|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||
International Journal of Medical and Biomedical Studies
Available Online at www.ijmbs.info
PubMed (National Library of Medicine ID: 101738825)
Index Copernicus Value 2018: 75.71
Original Research Article
Volume 4, Issue 4; April: 2020; Page No. 152-156

ASSESSMENT OF CLINICAL PROFILE OF RETINAL VASCULITIS IN IGIMS, PATNA, BIHAR

Dr. Poonam[1], Dr. Bibhuti Prassan Sinha[2]
[1]Senior Resident, Regional Institute of Ophthalmology, IGIMS, Patna, Bihar, India.
[2]Professor and Head, Regional Institute of Ophthalmology, IGIMS, Patna, Bihar, India.

Article Info: Received 04 April 2020; Accepted 28 April 2020
DOI: https://doi.org/10.32553/ijmbs.v4i4.1183
Corresponding author: Dr. Poonam
Conflict of interest: No conflict of interest.

Abstract

Retinal vasculitis (RV) is an intraocular inflammation that predominantly affects retinal vessels of either arterial and/or venous system and can be associated with numerous infectious and non-infectious disorders though many cases remain idiopathic. Inflammation of the retinal vasculature may occur as an isolated intraocular disorder or in association with various systemic diseases. The list of associated systemic diseases is extensive and includes various systemic disorders such as Behcet's disease, multiple sclerosis, sarcoidosis, systemic autoimmune disease as well as infectious diseases including herpetic viral infection, toxoplasmosis, and syphilis. Hence based on above findings the present study was planned for Assessment of Clinical Profile of Retinal Vasculitis in IGIMS, Patna, Bihar.

The present study was planned in Regional Institute of Ophthalmology, IGIMS, Patna, Bihar, India. The 50 cases of the retinal vasculitis were enrolled and evaluated in the present study. Patients were diagnosed with RV if the intraocular inflammation was located mainly in the retinal vasculature. Ocular findings included perivascular sheathing and inflammation located along the vessels associated with cotton wool spots, retinal exudates, retinal hemorrhages, ischemia or neovascularization.

The data generated from the present study concludes that the diagnosed cases of the primary retinal vasculitis shows no systemic disease association or infectious etiology could be ascertained after detailed history, clinical examination and tailored laboratory work-up. The finding that retinal vasculitis cases were primary in nature may lead to an approach where laboratory investigations are advised sparingly, based mainly on previous systemic history and clinical judgment.

Keywords: Clinical Profile, Retinal Vasculitis, IGIMS, Patna, Bihar, etc.

Introduction

Retinal vasculitis can be an isolated condition or a complication of local or systemic inflammatory disorders characterized by inflammation of the retinal vessels. It is a sight-threatening condition associated with various infective, auto-immune, inflammatory or neoplastic disorders.

The concept of retinal vessel inflammation was introduced by John Hunter in 1784, in the report 'Observations on the inflammation of the internal coats of the veins'.[1] Since then, there have been various epidemiological, imaging and clinico-pathological studies to improve the understanding of this condition. Since the inflammation of the retinal vessel wall is clinically visible, there has been a lot of interest generated in literature to study this disease. Initially, retinal vasculitis was thought to be an extension of the systemic disease.[2] However, there are major differences between the two, because of the unique microstructure of the retinal vessels. As an example, unlike systemic vasculitis, retinal vasculitis is not associated with vascular necrosis.[3]

Retinal vasculitis is used as a descriptive term to explain a conglomerate of typical clinical manifestations including perivascular sheathing or cuffing, vascular leakage and/or occlusion.[4][5] It may be associated with signs of retinal ischemia, including cotton-wool spots and intra-retinal hemorrhage. Involvement of retinal veins due to inflammation is termed as phlebitis whereas retinal arteriolar involvement is termed as arteriolitis.[6]

Retinal vasculitis may be associated with a variety of clinical conditions. Typically, a retinal vasculitis would occur as a part of an ocular or systemic disease. Rarely, it may be isolated, idiopathic condition, termed as idiopathic retinal vasculitis. It may also present as an initial manifestation of an underlying disorder. Isolated retinal vasculitis is seen in approximately 3% of the cases diagnosed with uveitis.[7] The annual incidence of retinal vasculitis is 1-2 per 10,000.[8] In one series, approximately 55% patients with retinal vasculitis had associated systemic inflammatory disease.[1][9] In another larger series including more than 1300 patients, retinal vasculitis was seen in approximately 15% patients with uveitis. In this series, systemic vasculitis was associated with retinal vasculitis in only 1.4% cases.[3]

Retinal vasculitis may be more common in individuals under the age of 40, with a slight preponderance in

females.[1][7] The mean age of diagnosis of retinal vasculitis is 34 without any gender differences.[2] This disorder is usually bilateral and is visual threatening. As many as one-third patients may suffer from severe visual loss (<20/200) as a result of retinal vasculitis and its complications.[10][11]

Despite precise clinical visualization of the retinal microvasculature, the exact pathophysiological mechanism of this condition is not clear.[2][5][6] In order to understand the pathogenesis of retinal vasculitis in humans, experimental animal models have been prepared. The manifestations of vascular sheathing and cuffing led to the belief that retinal vasculitis results due to type III hypersensitivity reaction. However, there is no proven human or animal model to support this hypothesis. A breakdown of blood-retinal-barrier secondary to intraocular or systemic inflammation resulting in clinical features of this disease is more likely. Due to the characteristic perivascular location of the inflammation, terms such as perivasculitis and periphlebitis have been suggested to denote the underlying pathology. [6]

Studies demonstrate presence of either a focal, segmental or diffuse retinal perivascular proliferation of lymphoplasmacytic infiltrates in eyes with retinal vasculitis. In granulomatous diseases such as sarcoidosis, there may be a collection of numerous epithelioid cells. In eyes with intermediate uveitis and retinal vasculitis secondary to lymphoma, histopathological studies demonstrate presence of lymphocytic cuffing with mural involvement of retinal veins. Characterization of lymphocytic cells in the perivascular region reveals predominance of CD4+ T cells as compared to CD8+ T cells or B lymphocytes. There is an upregulation of various inflammatory cellular markers including integrins and cell adhesion molecules. Increased expression of cell adhesion molecules along retinal vessels and blood-retinal-barrier cells may play an important role in inflammatory cell recruitment. The sera of patients with retinal vasculitis demonstrate an increase in the levels of type 1 interferons, mainly interferon-β. Other molecules that are up-regulated include E-selectin and s-intracellular adhesion molecules. [12]

Although there is a large pathological diversity among the retinal vasculitis etiologies, the manifestations of inflammatory changes resemble in many ways. In patients with infective retinal vasculitis, culture of live organisms such as mycobacteria may be possible from various systemic foci. Infectious organisms may involve retinal vasculature by various mechanisms, apart from direct vascular endothelial injury. They may result in release of toxins and may up-regulate molecules such as heat-shock proteins (HSPs).[26] Molecular mimicry may result in aberrant activation of immunological pathways resulting in pathological manifestations.[8]

In a subset of patients with retinal vasculitis, there is occlusion of blood flow through the retinal vessels. The pathology of occlusive retinal vasculitis may be distinct from vasculitis without evidence of obliteration of blood flow. Available literature suggests that eyes with occlusive vasculitis have a poorer prognosis with a higher number of complications such as cystoid macular edema (CME), neovascularization and epiretinal membrane formation.

Appropriate laboratory investigations aid in establishing the etiology for retinal vasculitis. A tailored approach to laboratory work-up is preferred to avoid unnecessary investigations and expenses to the patient. [13] The investigations must be based on systemic symptoms and signs, ocular examination and detailed history. The aim of laboratory work-up is to identify infectious, non-infectious, or immunologic causes as the treatment for each category may be different. In the absence of any laboratory positive result, malignancy should be kept in mind as one of the differential diagnosis.

Commonly performed laboratory evaluations include markers of systemic inflammation, such as erythrocyte sedimentation rate (ESR) and C-reactive protein. Based on the clinical features, infectious etiologies can be ruled out by performing specific investigations. Tuberculosis testing can be performed using Mantoux test (tuberculin skin test). The tuberculin skin test is negative in cases with sarcoidosis. Chest X-ray and Computed Tomography (CT) scan can be performed to establish the etiology in cases where the diagnosis is challenging. For diagnosis of viral and parasitic diseases, titers of antibodies or antigens can be assessed. Polymerase chain reaction has a higher sensitivity and specificity for diagnosis and can be very useful in patients with retinal vasculitis.

In patients where co-existent systemic vasculitidis is possible, investigations can include detection of anti-neutrophil cytoplasmic antibody, anti-DNA antibody, anti-nuclear antibody and rheumatoid factor among others. HLA testing can help identify diseases such as ABD (HLA-B5), birdshot chorioretinitis (HLA-A29) and systemic lupus erythematosus (HLA-DR3).

Investigations in patients without evidence of systemic or ocular disease, i.e. idiopathic retinal vasculitis, can be limited to fluorescein angiography, complete blood counts, syphilis serology, ESR, urine analysis, tuberculin and HIV testing and chest radiograph. [14] It is not recommended that every test is performed for every patient diagnosed with retinal vasculitis. Rather, as mentioned, the testing panel should be based in large on the findings from the review of systems and examination of the patient. There are various ocular and systemic etiologies that can present with retinal vasculitis. In a subgroup of patients without any underlying ocular or systemic cause, it is referred to as idiopathic retinal vasculitis.

Patients with retinal vasculitis must be periodically examined to evaluate the extent and severity of vascular leakage. The disease course can be effectively monitored using fluorescein angiography. Wide-field techniques assist the clinician to assess peripheral vascular lesions and aid in guiding further therapy. Infectious retinal vasculitis can be monitored by determining the load of the causative organisms using techniques such as quantitative polymerase chain reaction. As retinal vasculitis may be early manifestation of generalized vasculitis of the central nervous system (CNS), one needs to remember to evaluate and monitor the CNS vasculature (i.e. employing magnetic resonance imaging with contrast) as well when indicated. [15]

The management of retinal vasculitis depends on the underlying etiology. Adequate control of the intraocular inflammation is sine qua none for achieving remission of retinal vasculitis. This disease can be recurrent and aggressive in its course requiring steroid and immunosuppressive therapy.[6] Ocular sequelae resulting from uncontrolled retinal vasculitis can have deleterious consequences including severe visual loss. The mainstay of therapy for retinal vasculitis is medical management. Infectious etiology must be ruled out as the treatment for non-infectious disease consists of immunosuppressive therapy, which can possibly worsen intraocular infections.

Non-infectious retinal vasculitis is managed by systemic or local corticosteroids and steroid-sparing immunosuppressants. The local delivery of therapeutic agents can be done via intravitreal injections or periocular therapy, although the latter may not be sufficiently adequate for cases of severe retinal vasculitis. The choice of immunosuppressive agents must be tailored based on ocular manifestations, etiology and systemic co-morbidities. Use of advanced imaging techniques such as ultra-wide fundus photography and fluorescein angiography can aid in the management of patients with retinal vasculitis.

In a series of 56 patients with non-infectious uveitis, systemic prednisone (oral) was used for the treatment of two-third patients at an average dose of 27mg/day for a mean of 14 months.[1] Another study from Eastern India revealed that oral steroids were used in more than 80% patients with retinal vasculitis. In addition, periocular and intraocular steroids such as triamcinolone have been used in vasculitis associated with pars planitis. However, administration of steroid-sparing immunosuppressants are recommended in cases requiring more than 10mg/day dose of oral prednisone. [16]

Unlike systemic vasculitis that can be managed with colchicines and non-steroidal anti-inflammatory agents, retinal vasculitis due to causes such as ABD requires a more aggressive approach. Available immunosuppressive agents include cyclosporine, azathioprine, cyclophosphamide, mycophenolate mofetil or biologic agents such as infliximab or etanercept. Cyclosporine has been used as a drug of choice in previous studies. In eyes with vasculitis associated with birdshot chorioretinopathy, sarcoidosis and Harada's disease, azathioprine has been used for treatment. Alkylating agents such as chlorambucil and cyclophosphamide have also been used in combination with corticosteroids. Biologic agents have been increasingly used to achieve remission in eyes with retinal vasculitis. These include infliximab, tacrolimus and adalimumab, apart from other agents targeting molecules such as tumor necrosis factor and interleukins.

Infectious retinal vasculitis must be treated with appropriate anti-microbial agents depending upon the etiology. Infectious retinal vasculitis is a heterogenous cohort with various causative organisms such as bacteria, viruses and parasites. Anti-microbial therapy, including oral and intravitreal injections in various combinations with steroids have been used for the treatment of these disease entities. [17]

Retinal vasculitis (RV) is an intraocular inflammation that predominantly affects retinal vessels of either arterial and/or venous system and can be associated with numerous infectious and non-infectious disorders though many cases remain idiopathic. Inflammation of the retinal vasculature may occur as an isolated intraocular disorder or in association with various systemic diseases. The list of associated systemic diseases is extensive and includes various systemic disorders such as Behcet's disease, multiple sclerosis, sarcoidosis, systemic autoimmune disease as well as infectious diseases including herpetic viral infection, toxoplasmosis, and syphilis. Hence based on above findings the present study was planned for Assessment of Clinical Profile of Retinal Vasculitis in IGIMS, Patna, Bihar.

Methodology:

The present study was planned in Regional Institute of Ophthalmology, IGIMS, Patna, Bihar, India. The 50 cases of the retinal vasculitis were enrolled and evaluated in the present study. Patients were diagnosed with RV if the intraocular inflammation was located mainly in the retinal vasculature. Ocular findings included perivascular sheathing and inflammation located along the vessels associated with cotton wool spots, retinal exudates, retinal hemorrhages, ischemia or neovascularization.

All patients underwent complete ocular examination including slit lamp biomicroscopy, tonometry, and indirect ophthalmoscopy. Laboratory investigations included erythrocyte sedimentation rate, complete blood count, urine analysis, antinuclear antibody, serology for human

immunodeficiency virus (HIV)-type 1, and Treponema pallidum.

All the patients were informed consents. The aim and the objective of the present study were conveyed to them. Approval of the institutional ethical committee was taken prior to conduct of this study.
Following was the inclusion and exclusion criteria for the present study.
Inclusion Criteria: Patients more than 10 years of age were included in the study.
Exclusion Criteria: Patients with diabetic and hypertensive retinopathy and those who were not willing to participate in the study were excluded.

Results & Discussion:

Retinal vasculitis may occur as a primary syndrome called idiopathic retinal vasculitis, which affects the eye vasculature without evidence of any systemic, or eye disease. [18] More commonly, it is seen as a manifestation of systemic diseases including sarcoidosis, collagen vascular diseases, malignancy, neurologic conditions and systemic diseases. It also occurs in ocular conditions like parsplanitis or birdshot retinochoroidopathy. The various stages of disease can be described as stage of inflammation, stage of ischemia, stage of neovascularization and stage of complications. [19]

Inflammation of peripheral retinal vessels may be completely asymptomatic even in patients with associated systemic disease. They often complain of painless loss or blurring of vision. Areas of retinal infiltrates or haemorrhage can cause scotomata or floaters. [19] Anterior uveitis if present may be associated with redness, pain and photophobia. Some patients may present with sudden loss of vision due to vitreous haemorrhage.

The signs of vascular sheathing or cuffing can be found in inflammatory vascular disorders as well as in ischemic vasculopathies without inflammation. These two conditions should not be confused, as the approach to the diagnosis is different. If vascular sheathing is accompanied by vitreous cells, adjacent intra retinal edema, or infiltrates, it is more likely to be inflammatory in origin.

Table 1: Demographic Details

Age	No. of Cases
11 – 20	5
21 – 30	16
31 – 40	14
41 – 50	7
51 – 60	4
61 & above years	4
Sex:	
Males	38
Females	12
Total	50

Table 2: Signs

Signs	Observed in No. of Cases
Vascular sheathing	36
Vitritis	23
Sclerosed vessel	21
Neovascularization else where	15
Vitreous hemorrhage	15
Retinal hemorrhage	22
Anterior uveitis	4
Choroiditis	3
Neovascularization disc	2
Branch retinal vein occlusion	2
Subhyaloid hemorrhage	1
Pars plana membrane	1
Cataract	1
Rubiosis iridis	0
Glaucoma	0
Total retinal detachmen	0
Band-shaped keratopathy	0

Table 3: Macular Findings

Macular Findings	No. of Cases
Within normal limits	24
No view	6
Cystoid macular edema	6
Epiretinal membrane	4
ILM folds	3
Macular edema	2
Fibrovascular proliferation	1
RPE defect	1
Others	3
Total	50

Table 4: Treatment Undergone

Treatment	Observed in No. of Cases
Oral corticosteroids	23
None	17
Laser photocoagulation	16
Periocular steroids	7
Surgery	5
Immunosuppressive	2
Cryotherapy	1
Anti-VEGF	1
Antituberculous treatment	1

Gupta et al Evaluated polymerase chain reaction positive tuberculosis retinal vasculitis. 69.2% male and 30.7% were female mean age group of 20 years bilateral in a 9 cases out of 13 cases. The most consistent finding was the presence of vitritis in all eyes. Followed by snow ball opacities in (89.4%) neovascularisation (57.8%) focal Choroiditis (47.3%) vitreous / preretinal hemorrhage (26.3%) and serous retinal detachment in 15.7% over a median follow up of 12 months all showed resolution of vasculitis with no recurrences. [20]

S.P. Rai & et al evaluated A total of 44 cases of retinal vasculitis admitted in the tertiary care centre of the Armed Forces, between January ’98 and June 2000, were evaluated prospectively for evidence of healed or active

tuberculosis in the body. Retinal vasculitis was bilateral in 28 and unilateral in 16 patients, all were males; the average age was 31.7 years (range 16 to 53 years); only 2 patients had constitutional symptoms and no patient had past history of tuberculosis. [21]

Holland et al [22] reported the development of intraocular inflammatory reactions including vitritis, iridocyclitis, and retinal vasculitis without necrotizing retinal lesions in individuals with acquired systemic toxoplasmosis. These data strongly suggest that acquired systemic toxoplasmosis infection should be considered in the differential diagnosis of patients with retinal vasculitis, especially in the presence of constitutional symptoms suggesting systemic toxoplasmosis. In the study by Saurabh et al primary retinal vasculitis was more common and none of the patients were found to have a conclusively proven systemic disease. In another study conducted in Northern Thailand which included 47 patients, tuberculosis was the most frequently identified infectious cause. [23]

Classically the presenting feature of the Eales disease is repeated vitreous hemorrhage patients compliant of sudden appearance of floating spots, cobwebs, cloudy vision, or simply reduced vision. Vision often improves with time before a repeat hemorrhage affects vision again. The recovery of vision usually becomes less and less complete with recurrent episodes. Finally, the patient may be left with no useful vision. The gross loss of vision may be due to unresolving vitreous hemorrhage or such complications as traction retinal or macular detachments. Often a routine examination of the contra lateral eye reveals evidence of present or past phlebitis. A normal contra lateral eye, in the course of time, may develop the disease.

Conclusion:

The data generated from the present study concludes that the diagnosed cases of the primary retinal vasculitis shows no systemic disease association or infectious etiology could be ascertained after detailed history, clinical examination and tailored laboratory work-up. The finding that retinal vasculitis cases were primary in nature may lead to an approach where laboratory investigations are advised sparingly, based mainly on previous systemic history and clinical judgment.

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