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A new staging system for idiopathic retinal periphlebitis

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PURPOSE. *To develop and standardize a universally acceptable new staging system for idiopathic retinal periphlebitis (Eales disease).*

METHODS. *A new staging system was established and standardized based on standard terminology and features. Idiopathic retinal periphlebitis was classified as peripheral and central types. Peripheral disease consisted of four stages. Stage 1 is periphlebitis of small (1a) and large (1b) caliber vessels with superficial retinal hemorrhages. Stage 2a denotes capillary nonperfusion and 2b neovascularization elsewhere/of the disc. Stage 3a is classified as fibrovascular proliferation and 3b vitreous hemorrhage. Stage 4a is traction/combined rhegmatogenous retinal detachment whereas 4b is rubeosis iridis, neovascular glaucoma, complicated cataract, and optic atrophy. A total of 253 cases of idiopathic retinal periphlebitis (mean age, 24.7 ± 4.7 years, all male) presenting at this tertiary care center were classified prospectively according to the new staging system, by two independent observers (interobserver correlation = 0.7).*

RESULTS. *The new staging system was consistent, simple, and easy to recall. Peripheral and central types of idiopathic retinal periphlebitis were found in 94.07% and 5.93% of cases, respectively. The new staging system also defined the severity of the disease. Vitreous hemorrhage was found to be the commonest presenting feature (51.68%), whereas traction/combined rhegmatogenous detachment was found in 5.88% of cases.*

CONCLUSIONS. *The new staging system is useful in classifying and assessing the severity of disease. Management strategy can also be defined according to the stage of the disease. It is designed to promote the use of standard assessment with applications to clinical management and research. (Eur J Ophthalmol 2004; 14: 236-9)*

KEY WORDS. *Eales disease, Idiopathic retinal periphlebitis, Vitreous hemorrhage, Staging*

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INTRODUCTION

Eales disease is an idiopathic obliterative vasculopathy that primarily affects the peripheral retina in young adults (1). Eales disease was first described by Henry Eales, a British ophthalmologist, in 1880 and 1882 (2, 3). He found it in seven young male patients ranging in age from 14 to 29 years with recurrent vitreous hemorrhages. In addition, these patients had histories of headache, variation in peripheral circulation, chronic constipation, and epistaxis (3). In the next century, the disease was redefined by several investigators (4-7). Elliot first recognized the inflammation of retinal vein and described it as periphlebitis retinae (5). Subsequently, several investigators documented both venular and arteriolar inflammation (6, 8).

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Idiopathic retinal periphlebitis (Eales disease) is characterized by periphlebitis, peripheral retinal ischemia, and neovascularization. Visual loss is characteristically caused by recurrent vitreous hemorrhage. Central retinal periphlebitis is markedly uncommon compared to peripheral retinal periphlebitis (9-11).

Idiopathic retinal periphlebitis appears to be an immunologic reaction that may be triggered by an exogenous exposure. Our earlier study showed that retinal S-antigen and interphotoreceptor retinoid binding protein might play a role in the etiopathogenesis of this condition. An extraneous agent could result in the exposure of normally sequestered uveitopathogenic antigens of the immune system, leading to an immune response in the eye that may initiate the disease process (12). Antiretinal antibodies to retinal antigens have also been reported (13). Our earlier studies (13-17) and studies by other investigators (18-20) have highlighted the role of free radicals in pathogenesis of the disease. Mycobacterium tuberculosis DNA has also been detected by polymerase chain reaction in the vitreous of such patients (21-23).

Charamis (24) conveniently divided the ophthalmoscopic findings of Eales disease into several stages in 1965. Subsequently, two decades later, Das and Namperumalsamy (25) classified the disease, according to degree and extent of microangiopathy, proliferative retinopathy, and vitreous hemorrhage.

The natural course of idiopathic retinal periphlebitis is quite variable with temporary and even permanent remission in some cases and relentless progression to blindness in others. A universally accepted classification has not been worked out. A new staging system was established based on standard terminology and features, which would classify the severity of the disease and be universally acceptable. A tertiary care center-based prospective study was undertaken to categorize cases of idiopathic retinal periphlebitis according to the new staging system.

MATERIALS AND METHODS

Clinical manifestations of idiopathic retinal periphlebitis are due to three basic pathologic changes: inflammation (retinal phlebitis), ischemic changes (peripheral retinal capillary nonperfusion), and neovascularization of the retina or optic disc, which often leads to vitreous hemorrhage (26). Based on the above facts, a new staging system of idiopathic retinal periphlebitis was established, refined, standardized, and presented at two vitreoretinal scientific meetings (Tab. I).

In peripheral idiopathic retinal phlebitis, stage 1 is the stage of inflammation of small and subsequently large caliber retinal veins. Stage 2 is the stage of retinal ischemia and neovascularization. Stage 3 is the stage of retino-vitreal fibrovascular proliferation with resultant vitreous hemorrhage; stage 4 is the stage of complications. Central retinal periphlebitis includes inflammation and occlusion of the central retinal vein.

A total of 253 cases presenting in the Retina Clinic of this tertiary care center were included prospectively in this study. The eye with more severe disease was included. The mean age was 24.7 ± 4.7 years (range, 16–34 years). All were male. Systemic diseases such

TABLE I - STAGING OF IDIOPATHIC RETINAL PERIPHLEBITIS

Stages	Features	Eyes (%)
	A. Peripheral idiopathic retinal periphlebitis	238 (94.07%)
Stage 1a	Periphlebitis of small caliber vessels with superficial retinal hemorrhages	9 (3.78%)
Stage 1b	Periphlebitis of large caliber vessels with superficial retinal hemorrhages	17 (7.14%)
Stage 2a	Peripheral capillary nonperfusion	17 (7.14%)
Stage 2b	Neovascularization elsewhere/neovascularization of the disc	28 (11.76%)
Stage 3a	Fibrovascular proliferation	22 (9.24%)
Stage 3b	Vitreous hemorrhage	123 (51.68%)
Stage 4a	Traction/combined rhegmatogenous detachment	14 (5.88%)
Stage 4b	Rubeosis iridis, neovascular glaucoma, complicated cataract, and optic atrophy	8 (3.36%)
	B. Central idiopathic retinal periphlebitis	15 (5.93%)

as diabetes mellitus, hypertension, sickle cell hemoglobinopathy, blood dyscrasias, sarcoidosis, neurologic, and collagen vascular disorders were ruled out with a careful history and appropriate investigations. All the cases underwent full ophthalmologic examination, which included Snellen visual acuity, slit lamp biomicroscopy, indirect ophthalmoscopy, and fluorescein angiography. Peripheral idiopathic retinal periphlebitis (8, 26-28) was comprised of retinal periphlebitis, capillary nonperfusion, and neovascularization, whereas central idiopathic retinal periphlebitis (4, 29) was comprised of optic disc edema with dilated retinal veins, tortuosity of the major retinal veins, and variable degree of retinal hemorrhages. All the eyes were classified according to the new staging system by two independent observers (Tab. I). Interobserver correlation, using kappa statistics, was also computed.

RESULTS

In the new staging system, peripheral and central disease were found in 94.07% and 5.93% of cases respectively (Tab. I). Peripheral idiopathic retinal periphlebitis was divided into stages 1 to 4, with subsets a and b, which defined further the severity of disease. Interobserver correlation was computed as 0.7. Vitreous hemorrhage was observed in 51.68%, whereas traction/combined rhegmatogenous detachment was found in 5.88% of cases of Eales disease.

DISCUSSION

Idiopathic retinal periphlebitis is a distinct clinical entity comprised of characteristic funduscopic and fluorescein angiographic features (30). As the precise etiology of this disease is still undetermined, currently the disease may be labeled as a clinical syndrome with specific clinical picture and natural course (26).

A universally accepted staging system is not available for idiopathic retinal periphlebitis. In the past, ophthalmoscopic findings have been divided into several stages or have been classified according to degree and extent of microangiopathy, proliferative retinopathy, and vitreous hemorrhage (24, 25).

The new staging system, based on standard terminology and features, provides a simple method to categorize, according to the severity of the disease. This staging system takes into consideration the funduscopic and fluorescein angiographic variables that have been shown to be prognostic of visual outcome. In peripheral disease, management strategy can also be defined according to the stage of the disease. Stage 1, the stage of inflammation, is amenable to medical therapy. Stage 2, the stage of ischemia and neovascularization, requires observation/laser photocoagulation. Stage 3, the stage of proliferation, requires laser/pars plana vitrectomy and laser. Stage 4, the stage of complications, requires sophisticated surgical management strategies.

Idiopathic retinal periphlebitis was categorized into two types, according to the new system. The majority of cases (94.07%) were classified as peripheral type.

The new classification system for idiopathic retinal phlebitis is consistent and simple. It is easy to recall and is useful in assessing the severity of the disease. It can also be used to monitor the effect of medical, laser, and/or surgical treatment. This staging system is designed to promote the use of standard terminology and assessment with applications to patient care and research in idiopathic retinal periphlebitis.

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