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Research Article

Current Concepts of IRVAN Syndrome

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Abstract

IRVAN syndrome is a rare disease characterized by retinal vasculitis, retinal aneurysms and neuroretinitis. Patients are usually asymptomatic at diagnosis but over time, proliferative changes, macular hard exudates, macular edema and retinal vascular occlusions can lead to severe vision loss. In this article we review the signs, symptoms, workup and treatment options of this disease.

Keywords: *IRVAN syndrome; Vasculitis; Aneurysms; Neuroretinitis; Neovascularization; Retinal isquemia;*

Abbreviations: IRVAN: Idiopathic retinal vasculitis, aneurysms and neuroretinitis; IVFA: Intravenous Fluorescein angiography; VEGF: Vascular endothelial growth factor

Introduction

IRVAN syndrome is a rare disease that usually affects younger persons and is characterized by bilateral retinal vasculitis, retinal aneurysms and neuroretinitis combined with peripheral vascular nonperfusion which leads to retinal neovascularization [1,2]. It represents a local inflammatory disease localized to the retinal vasculature.

Diagnosis requires all three major criteria to be present (Table 1) [3]. Visual loss occurs secondary to proliferative changes, macular hard exudates, macular edema and retinal vascular occlusion.

Major Criteria	Minor Criteria
Retinal vasculitis	Peripheral capillary nonperfusion
Neuroretinitis	Retinal neovascularization
Aneurysmal dilations of the optic nerve head and retinal arterioles at or near their major branching sites	Macular exudation

Table 1: *Diagnostic criteria for IRVAN syndrome. All three major criteria must be present.*

IRVAN syndrome typically affects young healthy patients and is more common in women. Patients are usually asymptomatic at presentation despite important retinal findings. Although some patients are able to maintain good visual acuity, over time retinal isquemia secondary to neovascularization as well as exudative maculopathy and Neovascular glaucoma leads to severe visual loss. It is characterized by multiple leaking aneurysmal dilatations along the retinal arteriolar tree and over the optic nerve head. [1,2]. the diameter of the aneurysms usually measure between 75 and 300 μm and these can be triangular, Y-shaped or coiled. Neuroretinitis is characterized by optic nerve head swelling. Affected vessels tend to leak, therefore leading to exudative retinopathy. Subretinal, intraretinal or vitreous hemorrhage secondary to aneurysms is not a common finding in these patients. If vitreous hemorrhage is found, it is usually related to retinal neovascularization [1,4,5].

Etiology

The etiology of this disease is unknown. There is no consensus as to whether this disease is a vascular or inflammatory disorder. The presence of anterior chamber cells and vitritis indicate the process may be inflammatory related but treatment with steroids have had limited impact on halting the progression of the disease [1]. Positive perinuclear antineutrophil cytoplasmic antibody (P-ANCA) has been found in patients with IRVAN suggestive of a retinal form of P-ANCA associated vasculitis [6,7].

Differential Diagnosis

One of the differential diagnoses when faced with a patient with aneurysms is senile acquired macroaneurysms. A way to differentiate these two conditions is that the latter tend to occur in older patients with a history of hypertension. The aneurysms in senile acquired macroaneurysms tend to be round and are associated with hemorrhage and serous exudation.

Due to the presence of retinal vasculitis and peripheral nonperfusion, another differential diagnosis one must consider is Eales disease. In Eales disease affected patients are young males, with tuberculin hypersensitivity, uveitis, retinal venous inflammation and they lack macroaneurysms [2]. Inflammation in Eales disease is often more in the veins than the arterioles. The presence of multiple aneurysms and optic nerve head vascular tortuosity is usually enough to distinguish IRVAN from Eales disease [1].

The diagnosis of acute multifocal hemorrhagic retinal vasculitis should be considered in otherwise healthy patients that present with retinal vasculitis, retinal capillary nonperfusion, and retinal neovascuarization. These patients will also present with intraretinal hemorrhage, optic disk swelling and vitritis [4].

Workup

During eye examination, aneurismal changes are habitually present on the optic nerve head. The arteries passing through the optic nerve head have dilating changes that give the appearance of elongation. Exudative retinopathy is usually seen adjacent to the retinal and optic nerve head aneurysms [1]. Conventional fundus photos can demonstrate aneurismal changes although these are more prominently seen on fluorescein angiography [1]. Fluorescein and indocyanine green angiography are useful tools in identifying the aneurysms, peripheral capillary nonperfusion and disk staining abnormalities [1,5]. The staining of the arterial and venous walls corresponds to vasculitis. Neuroretinitis is seen by diffuse staining of the optic nerve head in late phase IVFA. These two studies also allow the visualization of retinal non perfusion.

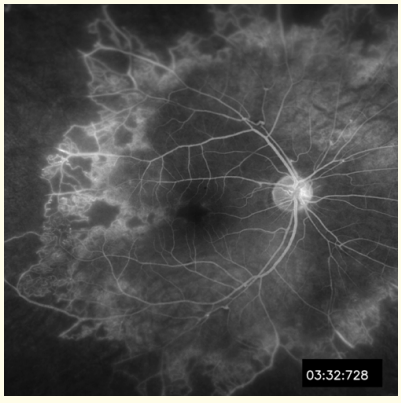

Figure 1: *Fluorescein angiography showing severe capillary non perfusion of the peripheral fundus, segmental staining of some arterioles and macroaneurysms.*

Classification

Samuel and colleagues proposed a classification based on ocular findings to evaluate the progression of the disease and the response to treatment [3].

Stage	Ocular Findings
1	Macroaneurysms, exudation, neuroretinitis and retinal vacuities
2	Capillary nonperfusion with angiographic evidence
3	Posterior segment neovascularization of disc or elsewhere and/ or vitreous hemorrhage
4	Anterior segment neovascularization (tubeosis iridis)
5	Neovascular glaucoma

Table 2: *IRVAN syndrome staging.*

Management and Prognosis

Several management options have been proposed depending on the clinical course. Observation for affected eyes without retinal neovascularization and no visual loss can be considered [1,8]. Interventional treatment options are medical treatment, laser photocoagulation and retinal surgery. Retinal photocoagulation (PRP) should be performed as early as possible if there are areas of widespread retinal nonperfusion. Eyes treated with photocoagulation as early as stage 2 maintain visual acuity and do not progress to an advance stage of the disease (figure 2) [3]. Other treatment options have been proposed, including oral and intravitreal glucocosteroids, immunosuppressive therapy, intravitreal anti VEGF injections. Pars plana vitrectomy has been performed in advanced cases with favorable results [9-14].

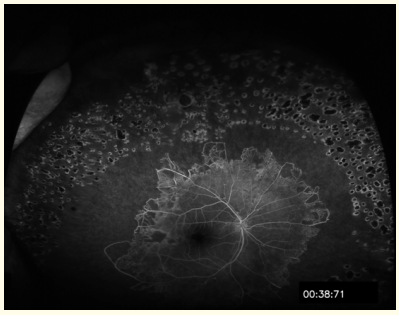

Figure 2: *Wide field fluorescein angiogram illustrating photocoagulation scars in the non-perfused peripheral retina.*

Discussion

There has been more awareness of this rare disease in recent years leading to a better diagnosis of affected patients. Although the clinical spectrum varies, the major causes of vision loss are retinal non perfusion and neovascularization. Patients have usually been treated with photocoagulation, steroids and surgery to prevent visual deterioration but the treatment is still controversial. PRP is the only well accepted treatment and is often effective, especially in disease stage 2 and 3. Systemic corticosteroids have been proposed as possible treatment options since the presence of anterior chamber cells and vitritis implies that there is an underlying inflammatory etiology, but these have not proved to stop the progression of neovascularization. The role that immunosuppressive or immunomodulatory agents play in the treatment of the disease is still unclear. There have been cases that suggest treatment with infliximab can reduce inflammation [15,16]. There has been a proposal to classify the disease based on ocular findings that would help monitor treatment response and disease progression.

Conflict of interest

The authors declare there exists no financial interest or any conflict of interest.

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