



Retinal vasculitis

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Abstract

Retinal vasculitis is an idiopathic inflammatory venous occlusion primarily affecting the peripheral retina of otherwise healthy young adults. Eales' disease is recognized as primary vasculitis of unknown etiology occurring in young adults. This article aims at the overall review of the etiopathogenesis, clinical presentations, pathology, management and prognosis of retinal vasculitis.

Key words: Retinal vasculitis, Eales' disease

Introduction

Eales' disease is an idiopathic inflammatory venous occlusion primarily affecting the peripheral retina of otherwise healthy young adults. It is the commonest cause of vitreous hemorrhage in young adults in the 2nd to 3rd decade of life in Nepal. It is one of the major causes of visual impairment and blindness after diabetes in patients attending the vitreo-retina clinic at B.P. Koirala Lions Centre for Ophthalmic Studies (personal experience of the authors).

Eales (1880, 1882)-a British ophthalmologist, described recurrent retinal hemorrhage in young adults. His seven patients were all young males with a common history of epistaxis, constipation and dyspepsia. He believed it to be a vasomotor neurosis with constriction of alimentary vessels and compensatory dilatation of those in the retinal and nasal vessels. Eales did not describe retinal vasculitis. However, five years later, Wadsworth (1887) described signs of retinal vasculitis.

Initially, Eales' disease was described as periphlebitis retinae (Elliot, 1948) because the affection was primarily of the mid peripheral retina. Later studies showed that both the arteries and veins were involved (Kimura et al 1956; Keith-Lyle and Wybark, 1961) and hence, it was named "retinal perivasculitis". In the following century, Henry Eales has been honored with the eponym for the disease characterized by idiopathic recurrent vitreous hemorrhage in otherwise young and healthy adults.

Patients' profile

Eales' disease typically affects healthy young adults of 20-30 years of age (average 26.9). Males account for 80%-90% of all cases (Patnik and Nagpal, 1998). In a study of 55 cases in the United States, there was equal involvement among male and female. In a study conducted in Nepal (Malla et al 1999) during 1993 to 1996 in a series of forty patients, 80% were between the age of 20 to 40 years and 90% of them were males. Another study conducted in Nepal (Joshi et al 2000) showed that 54.34% of the subjects were in the age group of 21 to 30 years and the male to female ratio was 19:1 and the disease was bilateral in 56.1% of the subjects. However, Duke Elder has mentioned the possibility of bilateral involvement in 90% of cases. In

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a retrospective study conducted by Palmer et al (1996) at St. Thomas Hospital on 53 patients, 48 of those patients had bilateral disease and 5 had unilateral disease. Eales' disease is now rare in developed countries but is commonly reported from the Indian sub-continent.

Aetiopathogenesis

Eales' disease is recognized as a primary vasculitis of unknown etiology occurring in young adults (Wadsworth, 1887). Various studies have been done to identify the etiology which can be classified as follows.

A) Systemic disorders associated with Eales' disease

Some authors have found association of tuberculosis with Eales' disease; however, many authors have found no association between the two at all (Patney et al 1965; Stock, 1937).

Madhavan et al (2002) showed presence of tubercular bacilli in epiretinal membrane of Eales' disease patients. Eales' disease has been shown to be associated with hypersensitivity to tubercular protein because of the fact that 90% of the patients in their series were Mantoux positive (Donders, 1958; Elliot, 1954). However, Eales' disease has been found in Mantoux negative patients as well and Mantoux positivity is seen in 67% to 90% of normal population in this part of the world. Some authors have shown the association of Eales' disease with thrombangitis obliterans, neurological diseases (Fielo and Foster 1962; Singhal and Dastur 1976; Opala et al 1988; Masson et al 1988; Gordon et al 1988), multiple sclerosis, cerebral stroke and hematological diseases (Khan et al 1963; Rahi et al 1969; Jain et al 1970; Bertrams et al 1989; Bryselbout et al 1989; Vanacore et al 1965; Boase et al 1980; Pathak et al 1977), such as acanthocytosis, coagulation disorders, etc.

B) Immunological studies in Eales' disease (Stock, 1937; Gilbert, 1935; Finoof, 1924)

The clinical picture of acute onset, steroid responsiveness, lymphocytic infiltration in histological study of the vitreous and epiretinal membrane and abnormal immunological parameters like low IgM, high IgG and IgA all indicate an immunological mechanism involved in Eales' disease. However, so far, a precise immunological mechanism has not been identified.

C) Biochemical studies in Eales' disease

Several studies have been done on the serum and vitreous samples (Rengarajan et al 1989; Pratap et al 1976). Studies have shown raised alpha-globulin and reduced albumin levels in the serum samples of patients with Eales' disease (Stanford et al 1987).

Stages of Eales' disease

Although a universally accepted classification has not been worked out, the ophthalmoscopic findings have been conveniently divided into several stages, although there may be an overlap between these stages.

Eales' I (stage of inflammation) is characterized by localized areas of peripheral retinal edema with sheathing of the small caliber vascular arcades. Minute retinal hemorrhage can be seen. In Eales' II disease (stage of ischemia), the same pathologic changes involve larger vessels and extend more posteriorly (Fig 1). Veins as well as arterioles can be sheathed. There are more widespread retinal hemorrhages and the vitreous body looks hazy. There are areas of retinal ischemia best seen on fundus fluorescein angiography. In the Eales' III stage (stage of neovascularisation), peripheral new blood vessels become apparent, with numerous and vitreous hemorrhages (Fig 2). The hemorrhage frequently recurs. The final stage, Eales' stage IV (stage of complication), is characterized by massive retinal proliferation protruding from the retinal surface into the vitreous cavity and associated with massive retinal and vitreous hemorrhages. With this advanced stage of the disease, the fibrous tissue components of the neovascular frond can also cause tractional or rhegmatogenous retinal detachment.

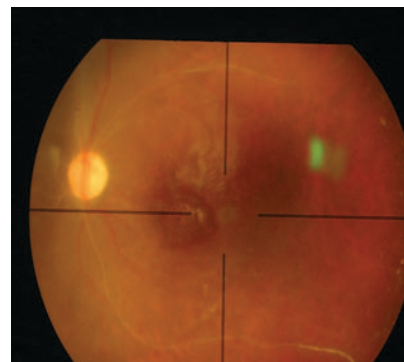


Fig 1- Extensive vascular sheathing

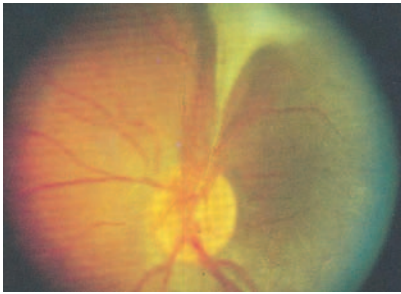


Fig 2- Neovascularisation at disc

Pathology

The clinical manifestations of the disease are due to three basic pathological changes - inflammation, ischemia and neovascularisation and its sequale. The site of involvement is predominantly the peripheral retina. Inflammation involves both the peripheral veins and arterioles, mainly the veins. Histopathological studies have uniformly demonstrated infiltration of chronic inflammatory cells, especially lymphocytes. In addition, Stock (1937) and Gilbert (1935) have demonstrated acid-fast bacilli on the peripheral retinal lesions and perivascular sheath respectively. The immuno-phenotyping of the lymphocytic infiltrate in the epiretinal and sub-retinal membrane in Eales' disease was found to be of predominantly T-cell type with few B cell type (Biswas and Rao, 1990).

Clinical features

Patients are asymptomatic if there is mild peripheral involvement only. Symptomatic patients complain of blurred or decreased vision. A study of 150 patients with vasculitis showed two-third to have visual acuity of 6/18 or better and 20% worse than 6/18 in both eyes (Graham 1989) on presentation. Retinal ischemia leads to scotoma formation and associated vitritis often causes floaters. Some patients may have defective color vision, difficulty in reading or metamorphopsia if the macula is involved.

Signs in the anterior chamber are mild but severe vitritis with inferior snowballs are often present in the vitreous. A review of the retinal signs in 67 patients with idiopathic retinal vasculitis showed that the most common retinal signs were peripheral vascular sheathing (64%) followed by macular edema (60%), retinal neovascularisation (16%), periphlebitis (15%) and retinal vein occlusion (10%)(Graham et al 1989).

Many patients with retinal vasculitis have it associated with prominent uveitis, optic disc edema or cystoid macular edema. Idiopathic retinal vasculitis is characterized by retinal phlebitis, peripheral nonperfusion and retinal neovascularisation.

1) Retinal phlebitis

Fundus examination reveals venous dilatation in the periphery with tortuosity and discontinuity of veins. Perivascular exudates are seen along the peripheral veins with characteristic venous sheathing. Perivascular sheathing ranges from thin white lines limiting the blood columns to heavy exudation, and characteristically peripheral vessels are involved. Though initially not involved, later, arteries are also attenuated. The involved vessels become obliterated and are better visualized with fluorescein angiography.

2) Peripheral non-perfusion

Intra-retinal hemorrhage first appears in the affected area, followed by increase in vascular tortuosity with frequent collateral formation around occluded vessels. The vascular abnormalities at the junction between the perfused and non-perfused retina include micro aneurysm, veno-venous shunts, venous beading, and occasionally hard exudates (Spitzans et al 1975; Elliot, 1975).

3) Neovascularisation

This complication is observed in 80% of patients with Eales' disease. The new vessels can form either on the disc (NVD) or elsewhere in the retina (NVE). Bleeding from the new vessel is common and recurrent and is the major cause of vision loss. In the favorable cases, no further episodes of bleeding occurs, but in recurrent cases, the fundus shows the evidence of old blood and fibrous organization, retinitis proliferens and even tractional retinal detachment. Some patients may develop uveitis, complicated cataract, rubeosis iridis, and secondary neovascular glaucoma in the late stage of the disease. The macula is usually not involved despite extensive peripheral non-perfusion. This preserves the central vision. However, in some cases non-perfusion may extend to the macula and macular edema develops.

Fluorescein angiography

Being essentially a retinal vascular disease, the various manifestations of retinal vascular disease are ideally shown by FFA (Malik and Patnaik, 1973; Theodosiadis,

1970). Active vasculitis is characterized by staining of the vessel wall or frank extravasations. Vascular sheathing due to gliosis without active inflammation does not show these features. Venous stasis due to venous obstruction is manifested by engorged tortuous veins distal to the obstruction, engorgement of the capillary bed, micro-aneurysm and macular edema. It also helps monitoring the regression and disappearance of new vessels during treatment and follow up (Fig 3).

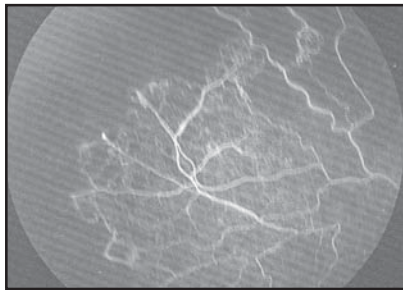


Fig 3- FA-Peripheral retinal nonperfusion

Management

Not all patients require therapeutic intervention. Indications for treatment are vision-limiting vitritis, capillary destruction around foveal avascular zone, broad areas of capillary drop out in FFA and cystoid macular edema.

The various modalities of management are the following.

Observations

If vision is 20/40 or better, and the patient is not bothered by vitreous opacities, mild vascular changes, non to minimal cystoid macular edema and the disease process does not appear to be progressive, the patient can be closely followed-up.

Medical therapy

Corticosteroid is the mainstay of treatment in the stage of active inflammation characterized by perivascular sheathing and infiltrations. Oral and periocular routes are the preferable ones and there is no role of topical steroids for posterior segment inflammation. The therapy is started with oral 1-2 mg/kg body weight then gradually tapered once vasculitis decreases. Periocular steroid injection, particularly posterior sub-tenon injection, is recommended for unilateral disease and oral-steroid contraindicated cases. Howe et al believed

that patients do better with prednisolone 80 mg for 4 days, 60 mg for 4 days and 40 mg for a month and then tapering the dose thereafter. Too rapid tapering may cause recurrence. Few studies have highlighted the role of anti-tubercular therapy in Eales' disease in patients with acute phlebitis with massive infiltration, nodule formation and obliteration of segments of veins. Immunosuppressive therapy is reserved for steroid-contraindicated cases and non-responders. Drugs used are alkylating agents (Cyclophosphamide, Chlorambucil), antimetabolites (methotrexate, azathioprine) or cyclosporine A.

Photocoagulation

Photocoagulation is mainly indicated for the ischemic and proliferative stages of Eales' disease. Stage I doesn't require photocoagulation whereas stage IV is too advanced for it. So the best time for photocoagulation is stage II and stage III of Eales' disease (Das and Namperumalsamy, 1987). Focal treatment at flat new vessel, sectoral laser at capillary drop out and direct treatment of neovascular frond in vitreous is quite effective (90% regression). Anchoring photocoagulation using moderate power laser is preferred in preventing subsequent tractional retinal detachment (Patnaik and Kalsi, 1987).

Anterior retinal cryoablation

This is indicated especially for stage II and stage III disease with hazy media, non-dilating pupil and recent-onset hemorrhage. The results are encouraging.

Vitrectomy

Vitreous hemorrhage is the prime cause for impaired vision in Eales' disease. Despite the available therapeutic measures, vitreous haemorrhages are still common. 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.

Pars plana vitrectomy is indicated in vitreous hemorrhage that has not cleared in two to three months, tractional retinal detachment involving posterior pole, multiple vitreous membranes with or without tractional RD and combined tractional and rhegmatogenous retinal detachment. In one study, forty eyes of forty patients with vitreous hemorrhage due to Eales' disease underwent simple vitrectomy (Malla et al 1999). Visual results were taken as criteria for improvement. More

than 36 eyes had visual improvements. Of these, in 30 eyes, the vision improved to 6/6-6/24. Visual improvement was better with few hemorrhagic episodes and a short duration of the disease. In our experience, early vitrectomy carries a better visual prognosis than waiting for the hemorrhage to clear. Early vitrectomy gives early visual recovery and probably removes the noxious stimuli from the vitreous and the inflammatory debris.

Vitrectomy in Eales' disease is found to be less risky than in diabetic retinopathy because of early and complete posterior vitreous detachment, though retinitis proliferans is fairly common in long-standing cases.

Conclusion

Usually patients with Eales' disease have extensive antero-peripheral non-perfusion but spare macula. Vitreous hemorrhage is the most common cause of visual loss. With the advent of sophisticated vitrectomy instruments, laser photocoagulation techniques and early vitrectomy in these patients, visual prognosis is usually good. The main sight-threatening complications are recurrent vitreous hemorrhage, tractional or rhegmatogenous retinal detachment, massive retinal proliferans and cataract.

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