

# Severe *Gemella haemolysans* endophthalmitis following ranibizumab intravitreal injection

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*Gemella haemolysans* is a commensal of the upper respiratory tract that is rarely involved in ocular pathology. We present a unique case of endophthalmitis with negative cultures and positive 16s ribosomal ribonucleic acid gene sequencing showing *G. haemolysans* infection after an intravitreal ranibizumab injection for wet age-related macular degeneration.

**Key words:** Endophthalmitis, *Gemella haemolysans*, Gram-positive bacteria, ranibizumab

Bacterial endophthalmitis is one of the most feared complications after any intraocular procedure. The most common organisms reported in cases of endophthalmitis following intravitreal anti-vascular endothelial growth factor (Anti-VEGF) injection are *Staphylococcus epidermidis*, unspciated coagulase-negative Staphylococci and Streptococcus species.<sup>[1]</sup>

## Case Report

We present the case of a 92-year-old lady with wet age-related macular degeneration who developed endophthalmitis after the 13<sup>th</sup> ranibizumab injection. The patient had been treated regularly for bilateral wet age-related macular degeneration. During her June 2015 visit, the patient received her 13<sup>th</sup> right eye and fifth left eye ranibizumab injections without any immediate complication. The patient developed severe right eye pain on her way home on the same day, but only presented to the hospital eye service 6 days later with no perception of light in the right eye. Preinjection best corrected visual acuity in the right eye was 6/48. The patient was otherwise healthy, and not taking any pills.

Ophthalmological examination showed an injected chemotic right eye with organized hypopyon and no view of the fundus. B-scan ultrasound examination revealed extensive vitreous debris [Fig. 1]. A diagnosis of suspected endophthalmitis was made.

The patient was admitted to hospital on the same day. Aqueous and vitreous specimens were obtained for bacterial cultures and gram staining. During posterior vitrectomy, a very opaque and thick vitreous was observed and it was not possible to remove all debris due to an inadequate view. A white sheet of material remained in the posterior pole. Intravitreal Vancomycin 0.5 mg and Amikacin 200 µg was injected at the end of the procedure. The patient was also started on oral Levofloxacin 500 mg twice daily.

On the 1<sup>st</sup> day following vitrectomy, the right eye was comfortable, with the perception of light vision. Topical ofloxacin, cycloplegics, and steroids were started. Prolonged bacterial cultures on solid and liquid media were negative. In view of the possibility of a toxic posterior segment syndrome, the patient was started on oral prednisolone 40 mg/day 3 days after the anterior chamber and vitreous biopsies came back negative.

Three weeks after vitrectomy, 16s ribosomal ribonucleic acid (rRNA) polymerase chain reaction (PCR) of the culture-negative vitreous sample was positive with a gene sequence consistent with *Gemella haemolysans*. One month after vitrectomy, the eye remained comfortable, with only perception of light vision. Slit-lamp examination showed an injected right eye with corneal decompensation and no fundus view [Figs. 2 and 3].

One month later, the patient presented with discomfort and elevated intraocular pressure in the right eye and was diagnosed with pupil block glaucoma for which she underwent YAG Laser peripheral iridotomies. Following the episode of elevated intraocular pressure, her visual acuity was permanently reduced to no perception of light.

## Discussion

This is the first reported case of *G. haemolysans* endophthalmitis after an intravitreal ranibizumab injection. Wet age-related macular degeneration is the most common cause of blindness in the elderly population, and intravitreal Anti-VEGF injections are a good treatment option with good results in preventing eyesight loss in the majority of patients. The risks of intravitreal injection therapy are inflammation, rise of intraocular pressure, lens touch, vitreous hemorrhage, retinal detachment, sterile uveitis, and most feared of all complications– endophthalmitis.

*G. haemolysans* is a commensal of the upper respiratory tract which was first described as an infectious causative agent for endocarditis.<sup>[2]</sup> It is a facultative anaerobic Gram-positive coccus and can be slow growing on conventional bacterial culture media. Negative culture endophthalmitis cases are difficult to manage, and diagnosis should always be reinforced by sending a sample for 16s rRNA PCR. This technique uses broad-spectrum PCR primers which detect sequences from all eubacterial

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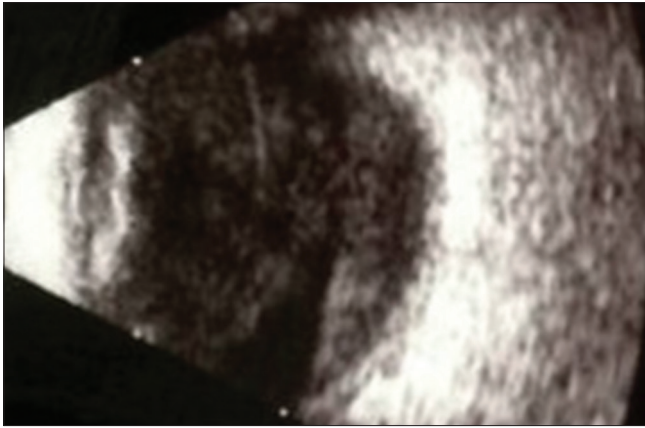
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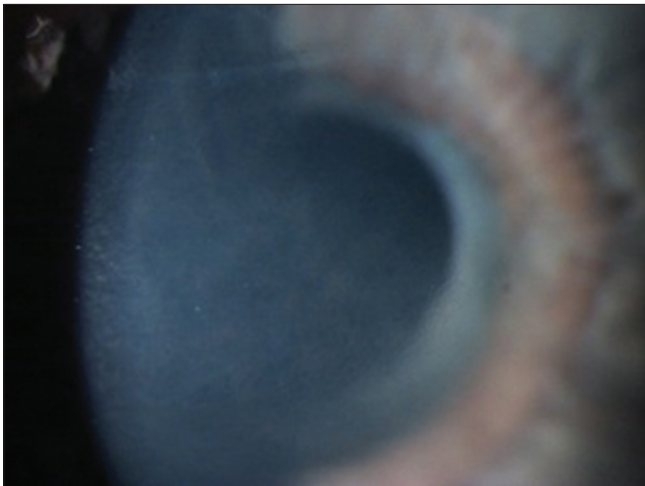
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**Figure 1:** B-scan ultrasound examination: extensive vitreous debris



**Figure 2:** Slit-lamp examination: injected right eye with corneal decompensation and no fundus view



**Figure 3:** Slit-lamp examination: focus on the corneal decompensation

species. The large amplified fragment is then sequenced and the organism identified by comparison to databases of previously identified species. This test is highly sensitive, and can reliably detect nonculturable bacteria. False-positives can occur due to

contamination during specimen collection or in the laboratory; in this case, the sample was collected and processed under strict aseptic conditions to minimize this risk.

The first ocular involvement of *G. haemolysans* was reported in a case of keratitis and consecutive endophthalmitis.<sup>[3]</sup> Since then, *G. haemolysans* endophthalmitis has been described after cataract surgery<sup>[4]</sup> and trabeculectomy<sup>[5]</sup>.

Another fact worth mentioning is that this is the second case of *G. haemolysans* endophthalmitis treated in our department, the first being after cataract surgery. There is a 12-year gap between the two cases, so hospital nosocomial infection can be ruled out. The case of endophthalmitis with *G. haemolysans* after cataract surgery had a similar presentation with ocular pain the afternoon after the surgical procedure. The patient presented to the hospital the next morning with only hand movement vision and antibiotic treatment was started early. Intravitreal vancomycin 2 mg and amikacin 300 µg were given, followed by oral Ciprofloxacin 500 mg twice daily and prednisolone 60 mg once a day. Gram staining suggested a Gram-positive coccus, cultures showed sensitivity to ciprofloxacin, and 16s rRNA PCR identified *G. haemolysans*. Vision improved to 6/4, demonstrating that an early start of treatment can have satisfactory results.<sup>[4]</sup>

The majority of endophthalmitis cases in the literature are caused by Gram-positive bacteria, which explains why vancomycin intravitreal injection is given as primary treatment after vitreous biopsy. Amikacin intravitreal injection covers the Gram-negative spectrum offering a good combination, especially until the cultures results are issued. Oral treatment with fluoroquinolones (such as levofloxacin or ciprofloxacin) covers Gram-positive and negative spectrums offering a good antibiotic treatment option whenever bacterial infection is suspected.

This is the first published case of *G. haemolysans* infection resulting in a visual outcome of no perception of light. The poor visual acuity can be related either to the late presentation of the patient or the bacterial pathogenicity, as well as the development of pupil block glaucoma. The literature shows that endophthalmitis following intravitreal injections is associated with an earlier presentation and poorer visual outcomes when compared with endophthalmitis following cataract surgery. Endophthalmitis after intravitreal injections has increased likelihood of final visual acuity of counting fingers or less and no improvement in visual acuity after antibiotic treatment.<sup>[6]</sup>

## Conclusion

This is a unique case of endophthalmitis with negative cultures and positive 16s ribosomal ribonucleic acid gene sequencing showing *G. haemolysans* infection after an intravitreal ranibizumab injection for wet age-related macular degeneration.

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All authors contributed equally to work. Each author participated in manuscript preparation and review. All authors believe that the manuscript represents honest work and all authors have read and approved the final manuscript.

All authors take responsibility for the integrity of the work as a whole from inception to the published article.

## Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have

given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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#### Conflicts of interest

There are no conflicts of interest.

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