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Original Research Article

Clinical outcome and compliance to treatment in patients with CNVM: Our experience

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ABSTRACT

Aim: To evaluate the outcome of treatment for CNVM and to estimate the compliance to treatment in patients diagnosed with CNVM.
Materials and Methods: A hospital-based retrospective descriptive study was done. Case record analysis of all the patients with diagnosis of CNVM, attending the retina clinic of a tertiary care centre was done. Records were studied for demographic and ocular characteristics and Ocular findings during initial and follow-up visits including best corrected visual acuity (BCVA) and findings on OCT.
Results: 45 cases were diagnosed to have vision loss due to CNVM. All the patients were counseled to undergo three doses of intravitreal Bevacizumab injection at monthly intervals. However out of 45 cases only 14 cases followed the protocol and completed 6 months follow up. All the patients received intravitreal Bevacizumab at monthly intervals for three months followed by injections as and when required. BCVA on LOGMAR improved from 1.032(+/- 0.05) to 0.75(+/- 0.037) at 6 months follow up. Reduction in the activity of CNVM was noted in all the patients with significant visual recovery. Of 45 cases diagnosed to have CNVM only 14 patients were compliant to treatment protocol and follow up. The compliance rate was found to be 31%.
Conclusion: CNVM is one of the leading causes of visual loss and irreversible blindness. Anti- VEGF drugs have been found to be efficacious in the treatment of CNVM. Intravitreal Bevacizumab found to be efficacious in reducing the CNVM activity and improving the visual acuity. However the treatment regimen has to be followed for successful clinical outcome. Compliance of patients to treatment and consequent treatment success outcome may be improved by addressing the underlying causative factors for non compliance.

1. Introduction

Blindness is an important public health problem in India. Blindness remains a major health and social issue in a vast country like India which has a population of over one billion and where providing access to health care and education remains a challenge.[1] In the study by Vijaya L et al. cataract was the leading cause of blindness and severe visual loss followed by glaucoma, optic atrophy, cystoid macular edema and corneal scars. Other leading causes included corneal decompensation, age related macular degeneration (AMD) and retinitis pigmentosa.[2]

Choroidal neovascular membrane (CNVM) secondary to AMD in the macular area is one of the leading causes of severe visual loss.[3] CNVM is defined as abnormal growth of new blood vessels that originate from the choroid and break through the Bruch's membrane to enter into the subretinal pigment epithelium or subretinal space.[4] Common causes of CNVM include AMD, Idiopathic polypoidal choroido vasculopathy (IPCV), pathological

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myopia, photocoagulation scars, angioid streaks, presumed ocular histoplasmosis syndrome, posterior uveitis, choroidal rupture. Various growth factors responsible for angiogenesis are known to be involved in the pathogenesis and development of CNVM, such as vascular endothelial growth factor (VEGF). Drugs targeting vascular endothelial growth factor, Anti-VEGFs have been used in treatment of exudative macular disorders presenting as CNVM, with considerable success.[5] The functional prognosis changed from almost-certain blindness to more than 90% chance of three-line visual improvement after two years of treatment with Anti-VEGFs.[6,7] Drugs like Ranibizumab, Bevacizumaband Aflibercept have been the frontline anti-VEGFs. Intravitreal injection of Ranibizumab is the current gold standard of treatment.[3] Intravitreal Bevacizumab(Off-label) is similar in therapeutic mechanism to Ranibizumab and has been found to be safe and comparatively cost-effective.[8]Treatment protocol includes three consecutive monthly injection of Anti-VEGF intravitreal injection followed by monthly follow-up with either repeat injections as and when needed[9] (PRN) or treat and extend regimen.[10] Gain in visual acuity and reduction in activity of CNVM is considered as desired response to treatment. However compliance of patients to adhere to the treatment schedule is desirable for better clinical outcome and prevention of irreversible vision loss.

2. Aim of the Study

To evaluate the outcome of treatment for CNVM and to estimate the compliance to treatment in patients diagnosed with CNVM.

3. Materials and Methods

A hospital-based retrospective descriptive study wherein case record analysis of all the patients with diagnosis of CNVM, attending the retina clinic of a tertiary care centre, between January 2015 to December 2017 was done. Institutional ethics committee clearance was obtained and the case records were retrieved using the Hospital Information System. All patients diagnosed to have treatment naïve CNVM attending the retina clinic during the period of Jan 2015 to Dec 2017 were included in the study. Demographic characteristics were noted.

All patients had undergone complete ophthalmic examination including BCVA (LOGMAR), slit lamp examination, intraocular pressure by Goldman Applanation Tonometer (APPA Associates), fundoscopy evaluation with slit lamp (+78D) and indirect ophthalmoscopy(+20D) and Optical coherence tomography(SD-OCT)(APPA Associates) at each visit.

Records were studied for demographic and ocular characteristics and Ocular findings during initial and follow-up visits including best corrected visual acuity (BCVA) and findings on OCT.

4. Results

Between January 2015 to December 2017, 45 cases were diagnosed to have vision loss due to CNVM. All the patients were counseled to undergo three doses of intravitreal Bevacizumab injection at monthly intervals. However out of 45 cases only 14 cases followed the protocol and completed 6 months follow up. Of 14 cases 6 were females and rest was males. 12 cases were in the age group of 35 to 65 years. Common cause for CNVM was Wet AMD followed by Myopia, IPCV and angiod streak (Figure 1). All the patients received intravitreal Bevacizumab at monthly intervals for three months followed by injections as and when required. BCVA was recorded in all cases before the first injection and during the subsequent visits. BCVA on LOGMAR improved from 1.032(+/- 0.05) to 0.75(+/- 0.037) at 6 months follow up (Figure 2). Reduction in the activity of CNVM was noted in all the patients with significant visual recovery (Figure 3).

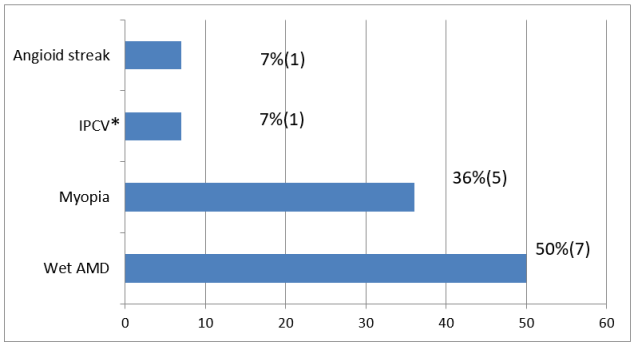

Fig. 1: Causes of CNVM (IPCV: Idiopathic Polypoidal choroidal vasculopathy, AMD: Age related macular degeneration)

Of 45 cases diagnosed to have CNVM only 14 patients were compliant to treatment protocol and follow up. Others deferred with respect to number of injections and the follow ups. The compliance rate was found to be 31%.

5. Discussion

In 2015, there were an estimated 253 million people with visual impairment worldwide. Of these, 36 million were blind.[11] Studies have shown that the prevalence of blindness is more in rural population as compared to urban population in India. This difference in prevalence of blindness suggests that probably the urban population has better access to ophthalmic care. However urban population blindness rate in India is higher than the urban blindness rates in other Asian countries. This could probably be due to the differences in socioeconomic conditions, health care practices, and access to vision care.[1] Common causes of blindness include glaucoma, optic atrophy, cystoid macular edema, corneal scars and macular diseases.[2]

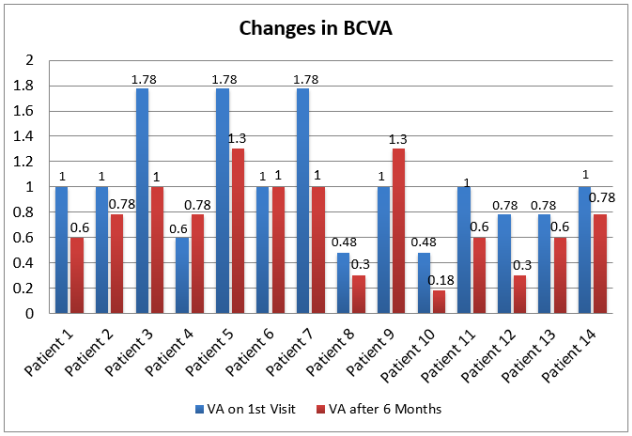

Fig. 2: BCVA of cases at first visit and at 6 months

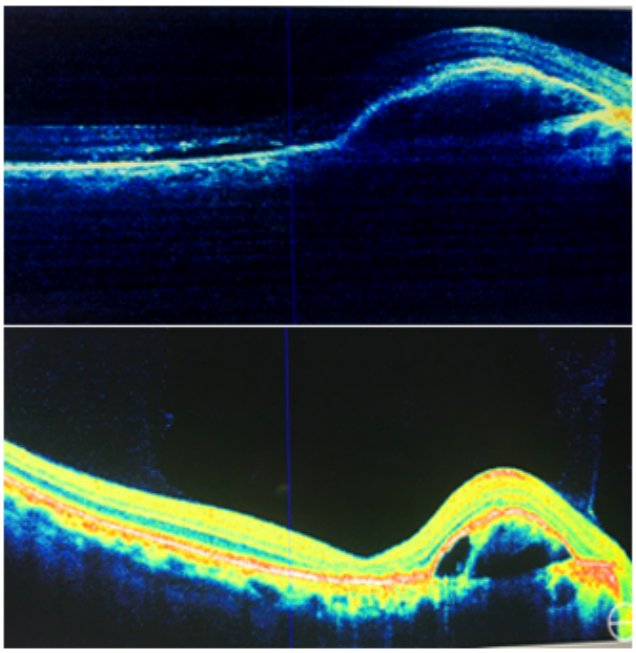

Fig. 3: OCT of macula showingin a case of IPCV **a**) Active CNVM (Pre-injection) and **b**) reduction in activity post 3rd injection

CNVM in the macular area is one of the leading causes of severe visual loss.[3] Common causes for CNVM include AMD, IPCV, angiod streaks, myopia, and intraocular inflammation as shown in different studies.[3] In our study, AMD was found to be the most common cause for CNVM followed by pathological Myopia that was comparable with other studies.[12] Various growth factors responsible for angiogenesis are known to be involved in the pathogenesis and development of CNVM, such as vascular endothelial growth factor (VEGF).[5] Drugs targeting vascular endothelial growth factor, Anti-VEGFs have been used in treatment of exudative macular disorders presenting as CNVM, with considerable success.[5]

Intravitreal injection of Ranibizumab is the gold standard in treatmentof AMD CNVM. Ranibizumab (Lucentis; Genentech Inc.,) is a humanized antigen-binding fragment against all forms of VEGF-A, thereby inhibiting angiogenesis and reducing vascular permeability.[13] The Minimally Classic/Occult Trial of the Anti-VEGF Antibody Ranibizumab in the Treatment of Neovascular AMD (MARINA) study and the Anti-VEGF Antibody for the Treatment of Predominantly Classic Choroidal Neovascularization in AMD (ANCHOR) study, both of which showed favorable outcome in the preservation of vision.[14] Clinical evidence has indicated that ranibizumab initiation with three consecutive monthly injections is optimal, providing the greatest best-corrected visual acuity (BCVA) gain.[4] Bevacizumab treated eyes also had a significant decrease in macular thickness and improvement in visual acuity.[15] In our study treated eyes had a decrease in CNVM activity and improvement in visual acuity that was comparable with other studies[15] No significant adverse effects like endophthalmitis, vitritis, cataract[3] were noted in our cases similar to observations done by Fung et al.[16]

The treatment regimen protocol consists of 3 consecutive monthly injections followed by additional injections given as and when needed according to OCT and visual acuity findings. Similar protocol was followed in other studies as well.[15] Percentage of patients who followed the protocol of three monthly injections with regular follow up upto six months was 33.1. In a study by Polat et al 39.8% were not compliant to treatment protocol.[17] In a review study by Mali Okada et al, the percentage of patients not compliant to treatment varied from 3.6 to 48.6.[18] The values were similar to the findings in our study. Compliance of patients to treatment and consequent treatment success outcome may be improved by addressing the underlying causative factors for non compliance. Patients' financial means, education level, sociocultural values, disease awareness, and access to treatment are better in developed countries compared to developing or undeveloped countries. In a study by Kelkar et al, fear of injection and not benefiting as expected from treatment were found to be the most common reasons stated by patients for not complying adequately with the treatment and follow-up.[19]

6. Conclusion

CNVM is one of the leading causes of visual loss and irreversible blindness. Age related macular degeneration is found to be one of the common causes of development of CNVM at macular area. Anti- VEGF drugs have been found to be efficacious in the treatment of CNVM. In our study we could determine that Intravitreal Bevacizumab was efficacious in reducing the CNVM activity and improving the visual acuity.

However the treatment regimen has to be followed for successful clinical outcome. 69% of our patients with

CNVM did not adhere to the treatment protocol and missed out on monthly injections. Compliance of patients to treatment and consequent treatment success outcome may be improved by addressing the underlying causative factors for non compliance. More studies are required to determine the causes for patient's non compliance to treatment and to take remedial measures to improve adherence to treatment protocol in order to prevent irreversible blindness from CNVM.

7. Source of Funding

None.

8. Conflict of Interest

The authors declare no conflict of interest.

9. Acknowledgement

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