Glomerella cingulata endophthalmitis

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ABSTRACT

Purpose: To report a case of an exogenous endophthalmitis caused by the fungal species Glomerella cingulata.

Observations: A 71-year-old male presented with an infectious keratitis that evolved into endophthalmitis. Combined cataract extraction and pars plana vitrectomy was performed and the vitreous specimen cultured Glomerella cingulata, a variant of the Colletotrichum gloeosporioides fungal species. Despite early treatment with topical, systemic and intravitreal doses of both voriconazole and amphotericin B, the patient had a poor visual and anatomical outcome.

Conclusions and Importance: Glomerella cingulata may rarely cause endophthalmitis with devastating visual outcomes.

1. Introduction

Colletotrichum gloeosporioides (C. gloeosporioides) is a rare fungus which is known to cause an infectious keratitis.1–6 In this case report, we present a rare human case of a non-traumatic endophthalmitis caused by Glomerella cingulata (G. cingulata).

2. Case report

A 71-year-old male presented with a 10-day history of right eye irritation that had failed to respond to topical chloramphenicol and flurometholone drops prescribed by his family physician. Past ocular history included regular intravitreal anti-vascular endothelial growth factor (anti-VEGF) injections with aflibercept (2mg/0.05mL) for diabetic macular edema, the last of which was given one month prior to his presentation. There was no history of ocular trauma.

On examination, his right eye visual acuity was 20/120 unaided. A corneal scrape was negative for any micro-organisms. Confocal microscopy did not reveal any fungal elements. Despite intensive topical ofloxacin 0.1% monotherapy and oral doxycycline 100mg daily, the patient progressively worsened with development of hypopyon, anterior chamber inflammatory cells, posterior synechiae and rapidly progressing cataract (Fig. 1A) over the course of 2 weeks from his initial presentation.

A B-scan ultrasonography showed hyperechoic densities consistent with vitritis, concerning for endophthalmitis secondary to the infectious keratitis. Attempts at vitreous biopsies were unsuccessful (dry taps) and an aqueous biopsy was negative for bacterial, fungal or viral causes. The patient was treated with intravitreal ceftazidime (2.25mg/0.1ml), vancomycin (1mg/0.1ml) and voriconazole (0.05mg/0.1ml). Oral voriconazole (400mg BD) was also prescribed due to clinical suspicion of fungal infection. Subsequently, the patient developed neovascular glaucoma in his right eye, and anti-glaucomatous agents (timolol 0.5% and apraclonidine 1% drops) together with an intravitreal ranibizumab
(0.3mg/0.05ml) injection were given.

Eight weeks after his initial presentation, the patient was found to have a progressive retrolental abscess on B-scan ultrasonography, prompting a combined cataract extraction and diagnostic pars plana vitrectomy. During the cataract extraction, a large fibrous plaque on the anterior lens capsule was removed and sent for histopathology with the vitrectomy. During the cataract extraction, a large fibrous plaque on the anterior lens capsule was removed and sent for histopathology with the vitrectomy. During the cataract extraction, a large fibrous plaque on the anterior lens capsule was removed and sent for histopathology with the vitrectomy. During the cataract extraction, a large fibrous plaque on the anterior lens capsule was removed and sent for histopathology with the vitrectomy. Following vitrectomy, the eye was injected with intravitreal ceftazidime, vancomycin, voriconazole and tenecteplase (50 μg/0.1ml).

Post-operatively, the patient was commenced on topical voriconazole, ofloxacin and prednisolone drops (Fig. 1B). The oral voriconazole was tapered to 200mg daily in response to renal and hepatic dysfunction. Four-weeks post-operatively, the vitrectomy biopsy identified the fungal species G. cingulata via DNA sequencing. This was confirmed on a second vitreous sample taken 2 weeks after the initial sample. As this organism is known to colonise fruit-bearing plants, further history was undertaken, revealing that the patient was growing mangoes at his residence. He however denied any direct ocular trauma from these fruit plants. Following consultation with an infectious disease specialist, serial intravitreal amphotericin (0.005mg/0.1ml) was given fortnightly for a period of six weeks, and the patient continued on systemic voriconazole.

Post-operatively, the patient developed choroidal detachments secondary to hypotony from a small persistent superior clear corneal incision leak. Despite re-suturing, the intraocular pressure remained low (Fig. 1C) due to development of a total retinal detachment (Fig. 1D) detected two weeks post-operatively. The eye progressed to phthisis bulbi requiring enucleation where histopathology demonstrated the patient had a total retinal detachment (Fig. 2A–D).

3. Discussion

As far as the authors are aware, this is the first reported human case of an exogenous endophthalmitis with no identifiable traumatic cause due to G. cingulata. This fungal species is a plant-based opportunistic pathogen, and a variant of the C. gloeosporioides species that has been reported to arise from certain fruits such as apples, mangoes, oranges and blueberries.1–12 Some other pathogenic variants of the Colletotrichum species known to cause infectious keratitis include: C. dematium, C. coccodes, C. graminicola, C. crassipes and C. truncatum.2,3,13 Other variants of the Glomerella species are also known including G. truncatum, G.acutata and G.magna, but these have not been reported to cause ocular infections.8,14–16 Ocular infections caused by C. gloeosporioides species have been reported (Table 1), but unlike our case these were predominantly associated with trauma. The only identifiable risk factors the patient had for an exogenous cause were his background of regular intravitreal aflibercept injections and his residential plantation of tropical mangoes which has been reported to be a source for C. gloeosporioides species, a pathogen that spreads via airborne spores.7,11,17 It is unlikely that the intravitreal aflibercept injections were contributory as the most recent injection was one month prior to initial presentation. However, a traumatic cause cannot be completely excluded as it is possible for the patient to have had a micro-trauma to the cornea. There was a reported case of a Glomerella genus endophthalmitis found in the literature, but the specific species was unidentified.1 This case had a favorable outcome following penetrating keratoplasty, vitrectomy, topical natamycin and intracameral and systemic voriconazole.

The management of the current case proved to be challenging in part due to the clinical presentation, a delay in culturing of the target organism, a poor fundus view from a dense fibrous pupillary plaque, and the absence of definitive effective antimicrobial treatment guidelines due to its rare occurrence.

Previous case studies on the treatment of fungal keratitis secondary to Colletotrichum species revealed mixed results (Table 1). Different variants were treated with different combinations of intravitreal, topical and systemic anti-fungal agents with the addition of either a keratoplasty or a vitrectomy as a definitive procedure for the removal of the fungal pathogens.1,4–6,13,20,23 Most studies have demonstrated that C. gloeosporioides is generally sensitive to amphotericin B and mixed responses to natamycin, suggesting that amphotericin B should be considered as first line therapy with this particular pathogen species. Unfortunately, the medical treatments options in our case became limited due to the patient developing significant renal and hepatic dysfunction from the systemic medications.

A case series on the management of filamentous fungal keratitis that had evolved into endophthalmitis suggested that aggressive early surgical management resulted in improved visual outcomes as 3 out of the 5 patients treated had a final best-corrected visual acuity of 20/20 after treatment.1 Currently there is no definitive treatment guidelines for the Colletotrichum species especially G. cingulata, which highlights the importance of further studies to obtain a better understanding of the pathogen regarding its pathogenesis in order to provide an effective treatment regimen.

Fig. 1. (A) Anterior segment photo of the patient’s right eye on initial presentation showing a temporal area of corneal thinning with an adjacent stromal plaque infiltrate and hypopyon. (B) Two weeks following cataract extraction combined with vitrectomy and intravitreal voriconazole, vancomycin plus ceftazidime, the corneal infiltrate is larger with re-sidual anterior vitreous abscess and hypopyon. (C) Two months post-operatively there is persistent hypotony due to phthisis bulbi; (D) B-scan ultrasonography shows an inoperable total retinal detachment.
Fig. 2. Histological haematoxylin and eosin stained slides of the enucleated globe showing the total retinal detachment at different sections of the globe. (A) Anterior segment including cornea (fold artefactual) (#), iris (λ), and retinal detachment (\(<\)) (x20); (B) anterior segment including the ciliary body (β) and cornea (α) (x20); (C) optic nerve with detached retina projecting into vitreous cavity (*) (x20); and (D) posterior sclera and overlying choroid (^) with retinal detachment (x40).

Table 1
A Summary of reported cases of keratitis and endophthalmitis caused by *C. gloesporioides* species\(^1,2,5,6,18-22\)

| Author/Year         | Organism(s)     | Risk factors                                                                 | Type of infection | Treatment                                                                                     | Outcomes                                                                 |
|---------------------|-----------------|------------------------------------------------------------------------------|-------------------|-----------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| Yamamoto et al., 2001 | *C. gloesporioides* | Cataract surgery (6 months ago)                                               | Keratitis         | Natamycin 5% Fluconazole drops and systemic Either: Amphotericin B 0.15% Natamycin 5% Itraconazole | Effective in resolving keratitis                                         |
| Fernandez et al., 2002 | *C. gloesporioides* | Trauma plant based liquid or branch Insulin dependent diabetes mellitus (IDDM) | Keratitis         | Amphotericin B 0.15% Natamycin 5% Itraconazole                                               | All cases sensitive to Amphotericin B and some cases sensitive to Natamycin |
| Shivaprakash et al., 2011 | *C. truncatum* | Wooden stick trauma Vegetable matter Insect fall Subconjunctival dexamethasone injection | Keratitis         | Amphotericin B 0.15% Natamycin 5% Itraconazole                                               | Effective with Amphotericin B plus Natamycin Plus systemic Antifungal therapy – Treatment duration ranged from 30 to 150 days |
| Shiraishi et al., 2011 | *C. gloesporioides* | Trauma from organic matter Trauma from sugarcane tree Plus immunosuppression | Keratitis         | Topical Voriconazole and Natamycin ointments Topical Fluconazole, Natamycin, Gentamicin PLUS Oral | Resolution in 2–3 weeks with sensitivities to Amphotericin B             |
| Ghatole et al., 2014  | *C. truncatum* | Trauma from sugarcane tree Plus immunosuppression | Keratitis         | Ciprofloxacin and Fluconazole Topical Amphotericin B 0.15% Natamycin 5% Voriconazole 1% PLUS Systemic Voriconazole PLUS Intrastromal Voriconazole | Resolution of keratitis after 9 days of treatment                        |
| Lamarca et al., 2016  | *C. gloesporioides* | Trauma from orange tree branch | Keratitis         | Topical Amphotericin B 0.15% Natamycin 5% Voriconazole 1% PLUS Intrastromal Voriconazole Cross-linking and a Penetrating keratoplasty | Resistant to medical therapy requiring a therapeutic penetrating keratoplasty with complication of a retinal and choroidal detachment which required further surgery Treatment duration – 3 months |
| Bui and Carvounis, 2016 | *C. gloesporioides* Glomerella species (strain not specified) | Unknown exogenous causes | Keratitis         | Topical and systemic voriconazole Penetrating keratoplasty Vitrectomy | 3 out of 5 cases resulted in resolution of the infection and a BCVA 20/20 |
| Wang et al., 2020     | *C. gloesporioides* | Trauma from apple tree branch Trabeculectomy + Trichodiagnosis (2yrs ago) | Keratitis         | Natamycin ointment Then Intravitreal Amphotericin B | Surgical washout required due to failure of abcess absorption Recommend combination antifungal therapy |
| Hung et al., 2020     | *C. gloesporioides* *C. truncatum* | Trauma from plant material Immunosuppression | Keratitis         | Topical Amphotericin B 0.15% Natamycin 5% Voriconazole 1% | C. truncatum patients required evisceration due to corneal perforation complications C. gloesporioides Responded to topical medical therapy |
Authorship

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

Patient consent

The patient provided written informed consent for the report.

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Declaration of competing interest

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