



Original Research Article

Intravitreal injection of avastin (Bevacizumab) from a single vial causing pseudo endophthalmitis

Kirthi Raj^{1,*}, Sadiqulla M²¹Dept. of Ophthalmology, Dr. Baba Sahib Ambedkar Medical College and Hospital, Bengaluru, Karnataka, India²Private Practitioner,, Bengaluru, Karnataka, India

ARTICLE INFO

Article history:

Received 20-04-2020

Accepted 24-04-2020

Available online 22-12-2020

Keywords:

Avastin (Bevacizumab)

Endophthalmitis

Intravitreal

Pseudo

ABSTRACT

Purpose: To study the occurrence of pseudo endophthalmitis among patients undergoing intravitreal avastin (Bevacizumab) under various indications.

Materials and Methods: A retrospective analysis of case records of patients who developed an inflammatory reaction after Intravitreal avastin (Bevacizumab) was done.

Results: Eight of the twenty-Eight patients (28.5%) developed pseudo endophthalmitis. However, the repeated culture of aqueous or vitreous samples did not show any bacterial or fungal growth. All patients showed precipitation of drug in vitreous with the resolution of symptoms after 10 weeks of intensive oral and topical steroid treatment.

Conclusion: Intravitreal avastin (Bevacizumab) can result in pseudo endophthalmitis though it is a diagnosis of exclusion given many complications, a larger clinical trial of intravitreal avastin (Bevacizumab) is needed to rationalize its use.

© This is an open access article distributed under the terms of the Creative Commons Attribution License (<https://creativecommons.org/licenses/by/4.0/>) which permits unrestricted use, distribution, and reproduction in any medium, provided the original author and source are credited.

1. Introduction

Intravitreal Bevacizumab has widely been used as a treatment for several ocular disorders such as proliferative vitreoretinopathy, persistent pseudophakic cystoid macular edema, exudative age-related macular degeneration, proliferative diabetic retinopathy etc.^{1,2} Pseudo endophthalmitis is defined as true intraocular inflammation following intravitreal injection. However, the etiology of pseudo endophthalmitis independent of the administered drug remains uncertain and multifactorial. Acute and painless vision loss has been observed after intravitreal avastin (Bevacizumab) injection in the majority of the cases causing pseudo inflammation. Dense posterior segment inflammation may be a common divisor, while anterior segment inflammation appears to be mild to moderate. In eyes with pseudo endophthalmitis, visual acuity improves progressively as the intraocular inflammation reduces.³

despite the advances in the recent diagnostic modalities, pseudo endophthalmitis should be a diagnosis of exclusion because of the devastating visual prognosis an intraocular infection may cause if left untreated. This paper reports a series of cases that developed severe posterior segment inflammation and repeated culture-Negative of samples that responded to intensive oral and topical steroidal treatment.

2. Materials and Methods

A retrospective analysis of case records of a total of 28 patients with various etiologies ranging from cnvm, choroidal neovascularization to retinal vein thrombosis with macular edema and diabetic macular edema received intravitreal avastin (Bevacizumab) from a single common vial on the same day under strict aseptic precautions in major operation theatre at the regional institute of ophthalmology. The age varied from 35 to 56 years and 34-54 years among men and women respectively.

* Corresponding author.

E-mail address: drkirthiraj@gmail.com (K. Raj).

3. Results

Out of 28 patients 8 developed pseudo endophthalmitis among them were four men and four were women within the group. The various 8 cases were:

1. Retinal vein occlusion with macular oedema was found among four patients.
2. Two had moderate non proliferative diabetic retinopathy (NPDR with CSME).
3. Two had traumatic and myopic choroidal neovascularization each.

During the last 4 months, 2 patients had received prior intravitreal avastin injections. A series of eight of those patients who were stable on the first four days following injection subsequently developed intense anterior and posterior inflammation. On the 8th day after injection, three patients with severe vitreous inflammation and worsening of vision had to undergo pars plana vitrectomy and they also received multiple intravitreal antibiotics. None of these patients showed any positive culture reports of aqueous, vitreous samples and on the culture of the vial and the remaining drug.

Total posterior vitreous detachment was noted in all patients along with drug deposits. Intense anterior and posterior inflammation with hypopyon on day two was noted in two patients with choroidal neovascularization which subsequently resolved after steroid therapy.

4. Discussion

The incidence of pseudo endophthalmitis has been described between 0.09% and 1.1% of intravitreal bevacizumab injections (IBV).^{4,5}

Pain or chemosis or any such sign of infective endophthalmitis was not seen among all the eight cases. All the patients were assumed to have endophthalmitis received multiple subconjunctival, intravitreal vancomycin and ceftazidime injections but showed no clinical improvement for three weeks. However, total posterior vitreous detachment was noted among all patients. hypopyon was seen among two patient that resolved within three days of post-Treatment. Bacterial or fungal culture after repeated aqueous and vitreous tap remained sterile. Three of the eight patients underwent pars plana vitrectomy and the aqueous or vitreous culture for bacteria or fungi remained sterile.

Oral steroids at tapering dose were dispensed after physician consent. Dramatic improvement was observed from the third week. On b-scan vitritis revealed signs of resolution. After about three weeks of intensive treatment, there was total posterior vitreous detachment in eight patients. After ten weeks, all the patients showed precipitation of drug particles which eventually started clearing. The patients showed improvement after ten weeks

of intravitreal avastin (Bevacizumab) possibly due to pseudo endophthalmitis.

Avastin (Bevacizumab) certified by the us FDA is a full-length humanized monoclonal nonselective antibody is used counter to vascular endothelial growth factor for the treatment of

1. Colorectal cancer
2. Kidney cancer
3. Combination with chemotherapy

Rosenfeld et al. described for the first time the use of intravitreal bevacizumab (IVB) for the treatment of macular oedema secondary to retinal vein occlusion and exudative age-Related macular degeneration.⁶

The protection and effectiveness of intravitreal injections are not independent merely on the surgical technique, but also on the traits of the dispensed drug. Endophthalmitis is the most dreaded and potentially destructive complication of intravitreal injections. Vitreous tap for microbiological study and administration of intravitreal antibiotics must be done once the diagnosis of acute infectious endophthalmitis is suspected, while pars plana vitrectomy will have to be performed in many patients.⁷

In our reflection, 100% of the patients presented with

1. Blurred vision
2. Redness
3. Floaters
4. Showed signs of anterior segment inflammation in 50% on day 3 and 100% of vitreous inflammation on day 6.

A similar report of 44 cases witnessed by Chong et al.⁵ Demonstrated blurred vision present in 73% of the patients, floaters in 43% and pain in 34%. Most of the patients had signs of inflammation in the anterior chamber (77%) as well as in the vitreous cavity (80%). Following about 90 days of the injection improvement in mean visual acuity of five of the six patients were observed, much extended than what has been reported by various studies quoted by Joaquín et al. (37-71 days).³

In our study two patient who had developed hypopyon had formerly received two doses of intravitreal bevacizumab for traumatic cnvm and another patient with myopic cnvm also had intense inflammation. The repeated injection could increase the probability of pseudo endophthalmitis, as bevacizumab is a full-length humanized igg antibody. Wickremasinghe et al. reported 19 cases of inflammation after intravitreal bevacizumab, suggested the probability of contamination with trace endotoxin of a level not sufficient to cause any symptoms when administered systemically, which could have resulted in the intraocular inflammation. In this study, 2 eyes developed inflammation that had prior intravitreal bevacizumab injections. Early recognition and

Table 1:

S. No	Age	Sex	Cause	Dose	V/A
Patient 1	38	F	Myopic cnvm	2	6/36
Patient 2	50	M	Branch retinal vein occlusion+Macular oedema	1	6/60
Patient 3	54	M	Branch retinal vein occlusion+Macular oedema	1	6/60
Patient 4	38	M	Traumatic cnvm	2	6/60
Patient 5	53	F	Branch retinal vein occlusion+Macular oedema	1	Cf-2m
Patient 6	43	F	Moderate npdr + csme	1	6/60
Patient 7	36	F	Myopic cnvm	2	6/36
Patient 8	53	F	Branch retinal vein occlusion+Macular oedema	1	Cf-2m

Table 2:

S. No	Day 1	Day 3	Day 7	1 month	6 months
Patient 1	6/36	CF-CF	CF2M	6/60	6/24
Patient 2	6/60	HM	HM	CF 3m	6/36
Patient 3	6/60	PL	HM	CF2M	6/24
Patient 4	Cf-2m	CF-CF	CF1M	CF 3m	6/60
Patient 5	6/60	PL	CF1M	CF2M	6/18
Patient 6	6/60	HM	CF1M	6/60	6/24
Patient 7	6/36	CF-CF	CF2M	6/60	6/24
Patient 8	6/60	PL	CF1M	CF2M	6/18

CF- Counting fingers close to face; HM- Hand movements

management of inflammation with steroids could help in speedier healing and restrict incapacity.

Once dispensed systemically bevacizumab is mostly well accepted. Bevacizumab coupled infusional reactions are rare, 3% observed during a clinical test setting; intense reactions were noted just in 0.2% of patients. consequences like hypersensitivity, fever, hypertension, hypertensive crisis, etc have been reported in the literature.⁸ However, the probability of a delayed hypersensitivity reaction following intravitreal injection cannot be ruled out as this infection occurring in eyes that had obtained prior intravitreal bevacizumab.

Even though it seldom causes acute intraocular inflammation (Or 'pseudo endophthalmitis') it is a more serious ocular adverse event. The catt trial at the end of 24 months stated only two cases of 'pseudo-Endophthalmitis, one case in each of the bevacizumab group and ranibizumab group⁹ it is still uncertain if either bevacizumab poses a safety advantage to the patient. Lately, a series of cluster endophthalmitis was reported elsewhere in India.¹⁰

5. Conclusion

In conjecture, the intravitreal injection of anti -VEGF agent avastin (Bevacizumab) can produce pseudo endophthalmitis and its pattern may be as destructive as any other infective etiology. Although it's a diagnosis of exclusion, it calls for early detection and intensive anti-Inflammatory therapy to avoid these sequelae.

6. Conflict of Interest

None.

7. Source of Funding

None.

References

- Gupta SK, Yadav I, Deshmukh S, Maurya RP, Singh VP Predictors of visual response to Intravitreal Bevacizumab for treatment of Diabetic Macular Edema. *Indian J Clin Exp Ophthalmol.* 2015;1(1):35–40.
- Maurya RP. Dabetic macular edema: An overview. *Indian J Clin Exp Ophthalmol.* 2019;5(1):1–2. doi:10.18231/2395-1451.2019.0026.
- Marticorena J, Romano V. Sterile Endophthalmitis after Intravitreal Injections. 2012;2012. doi:10.1155/2012/928123.
- Wu L, Martínez-Castellanos MA, Quiroz-Mercado H, Arevalo JF, Berrocal MH, and MEF. Twelve-month safety of intravitreal injections of bevacizumab (Avastin®): results of the Pan-American Collaborative Retina Study Group (PACORES). *Graefes Arch Clin Exp Ophthalmol.* 2007;246:81–7. doi:10.1007/s00417-007-0660-z.
- Chong DY, Anand R, Williams PD, Qureshi JA, Callanan DG. Characterization of sterile intraocular inflammatory responses after intravitreal bevacizumab injection. *Retina.* 2010;30:1432–40. doi:10.1097/iae.0b013e3181dc04da.
- Rosenfeld. 2005.
- Results of the Endophthalmitis Vitrectomy Study. A randomized trial of immediate vitrectomy and of intravenous antibiotics for the treatment of postoperative bacterial endophthalmitis. Endophthalmitis Vitrectomy Study Group. *Arch Ophthalmol.* 1995;113(12):1479–96.
- Kang SP, Saif MW. Infusion-related and hypersensitivity reactions of monoclonal antibodies used to treat colorectal cancer—identification, prevention, and management. *J Support Oncol.* 2007;5(9):451–7.
- Comparison of Age-related Macular Degeneration Treatments Trials: Lucentis-Avastin Trial. Available from: <https://clinicaltrials.gov/ct2/show/NCT00593450>.
- Khan P, Khan L, Mondal P. Cluster endophthalmitis following multiple intravitreal bevacizumab injections from a single use vial. *Indian J Ophthalmol.* 2016;64(9):694–6. doi:10.4103/0301-4738.99855.

Author biography

Kirthi Raj, Assistant Professor

Sadiqulla M, Consultant

Cite this article: Raj K, Sadiqulla M. Intravitreal injection of avastin (Bevacizumab) from a single vial causing pseudo endophthamitis. *Indian J Clin Exp Ophthalmol* 2020;6(4):554-557.