Introduction

Choroidal neovascularization developing in individuals < 50 years without any apparent ocular cause is known as idiopathic CNV (ICNV). In others CNV develops secondary to some predisposing conditions such as pathological myopia, angioid streak, trauma, or inflammation like ocular histoplasmosis syndrome. In a significant number of young patients with CNV, these membranes are usually unilateral and final visual outcomes are considered to be more favorable than CNV due to age-related macular degeneration (AMD). Unlike AMD, sparse information exists on the natural course and treatment of subfoveal ICNV.

Photodynamic therapy (PDT) has been shown to be effective in idiopathic CNV in many studies. Encouraged by the preliminary findings of the ranibizumab trials in patients with AMD and subfoveal lesions, many physicians began to investigate a related compound, bevacizumab (Avastin; Genentech, Inc, South San Francisco, California), as a treatment for neovascular AMD with encouraging short term effects in selected patients.

Intravitreal injection of anti VEGF agents is the current standard of care treatment in treatment of neovascular age related macular degeneration (AMD). Intravitreal anti-VEGF therapy is also being used increasingly in cases of retinal veno-occlusive disease, proliferative diabetic retinopathy and non AMD related CNV from causes like myopia, idiopathic, postinflammatory. Intravitreal ranibizumab and bevacizumab are the most commonly used anti-VEGF medications for intravitreal use. As of now the current usage of bevacizumab in the treatment of various retinal diseases is "off-label". For ocular use the hospital or the compounding pharmacies aliquot individual doses of bevacizumab into syringes for intravitreal use, usually 1.25mg/0.05ml or 2.5mg/0.1 ml.

Methods

The charts of patients with angiographically documented choroidal neovascular membrane in patients below the age of 50 years, from 2004 to 2010 were reviewed.

Inclusion Criteria

All patients < 50 years with angiographically proven choroidal neovascular membrane without any obvious ocular cause were included.

Exclusion Criteria

All patients < 50 years of age with a previous history of laser, clinical features of CSR, old trauma, coexisting retinal disease, recent ocular surgery clinical features of anterior or posterior uveitis. Patients without a minimum follow up of 6 months.

Outcome Measures

The BCVA at presentation, and at the end of the treatment. For assessing the change in BCVA, a 2 line drop was considered as a “drop” in BCVA, while a gain of 1 line was considered as “gain”. If the BCVA remained the same, it was considered to be “stabilized”. [NB: BCVA < 6/60 was considered to be the same level, i.e. CF improving to 5/60 was considered as “stabilization” and not improvement].

Baseline evaluation

All patients had their BCVA assessment by Snellen’s chart, slit lamp biomicroscopic examination and dilated fundus examination. Fluorescein angiography and Optical Coherence Tomography were done.

Treatment Modalities

The various treatment modalities used in our series included loading dose of Bevacizumab, PRN dosing of Bevacizumab, combination therapy PDT with Visudyne with anti VEGF agents, IVTA and thermal laser.

Loading dose of Bevacizumab included 3 monthly injections of Bevacizumab followed by repeat angiogram at the end of the 4th month. Residual activity on angiogram warranted further injections. Retreatment was based on demonstration of serous macular detachment on OCT. The anti-VEGF intravitreal therapy was repeated at a 4-week interval if OCT showed serous macular detachment. The patient was subsequently reviewed at monthly intervals.

In case of PRN dosing of Bevacizumab, serial OCTs at monthly intervals were performed and at the evidence of membrane activity, as evidenced by serous macular detachment, the patient was treated with Bevacizumab injections till the complete resolution was achieved.

In combination therapy with PDT with Visudyne and anti-VEGF agents, the lesion size was assessed angiographically. PDT was given with a 689 nm diode laser for 83 seconds with a laser spot size 1000 microns larger than the greatest linear dimension of the lesion. Anti VEGF injection was given on the following day. A repeat angiogram was done at the end of 3 months to look for signs of closure of CNV. In case of residual activity of CNV additional cycle of PDT with anti-VEGF agents was given.
Thermal laser was used in cases of a small extrafoveal lesion. IVTA was used in cases presenting in the pre anti-VEGF era.

**Results**

In our study, 18 eyes of 18 patients were enrolled and studied. The patients comprised of 38.8% females and 61.1% males. The mean age of the patients was 40 years (range 22-49 years). The mean period of follow up was 12.9 months (range 6-36 months).

All patients had unilateral disease at presentation although one patient (representative case no.1) developed CNV in the other eye during the follow up period. Angiographically the data showed classic CNV in all the patients out of whom 72% were subfoveal, 22.2% were juxtafoveal and 5% were peripapillary.

The median BCVA was 6/60. With the treatment, the visual acuity improved in ten patients (55.5%), 5 patients (27.8%) maintained a stable vision, while 3 patients (16.7%) showed a drop in visual acuity [Table 1]. All the patients who showed a decline in the BCVA showed a scarring of the CNV on examination.

The treatment modalities included loading dose of Bevacizumab (Avastin) in 55.5%, combination therapy with PDT with Visudyne and Bevacizumab in 16.67%, thermal laser in 5% and Bevacizumab on PRN basis in 10%. Thermal laser was used in the patient with a juxtafoveal CNV.

In the cases receiving loading dose of Bevacizumab, the mean number of injections was 3.2 [range 3-5] in the patients who received loading dose of Bevacizumab. Out of the ten patients, one patient received 2 additional injections after the loading dose. The remaining 9 patients received 3 doses of Bevacizumab.

In the patients treated with PRN dosing of IVTA, one patient received only one injection while the other patient received two injections.

Out of the three patients treated with combination therapy with PDT with Visudyne with anti VEGF agents, one patient additionally received one dose of Bevacizumab. Another patient received just one cycle of PDT with Bevacizumab. The third patient received two cycles of PDT with Bevacizumab.

The patient receiving thermal laser required only one sitting of laser. No anti VEGF injections were required.

All forms of treatment were well tolerated and none of the patients developed any adverse side effects to the treatment modalities used.

**Discussion**

Although the clinical course of subfoveal CNV secondary to AMD is well documented in the literature, sparse information exists on both the natural history and treatment of subfoveal CNV secondary to idiopathic etiology.

In our study 88.9% 16 of the total 18 patients achieved stabilization or improvement of vision. As this result includes all the treatment groups in the study compounded with the small sample size the data of our study cannot be directly compared with data from other studies, but it conveys that the results of treatment in cases of idiopathic CNV are more favorable than CNV due to age related macular degeneration.

Although the most effective dose of intravitreal Bevacizumab required for the treatment of CNV has not been studied, idiopathic CNV may require a lesser amount of injection in comparison with neovascular AMD. However, only a comparative study can confirm this presumption. Amongst the patients who received Bevacizumab, the improvement in visual acuity could have been attributed to the dose used in our series (2.5mg/0.1ml). Bashshur et al administered 3 injections of 2.5 mg/0.1 mL every 4 weeks as per their protocol in CNV from AMD and found complete resolution of SRF in 13 of 17 eyes (76%) at 12 weeks' follow-up.

Given the retrospective nature of the study, inherent weaknesses in the article exist that cannot be avoided. Visual acuity was measured in a nonstandardized fashion using the Snellen chart. Since no single treatment protocol was followed the data from our series cannot be directly extrapolated to other available data.

**Representative Cases**

**Case No.1**

A 26 year old male developed diminution of vision OD to 6/12 N8. Ocular examination, fundus photography, FA and OCT showed subfoveal active ICNV (Fig 1a). Combination therapy was done. Repeat FA showed residual activity so a second cycle of combination therapy was given. BCVA was 6/18 N18 at 4 and 6 months. He additionally received 3 pm doses of Bevacizumab. Final BCVA was 6/60 N18 with scarring of the CNV (Fig 1b). Later the other eye developed CNV.

![Figure 1a](image-url)
Fig 1. a: Shows the pre treatment angiogram showing an active subfoveal classic CNVM in OD. The corresponding OCT shows a fusiform lesion at the RPE–choriocapillaris complex with overlying intraretinal edema. Fig 1b: Post 1st cycle of PDT with Bevacizumab, residual activity of the CNV seen. Fig 1c: Post 2nd cycle of PDT with Bevacizumab. FA shows RPE window defects and a scar. OCT shows resolution of intraretinal edema.

Case No. 2

A 39 year old female developed diminution of vision OD to 6/12. Ocular examination, fundus photography, FA and OCT showed classic subfoveal active ICNV (Fig 2a). She received a loading dose of Bevacizumab. BCVA was 6/18 N18 at 4 and 6 months. The BCVA at 4th and 6th month was 6/6 N6. At end of 1 year she maintained a BCVA OD 6/6 N6 with no additional injections. (Fig 2b).

Fig 2a: Pretreatment FA showing an active subfoveal classic CNV and OCT showing a fusiform lesion at the RPE-choriocapillaris complex. Post loading dose of Bevacizumab, FA shows only RPE window defects. OCT shows complete resolution of the lesion.

Conclusion

In patients younger than the age of 50 years at diagnosis, the prognosis of idiopathic choroidal neovascularization differs from eyes with age-related macular degeneration, and the prognosis often being favorable. Various trials have shown promising results with the various treatment options namely PDT, IVTA and anti-VEGF agents and thermal laser in selected patients. Prompt treatment is the key to successful visual outcomes.

Table-1: Change in the BCVA in patients [Parentheses show the LogMAR equivalent as per the AJO guidelines]

<table>
<thead>
<tr>
<th>Patients</th>
<th>Baseline BCVA</th>
<th>Final BCVA</th>
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References
1. Intravitreal Bevacizumab for Subfoveal Idiopathic Choroidal Neovascularization Subrata Mandal; Satpal Garg; Pradeep Venkatesh; Charu Mithal; Rajpal Vohra; Abhas Mehrotra, Arch Ophthalmol. 2007;125(11):1487-1492

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