Idiopathic Retinal Vasculitis, Aneurysm, Neuroretinitis Syndrome; Case Report

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ABSTRACT

Idiopathic retinal vasculitis, aneurysm, neuroretinitis (IRVAN) syndrome is an idiopathic disease that usually affects young women. Macular edema and neovascular complications secondary to retinal ischemia are the main causes that threaten vision. There is no accepted standard algorithm in the treatment of IRVAN syndrome. Laser photocoagulation is used for retinal ischemia, and intravitreal antivascular endothelial growth factor or dexamethasone implant injection is applied in the presence of macular edema. In systemic treatment, steroids, conventional immunosuppressive or biological agents are used. Fundus fluorescein angiography and optical coherence tomography are used in the diagnosis and follow-up of patients. In this case report, the clinical and angiographic findings of two female patients who were diagnosed with IRVAN and received local and systemic treatment are described.

Key words: retinal vasculitis, aneurysm, neuroretinitis, IRVAN syndrome

INTRODUCTION

The clinical picture in which retinal vasculitis, retinal/optic nerve head aneurysms and neuroretinitis is defined as idiopathic retinal vasculitis-aneurysm-neuroretinitis syndrome (IRVAN) [1]. Six criteria have been established to diagnose IRVAN syndrome. These criterias are, multiple aneurysmal dilatations, neuroretinitis, retinal vasculitis, retinal neovascularization, macular exudation and peripheral capillary nonperfusion.[1] The classical triad is seen in most patients at the time of diagnosis. However, in some patients, not all findings are seen initially and the triad is completed during follow-up.[1-4] It is stated that the neuroretinitis seen in IRVAN syndrome is not a true neuroretinitis and that the picture should be defined as idiopathic retinal vasculitis, aneurysm and retinal exudate (IRVARE).[5]

The disease is often seen in young women. Although the etiology is generally idiopathic, it can also be seen together with various systemic vascular diseases.[3-6] IRVAN syndrome causes vision loss due to neovascular complications secondary to retinal ischemia or edema and exudations in the macula. There are five stages of the disease. Exudation and aneurysm in the retinal arteries are observed in the first stage, retinal ischemia in the second stage, neovascularization and secondary hemorrhages in the third stage, neovascularization in the angle and iris in the fourth stage, and neovascular glaucoma in the fifth stage.[2,3]

It has been reported that there is no specific treatment algorithm for the disease, and laser photocoagulation can be used for aneurysm and ischemic areas, intravitreal anti-vascular endothelial growth factor (anti VEGF) agents and dexamethasone implant can be used in the

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presence of macular edema, and steroids, conventional immunosuppressive and biological agents can be used in systemic treatment.[3,7-12]

In this case report, the clinical and angiographic findings and treatments of two patients diagnosed with IRVAN syndrome and followed up will be discussed.

CASE-1

A 29-year-old female patient was investigated at an external center with complaints of headache and decreased vision that had been going on for 4-5 years. The patient's cranial MRI was found to be normal, and CSF opening pressure was found to be high in the lumbar puncture, and she was diagnosed with idiopathic intracranial hypertension and acetazolamide (Diazomid, Sanofi, İstanbul, Türkiye) was started. However, since clinical improvement could not be achieved, a shunt operation was performed. The patient, who developed poor vision during follow-up, and stated that laser photocoagulation was applied because she had vascular occlusion in her eyes was referred to our clinic for evaluation. On examination, the patient's vision was 0.4/0.2 and the anterior segment was normal. Intraocular pressures were at 12/17 mmHg. There were bilateral 1+ cells in the vitreous, increased vascular tortuosity in the fundus, hyperemia in the optic disc, and peripapillary exudation in the left eye. Fundus fluorescein angiography revealed aneurysmal dilatations in the vascular bifurcations and ischemia in the bilateral temporal periphery (figure 1a). On optic coherence tomography (OCT), there were hyperreflective spots belonging to exudates, but there was no macular edema. With these findings, the patient was diagnosed with stage 2 IRVAN syndrome. Systemic investigation revealed no disease other than benign intracranial hypertension. Laser photocoagulation was applied to ischemic areas. Azathioprine (Imuran, Aspen Europe GmbH, Feucht, Germany) 100 mg/day was started. Although peripapillary exudations increased during follow-up, there was no decrease in visual acuity and OCT was normal. Since macular edema, new capillary nonperfusion area and neovascularization did not develop, no change was made in the patient's systemic treatment (figure 1b).

CASE-2

A 26-year-old female patient applied with the complaint of decreased vision in her left eye. On examination, visual acuity was 1.0 on the right eye and 0.05 on the left eye. The anterior segment was bilaterally normal and there was bilateral 1+ vitritis. Hard exudates were observed in the right posterior pole, scarring in the left macula, and thin fibrous tissue in the left optic nerve head. In the patient's OCT, right macula was normal and there was a scar in the left macula. The patient, whose angiography revealed ischemia in the periphery, was diagnosed with stage 2 IRVAN. Laser photocoagulation was applied to the ischemic areas of the patient, whose systemic investigation revealed no pathology. Because permanent vision loss developed in one eye due to macula scarring and the patient was breastfeeding, adalimumab (Humira, AbbVie,Ravensburg, Germany) 40 mg/2 weeks was started. During follow-up, it was observed that the ischemic area widened and neovascularization developed in the same eye and the stage was progressed to stage 3 IRVAN syndrome (figure 2). Laser photocoagulation was applied to the new ischemic areas. No additional ocular complications developed during the follow-up of the patient, and adalimumab was contiuned.

DISCUSSION

Retinal and vitreous hemorrhage, macular edema, and neovascular glaucoma secondary to ischemia are important vision-threatening complications in IRVAN syndrome. It is essential to evaluate the patient with fundus fluorescein angiography (FFA) during follow-ups to protect the patient's vision and provide effective treatment. FFA shows aneurysmal dilatations, leakage at the optic nerve head, late phase staining, and focal or segmental vascular leakage. In addition, capillary nonperfused areas, leakage due to neovascularization and macular edema are other findings detected. [3,4,6,13,14]

In IRVAN syndrome, inflammation and necrosis occur in the vessels. The resulting inflammation mainly affects the retinal arterial smooth muscles. It has been shown that, due to the possible effect of intravascular hydrostatic pressure, the vessel wall weakens in a segment of the inflamed vascular structure, resulting in fusiform expansion and ectasia.[15,16] It has been argued that tumor necrosis factor alpha (TNF-alpha) plays a role in this inflammation, and it has been reported that this aneurysm appearance may disappear with the regression of inflammation. It has been emphasized that in some cases, new aneurysms may develop in areas

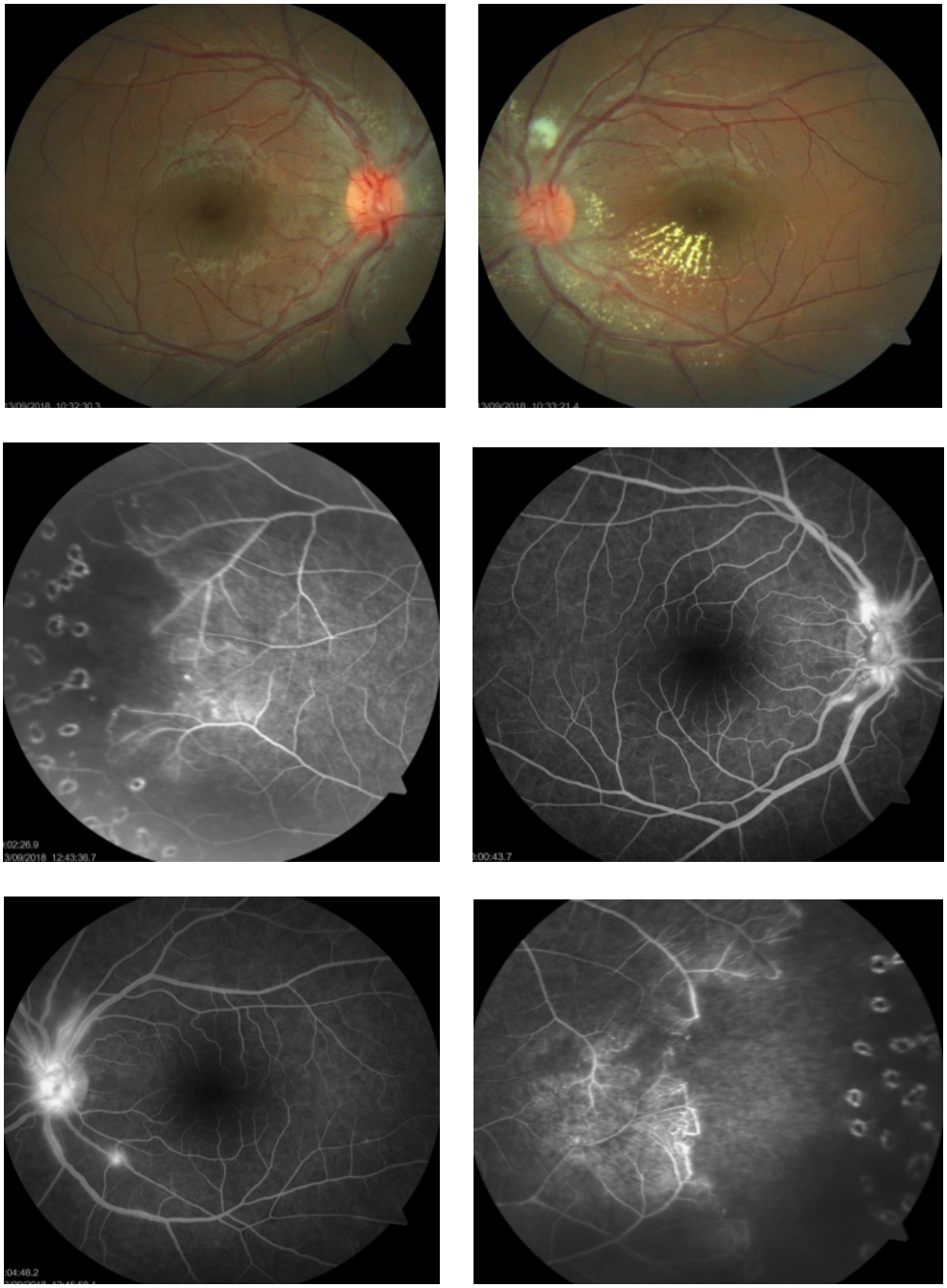

Figure 1a: *In the fundus image of the first case, hyperemia in both optic discs, exudation in the left macula, and hyperfluorescence of aneurysms and nonperfused areas in both temporal peripheries are noted in the angiography images.*

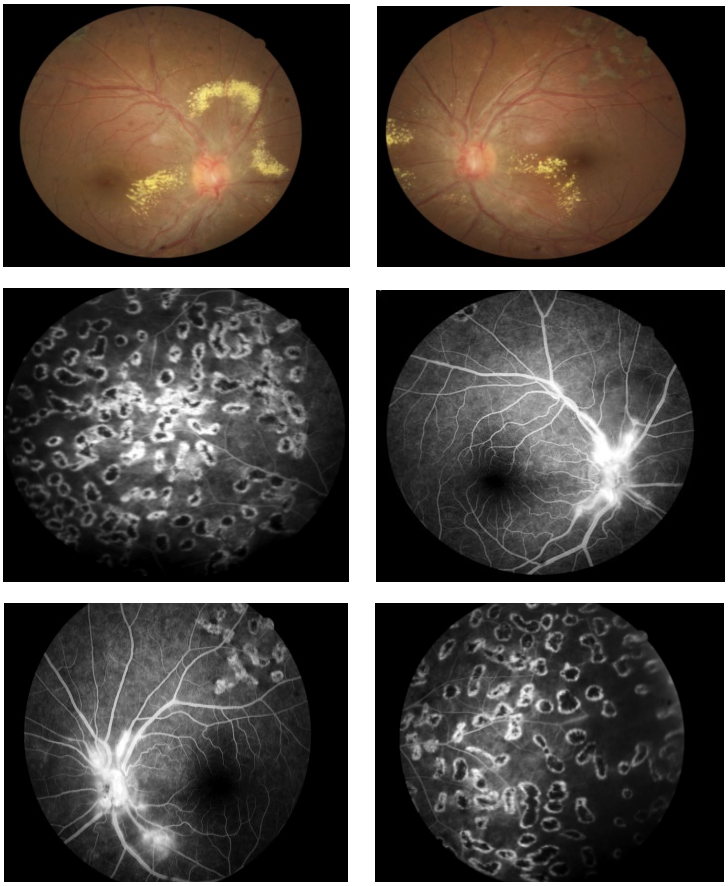

Figure 1b: *In the last fundus photograph of the same case, it is seen that exudations increased in both eyes and ischemic areas in the periphery were treated with laser photocoagulation.*

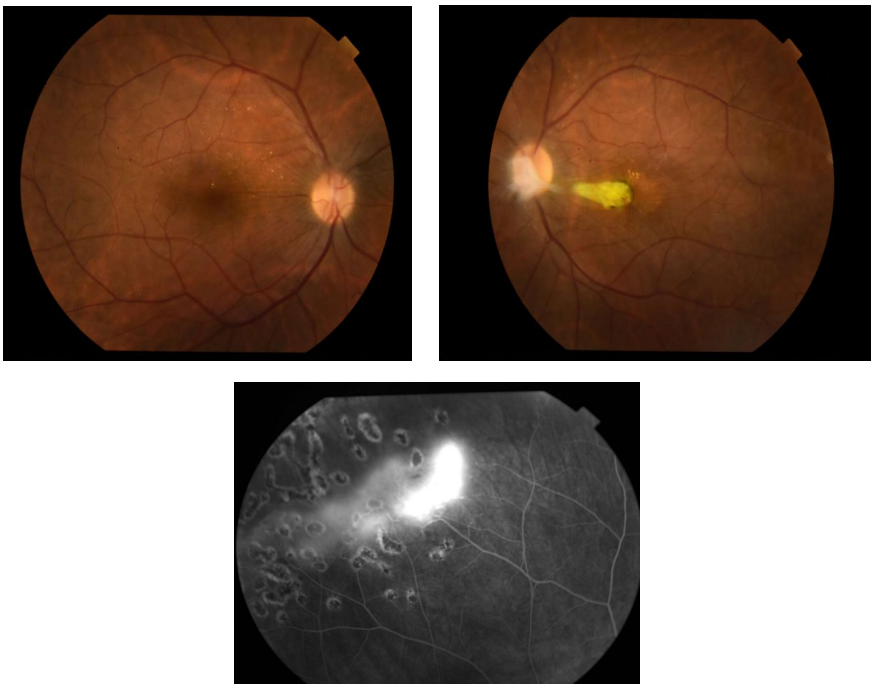

Figure 2: *The fundus photo of the second case shows exudates in the right posterior pole, scar in the left macula, and angiography shows ischemia in the upper periphery and leakage from neovascularization.*

adjacent to regressed aneurysms.[15] Aneurysmal dilatations are frequently seen at retinal bifurcation points and arterioles in the optic nerve head. Leakage and lipid exudation from these aneurysms, especially those occurring in the posterior pole, cause macular involvement and a decrease in visual acuity.[1-3,6,15] It has been reported that no aneurysm was observed in some of the patients.[11] Although widespread aneurysms were seen in the optic nerve head and posterior pole in our first case, the absence of an aneurysm in our second case is important in that the classic triad of IRVAN disease may not be seen in all patients at the time of first presentation. It is also thought that the fibrous tissue in the left optic nerve head of the second patient may be a sequela finding due to a leaky regressed aneurysm.

The disease is often idiopathic. However, it has been reported that some patients have perinuclear antineutrophil cytoplasmic antibodies (p-ANCA) positivity.[17] It has been argued that in some cases, IRVAN disease develops as a result of hypersensitive reaction to fungal or tuberculin antigen and inflammation. It has also been stated that it would be useful to evaluate patients for sarcoidosis and to check the lupus anticoagulant and antiphospholipid antibodies[3,.4,18,19] It has been reported in the literature that idiopathic intracranial hypertension occurs together with IRVAN syndrome, like our first case. In a case report, intracranial venous obstruction was observed and it was thought that the increase in pressure might be related to this pathology.[20] Unlike this case report, no pathological findings were found in the magnetic resonance imaging performed in our first case who diagnosed with intracranial hypertension. This association should be taken into consideration in patients diagnosed with IRVAN, and if the patient is accompanied by headache, intracranial pressure control should be performed.

Although arterial involvement is prominent in IRVAN, periphlebitis can often be observed. Nonperfused areas may develop as a result of vasculitis and microvascular occlusion, VEGF secreted from peripheral capillary nonperfused areas causes neovascularization.[6] It was shown that areas of capillary nonperfusion are associated with poorer vision and a higher incidence of complications.[3,6] Laser photocoagulation is recommended for ischemic areas in IRVAN syndrome and this treatment eliminates nonperfused areas and provides a reduction in neovascular processes, aneurysm regression and leakage.[3,4] Stage II and III cases are treated with laser photocoagulation alone or in combination with systemic steroids to prevent ischemia and related complications. In addition, intravitreal dexamethazone implants or anti-VEGF injections combined with photocoagulation have been shown to be effective in some cases with macular exudation and edema.[6-10] In our patients peripheral capillary nonperfusion areas were observed and both of them had underwent only one session laser photocoagulation. Although no new ischemic areas developed during follow-up in the first case, the expansion of the ischemic area and the development of neovascularization in the second case shows the progression may differ among patients and the importance of FFA in the follow-ups.

In IRVAN syndrome, macular edema is treated with anti-VEGF agents or intravitreal dexamethasone implant. Patients who develop retinal detachment, tractional membrane, and vitreous hemorrhage undergo pars plana vitrectomy.[3,7-9] It has been reported in case reports that systemic steroids, conventional immunosuppressives or biological agents were used in addition to local treatments.[3,10-12] In our first patient we couldn't use systemic steroid because of intracranial hypertension so we added azathioprine to control the disease. There was no decrease in visual acuity as macular edema did not develop during follow-up. In the second case, the patient was pregnant and had advanced vision loss in one eye. Laser photocoagulation was performed for ischemic areas and adalimumab, a TNF alpha blocker thought to play a role in the etiology of IRVAN, was added to the treatment. Neovascularization and ischemia that developed during follow-up were treated with laser photocoagulation and no progression was observed. Intravitreal injection was not needed because macular edema did not develop in either case.

In conclusion, IRVAN syndrome is an idiopathic retinal vascular disease usually seen in young women. The aim of treatment is to close angiographically detected ischemic areas with laser photocoagulation and to apply anti-VEGF or dexamethasone implants to improve macular edema. In some patients immunosuppressive treatment can prevent blindness.

Informed consent: Informed consents were obtained from the patients.

Conflict of interest: No conflict of interest was declared by author.

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