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Evaluation of Aetiological Factors of Vasculitis Retinae in a Tertiary Specialized Eye Hospital in Bangladesh

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Abstract

Vasculitis retinae (VR) is a potentially sight threatening inflammatory condition of eye which may occur as isolated intraocular disorder or in association with various systemic diseases. It may occur as an idiopathic condition, as a manifestation of infections or non-infectious auto immune disorders. Impractical or unthoughtful approach increases the burden of treatment cost because of long investigation list. This prospective, observational study was carried out at the National Institute of Ophthalmology & Hospital (NIOH), a tertiary specialized eye hospital, Dhaka, Bangladesh, between March 2020 and February 2021, which aims to determine the common aetiology of VR patients. A total of 45 patients of VR were prospectively examined and investigated thoroughly. The mean age of mean age of onset of disease was 29.5 years where 82.2% were male. Among the 72 eyes of 45 patients of vasculitis retinae, the most common aetiology was Eales disease (52.8%), followed by tubercular VR (33.3%). Other causes of VR found in the study were toxoplasmosis (8.3%), systemic lupus erythematosus (SLE) (2.8%) and sarcoidosis (2.8%). The most common cause of VR was found Eales disease followed by Tubercular VR. Although the study has the limitations of being cross sectional and hospital based, the information from the study can be used by the ophthalmologist while dealing with the VR patients.

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Introduction

Vasculitis retinae (VR) is a potentially sight threatening inflammatory eye condition characterized by perivascular sheathing and vascular leakage or occlusion on fluorescein angiogram of retinal vessels. It can be a common clinical finding in various infective, inflammatory and neoplastic processes within the body. However a subgroup termed as primary retinal vasculitis, an idiopathic condition where no positive correlation can be established.[1] The actual incidence of VR in the USA has been estimated as 1 to 2 per 100000.[2] VR occurs in approximately 1 (One) in 8 (eight) eyes of uveitis.[3] There are significant regional & geographical variations. Limited data are available regarding VR in Asia.[4,5] Eales disease

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is reported in 1 (one) in 200-250 ophthalmic patient in India while it is rare in developed counties.[6]

The evaluation of the aetiology of VR is very important for the modality of treatment as it is a manifestation of infectious disease such as tuberculosis, syphilis, toxoplasmosis, Lyme disease or acute retinal necrosis; as a part of neurological disorders such as multiple sclerosis or in association with a systemic immune mediated diseases such as SLE, RA, Behcet disease. Autoimmune processes are thought to be responsible when retinal vasculitis occurs without systemic manifestations.[7] Apart from infective and neoplastic VR, most of the cases of retinal vasculitis which are secondary to systemic inflammation and those of primary category have indiscriminate clinical presentation making it difficult of pinpoint the etiology based on clinical examination alones.[8] Tailored laboratory investigations have been advocated as the only way to find out the etiology of such cases of VR.[9] Adequate knowledge of the frequency of aetiology of VR on regional basis is important as the disease pattern is different in our country from the other parts of the world, where infectious disease are more common than autoimmune diseases. Good prognosis can be expected with early diagnosis and adequate treatment. In this study, we analyze the patients with VR to evaluate the common aetiological factors in a tertiary eye care center in Bangladesh.

Methods

This prospective, observational study was carried out at the National Institute of Ophthalmology & Hospital (NIOH), a tertiary specialized eye hospital, Dhaka, Bangladesh, between March 2020 and February 2021. In this study, 72 eyes of 45 patients of vasculitis retinae were prospectively examined and investigated consecutively who had attended at the retina clinic of the hospital. Patients were diagnosed as vasculitis retinae if the inflammation was identified in the retinal blood vessels which manifests by perivascular sheathing and inflammation located along the vessels associated with cotton wool spots, retinal exudates, retinal hemorrhages or neovascularization on clinical examination or by ischemia, vascular occlusion and/or leakage as identified by fluorescein angiogram (FA) at any time while attending the clinic. Age at initial consultation, sex, laterality of the disease and duration of symptoms were recorded.

All patients underwent complete ocular examination including slit lamp biomicroscopy, tonometry and indirect ophthalmoscopy. Laboratory investigations included complete blood count (CBC), erythrocyte sedimentation rate (ESR), urine analysis, antinuclear antibody (ANA), Chest X-ray (CXR) was the routine laboratory investigations. Tuberculin skin test (TST) was performed in all patients with suspected diagnosis of ocular tuberculosis, i.e in all patients with ocular features consistent with the diagnosis of Eales disease and patient with abnormal CXR. Due to the fact that the study was done in the tubercular endemic area and country with obligatory Bacillus Calmette Guerin (BCG) vaccination, considering TST positive when the reaction was at least 10 mm in diameter. Quantiferon TB Gold was done on suspected TB patients. Chest computerized tomography (CT) was performed in patients who had positive TST

and/or abnormal CXR. A measurement of angiotensin-converting enzyme (ACE), serum lysosome, serum calcium, IgM and IgG for toxoplasma, serology for human immunodeficiency virus (HIV) type 1 and Treponema pallidum were done in selective cases.

Intraocular fluid (aqueous and/or vitreous) analysis by polymerase chain reaction (PCR) for cytomegalovirus (CMV), herpes simplex virus (HSV), varicella zoster virus (VZV) was performed in selective patients based on clinical presentation. Aqueous sampling was performed by standard anterior chamber tap and vitreous sampling was principally performed in patients requiring therapeutic vitrectomy for the complications of vasculitis retinae. Sample was taken from one eye (more affected eye) in case of bilateral involvement.

Fluorescein angiography was performed in patients who has active vasculitis retinae and ocular media clear enough to allow photography and also in patients after vitrectomy operations. Uveitis was classified according to the anatomical location recommended by Standardization of Uveitis Nomenclature (SUN) working group.[10] Diagnosis of Eales disease (ED) was made in the patients with no sign or symptom of associated systemic disease and was based on the clinical features of peripheral retinal phlebitis in combination with peripheral retinal capillary non-perfusion, sometimes complicated by neovascularization with or without accompanying vitreous hemorrhages[11] and was considered a noninfectious disorder. Diagnosis of systemic lupus erythematosus (SLE) was based on the criteria of American College of Rheumatology.[12] Tubercular vasculitis retinae was diagnosed when vasculitis retinae was associated with systemic TB at any site or ocular lesions (choroiditis, chorioretinitis or choroidal scar) consistent with ocular TB and had either abnormal CXR or one positive immunological test (TST or QTB gold test).

The study was approved by the Institutional Review Board of the National Institute of Ophthalmology & Hospital (NIOH), Dhaka, Bangladesh.

Results

Among the 45 patients, 37 were male (82.2%) while the mean age of the patients was 29.5±5.3 years. The mean duration of symptoms was 2.1±0.3 months (Table-I). According to ocular findings, two third (66.7%) of the patients had vitritis, less than half (45.8%) had vascular sheathing. Sclerosed vessels were evident in one fourth (25%) patients. Most of the patients had venous involvement (90.3%) while in 86.1% cases, the locations of vessels were both central and peripheral (Table-II). The most common aetiology of vasculitis retinae was Eales disease (52.8%), followed by tubercular VR (33.3%). Other causes of VR were toxoplasmosis (8.3%), systemic lupus erythematosus (SLE) (2.8%) and sarcoidosis (2.8%) (Fig. 1).

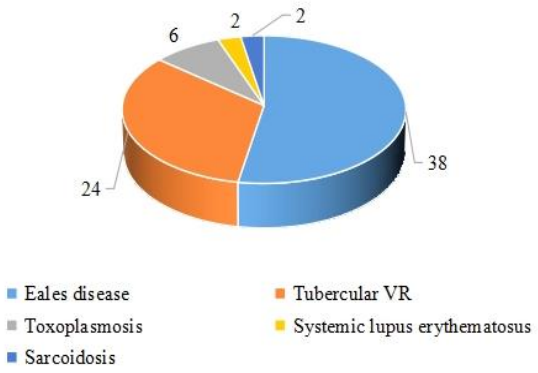
Table-I: Baseline characteristics of the patients (n=45)

Baseline criteria	Frequency (percentage)
Male gender	37 (82.2)
Age (in years) (Mean ±SD)	29.5 ±5.3 (range 21-55)
Bilateral eye involvement	27 (60.0)
Duration of symptoms (in months)	2.1 ±0.3 (range 0.5-6)

Table-II: Distribution of vessel involvement in patients of vasculitis retinae (n=72)

Vessel involvement	Frequency (percentage)
Type of vessel	
Artery	5 (6.9)
Vein	65 (90.3)
Both artery and vein	2 (2.8)
Location of vessel	
Central	3 (4.2)
Peripheral	7 (9.7)
Both central and peripheral	62 (86.1)

Fig. 1: Etiology of vasculitis retinae (n=72)



Discussion

Retinal vasculitis, an uncommon eye disease which has the potential for significant visual morbidity. Most of the cases of vasculitis retinae have elusive diagnosis which complicates the successful management. Main dilemma in management of vasculitis retinae is to identify whether the aetiology was infectious or non-infectious, as their management are completely different. Control of intraocular inflammation is sufficient in non-infectious vasculitis retinae but appropriate antimicrobial therapy alongside anti-inflammatory and/or immunosuppressive therapy is required for infectious vasculitis retinae. On the other spectrum of aetiology of vasculitis retinae are the cases associated with systemic immunological disease conditions. Onset of vasculitis retinae in these cases heralds worsening of the systemic disease as well as forecasts vision loss if these cases are not identified and treated aggressively.[13]

Still there are another group of vasculitis retinae patient who do not give any positive clue on history and clinical examination and have negative laboratory investigations, termed as Eales disease (ED).[14] Such cases of vasculitis retinae are the majority and are often given a lot of laboratory investigations, yielding no confirmatory result.[1,15-17] More than half of the cases in this study were Eales disease (52.8%) and majority (75%) of the patient of ED have bilateral involvement. This finding is in keeping with that of Saxena *et al*., who have studies 159 cases of Eales disease in india[14] and Saurav *et al*., who studies 70 patients of Eales disease in Eastern India.[18] Male preponderance and occurrence of cases in 3rd and 4th decade of life are simillar to previous reports.[17,18] Tuberculous VR was the second most common cause of vasculitis retinae next to Eales disease and the most common infectious cause of vasculitis retinae in the series. Apinyawasisuk *et al.*[19] who studied 47 patients of vasculitis retinae in Thailand have similar observation, though the frequency was much higher in the current study; 53% vs 23% ED and 31% vs 13% in tuberculous vasculitis retinae.

In this study, the most cases were non-infectious VR, similar to the other current studies.[18,19] However, there were differences in aetiology of non-infectious as well as infectious cause of vasculitis retinae in contrast to other studies.[19] SLE and Sarcoidosis were the two causes of vasculitis retinae in this series in non-infectious

vasculitis retinae. In contrast, SLE and Bechet's disease were other frequently occurring causes of non-infectious vasculitis retinae observed by Apinyawasisuk *et al*.[19] Cytomegalovirus (CMV) and Herpes simplex virus (HSV) the two frequently occurring infectious cause of vasculitis retinae next to tuberculous vasculitis retinae observed in the same study. But in this study toxoplasma retinitis with vasculitis was the second cause of vasculitis retinae. In the study by Apinyawasisuk *et al*.[19] there were high rate of undifferentiated VR (32%) in contrast this study has none. This variations in part may be due to inclusion of undifferentiated vasculitis retinae patients in ED group in this study, though they have not defined 'undifferentiated vasculitis retinae.

Retinal vasculitis can be classified into descriptive subsets depending on the location of affected vessels such as central vasculitis, peripheral vasculitis; on the basis of types of vessels involvement as predominantly phlebitis, predominantly arteries or involvement of the retinal arterioles with venules. These distinctions can be helpful to determine the aetiology, severity and prognosis of VR. In this series, the peripheral vascuiitis and phlebitis were the most common (91.66% and 84.72% respectively) presentation comparable to previous studies[18,19] though we observed a higher percentage of Eales disease.

The present study was a cross-sectional one in a tertiary government hospital with its known limitations. It prevents the study from providing prevalence of various aetiological factors associated with vasculitis retinae. It did not include the patients from all walks of life as mostly middle- and low-income group patients come for service in such government tertiary hospital.

Conclusion

Our study revealed that the most common cause of VR is Eales disease in our country. Tubercular VR was the most common infectious cause of VR as well as the second most common cause of VR. However, a large population-based study to know the prevalence of etiological factors associated with VR is necessary. According to many authors Eales disease occurs secondary to immunological reaction to tubercular protein. In that perspective present or past MTB infection and latent TB infection should be excluded at the very beginning while dealing with a case of vasculitis in TB endemic country like ours.

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