Beijingensis* | 0.2; 2.3 | 0.3; 2.3 | - oral prednisolone<br>- LE vitrectomy + silicone oil + subretinal biopsy<br>- systemic meropenem, ceftriaxone, trimethoprim-sulphamethoxazole and amikacin<br>- RE 3 x intravitreal amikacin | RE worse VA; LE same VE |
| 42 | Tsai, BMC Ophthalmol | not isolated | N/A | 0 | - vitrectomy + intravitreal ceftazidime and amikacin<br>- intravenous ceftriaxone | N/A |
| 43 | Kamath, BMK | *Mycobacterium TB* | 1.8 | N/A | - ATT (rifampicin, pyrazinamide, isoniazid and ethambutol)<br>- oral steroids | N/A |
| 44 | Schlaenm Ret Cas Brief Rep | *Fusarium Solani* | 1.9 | N/A | - systemic piperaciline, tazobactam, imipenem, voriconazole<br>- vitrectomy + SRA drainage + intravitreal amphotericin and voriconazole<br>- intravenous amphotericin | N/A |
| 45 | Venkatesh, Int J Ret Vitr | not isolated | 1.9 | 0.6 | - intravenous vancomycin and ceftriaxone<br>- intravitreal vancomycin and ceftazidime<br>- vitrectomy + SRA intralesional vancomicin | better VA |
| 46 | Soria, Cas Rep Ophthalmol | *Mycobacterium TB* | 1.9 | 1.9 | ATT (isoniazid, rifampin, pyrazinamide, and ethambutol) | same VA |
| 47 | Martel, J Fran Ophtalmol | *Klebsiella P.* | 0.2 | 0 | - IV ceftriaxone and amikacin, then levofloxacin<br>- intravitreal 13 x ceftazidime and 7 x vancomicin<br>- dexamethasone drops | better VA |
| 48 | Ganesh, Indian J Ophthalmol | *Mycobacterium TB* | 1.0; 0.3 | 1.5; 0.2 | - ATT (isoniazid, rifampicin, pyrazinamide) + oral steroids<br>- azathioprine + intravenous steroids<br>- vitrectomy | RE worse VA; LE better VA |
| 49 | Kimura, Cas Rep Ophthal | *Klebsiella P.* | N/A | 3.0; 1.7 | - BE intravitreal ceftazidime<br>- intravenous linezolid<br>- LE vitrectomy + silicone oil | N/A |

**Table 4** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 50 | Boonsopon, J Med Cas Rep | *Mycobacterium TB* | 3.0 | – | - isoniazid, rifampicin, pyrazinamide and ethambutol<br>- intravenous amikacin, levofloxacin, oral clarithromycin and para-aminosalicylic acid<br>- intravenous ceftriaxone, oral ciprofloxacin<br>- exenteratio | exenterated |
| 51 | Pittenger, BMJ | *S. aureus* | N/A | 0 | - intravenous vancomycin<br>- intravitreal vancomycin and ceftazidime | N/A |
| 52 | Fortun, Ophthal Surg Las | *S. aureus* (all) | N/A | 0 | - systemic vancomicyn and gentamicin | N/A |
| | | | 0; 1 | 0; 0 | - intravitreal vancomicyn and foscarnet<br>- systemic trimetoprim-sulphametoxazole | RE same VA; LE better VA |
| | | | 1 | 0.4 | - intravitreal vancomycin and ceftazidime<br>- systemic vancomycin | better VA |
| | | | 1.7 | 1.7 | - intravitreal vancomycin, ceftazidime and foscarnet<br>- systemic trimethoprim-sulfamethoxazole and foscarnet | same VA |
| | | | 0; 1.7 | 0; 0 | - intravitreal vancomycin<br>- systemic vancomycin | RE same VA; LE better VA |
| | | | 0.5; 1.9 | 0.6; 1.2 | - intravitreal vancomycin and ceftazidime<br>- systemic trimethoprim-sulfamethoxazole and vancomycin | |
| | | | N/A; N/A | 1.2; 3 | - intravitreal vancomycin and ceftazidime<br>- systemic vancomycin<br>- RE vitrectomy + buckling + silicone oil | N/A |
| 53 | Oduard, Clin Exp Ophthalmol | *Klebsiella P.*<br>*Klebsiella P.* | 1.9 | 0.5 | - intravitreal ceftazidime × 2 and vancomycin<br>- intravenous ceftriaxone<br>- topical prednisolone and phenylephrine<br>- vitrectomy + SRA drainage + silicone oil | better VA |
| | | | 0.3; 2.3 | 0.3; 0.6 | - BE intravitreal vancomycin and ceftazidime: RE × 4 and LE × 5<br>- BE intravitreal dexamethasone: RE × 4 and LE × 5<br>- intravenous ceftriaxone<br>- oral steroid<br>- BE topical steroid<br>- RE 1st vitrectomy<br>- RE 2nd vitrectomy + SRA drainage + silicone oil<br>- LE vitrectomy + SRA drainage + silicone oil | RE same VA; LE better VA |

**Table 4** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 54 | Pappuru, Int Ophthalmol | *Mycobacterium TB* | 1.8 | 0.3 | - ATT<br>- oral steroids | better VA |
| 55 | Bendhe, J Ophthal Inflamm Infect | *Roseomonas Mucosa* | 1.9 | 1.3 | - 2 x intravitreal ceftazidime and vancomycin<br>- oral cefotaxime<br>- topical moxifloxacin, tobramycin, homatropine and prednisolone<br>- vitrectomy + SRA drainage + silicone oil | better VA |
| 56 | Dutta-Majumder, Ocul Imm Inflamm | *Mycobacterium TB* (all) | 0.8 | 0.5 | ATT, topical and oral steroid | better VA |
| | | | 1.9 | 1.3 | ATT, topical steroid | better VA |
| | | | 1.5 | 1.8 | ATT, periocular steroid | worse VA |
| | | | 2.7 | 0.5 | ATT, topical and oral steroid | better VA |
| | | | 1.9 | 0.2 | ATT, topical steroid | better VA |
| | | | 2.7 | 2.7 | ATT, topical and oral steroid | same VA |
| | | | 1.9 | 1.9 | ATT, topical and oral steroid | same VA |
| | | | 1.5 | 1.9 | ATT, topical and oral steroid | worse VA |
| | | | 0.8 | 0 | ATT, topical steroid | better VA |
| | | | 1.9 | 0.5 | ATT, topical and oral steroid | better VA |
| | | | 0.5 | 2.7 | ATT, topical and periocular steroid | worse VA |
| | | | 1.9 | 1.0 | ATT, oral steroid | better VA |
| 57 | Harvey, BMJ Cas rep | *S. aureus* | 2.3 | 1.9 | - intravenous flucloxacillin and ceftriaxone<br>- topical steroid<br>- oral antibiotics (not specified) | better VA |
| 58 | Prajapati, BMJ Cas Rep | *S. aureus* | 2.3 | 1.0 | - intravenous clindamycin, meropenem, flucloxacillin, ganciclovir<br>- oral pyrimethamine | better VA |
| 59 | Zafar, BMC Res Not | *Candida A.* | 1.9 | N/A | - intravitreal amphotericin<br>- vitrectomy + intravitreal amphotericin<br>- oral voriconazole | N/A |
| 60 | Chawla, Middle East Afr J Ophthalmol | *Mycobacterium TB* | 1; 1.8 | 0.3; 1.5 | - oral ATT (isoniazid, rifampicin, ethambutol, and pyrazinamide)<br>- topical steroid and cycloplegic | BE better VA |
| 61 | Puri, Am J Ophthalmol | *Nocardia Farcinica* | N/A | 0.7 | - intravenous vancomycin, piperacillin-tazobactam and micafungin<br>- intravitreal amikacin<br>- oral bactrim and augmentin | N/A |

**Table 4** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 62 | Xu, BMC Ophthalmol | *Nocardia* | 1.9 | 1.0 | - intravitreal vancomycin and ceftazidime<br>- topical levofloxacine and steroids<br>- oral trimethoprim and sulfamethoxazole + oral prednisone | better VA |
| 63 | Tran, Clin Exp Ophthal | *Nocardia Farcinica* | 0.5 | – | - systemic moxifloxacin, voriconazole and amphotericin<br>- intravitreal multiple injections of voriconazole, vancomicin, ceftazidime and foscarnet<br>- evisceratio | eviscerated |
| 64 | Scavelli, Am J Cas Rep | *Nocardia Farcinica* | 1.9 | 0.3 | - systemic sulfamethoxazole/trimethoprim and imipenem<br>- intravitreal amikacin × 4 | better VA |
| 65 | Manoharam, JRSM Open | *Proteus Mirabilis*, *Enterococcus Faecium*, *E. coli* | 1.9 | 1.9 | - intravitreal vancomicin × 2, ceftazidime × 2<br>- topical antibiotics, steroid and cycloplegic drops<br>- oral antibiotics (not specified)<br>- intravenous linezolid, meropenem and fluconazole | same VA |
| 66 | Mohd-Ilham, Cureus | *Klebsiella P.* | 1.0 | 0.8 | - intravenous cefepime and ciprofloxacin<br>- intravitreal vancomycin and ceftazidime<br>- topical cefuroxime, gentamicin and dexamethasone)<br>- vitrectomy + silicone oil | better VA |
| 67 | Angermann, Ocul Imm Inflamm | *Nocardia Cyriacigeorgica* | N/A | N/A | - vitrectomy + SRA biopsy<br>- systemic trimethoprim-sulfamethoxazole | N/A |
| 3.1.4.68 | Dogra, Ocul Imm Inflamm | *Klebsiella P.* | 1.9 | 0.8 | - intravitreal vancomycin and ceftazidime<br>- topical moxifloxacin, prednisolone and cycloplegics<br>- intravenous piperacillin/tazobactam<br>- intravitreal piperacillin/tazobactam + dexamethasone | better VA |
| 69 | Yiesiltas, Ocular Imm Inflamm | *Candida A.* | 1.9 | 1.9 | - oral methylprednisone +<br>co-trimoxazole<br>- intravenous amphotericin<br>- topical steroid and cyclopentolate<br>- intravitreal voriconazole and amphotericin<br>- oral fluconazole<br>- vitrectomy + silicone oil | same VA |
| 70 | Shen, Retina | *Klebsiella P.* | 2.3 | 2.3 | - intravitreal vancomycin | same VA |

**Table 4** (continued)

| S/N | Study | Pathogen | Initial VA (logMAR) | Final VA (logMAR) | Treatment | Outcome |
|---|---|---|---|---|---|---|
| 71 | Hojjatie, J Ophthalmic Inflamm Infect | *Nocardia Farcinica* | 1.2 | 0.7 | - intravitreal voriconazole, vancomycin and amikacin<br>- topical steroids and cycloplegics<br>- vitrectomy | better VA |
| 72 | Vamsidhar, J R Coll Physicians Edinb | *S. aureus* | 1.3; 1.8 | 0.5; 0.5 | - intravenous ceftazidime, vancomycin and cloxacillin<br>- oral ATT<br>- oral cloxacillin | BE better VA |
| 73 | Lim, Case Rep Ophthalmol Med | *Klebsiella P.* | 2.3 | 1.0 | - intravenous ceftriaxone, metronidazole and amikacin<br>- intravitreal vancomycin × 1, ceftazidime × 9 and dexamethasone × 4<br>- topical antibiotics<br>- vitrectomy + intravitreal ceftazidime | better VA |
| | | not isolated | 1.9 | 2.3 | - oral moxifloxacin, intravenous ceftriaxone, amikacin and metronidazole<br>- intravitreal vancomicin, ceftazidime, ceftriaxone and dexamethasone<br>- vitrectomy + intravitreal ceftriaxone and vancomycin | better VA |
| 74 | Nair, Indian J Ophthalmol | *Mycobacterium TB* | 1.9 | 0.4 | - oral ATT (isoniazid, rifampicin, ethambutol and pyrazinamide)<br>- steroids | better VA |
| 75 | Kapoor, Indian J Ophthalmol | not isolated | 2.7 | 1.0 | - intravenous ceftriaxone<br>- intravitreal vancomicin, piperacillin and amphotericin<br>- vitrectomy | better VA |
| 76 | Malik, BMJ Cas Rep | *Nocardia* | 0.7 | 0.7 | - intravitreal amikacin, vancomicin and amphotericin<br>- intravenous amikacin and imipenem<br>- oral trimethoprim-sulfamethoxazole and linezolid<br>- vitrectomy | same VA |
| 77 | Fan, Ret Cas Brief Rep | *Klebsiella P.* | 2.3 | N/A | - vitrectomy + phaco + AC washout + intravitreal ceftazidime, vancomicine and amikacin<br>- intravenous vancomicin and cefepime<br>- enucleation | enucleated |
| 78 | Cunha, Ret Cas Brief Rep | *Nocardia Abscessus* | 0.4 | 0.3 | - systemic trimetoprim-sulfalethoxazol, imipenem and cefipime<br>- intravitreal bevacizumab | better VA |

*S/N* Study number, *RE* Right eye, *LE* Left eye, *BE* Both eyes, *M* Male, *F* Female, *SRA* Subretinal abscess, *N/A* Not available

enucleation or evisceration. Some of the cases with poor prognosis may be related to delay in diagnosis and management or to systemic factors as immunosuppressive medication intake that may have an impact on the natural history of the disease.

No standard approach exists for the management of SRA because, unlike endophthalmitis, no guidelines are available at present and there is no consensus on the various proposed therapeutic approaches. Systemic and intravitreal antibiotics/antifungals and vitrectomy are the mainstay treatment in the majority of cases, but there is no consensus on the timing of vitrectomy, which in fact differed between the two groups: in group 1 vitrectomy was performed with similar frequency as first or second line treatment, while for group 2 it was mostly performed when previous non-surgical treatments failed. While for endogenous endophthalmitis the standard of care includes vitreous biopsy and intravitreal antibiotics combined with systemic antibiotics and oral steroids (once fungal infection has been ruled out), for SRA there is no universal approach. In case of no vitreous involvement a prompt systemic treatment can achieve an excellent prognosis, but a close follow-up is essential to identify the potential progression of SRA into the vitreous cavity, needing immediate revision of the therapeutic strategy. The effectiveness of intravitreal antibiotics, including vancomycin for Gram positive and ceftazidime for Gram negative bacteria, is controversial as they may not fully penetrate into the subretinal space. Surgical treatment of SRA, including pars plana vitrectomy and abscess drainage, is considered a second-line therapy when conservative treatments are not effective. However, for very aggressive pathogens some authors advocate an early surgical intervention. Some authors adopted the technique of intralesional antibiotics, namely injection of antibiotics into the subretinal space through a small retinotomy. Compared to abscess drainage, the technique has the advantage of carrying a lower risk of retinal detachment [20, 21], but in isolated SRA it could favor the invasion of the vitreous cavity by the pathogen. Tsai and Peng suggested that if the SRA is smaller than four disc areas, pars plana vitrectomy with intravitreal antibiotic injection could be successful, whereas, in larger lesions, vitrectomy with retinectomy to remove the abscess should be considered [22]. Internal drainage of the SRA leads to resolution of the infection, but carries the risk of postoperative retinal detachment due to proliferative vitreoretinopathy and therefore should be considered in cases that fail to respond to conventional therapy. Eschle-Meniconi et al. suggested fluorescein angiography as a guide for the management strategy as it helps understanding which layer is affected by the infection and identify a potential early invasion of the vitreous: if at presentation a late leakage of the lesion is observed, it means that the retinal pigmented epithelium is disrupted and the vitreous is affected and then vitrectomy and subretinal biopsy should be performed in the first instance. If no late leakage is seen, the infection is at an initial stage and limited to the subretinal space and a trans-vitreal fine needle biopsy or vitreous tap, intravitreal antibiotics and systemic treatment are the preferred options to start with. If the patient is already under treatment for an infection site elsewhere, then a late leakage on angiography would indicate the need for intravitreal antibiotics in case of small and peripheral SRA or for vitrectomy for larger ones [23]. However, vitreous involvement in practice can be identified by clinical assessment and multimodal imaging with no need for invasive tests.

## Conclusion

Although SRA can develop even in the absence of clinically detectable systemic infectious foci it is of primary importance to perform a prompt physical examination and systemic investigations in order to identify or rule out a source of infection elsewhere or masquerading conditions. Our review showed that no universal approach exists for SRA. Systemic broad-spectrum antibiotics are of primary importance and should be used in all cases of SRA, even in the absence of vitreous involvement and of identifiable infective foci, given the high risk of an undiagnosed underlying systemic infection.

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## Publisher's Note