

Original Article

Proper Diagnosis for a Proper Management of Retinal Vasculitis

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Citation: Boyd S (2016) Proper Diagnosis for a Proper Management of Retinal Vasculitis. Gavin J Ophthalmol 2016: 7-10.

Received: 26 April, 2016; **Accepted:** 16 May, 2016; **Published:** 30 May, 2016

Abstract

Retinal vasculitis is an inflammatory disease of the blood vessels of the retina that may be associated with primary ocular conditions. Retinal vasculitis is also defined as vascular leakage and staining of vessel walls on fluorescein angiography, with or without the clinical appearance of fluffy, white perivascular infiltrates in the eye.

Introduction

Retinal vasculitis is a sight-threatening inflammatory eye disease involving the retinal blood vessels [1-3]. It is characterized by focal, perivascular and creamy-colored cuffs, sheathing the retinal blood vessels [2,4-6].

The terms retinal vasculitis and retinal perivasculitis are used interchangeably as clinical descriptions of the fundus copic sign of this exudative sheathing of the retinal blood vessels. These changes most commonly occur around retinal veins and are called retinal periphlebitis.

They can be subtle and overlooked by ophthalmoscopy, but can be revealed by Fluorescein Angiography (FA).

Different causes of retinal vasculitis carry variable risks of developing retinal ischemia ranging from being common in presumed tuberculous retinal vasculitis and Behçet's disease to a more rare association in sarcoidosis and multiple sclerosis [6].

Epidemiology

Intraocular inflammation occurs in about 80% of patients with retinal vasculitis, but is more common in men than in women. Men are also more likely to develop posterior segment involvement and macular lesions. Uveitis is not usually the first manifestation of the disease, but may arise soon after the onset.

Those who develop the disease aged <25 years have a higher incidence of eye inflammation.

Retinal vasculitis is seen more commonly as a manifestation of ocular or systemic inflammatory or infectious diseases, such as Adamantiades-Behçet's Disease (ABD) or TB [7]. The incidence of these diseases varies throughout the world. Therefore, data from centers with a predominantly white population do not reflect the incidence of retinal vasculitis in other regions, such as Africa, India, Brazil or Japan.

In one series, approximately 55% patients with retinal vasculitis had associated systemic inflammatory disease [8,9]. 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]. 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]. Retinal vasculitis may be associated with a number of systemic and local diseases (Table 1) [12,13].

Classification

Systemic vasculitis has been classified by the International Chapel Hill Consensus Conference on the Nomenclature of Vasculitides [14].

The retinal vasculitis may be divided by:

-Predominantly involved vessels.

1. Infectious	
a. Bacterial	Tuberculosis, Whipple's disease Endophthalmitis, Syphilis, Lyme's disease, Brucellosis, Bartonella, Leptospirosis
b. Viral	Cytomegalovirus, Human T-cell Lymphoma Virus type 1 (HTLV-1), Herpes Simplex Virus, Herpes Zoster Virus, West Nile Fever virus, Rift Valley Fever Virus, Hepatitis B and C, Human Immunodeficiency virus, Acute retinal necrosis, Infectious mononucleosis, Dengue Fever virus,
c. Fungal	Coccidiomycosis, Candidiasis
d. Parasitic	Toxoplasmosis, toxocariasis, amoebiasis
e. Rickettsia	Mediterranean spotted fever
2. Ocular disorders	
	Eales' disease
	Birdshot chorioretinopathy
	Pars planitis
	Idiopathic Retinal Vasculitis, Aneurysms and Neuroretinitis (IRVAN)
	Acute Multifocal hemorrhagic retinal vasculitis
	Idiopathic recurrent branch retinal arterial occlusion
	Frosted Branch Angiitis (FBA)
	Vogt-Koyanagi-Harada Syndrome
	Sympathetic ophthalmia
	Idiopathic
	Drug-induced
3. Systemic Inflammatory Diseases	
	Adamantiades-Behcet's disease
	Sarcoidosis
	Wegener's Granulomatosis
	Systemic Lupus Erythematosus
	Relapsing Polychondritis
	Crohn's disease
	Takayasu's disease
	Polyarteritis Nodosa
	Churg-Strauss Syndrome
	Sjorren's Syndrome
	Rheumatoid Arthritis
	Dermatomyositis/polymyositis
	Buerger's disease
	Post-vaccination
	Multiple sclerosis
	Seronegative arthritis
4. Malignancy	
	Leukemia
	Lymphoma
	Paraneoplastic Syndromes
	Cancer-associated retinopathy

Table 1: Systemic and local intraocular conditions associated with retinal Vasculitis.

-Artery- Acute Retinal Necrosis (ARN), Idiopathic Retinal Vasculitis, Aneurysm and Neuroretinitis (IRVAN), Systemic Lupus Erythematosus (SLE), Polyarteritisnodosa (PAN), syphilis, Progressive Outer Retinal Necrosis (PORN) and Churg Strauss Syndrome. Intermediate uveitis, sarcoidosis,

multiple sclerosis, tuberculosis, Birdshot chorioretinitis, HIV paraviral syndrome, frosted branch angiitis, toxoplasmosis, relapsing polychondritis, granulomatosis with polyangiitis (Wegener), Crohn's disease.

-Involvement of peripheral vessels or vessels around the posterior pole.

Clinical Characteristics & Diagnosis

Examination of patients with retinal vasculitis is performed using both, slit-lamp biomicroscopy with 90 or 78-diopter lens and indirect ophthalmoscopy with either 20 or 28- diopter lens.

The classic symptom of retinal vasculitis is a painless decrease in vision (Figure 1). Other symptoms may include a blind spot from ischemia-induced scotomas or floaters from vitritis. With macular involvement, patients may present with metamorphopsia or abnormalities in color vision. Retinal vasculitis can also be asymptomatic.



Figure 1: Color fundus photograph shows tortuous veins with scattered hemorrhages, cotton and perivascular exudation.

The usual clinical manifestations of retinal vasculitis are demonstrable by ophthalmologic examinations or fluorescein angiography (Figure 2). These findings also include vascular sheathing (visible accumulation of inflammatory cells along vessel walls) and vitreous hemorrhage. The peripheral vessels are often more involved than central arteries and veins, and there are frequently skip areas. With certain disorders such as sarcoidosis, lesions resembling candle-wax drippings or extensive perivascular inflammation may also be observed [15-16]. There are various diseases associated to retinal vasculitis, as listed below.

Intermediate uveitis is characterized by vitritis, snowball exudates, peripheral retinal periphlebitis and pars plana exudates. The classic feature of the vasculitis is presence of sheathing around the vessel wall.

Eales'disease is an idiopathic obliterative periphlebitis, which commonly occurs in healthy young males between 15-40 years of age [17-19]. It starts anterior to the equator and

progresses posteriorly and ultimately involves multiple quadrants of the retina. This inflammation induced vascular occlusion leads to proliferative vascular retinopathy with sequelae as recurrent vitreous hemorrhage and tractional detachment [20-22]. The etiology of this disease is still unknown however it is believed to be due to hypersensitivity to tuberculo-protein.

Birdshot retinochoroidopathy is a bilateral panuveitis where fundus examination shows cream colored, deep, round lesions, retinal vasculitis and cystoid macular edema [23].

Frosted branch angiitis is a rare vasculitis where thick inflammatory infiltrates surround the retinal arterioles and venules creating an appearance of frosted tree branches [24]. The sheathing of the blood vessels is so extensive that the underlying vessels are obscured. Mostly it is idiopathic, but cases have been reported in herpes, rubella, cytomegalovirus infections and malignancies.

Retinal necrosis is associated to infectious forms of uveitis. This is commonly seen in eyes with toxoplasmosis, [25] viral infections such as varicella zoster [26] or herpes simplex, [27] cytomegalovirus [28] and human T-cell lymphoma virus type 1 [29]. Toxoplasmosis is often associated with reactivation of the retinal lesion adjacent to a previous scar. Kyrleis arteriolitis is an accumulation of periarteriolar exudates in eyes with toxoplasmosis leading to retinal necrosis. Foci of chorioretinitis and chorioiditis may be closely associated with retinal vasculitis.

Fluorescein Angiography

Fluorescein angiography can be done in active or healed vasculitis. It shows staining and leakage of retinal veins, areas of capillary non-perfusion, retinal neovascularization, sclerosis of vessels, optic disc leakage, cystoid macular edema, vascular occlusion and macular ischemia [30-31]. Optical coherence tomography may also be done in cases of refractory macular edema to follow them and see the response of treatment when it is not clinically apparent.

Differential Diagnosis

The differential diagnoses of retinal vasculitis have been listed in (Table 1). 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.

Although a good prognosis can be expected with adequate treatment, poor visual outcome despite therapy often is associated with complications such as macular ischemia, branch retinal vein occlusion, central retinal vein occlusion, branch retinal artery occlusions, persistent neovascularization, vitreous hemorrhage, and tractional retinal detachment.

Management

The main goal of treatment in retinal vasculitis is suppression of intraocular inflammation in order to prevent



Figure 2: Fundus fluorescein angiography shows capillary non perfusion, microaneurysms and leakage of fluorescein dye.

visual loss and long-term complications. The mainstay of therapy is corticosteroids and immune suppressive [32-36]. In case of an infective lesion, specific therapy against the infective agent with or without corticosteroids may be required. Corticosteroids may be given either systemically or by posterior subtenon's injection. Periocular steroids are useful in patients with unilateral and mild inflammation [37].

Though this route avoids the systemic side effects, it carries a risk of raised intraocular pressure and globe perforation. Oral corticosteroids are given in patients with moderate to severe bilateral inflammation and a marked decrease in visual acuity. Severe cases of sight threatening retinal vasculitis involving the posterior pole may require intravenous methyl prednisolone followed by oral corticosteroids and immunosuppressives. Intravitreal steroid injections can also be given in cases of refractory macular edema [38-41].

Other therapeutic options such as pan-retinal photocoagulation have been tried in order to control retinal vasculitis [42]. Cryotherapy has been used in the past to treat retinal vasculitis associated with pars planitis.

In conclusion, retinal vasculitis can be a difficult sight threatening condition with pathognomic clinical features identifiable on clinical examination. A thorough diagnostic work up observed by the patient's symptoms and signs it is crucial in this disease. A number of systemic associations occur with retinal vasculitis, and it is the responsibility of the ophthalmologist to help direct such a search, particularly in cases where systemic findings are scarce.

References

1. Holland GN (1991) Retinal vasculitis. West J Med 154: 218-220.
2. Duke-Elder S, Dobree JH (1967) Diseases of the Retina. Henry Kimpton, London, UK. Pg no: 218-236.
3. Pleyer U, Forrester J (2009) Uveitis and Immunological Disorders: Progress III, Volume 3. Springer, Berlin, Germany.
4. Graham E, Stanford M, Whitcup S (1996) Retinal Vasculitis. In: Pepose J, Holland GN, Wilhelmus KR (eds.). Mosby, St Louis, USA. Pg no: 538-551.

5. Nussenblatt RB, Whitcup SC (2010) *Uveitis. Fundamentals and Clinical Practice*. Elsevier, Philadelphia, USA.
6. Abu el-Asrar AM, Tabbara KF (1997) Retinal vasculitis. *Curr Opin Ophthalmol* 8: 68-79.
7. George RK, Walton RC, Whitcup SM, Nussenblatt RB (1996) Primary retinal vasculitis. Systemic associations and diagnostic evaluation. *Ophthalmology* 103: 384-389.
8. Hughes EH, Dick AD (2003) The pathology and pathogenesis of retinal vasculitis. *Neuropathol Appl Neurobiol* 29: 325-340.
9. Graham EM, Stanford MR, Sanders MD, Kasp E, Dumonde DC (1989) A point prevalence study of 150 patients with idiopathic retinal vasculitis: 1. Diagnostic value of ophthalmological features. *Br J Ophthalmol* 73: 714-721.
10. Rothova A, Suttrop-van Schulten MS, Frits Treffers W, Kijlstra A (1996) Causes and frequency of blindness in patients with intraocular inflammatory disease. *Br J Ophthalmol* 80: 332-336.
11. Palmer HE, Stanford MR, Sanders MD, Graham EM (1996) Visual outcome of patients with idiopathic ischaemic and non-ischaemic retinal vasculitis. *Eye (Lond)* 10: 343-348.
12. El-Asrar AM, Herbert CP, Tabbara KF (2010) A clinical approach to the diagnosis of retinal vasculitis. *Int Ophthalmol* 30: 149-173.
13. Abu El-Asrar AM, Herbert CP, Tabbara KF (2009) Differential diagnosis of retinal vasculitis. *Middle East Afr J Ophthalmol* 16: 202-218.
14. Charles JJ (2013) Overview of the 2012 Revised International Chapel Hill Consensus Conference Nomenclature of Vasculitides. *Clin Exp Nephrol* 17: 603-606.
15. Stanford MR, Graham EM, Kasp E, Brown EC, Dumonde DC, et al. (1987) Retinal vasculitis: correlation of animal and human disease. *Eye (Lond)* 1: 69-77.
16. Empeklidis T, Konidaris V, Brent A, Vardarinos A, Deane J (2013) Kyrieleis plaques in herpes zoster virus-associated acute retinal necrosis: a case report. *Eye (Lond)* 27: 1110-1112.
17. Sanders MD, Graham EM (1988) Retinal vasculitis. *Postgrad Med J* 64: 488-496.
18. Rosenbaum JT, Robertson JE, Watzke RC (1991) Retinal vasculitis—a primer. *West J Med* 154: 182-185.
19. Henderly DE, Genstler AJ, Smith RE, Rao NA (1987) Changing patterns of uveitis. *Am J Ophthalmol* 103: 131-136.
20. Schumacher HR, Klippel JH, Koopman WJ (1993) *Primer on the Rheumatic Diseases*. Arthritis Foundation, Atlanta, USA.
21. Jabs DA, Fine SL, Hochberg MC, Newman SA, Heiner GG, et al. (1986) Severe retinal vaso-occlusive disease in systemic lupus erythematosus. *Arch Ophthalmol* 104: 558-563.
22. Robin JB, Schanzlin DJ, Meisler DM, deLuise VP, Clough JD (1985) Ocular involvement in the respiratory vasculitides. *Surv Ophthalmol* 30: 127-140.
23. Spalton DJ, Graham EM, Page NG, Sanders MD (1981) Ocular changes in limited forms of Wegener's granulomatosis. *Br J Ophthalmol* 65: 553-563.
24. Haynes BF, Fishman ML, Fauci AS, Wolff SM (1977) The ocular manifestations of Wegener's granulomatosis. Fifteen years experience and review of the literature. *Am J Med* 63: 131-141.
25. Straatsma BR (1957) Ocular manifestations of Wegener's granulomatosis. *Am J Ophthalmol* 44: 789-799.
26. Isaak BL, Liesegang TJ, Michet CJ (1986) Ocular and systemic findings in relapsing polychondritis. *Ophthalmology* 93: 681-689.
27. Elliot JH (1994) Introduction to uveitis. In: DM Albert, FA Jakobiec (eds.). *Principles and practice of ophthalmology: clinical practice*. Volume 1, WB Saunders, Philadelphia, USA.
28. Levy-Clarke GA, Buggage RR, Shen D, Vaughn LO, Chan CC, et al. (2002) Human T-cell lymphotropic virus type-1 associated t-cell leukemia/lymphoma masquerading as necrotizing retinal vasculitis. *Ophthalmology* 109: 1717-1722.
29. Chazalon E, Conrath J, Ridings B, Matonti F (2013) [Kyrieleis arteritis: report of two cases and literature review]. *J Fr Ophthalmol* 36: 191-196.
30. Majumder PD, Sudharshan S, Biswas J (2013) Laboratory support in the diagnosis of uveitis. *Indian J Ophthalmol* 61: 269-276.
31. Barry RJ, Nguyen QD, Lee RW, Murray PI, Denniston AK (2014) Pharmacotherapy for uveitis: current management and emerging therapy. *Clin Ophthalmol* 8: 1891-1911.
32. Saurabh K, Das RR, Biswas J, Kumar A (2011) Profile of retinal vasculitis in a tertiary eye care center in Eastern India. *Indian J Ophthalmol* 59: 297-301.
33. Benitez Del Castillo Sanchez JM, Garcia Sanchez J (2001) [Intravitreal injection of triamcinolone acetonide in non infectious uveitis]. *Arch Soc Esp de Oftalmol* 76: 661-664.
34. Kok H, Lau C, Maycock N, McCluskey P, Lightman S (2005) Outcome of intravitreal triamcinolone in uveitis. *Ophthalmology* 112: 1-7.
35. Jabs DA, Rosenbaum JT, Foster CS, Holland GN, Jaffe GJ, et al. (2000) Guidelines for the use of immunosuppressive drugs in patients with ocular inflammatory disorders: recommendations of an expert panel. *Am J Ophthalmol* 130: 492-513.
36. Comarmond C, Wechsler B, Cacoub P, Saadoun D (2013) Approaches to immunosuppression in Behcet's disease. *Immunotherapy* 5: 743-754.
37. Whitcup SM, Salvo EC, Nussenblatt RB (1994) Combined cyclosporine and corticosteroid therapy for sight-threatening uveitis in Behcet's disease. *Am J Ophthalmol* 118: 39-45.
38. Ozdal PC, Ortac S, Taskintuna I, Firat E (2002) Long-term therapy with low dose cyclosporin A in ocular Behcet's disease. *Doc Ophthalmol* 105: 301-312.
39. Greenwood AJ, Stanford MR, Graham EM (1998) The role of azathioprine in the management of retinal vasculitis. *Eye (Lond)* 12: 783-788.
40. Palmares J, Castro-Correia J, Coutinho MF, Araujo D, Delgado L (1995) Immunosuppression in Behcet's disease Clinical management and long-term visual outcome. *Ocular immunology and inflammation* 3: 99-106.
41. Davatchi F, Sadeghi Abdollahi B, Shams H, Shahram F, Nadiji A, et al. (2014) Combination of pulse cyclophosphamide and azathioprine in ocular manifestations of Behcet's disease: longitudinal study of up to 10 years. *International journal of rheumatic diseases* 17: 444-452.
42. Pasadhika S, Rosenbaum JT (2014) Update on the use of systemic biologic agents in the treatment of noninfectious uveitis. *Biologics* 8: 67-81.