Original Article

Inflammatory choroidal neovascularization in Indian eyes: Etiology, clinical features, and outcomes to anti-vascular endothelial growth factor

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Background and Objectives: The aim was to study the clinical profile of inflammatory choroidal neovascularization (CNV) and its treatment response to intravitreal bevacizumab or ranibizumab on pro re nata (PRN) basis in Indian eyes. **Materials and Methods:** This was a retrospective case series of consecutive patients with inflammatory CNV treated with anti-vascular endothelial growth factor (anti-VEGF) in a tertiary eye care center in Eastern India between 2009 and 2014. The data about clinical features, investigations, treatment, and outcomes were obtained from the medical records. We included patients with active inflammatory CNV but with no evidence of inflammation and were treated with anti-VEGF alone, with a minimum follow-up of 6 months. Main outcome measures were a clinical and etiological profile of inflammatory CNV in Indian eyes and their response to treatment. **Results:** Thirty eyes of 28 patients were included in the study. The mean follow-up was 17.93 ± 14.28 months (range 6–53 months). In our cohort, seven (23.33%) eyes had inflammatory CNV secondary to idiopathic choroiditis, four (13.33%) eyes had toxoplasmosis, idiopathic panuveitis, and Vogt Koyanaki Harada's disease each. Three (10%) eyes had geographic helicoid peripapillary choroidopathy and tubercular choroiditis each. Remaining two (6.66%) eyes had punctate inner choroidopathy, while multifocal choroiditis with panuveitis, resolved endogenous endophthalmitis and Hansen's diseases were the etiology in one (3.33%) case of inflammatory CNV each. The mean number of injections were 2.76 (range 1–5). Among thirty eyes of inflammatory CNV, 16 (53.3%) eyes showed improvement, eight (26.6%) maintained the same vision, whereas six (20%) eyes showed deterioration of vision. **Interpretations and Conclusion:** Idiopathic choroiditis was the most common cause of inflammatory CNV and PRN intravitreal anti-VEGF (ranibizumab or bevacizumab) appears to have effective treatment response.

Key words: Bevacizumab, choroidal neovascularization, inflammatory choroidal neovascularization, ranibizumab

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Inflammation represents the third most common cause of choroidal neovascularization (CNV) after age-related macular degeneration (AMD) and myopia.[1] Inflammatory CNV is a sight threatening complication of posterior segment intraocular inflammation.[2] Various conditions such as toxoplasma retinochoroiditis, multifocal choroiditis with panuveitis (MCP), Vogt Koyanaki Harada's disease (VKH), geographic helicoid peripapillary choroidopathy (GHPC), punctate inner choroidopathy (PIC), and presumed ocular histoplasmosis syndrome can be complicated by CNV.[3-8]

The development of CNV is a result of angiogenic drive mediated by local inflammation or secondary to degenerative disruption of the retinal pigment epithelium (RPE) - Bruch's membrane complex. It can also be due to a combination of both mechanisms. The natural course and visual prognosis of inflammatory CNV are generally considered to be more favorable than the CNV resulting from AMD.[9-11] It may be due to the classic nature and smaller size of the membrane and younger age of patients as compared to AMD-related CNV.[2]

Treatment modalities for inflammatory CNV include laser photocoagulation,[12] photodynamic therapy,[12] systemic or local steroid,[11,13,14] and surgical removal of the membrane.[15] These treatment modalities do have potential limitations and can be associated with high rate of recurrence or complications.[11-16] Anti-vascular endothelial growth factor (anti-VEGF) has emerged as primary therapy against CNV. Currently used anti-VEGF agents are pegaptanib sodium (Macugen; OSI Eyetech Pharmaceuticals, Melville, NY, USA), ranibizumab (Lucentis, Genentech, Inc., South San Francisco, CA, USA), and bevacizumab (Avastin, Genentech, Inc.,). Marina[17] and Anchor[18] studies have shown the beneficial role of anti-VEGF agents in CNV secondary to AMD.[13,16] A few case series have shown the promising role of anti-VEGF agents in the treatment of inflammatory CNV as well.[3-7]

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Kramer *et al*.,[4] Rouvas *et al*.[5] and Arevalo *et al*.[6] have studied the etiologies, treatment, and outcomes of inflammatory CNV. Epidemiological data based on studies by Baxter *et al*. provides us information on inflammatory CNV in uveitic eyes. They have found that among 4041 eyes of 2307 patients with posterior or panuveitis, 81 (2.0%) presented with CNV. The cumulative 2-year incidence of CNV was 2.7% in their cohort of patients with posterior uveitis.[19] However, there are very few case reports on etiologies and outcomes of inflammatory CNV in Indian eyes. The objective of this study was to evaluate the etiology and clinical features of inflammatory CNV in Indian eyes. We also aimed to study the treatment response to intravitreal anti-VEGF, that is, bevacizumab (IVB) and ranibizumab (IVR) on pro re nata (PRN) basis.

Materials and Methods

This was a retrospective case series of consecutive patients with inflammatory CNV treated with anti-VEGF in a tertiary care eye hospital in Eastern India between 2009 and 2014. The study was approved by the institutional review board. We included patients with inflammatory CNV treated with at least one intravitreal anti-VEGF injection and had a minimum follow-up of 6 months. Intravitreal anti-VEGF injections were given only after control of inflammation with topical and/or oral anti-inflammatory medications. Eyes with no inflammatory activity, but active CNV were selected. Patients who had previously undergone photodynamic therapy (PDT) or had received anti-VEGF injection in past were excluded from the study.

All patients underwent comprehensive ophthalmic examination at each visit, which included best-corrected visual acuity (BCVA) recording with Snellen's chart, intraocular pressure measurement with Goldmann's applanation tonometry, slit lamp biomicroscopy, and fundus examination by 90D and 20D lens. They also underwent fundus fluorescein angiography (FA) using a Carl Zeiss FF 450 Plus (Carl Zeiss Medictec, Dublin, CA, USA) at first visit for confirmation of diagnosis and assessment of the activity. Optical coherence tomography (OCT) was performed using a Topcon 3D 2000 (Topcon Medical Systems, Oakland, NJ, USA) at each visit to assess the activity and response to treatment. Every patient underwent detailed physician evaluation. Patients with a history of uncontrolled hypertension and recent thromboembolic events or any history of cerebrovascular accidents, myocardial infarction were not injected with anti-VEGF.

Systemic corticosteroids were given in a dose of 1 mg/kg body weight orally with 10 mg/week tapering for 6–10 weeks. The sight-threatening inflammatory disease was treated initially with intravenous methyl prednisolone 1 g/day for 3 consecutive days followed by oral corticosteroids. Oral azathioprine (2.5 mg/kg body weight over three divided doses) was used for steroid nonresponders or for patients having a recurrence on steroids.

Diagnostic criteria for uveitis

The diagnosis for specific ocular uveitic entities or systemic disease association was based on a detailed clinical history, ophthalmological examination, general physical examination, and necessary investigations. The anatomical classification of uveitis was based on the International Uveitis Study Group classification system.[20] The short differential diagnosis was made in each case, and subsequently, a tailored laboratory approach was adopted as described by Smith and Nozik.[21] In our case series, acute yellow-white confluent lesions at the level of RPE and choroid starting at the peripapillary region with serpiginous projections spreading centrifugally was considered diagnostic of serpiginous choroiditis. Laboratory investigations were carried out in all patients to rule out other infective agents causing serpiginous-like choroiditis.

The laboratory investigations included complete blood counts, erythrocyte sedimentation rate, Mantoux skin test, *Treponema pallidum* hemagglutination test, serum angiotensin converting enzyme levels, enzyme-linked immunosorbent assay for Toxoplasma, Toxocara, human immunodeficiency virus, quantiferon tuberculosis (TB) gold test, and human leukocyte antigen typing. Radiological investigations included X-rays and high-resolution computed tomography of the chest, X-rays of sacroiliac joints and knee joints. Aqueous and vitreous taps were done wherever felt necessary for cytological examination and polymerase chain reaction. Consultations were sought with internist, rheumatologist, and pulmonologist whenever required to reach the final etiological diagnosis.

Treatment guidelines and technique

All patients underwent IVB (Avastin; Genentech, CA, USA) or IVR (Lucentis; Genentech, CA, USA) on PRN basis. Off-label use of the drugs, potential risks, and benefits and other treatment options were discussed in detail with each patient. Bevacizumab was drawn from a multi-dose vial whereas ranibizumab was withdrawn from single dose vial into a tuberculin syringe under aseptic conditions. After the eye had been prepared with standard pre-operative preparations using 5% povidone-iodine cleaning and antiseptic draping, an eyelid speculum was used to stabilize the eyelids. Intravitreal injection of 1.25 mg (0.05 ml) of bevacizumab or injection of 0.3 mg (0.05 ml) of ranibizumab was given 3.5–4 mm posterior to the limbus, through the inferotemporal pars plana with the help of a 30-gauge needle under topical anesthesia in an operation theater with every aseptic precaution. After the injection, intraocular pressure and retinal artery perfusion were checked and patients were instructed to administer topical antibiotics four times per day for 5 days. Patients were examined at first and third postinjection day and thereafter 1 month after each injection. Re-treatment criteria were persistent or recurrent intraretinal edema, subretinal fluid, increased retinal thickening (>100 μ), and subretinal hemorrhage on clinical examination and on OCT.

Statistical analysis

Statistical analysis was performed using Statistical Package for Social Service (SPSS Ver. 17, IBM Corp., USA). BCVA readings were converted to LogMAR values for the statistical analysis. Values of numerical characteristics were tested for normality and are presented as mean value (± standard deviation), if normally distributed. Student's paired sample *t*-test was used for statistical analysis. A $P < 0.05$ was considered statistically significant.

Results

A total of thirty eyes of 28 patients with inflammatory CNV were included in the study. There were 19 (67.85%) males and 9 (32.14%) females; aged 9–52 years (mean 37.37 ± 12.63 years). The duration of complaints ranged from 7 to 365 days

(mean 119.97 ± 129.53 days). Out of 28 patients, 26 (92.85%) had unilateral presentation, and two (7.14%) had bilateral disease. Among 26 patients with unilateral presentations, 14 (53.84%) had CNV in the right eye and 12 (46.15%) in the left eye [Table 1].

Seven (23.33%) eyes had inflammatory CNV secondary to idiopathic choroiditis. Four (13.33%) eyes had Toxoplasmosis, four (13.33%) had idiopathic panuveitis, four (13.33%) eyes had VKH, three (10%) eyes had GHPC, three (10%) had tubercular choroiditis, two (6.66%) had PIC, and one eye (3.33%) had MCP, sequelae of endogenous endophthalmitis and Hansen's disease each.

Table 1: Demography and baseline characteristics of study eyes

Characteristics	Total (%)
Number of patients	28
Number of eyes	30
Male/female	19/9
Unilateral	26 (92.85)
Right/left	14/12
Location	
Subfoveal	23 (76.66)
Juxtafoveal	3 (10.00)
Para papillary	4 (13.33)
BCVA (Log MAR)	
Baseline	0.60±0.49
Final	0.40±0.49
Visual outcome	
I	16 (53.3)
S	8 (26.6)
D	6 (20.0)

BCVA: Best-corrected visual acuity, I: Improvement in final BCVA, S: No change in final BCVA, D: Deterioration in final BCVA, Log MAR: Log of the minimum angle of resolution

Of thirty eyes, 26 (86.70%) eyes underwent OCT which revealed Type 2 (subretinal) CNV in 22 eyes (84.61%) and Type 1 (sub-RPE) CNV in four eyes (15.38%). Eighteen (60%) eyes underwent FA which revealed predominantly classic CNV in 17 (94.44%), occult CNV in one (5.55%) eye. Twenty-three eyes (76.7%) had subfoveal CNV, three (10%) eyes had juxtafoveal and four (13.3%) eyes had parapapillary CNV.

In this study, all patients underwent treatment with intravitreal anti-VEGF injections alone. A total of 83 injections were given of which 52 (62.65%) were IVB and 31 (37.34%) were IVR. Out of thirty eyes, twenty received IVB alone and nine received IVR alone. One patient received both as he switched from IVR to IVB due to financial reasons. The mean number of injections was 2.76 (range 1–5). None of the patients had any postinjection systemic side effects. Three (10%) eyes had increased intraocular pressure following injection and were treated with topical anti-glaucoma medication. There was no episode of flaring up of intraocular inflammation following injection. No patient had active inflammation at the time of injection. Out of 28 patients, 20 were not on any concomitant immunomodulators while eight patients were on maintenance therapy either with systemic steroids or immunosuppressants. Table 2 summarizes response to anti-VEGF in individual uveitic subgroups.

The mean follow-up was 17.93 ± 14.28 months (range 6–53 months). The mean of baseline BCVA was 0.60 ± 0.49 and final BCVA was 0.40 ± 0.49. Using paired *t*-test, *P* value was 0.083, that is, statistically not significant. Among thirty eyes of inflammatory CNV, 16 (53.3%) showed improvement, eight (26.6%) maintained the same vision, whereas six (20%) eyes showed deterioration of vision. In our cohort, 25 (83.33%) eyes did not have any recurrence whereas five (16.66%) eyes had a recurrence of CNV activity. These

Table 2: Clinical details and response to anti-vascular endothelial growth factor in study eyes

Diagnosis	Number of eyes, *n* (%)	Mean number of injection	BCVA			Recurrence, *n* (%)
			I	S	D	
Postuveitis	20 (66.66)					
Focal	5 (16.66)					
Toxoplasmosis	4 (13.33)	2.25	1	2	1	0
Idiopathic	1 (3.33)	2	0	1	0	1 (100)
Multifocal	15 (50.00)					
Idiopathic	6 (20.00)	3.16	5	1	0	1 (16.66)
Tuberculosis	3 (10.00)	2	3	0	0	0
GHPC	3 (10.00)	3.33	1	0	2	1 (33.33)
PIC	2 (6.66)	3.5	0	1	1	0
MCP	1 (3.33)	2	1	0	0	0
Panuveitis	10 (33.33)					
VKH	4 (13.33)	1.75	2	1	1	0
Idiopathic	4 (13.33)	3.75	3	0	1	2 (50.00)
Hansen	1 (03.33)	3	0	1	0	0
Endophthalmitis	1 (03.33)	3	0	1	0	0

BCVA: Best-corrected visual acuity, I: Improvement in final BCVA, S: No change in final BCVA, D: Deterioration in final BCVA, GHPC: Geographic helicoid peripapillary choroidopathy, PIC: Punctate inner choroidopathy, MCP: Multifocal choroiditis with panuveitis, VKH: Vogt Koyanaki Harada's disease

recurrences were treated with same PRN intravitreal anti-VEGF leading to resolution of CNV.

Discussion

Inflammatory CNV is a sight-threatening multifactorial complication of posterior segment intraocular inflammation. In this study, we report etiology, clinical profile of patients with inflammatory CNV in Indian eyes and their response to intravitreal anti-VEGF therapy. We had cohort of thirty eyes of consecutive inflammatory CNV.

In our study group, patients had a mean age of presentation 37.37 years which was comparable to the mean age in the study by Arevalo *et al*.[6] (41.74 years), Rouvas *et al*.[5] (46 years) and Kramer *et al*.[4] (44 years) [Table 3]. Most of our patients were male (66.7%) which is in contrast to other studies from Western population which had female preponderance. Similar to studies by Kramer *et al*.,[4] Rouvas *et al*.[5] and Arevalo *et al*.,[6] we also had the majority of the patients (92.85%) presenting with unilateral disease. We followed patients for minimum 6 months with mean follow-up of 17.93 ± 14.285 months (range 6–53 months).

Various studies are there from India about the pattern of uveitis in the subcontinent but none about pattern of inflammatory CNV except for few individual case reports. Rathinam and Namperumalsamy[22] and Singh *et al*.[23] have reported idiopathic and GHPC to be the most common cause of posterior uveitis respectively whereas for panuveitis they reported idiopathic and TB to be most common, respectively. Recently, Das *et al*.[24] reported TB to be most common cause of posterior and panuveitis. In our cohort, we found idiopathic choroiditis to be the most common cause of posterior uveitis induced inflammatory CNV. Whereas inflammatory CNV secondary to panuveitis we had equivocal cases of VKH and idiopathic panuveitis.

Rishi *et al*.[25] and Shah and Shah.[26] have reported inflammatory CNV secondary Toxoplasmosis from the Indian subcontinent. Rishi *et al*. reported the efficacy of combined therapy, that is, PDT + IVB and Shah and Shah. reported resolution after single IVR injection. Both have noted gain in visual acuity following resolution of CNV. In our cohort we had four eyes with Toxoplasmosis with inflammatory CNV. Of these four eyes, one received single IVB with resolution of CNV. Another one eye had two IVR with gain in visual acuity, whereas remaining two eyes had three IVB each with the deterioration of vision in one eye and maintenance in the other eye. None of these four eyes had any recurrence.

Rao *et al*.[27] have reported a case of PIC in which there was flaring up of choroiditis and CNV due to pregnancy. There is no other report of inflammatory CNV secondary to PIC from India. In our series, we had two eyes with inflammatory CNV secondary to PIC. One eye received total of four injections (2 IVB + 2 IVR) with the maintenance of BCVA. Other eye received three IVR with the deterioration of BCVA. None of them had any recurrence. Arevalo *et al*.[6] have reported eight cases of PIC-induced inflammatory CNV, out of which seven had stable or improved vision and one case had deterioration in BCVA. We had a single eye with MCP who gained vision without any recurrence.

To the best of our knowledge, there is no report in the literature about VKH, GHPC, panuveitis or idiopathic choroiditis related inflammatory CNV from the Indian subcontinent. We had four eyes with VKH which underwent IVB with resolution of CNV and no recurrence. In series by Kramer *et al*.[4] and Rouvas *et al*.[5] none of the patient had VKH. Arevalo *et al*.[6] reported one case in there series who had 5 IVB injections with improvement in visual acuity. In our series, we had three eyes with GHPC and out of these two had deterioration of vision; of these two, one had recurrence of CNV. Arevalo *et al*. reported six eyes with GHPC and none had deterioration of vision, they had either improvement or maintained the baseline visual acuity.

Out of thirty eyes, we had 7 eyes with idiopathic choroiditis in which two had recurrences, but all eyes either maintained or gained visual acuity. Mansour *et al*.[7] have reported maintenance or gain in BCVA in their series of 12 eyes with idiopathic choroiditis related CNV. We had four eyes with idiopathic panuveitis in which two eyes developed recurrence out of which one eye had drop in final visual acuity and other had gain in vision. Kramer *et al*. have reported two eyes with inflammatory CNV secondary to panuveitis, in which they have not mentioned etiology of panuveitis. Both eyes had gain in visual acuity.

There is no report of tuberculous choroiditis related CNV in literature. We had three such eyes in our series who gained vision without recurrence. Our study reports inflammatory CNV secondary to endogenous endophthalmitis and Hansen's panuveitis for the first time. Both cases have maintained visual acuity without recurrence.

In concordance with all studies on inflammatory CNV, majority of our patients had classic (94.44%) and Type 2 (84.61%) presentation on FFA and OCT, respectively. We have found subfoveal CNV to be the most common, that is, 76.7% which was similar what Rouvas *et al*.[5] have reported. The mean number of injections given was 2.76 (range 1–5) which is similar to what Kramer *et al*.[4] (2.7 ± 2) and Rouvas *et al*.[5] (2.3). In ours

Table 3: Comparison with other studies

	Year	Number of eyes	Anti-VEGF	Follow up (months)	Number of injections (mean)	Recurrence, *n* (%)
Adán *et al*.[3]	2007	9	IVB	7.1	NA	1 (11.11)
Kramer *et al*.[4]	2010	10	IVB	13±8	2.7±2	1 (10.00)
Rouvas *et al*.[5]	2011	16	IVR	17.6±6	2.3	0
Arevalo *et al*.[6]	2011	23	IVB	24	1.73±1.17	9 (39.13)
Mansour *et al*.[7]	2012	27	IVB	24	3.6±4.2	NA
Present study	2016	30	IVB/IVR	17.93±14.28	2.76	5 (16.66)

Anti-VEGF: Anti-vascular endothelial growth factor, IVB: Intravitreal bevacizumab, IVR: Intravitreal ranibizumab, NA: Not available

and Rouvas *et al*.[5] study, population none of the patients had any systemic side effects or local side effects like intraocular inflammation as experienced by Kramer *et al*.[4] and Arevalo *et al*.[6] In our series, number of injection did not correlate with etiology of inflammatory CNV. Like eyes which received just single anti-VEGF injection were having VKH, tuberculous choroiditis and Toxoplasmosis. Eyes which underwent maximum injections had idiopathic choroiditis and idiopathic panuveitis.

Although we achieved gain in BCVA with treatment; it was not statistically significant. Similar to Rouvas *et al*. and Kramer *et al*.,[5,4] we also note that a maximum number of patients (53.3%) had showed improvement of visual acuity but few BCVA in few patients (26.7%) remained static. Unlike others; except Arevalo *et al*.[6] we found 20% of our patients had deterioration in visual acuity.

We had five eyes with recurrence of CNV following treatment. Similarly, Kramer *et al*. and Arevalo *et al*.[4,6] had recurrences in one and nine eyes, respectively. Of 28 patients, none had active inflammation though eight patients were on maintenance therapy with immunomodulators. Kramer *et al*.[4] also had five patients who received steroids and out those two had active inflammation.

Added to the varied presentation, the absence of randomized clinical trials on treatment of inflammatory CNV makes the management of this disease an evolving process. PDT has been used for treatment, with the understanding that it provides a favorable outcome in classic CNV; however, the results have been variable. Anti-VEGF is increasingly being used for the treatment of inflammatory CNV, though the injection protocol remains uncertain. Heier *et al*.[28] compared the efficacy of monthly IVR with 3 monthly IVR followed by PRN injections for non-AMD CNV and had found comparable efficacy with both treatment protocols. They have also mentioned that patients on PRN protocol received 38% fewer injections than those on monthly injection protocols to achieve a similar outcome. Although there is no similar study comparing different injection protocols for IVB or IVR, multiple studies show the efficacy of PRN IVB or IVR in inflammatory CNV. Although ours was a retrospective study we did find that 80% of patients maintained or gained vision at final follow-up; which adds to evidence that IVB or IVR on PRN basis achieve desired outcomes in eyes with inflammatory CNV.

Conclusion

Idiopathic choroiditis is the most common cause of inflammatory CNV and anti-VEGF (ranibizumab or bevacizumab) used on PRN basis appears to have effective treatment response.

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Conflicts of interest

There are no conflicts of interest.

References

1. Perentes Y, Van Tran T, Sickenberg M, Herbort CP. Subretinal neovascular membranes complicating uveitis: Frequency, treatments, and visual outcome. Ocul Immunol Inflamm 2005;13:219-24.
2. Winterhalter S, Joussen AM, Pleyer U, Stübiger N. Inflammatory choroidal neovascularisations. Klin Monbl Augenheilkd 2012;229:897-904.
3. Adán A, Mateo C, Navarro R, Bitrian E, Casaroli-Marano RP. Intravitreal bevacizumab (Avastin) injection as primary treatment of inflammatory choroidal neovascularization. Retina 2007;27:1180-6.
4. Kramer M, Axer-Siegel R, Jaouni T, Reich E, Hemo I, Priel E, *et al.* Bevacizumab for choroidal neovascularization related to inflammatory diseases. Retina 2010;30:938-44.
5. Rouvas A, Petrou P, Douvali M, Ntouraki A, Vergados I, Georgalas I, *et al.* Intravitreal ranibizumab for the treatment of inflammatory choroidal neovascularization. Retina 2011;31:871-9.
6. Arevalo JF, Adan A, Berrocal MH, Espinoza JV, Maia M, Wu L, *et al*. Intravitreal bevacizumab for inflammatory choroidal revascularization: Results from the Pan-American collaborative retina study group at 24 months. Retina 2011;31:353-63.
7. Mansour AM, Arevalo JF, Ziemssen F, Mehio-Sibai A, Mackensen F, Adan A, *et al.* Long-term visual outcomes of intravitreal bevacizumab in inflammatory ocular neovascularization. Am J Ophthalmol 2009;148:310-6.e2.
8. Neri P, Lettieri M, Fortuna C, Manoni M, Giovannini A. Inflammatory choroidal neovascularization. Middle East Afr J Ophthalmol 2009;16:245-51.
9. Cohen SY, Laroche A, Leguen Y, Soubrane G, Coscas GJ. Etiology of choroidal neovascularization in young patients. Ophthalmology 1996;103:1241-4.
10. Ho AC, Yannuzzi LA, Pisicano K, DeRosa J. The natural history of idiopathic subfoveal choroidal neovascularization. Ophthalmology 1995;102:782-9.
11. Chan WM, Lai TY, Lau TT, Lee VY, Liu DT, Lam DS. Combined photodynamic therapy and intravitreal triamcinolone for choroidal neovascularization secondary to punctate inner choroidopathy or of idiopathic origin: One-year results of a prospective series. Retina 2008;28:71-80.
12. Macular Photocoagulation Study Group. Argon laser photocoagulation for ocular histoplasmosis: Results of a randomized clinical trial. Arch Ophthalmol 1983;101:1347-57.
13. Flaxel CJ, Owens SL, Mulholland B, Schwartz SD, Gregor ZJ. The use of corticosteroids for choroidal neovascularisation in young patients. Eye (Lond) 1998;12(Pt 2):266-72.
14. Dees C, Arnold JJ, Forrester JV, Dick AD. Immunosuppressive treatment of choroidal revascularization associated with endogenous posterior uveitis. Arch Ophthalmol 1998;116:1456-61.
15. Essex RW, Tufail A, Bunce C, Aylward GW. Two-year results of surgical removal of choroidal neovascular membranes related to non-age-related macular degeneration. Br J Ophthalmol 2007;91:649-54.
16. Postelmans L, Pasteels B, Coquelet P, Caspers L, Verougstraete C, Leys A, *et al.* Photodynamic therapy for subfoveal classic choroidal neovascularization related to punctate inner choroidopathy (PIC) or presumed ocular histoplasmosis-like syndrome (POHS-like). Ocul Immunol Inflamm 2005;13:361-6.
17. Rosenfeld PJ, Brown DM, Heier JS, Boyer DS, Kaiser PK, Chung CY, *et al.* Ranibizumab for neovascular age-related macular degeneration. N Engl J Med 2006;355:1419-31.
18. Brown DM, Kaiser PK, Michels M, Soubrane G, Heier JS, Kim RY, *et al.* Ranibizumab versus verteporfin for neovascular age-related macular degeneration. N Engl J Med 2006;355:1432-44.
19. Baxter SL, Pistilli M, Pujari SS, Liesegang TL, Suhler EB, Thorne JE, *et al.* Risk of choroidal neovascularization among the uveitides. Am J Ophthalmol 2013;156:468-77.e2.
20. Bloch-Michel E, Nussenblatt RB. International Uveitis Study Group

recommendations for the evaluation of intraocular inflammatory disease. Am J Ophthalmol 1987;103:234-5.

21. Smith RE, Nozik RA. Uveitis: A Clinical Approach to Diagnosis and Management. 2nd ed. Baltimore: Williams and Wilkins; 1989. p. 23-6.
22. Rathinam SR, Namperumalsamy P. Global variation and pattern changes in epidemiology of uveitis. Indian J Ophthalmol 2007;55:173-83.
23. Singh R, Gupta V, Gupta A. Pattern of uveitis in a referral eye clinic in North India. Indian J Ophthalmol 2004;52:121-5.
24. Das D, Bhattacharjee H, Das K, Tahiliani PS, Bhattacharyya P, Bharali G, *et al.* The changing patterns of uveitis in a tertiary institute of Northeast India. Indian J Ophthalmol 2015;63:735-7.
25. Rishi P, Venkataraman A, Rishi E. Combination photodynamic therapy and bevacizumab for choroidal neovascularization associated with toxoplasmosis. Indian J Ophthalmol 2011;59:62-4.
26. Shah NJ, Shah UN. Intravitreal ranibizumab for the treatment of choroidal neovascularization secondary to ocular toxoplasmosis. Indian J Ophthalmol 2011;59:318-9.
27. Rao VG, Rao GS, Narkhede NS. Flare up of choroiditis and choroidal neovasculazation associated with punctate inner choroidopathy during early pregnancy. Indian J Ophthalmol 2011;59:145-8.
28. Heier JS, Brown D, Ciulla T, Abraham P, Bankert JM, Chong S, *et al.* Ranibizumab for choroidal neovascularization secondary to causes other than age-related macular degeneration: A phase I clinical trial. Ophthalmology 2011;118:111-8.