Choroidal Neovascular Membrane In Paediatric Population – Etiology, Clinical Features And Visual Outcome

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**Objective**: To study the clinical features and outcome of CNVM in pediatric population

**Design**: Retrospective case series

**Materials and Methods**: All patients <18 years of age with angiographic evidence of CNV from 2004 to 2010 were included.

**Results**: 16 eyes of 16 patients were enrolled of which 14 eyes with adequate follow up were analyzed. The mean age of the patients was 14.5 years (Range 7-18 years) with a mean period of follow up of 27.5 months (Range 6-89 months). Angiographic characteristics included 78.57% predominantly classic and 21.4% occult. Location was subfoveal-50%, juxtafoveal-42.87% and peripapillary-7.1%. The etiologies included post inflammatory-48.57%, posttraumatic-7.1% and CNV secondary to Best’s disease in 7.1% and idiopathic in 48.57%. The treatment modalities included loading dose Bevacizumab in 35.7%, combination therapy with PDT and antiVEGF in 14.28%, thermal laser with IVTA in 7.1%, Bevacizumab on PRN basis in 14.28%, IVTA in 14.28%. In 2 patients no treatment was administered. 35.7% achieved stabilization of visual acuity, 28.6% showed an improvement in visual acuity while 35.7% showed a drop in visual acuity.

**Conclusion**: CNVM in pediatric age group is a rarity posing challenges in the management and 64.28% show stabilization or improvement of vision with treatment.

**Introduction**

Subfoveal choroidal neovascularization in children is a rare event, typically occurring as a complication of inflammatory or infectious chorioretinal disease. Visual acuity may be compromised by the subfoveal location of the choroidal neovascular complex, exudative macular detachment, subretinal or subretinal pigment epithelial hemorrhage, and cystoid degenerative changes of the neurosensory retina. Wilson and Mazur and Goshorn et al reported that 58% of subretinal neovascular membranes in children and adolescents undergo spontaneous involution, with 29% achieving a final visual acuity of 20/50.

The prognosis for subfoveal neovascularization in children is reportedly more favorable than for adult neovascularization from either exudative age-related macular degeneration (AMD) or presumed ocular histoplasmosis (POHS).

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.

**Methods**

The charts of patients with angiographically documented choroidal neovascular membrane in patients below the age of 18 years, from 2004 to 2010 were reviewed.

**Inclusion Criteria**

All patients <18 years with angiographically proven choroidal neovascular membrane were included.

**Exclusion Criteria**

All patients < 18 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 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**

16 eyes of 16 patients were enrolled of which 14 eyes with adequate follow up were analyzed. The mean age of the patients was 14.5 years (Range 7-18 years) with a mean period of follow up of 27.5 months (Range 6-89 months). The sex distribution was equal. All patients except one had unilateral disease. The patient with the bilateral disease had CNV secondary to Best’s disease. The etiologies included post inflammatory in 48.57%, posttraumatic in 7.1% and CNV secondary to Best’s disease in 7.1% and idiopathic in 48.57%.

<table>
<thead>
<tr>
<th>Patients</th>
<th>Baseline BCVA</th>
<th>Final BCVA</th>
<th>Change in BCVA</th>
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<td>CF 1 (2.7)</td>
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<td>16</td>
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<tr>
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</table>

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

The median baseline BCVA was 6/36. In terms of BCVA change at the end of the treatment, 35.7% (five patients) achieved stabilization of visual acuity, 28.6% (four) showed an improvement in visual acuity while 35.7% (five) showed a drop in visual acuity. [Table 1]

The treatment modalities included loading dose Bevacizumab in 35.7%, combination therapy with PDT and anti VEGF in 14.28%, thermal laser with IVTA in 7.1%, Bevacizumab on PRN basis in 14.28%, IVTA in 14.28%. In two patients (14.28%) no treatment specific to CNV was given, these patients developed scarring of the CNV while only on antitoxoplasma medications.

In the patients who were treated with loading dose of Bevacizumab, the mean number of injections was 2.4 (range 3-5). Two patients had a residual CNV on angiogram at the end of initial loading regime and were advised 2 more injections. Out of these 2 only one patient (representative case no.1) took the additional injections. Repeat angiogram showed no residual activity of the membrane.

In the p.r.n dosing group one patient received three doses of Bevacizumab while another patient received only one injection along with antitoxoplasma therapy. Both of these patients developed scarring of the membrane.

Amongst the patients treated with IVTA, only one patient developed raised IOP which was successfully managed medically with topical antiglaucoma medications.

Of the patients treated combination therapy, both patients received one cycle of PDT with anti VEGF agent on the subsequent day. One of these patients developed recurrence and was managed with 2 additional doses of Bevacizumab. Only one patient underwent combination with thermal laser and IVTA.

Apart from one instance of raised IOP none of the patients developed any complications to the therapies instituted.
Representative Cases

Case No.1

A 17 year old male developed diminution of vision OD to 6/60 N36. Ocular examination, fundus photography, FA and OCT showed subfoveal active CNV (Figure 1a). Loading dose of Bevacizumab was given at monthly intervals. Repeat FA (Figure 1b) showed residual activity so two additional doses of Bevacizumab were given at monthly intervals. BCVA was 6/9 N6 at 6 months and repeat FA showed scar with staining. (Figure 1c)

Case No.2

A 12 year old female developed diminution of vision OS to 6/36 N36. Ocular examination, fundus photography, FA and OCT showed subfoveal active CNV (Figure 2a). Combination therapy with IVTA and thermal laser was done. Repeat FA showed total resolution. BCVA was 6/6 N 8p at 6 months. The BCVA improved to 6/6 N6 at 1 year and she has maintained the same BCVA till her last follow up (38months).
Figure 2 (a) Shows the pre treatment FA showing juxtafoveal classic CNV and the OCT showing a pre RPE fusiform lesion. Figure 2(b) Post treatment with IVTA with thermal laser, FA showing scarring of the CNV with no residual activity. OCT shows hyperreflectivity in the juxtafoveal region with no residual intraretinal edema or serious macular detachment.

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 CNV in the pediatric age group. Due to the rare occurrence of this entity, there are not many published reports in the available literature; it poses challenges in the management. Von Eiken et al reported photodynamic therapy to be successful in 1 case of a 5-year-old girl with subfoveal CNVM.

The successful use of anti-VEGF therapies in younger patients, most notably in neonates with retinopathy of prematurity, has allowed for application of this treatment to other pediatric conditions. Cakir and colleagues reported two children with choroidal neovascular membrane that regressed following treatment with bevacizumab with documented improvement in visual acuity. Avery has discussed the potential uses of anti-VEGF agents in pediatric diseases. He also raised concern and demanded caution in the use of these powerful agents, especially bevacizumab, which has a long systemic half-life.

In our series however none of the patients developed any adverse effect. Adverse effects are typically uncommon and therefore unlikely to be seen with relatively small numbers of patients.

In our series 64.28% of the total patients achieved stabilization or improvement of vision. As this result includes all the treatment groups in the study, compounded with the small sample size and the substantial lack of literature, these results cannot be overtly generalized. However it seems that pediatric CNV fare off better than its age related counterparts. 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). However, Bashshur et al administered 3 injections of 2.5 mg/0.1 mL every 4 weeks as per their protocol in CNV from AMD. Still this is just an extrapolation and it is wise to be exerting caution for the overzealous in the use of these agents in pediatric cases.

This series suffers from many shortcomings. One is that it is retrospective. Another is that it is not a randomized treatment trial so the inherent weaknesses in the article cannot be avoided. Visual acuity was measured in a non standardized 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.

Conclusion

Choroidal neovascular membrane in pediatric age is a potentially treatable but rare entity and in the lack sufficient trial and guidelines for the management, treating this subgroup of diseases is challenging. The treatment options which include PDT, thermal laser, IVTA and anti-VEGF agents have their own benefits and risks. Various investigators have shown the results of treatment with various modalities to be favorable. Timely and judicious management yields good visual outcomes.

References