



Original article

Changing trends in idiopathic retinal vasculitis in a tertiary eye care centre of Nepal over a ten-year period

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Abstract

Objectives: To study the demographic profile, clinical presentations, management and visual outcome of retinal vasculitis in a tertiary eye care center of Nepal

Materials and methods: A retrospective, record based study of retinal vasculitis cases in the retina clinic of a tertiary care centre in Nepal from January 2009 to January 2011 was carried out. Results of the study were compared to those from the study conducted in a similar set-up between 1998 and 2000.

Results: Sixty-nine eyes of 51 affected patients were evaluated in the study. The male/female ratio was 2.64:1 vs 19:1 a decade ago ($p=0.0027$). The mean age of the patients was 33.53 ± 12.29 years in the present study. Bilateral ocular involvement was present in 18 cases (35.3%) vs 56.14% in the past decade ($p=0.044$). The common symptoms were dimness of vision (29.4%), floaters (25.5%) and flashes of light (3.92%). Seventy-one eyes (69.6%) had the best corrected visual acuity of 6/18 or better. Four eyes (3.92%) had no light perception. Vascular sheathing was the most common finding (32.35%), followed by vitritis (30.39%). Corticosteroids were primarily used to manage retinal vasculitis (39.21%). No association of retinal vasculitis with tuberculosis was found.

Conclusion: The demographic pattern and clinical presentation of idiopathic retinal vasculitis has changed over a decade period in Nepal.

Key-words: Eales' disease, steroid, tuberculosis, vitreous haemorrhage

Introduction

Eales' disease is named after Henry Eales, a British ophthalmologist, who described the clinical picture of recurrent retinal haemorrhages in young adults aged 14 to 29 years in 1880 (Eales et al, 1882). The disease affects healthy young adults with male predominance in up to 97.6% of cases (Biswas et al, 2002). After diabetes, it is one of the major

causes of visual impairment and blindness in patients attending the vitreo-retina clinic at BP Koirala Lions Centre for Ophthalmic Studies, Kathmandu (Shrestha et al, 2009).

To date, the exact etiology of Eales' disease is unknown. Recent studies have revealed no definite association between this disease and tuberculosis, hypersensitivity reaction to tuberculo-protein, thrombocytopenic purpura, multiple sclerosis and various neurological and haematological disorders. Immunological, molecular biological and

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biochemical studies have indicated the role of human leukocyte antigen, retinal autoimmunity, mycobacterium tuberculosis genome, and free radical mediated damage in the etiopathogenesis of this disease (Biswas et al 2002).

Clinical manifestation of this disease is due to three basic pathological changes: inflammation (peripheral retinal perivasculitis), ischemic changes (peripheral retinal capillary non-perfusion); and neovascularisation of the retina or disc, which often leads to vitreous hemorrhage (Biswas et al 2002). Based on the clinic-pathological features, Eales' disease is classified into four stages (Charmis et al, 1965). Stage I (inflammation) is characterized by mild periphlebitis of small peripheral retinal capillaries with localized areas of peripheral retinal edema. Perivasculitis of the venous capillary system is widespread and associated with retinal haemorrhages in stage II (ischemia). New vessel formation with abundant haemorrhage in the retina and vitreous is seen in stage III (neovascularisation) and the stage IV (complications) is the end result of massive and recurrent vitreous haemorrhages with retinitis proliferans and tractional retinal detachment.

Prognosis for patients with Eales' disease may vary depending on the availability of medical care. Many patients in Nepal live in the areas that are underserved by medical care. In locations where specialized medical care is available, the outcomes tend to be better with treatment. This study was carried out to assess the demographic pattern, clinical presentation and treatment outcome of idiopathic retinal vasculitis in Nepal and compare these parameters with those of a similar study conducted roughly a decade ago in the same centre.

Materials and methods

A retrospective review of medical records was conducted on patients presenting between January 2009 and January 2011 at the retina clinic of BP Koirala Centre for Ophthalmic Studies, a tertiary eye centre of Nepal. Informed written consent was obtained from the patients. The study was conducted adhering to the principles of the

Declaration of Helsinki and was approved by the Institutional Review Board. Diagnosis of the retinal vasculitis was done based on retinal findings and supporting fundus fluorescein angiography findings. Diabetes mellitus, tuberculosis, sickle cell hemoglobinopathy, blood dyscrasias, sarcoidosis and collagen vascular disorders were ruled out after proper history, examination and investigations. All the eyes were staged according to the Charmis classification (1965).

A total of 51 patients were enrolled in the study. Each patient received a comprehensive eye examination as per the pro forma. Detailed scrutiny of each patient's systemic history, drug history and laboratory findings was performed.

Presenting, best-corrected and final visual acuity was measured using the Snellen's acuity chart. Slit-lamp bio-microscopy and indirect ophthalmoscopy was used for ocular examination. Cellular grading was performed according to Hogan's classification system. Fundus examination of every patient was performed under mydriasis. Fluorescein angiography was used to note the presence of capillary non-perfusion, collaterals, neovascularization and status of the macula. Details of the treatment provided were noted for each subject.

The findings of the present study were compared to a similar study performed at the same centre between 1998 and 2000. The previous study included 89 eyes of 57 cases of Eales' disease. All data were recorded in a pro forma and analyzed using SPSS statistics software version 17 (SPSS Inc., Chicago, IL, USA).

Results

Among 51 cases, 18(35.3%) were inhabitants of the Kathmandu valley and 33(64.7%) were from outside the valley. Of them, 37 (72.5%) were males and 14(27.5%) were females, the male to female ratio being 2.64:1. The mean age of the patients was 33.53 ± 12.29 years with the range of 18 -74 years. Twenty-one patients (41.1%) were of the

age 21-30 years. Fifteen were in the age group of 31-40 years (29.3%, Table 1).

Bilateral ocular involvement was present in 18 cases (35.3%) and unilateral in 33 (64.7%). Of the unilateral cases right eye was involved in 22 and left eye in 11 cases. A total of 69 eyes in 51 patients were involved.

The mean duration of the ocular symptoms was 578 ± 89 days. Of the 102 eyes, the three most common symptoms were dimness of vision (30; 29.4%), floaters (26; 25.5%) and flashes (4; 3.92%). Other symptoms noted were redness, ocular discomfort and foreign body sensation.

Of the 102 eyes, 71 eyes (69.6%) had a best-corrected visual acuity of 6/18 or better. Thirteen

eyes (12.74%) had the visual acuity between 6/24 and 3/60; and fourteen eyes (13.72%) had less than 3/60. Four eyes (3.92 %) had no light perception.

The lens was clear in 88 eyes (86.27%), posterior sub-capsular cataract was present in 3 eyes (2.94%), Senile cataract in 5 eyes (4.90%), 3 eyes were pseudophakic (2.94 %) and 1 eye (0.98 %) was aphakic. Vascular sheathing (Figure-1) was noted in 33 eyes (32.35%) and vitritis in 31 (30.39%) making these two the most common findings in retinal vasculitis. Vitreous haemorrhage was the most common type of haemorrhage noted. Of the 23 (22.54%) eyes affected by vitreous haemorrhage, 15 eyes (14.7%) had a fresh haemorrhage and 8 eyes (7.84%) had old haemorrhage.

Table 1
Age distribution of patients of Eales' disease

Age group	Gender		Total	Percentage (%)
	Male	Female		
0-10 years	0(0%)	0(0%)	0	0%
11-20 years	5(9.8%)	0(0%)	5	9.8%
21-30 years	17(33.3%)	4(7.8%)	21	41.1%
31-40 years	9(17.6%)	6(11.7%)	15	29.3%
41-50 years	2(3.9%)	3(5.8%)	5	9.8%
51-60years	2(3.9%)	0(%)	2	3.9%
61-70years	1(1.9%)	1(1.9%)	2	3.9%
71-80 years	1(1.9%)	0(0%)	1	1.9%
Total	37(72.54%)	14(27.45%)	51	100%

Retinal neovascularization at the disc and elsewhere was present in 18 eyes (17.64%). Macular involvement was also observed in the form of epiretinal membrane with tractional retinal detachment (6.86%), macular branch venous occlusion (3.92%) and cystoid macular oedema (1.96%).

The most common stage of presentation was the stage of resolution (41.17%), followed by the stage of ischemia (13.72%), the stage of neovascularization (9.8%) and finally the stage of inflammation (5.88%).

The mean IOP was 14.10 ± 2.4 mmHg. Capillary non-perfusion (12.74 %) was the most common angiographic finding followed by collaterals (7.84%).

Corticosteroids were the mainstay of management of retinal vasculitis. Oral steroids were administered in 20 cases (39.21%) and intravenous methylprednisolone in 1 individual (1.96%). No immunosuppressive agents were used. But intra-vitreous bevacizumab was given to 1 individual (1.96%) with active neovascularisation.

Retinal laser photocoagulation therapy was the modality of treatment in 22 eyes (21.56%). Six eyes (5.88%) underwent pars plana vitrectomy for vitreous haemorrhage. Though the Mantoux test was positive in 18 cases (35.3%), tuberculosis was confirmed with X-ray chest and sputum examination for acid fast bacilli in only 1 individual (1.96%) who was commenced on anti-tubercular therapy.

Thirty-four (66.7%) patients had history of treatment for retinal vasculitis for the past episode or for a

recent attack before visiting our centre. Only 17(33.3%) cases were new.

Twenty eyes (19.6%) gained one or more lines on Snellen's distant visual acuity chart, 7 eyes (6.86%) lost one or more lines and 4 eyes (3.92%) had no perception of light. However, 71 eyes (69.60%) maintained their initial visual acuity through the available follow-up period.

The above results were compared with the results of the study conducted a decade ago among the patients in the same clinic (Table-2).

Table 2
Comparison of the present study with the similar study of 10 years ago

Parameters	Study of 1998-2000	Study of 2009-2011	Remarks
No. of patients	57	51	
Male/Female ratio	19:1	2.64:1	p= 0.0027
Age group affected	31 – 40 years (54.43%)	21 – 30 years (43.13%)	
Laterality of involvement	Bilateral (56.14%) Unilateral (43.86%)	Bilateral (35.3%); Unilateral (64.7%)	p= 0.0044
Presenting visual acuity	Normal : 48.24% Blindness: 27.19%	Normal: 69.6% Blindness: 17.64%	
Final visual acuity	Normal: 50.27% Blindness: 22.80%	Normal: 71.8% Blindness: 12.64%	
Stage of presentation	Stage III: 40.44% Stage I: 28.08% Stage IV: 20.22% Stage II : 11.23%	Stage IV: 41.17% Stage III: 13.72% Stage II: 9.8% Stage I: 5.88%	
Association with pulmonary tuberculosis	2 cases (3.5%)	1 case (1.96%)	
Mean IOP	13.54± 1.875mmHg	14.10 ± 2.375mmHg	

Discussion

Eales' disease, observed more commonly in the Indian subcontinent than in the rest of the world, occurs in young healthy adult males, initially presenting as retinal periphlebitis and later as retinal ischemia that may lead to vascular alterations and neovascularization (reference required).

In the previous study from this centre, bilateral involvement was found in 56.14%. In the present

study, unilateral (64.7%) presentation was more than bilateral (35.3%), which is statistically significant (p = 0.0044). This disparity could be due to an increased awareness among the symptomatic patients to seek care at a tertiary centre. It could also be due to the duration of the study. Clustering of cases in second to fourth decade of life is similar to the reports from India. Kumar et al (year of



publication and listing in the references) found that the range of age of the patients was 12-62 years and mean age was 32.9 ± 11.4 years. The means of age of male and female cases were 33 ± 11.1 and 32.4 ± 13.6 years respectively. In the present study, the mean age of patients was 33.53 ± 12.29 years with the range of 18-74 years. The previous study from our centre had an age range from 16-60 years with male to female ratio of 19:1 which is in sharp contradiction to 2.64:1 in the present study. Higher prevalence of Eales' disease in female may be the result of an increased female literacy rate and increasing awareness of the need for eye exams in this population. According to Graham (Graham et al, 1989) idiopathic retinal vasculitis usually occurs in young people with equal male to female ratio. He also reported that 75% cases of Eales' disease were present before 50 years of age. Our study is comparable as 82.7% presented before 40 years of age.

In the present study, most of the cases (69.6%) had a best corrected visual acuity of 6/18 or better at presentation. However fourteen eyes (13.72%) had vision less than 3/60 and four eyes (3.92%) had no light perception of light. The study of Kumar et al (poor vision was present in 10.6% and no light perception in 1.8%) is very comparable to the present study. Over the past decade, there has been a decrease in the number of patients with poor vision, from 27.19% to 10.6%. This could be due to the increased awareness of the disease and eye health care, improved treatment modality, earlier presentation and fewer economic constraints.

The most common ocular manifestation of idiopathic retinal vasculitis was vascular sheathing (32.35%) which is comparable with the study done previously in this centre (47.19%). This lower percentage, when compared to the studies of Kumar (68.1%), Graham (64%) and Abraham (84%), may be due to the prior treatment in other centres and or late presentation of the disease. Saxena et al (year of publication and listing in references) reported vitreous haemorrhage as the most common

presenting sign and this difference might be due to the fact that all cases of primary retinal vasculitis are not Eales' disease, which is considered a specific disease entity.

Tuberculosis is a prevalent disease in Nepal. A positive Mantoux test was found in 18 cases (35.3%) in our study group but radiological and microbiological confirmation was found in only 1 case (1.96%). The previous study at our centre revealed 16 cases (28.07%) with a positive Mantoux test, but only two confirmed cases of tuberculosis. Kumar et al reported a positive Mantoux test in 21 (30%) individuals, but only four (5.71%) individuals with confirmed tuberculosis. Habibullah et al (Year of publication and listing) found no statistically significant association between Mantoux positivity and tuberculous retinal vasculitis. In a case-control study of Eales disease in India, no statistically significant difference in Mantoux positivity was seen between cases and controls (Biswas et al 1997). This trend could apply to our study population as well.

In another study, 11 of 23 epiretinal membranes removed from eyes with Eales disease showed mycobacterium tuberculosis genome 106 by nested PCR technique. However, culture of vitreous specimen did not show any growth of mycobacterium tuberculosis (Madhavan et al, 2000). Thus, the role of mycobacterium tuberculosis genome in the pathogenesis of Eales disease is yet to be ascertained.

Despite the available therapeutic measures, vitreous haemorrhages are still the primary cause for impaired vision in Eales' disease. The first episode of vitreous hemorrhage usually clears but recurrent vitreous haemorrhages may lead to formation of traction bands and membranes in the vitreous and subsequent complications. In a study from Nepal (Malla et al, 1999), 40 eyes of forty patients with vitreous hemorrhage due to Eales' disease underwent simple vitrectomy. In the previous similar study of a decade ago, vitreous haemorrhage was present in 29 eyes (32.5%) and vitrectomy was

done in 9 eyes (10.11%) with better and earlier visual outcomes. In the present study, vitreous haemorrhage was present in 23 eyes (22.54%) out of which 6 eyes (5.88%) underwent pars plana vitrectomy, the results of which are comparable to the study by Kumar and Abraham et al (proper citation required). Early vitrectomy has better prognosis as it gives early visual recovery and probably removes the noxious stimuli from the vitreous and the inflammatory debris.

Usually patients with Eales' disease have extensive antero-peripheral non-perfusion with spare macula, but in our study, macular ischemia was also present leading to profound loss of vision.

Capillary non-perfusion (12.74 %) was the most common angiographic finding followed by collaterals (7.84%) which is comparable to the previous study from this institute.

The most common stage of presentation in the 1998-2000 study was the stage of ischemia (40.44%) followed by stage of inflammation (28.08%). The results of the study done decade later show the stage of resolution (41.17%) and stage of ischemia (13.72%) as the two most common stages of presentation. Late presentation in our facility may be due to the improved treatment facility in the peripheral hospitals.

Howe et al (1994) believed that high doses of oral steroids should be used for the initial management of patients with idiopathic retinal vasculitis. Similarly in our study, patients presenting at the stage of inflammation, received oral corticosteroids (39.21%) and intravenous methylprednisolone (1.96%). Those presenting at the stage of ischemia, underwent retinal photocoagulation (21.56%). Intra-vitreous bevacizumab was given in 1 individual (1.96%) with active neovascularisation.

Among our study population, 66.7% cases had received treatment for retinal vasculitis prior to visiting our centre. This result is comparable to the previous study from this centre (64.9%).

Conclusion

Over the past decade, the profiles of Eales' disease in a tertiary eye hospital in Nepal seem to be changing. Earlier, the disease showed significant male predominance but now the trend has changed, and females affected with Eales' disease are emerging. Unilateral presentation has become more common than bilateral. Though vitreous hemorrhage is still the most common cause of visual loss, visual prognosis is usually good due to the advent of sophisticated vitrectomy instruments, laser photocoagulation techniques and early vitrectomy.

As the aetiopathogenesis of Eales' disease still remains to be ascertained, it is essential that a multidisciplinary and multicentre collaborative approach would unravel the exact pathogenic mechanism.

References

- Abraham C, Baig SM, Badrinath SS (1997). Eales's disease. Proc all India ophthal SOC 33;226.
- Biswas J, Narain S, Roy S, Madhavan HN (1997). Evaluation of lymphocyte proliferation assay to purified protein derivative, enzyme linked immunosorbant assay, and tuberculin hypersensitivity in Eales disease. Indian J Ophthalmol 45:93-7.
- Biswas J, Sharma T, Gopal L et al (2002). Eales Disease: An update Surv Ophthalmol 47:(3);197-204.
- Charmis J (1965). On the classification and management of the evolutionary course of Eales' disease. Trans Ophthalmol Soc UK. 85:157.
- Das T, Biswas J, Kumar A, et al. Eales disease (1994). Indian J Ophthalmol; 42:3-18.
- Eales H: Primary retinal haemorrhage in young men (1882). Ophthalmic Rev 1:41.
- Gadkari SS, Kamdar PA, Jehangir RP, et al (1992). Pars plana vitrectomy in vitreous haemorrhage due to Eales disease. Indian J Ophthalmol 40:35-7.



Graham EM (1989). A point prevalence study of 150 patients with idiopathic retinal vasculitis. *BJO* 73:714-721.

Howe L J, Stanford MR, Edelsten C (1994). The efficacy of systemic corticosteroid in sight threatening retinal vasculitis. *Eye*; 8:443-447.

Madhavan HN, Therese KL, Gunisha P (2000). Polymerase chain reaction for detection of *Mycobacterium tuberculosis* in epiretinal membrane

in Eales disease. *Invest Ophthalmol Vis Sci*; 41:822-5.

Malla OK, Shrestha J, Dhital S, Miller S.D (1999). A retrospective study of vitrectomy on 40 eyes with vitreous haemorrhage due to Eales' Disease. *JNMA* 38;14-17.

Shrestha J K, Khadka D, Lamichhane G, Khanal S (2009). Retinal vasculitis. *Nep J Oph* .1(1):66-71.

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