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CASE REPORT

Further observations on a bilateral IRVAN syndrome case

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Abstract

Purpose Reporting clinical features of the late course of the disease after long-term follow-up in a bilaterally affected patient with idiopathic retinitis, vasculitis, retinal aneurysms and neuroretinitis (IRVAN) and new peripheral retinal findings on wide-field angiography and multimodal imaging.

Methods This was a retrospective observational study, based on current diagnostic studies including wide-field fluorescein angiography, optical coherence tomography (OCT) and treatment of aneurysms with argon laser photocoagulation.

Results A 21-year-old female with bilateral IRVAN syndrome—stage 2 in the right eye and stage 3 in the left eye—previously treated bilaterally with laser photocoagulation for retinal macroaneurysms and ischemic areas between 1985 and 1992. Follow-up interrupted on two occasions, with subsequent fundus re-examinations confirming the prevention of retinal neovascularization in both eyes, as recently evidenced on wide-field angiography.

Conclusions A case of bilateral IRVAN disease with multiple retinal aneurysms, neuroretinitis and peripheral capillary nonperfusion successfully treated with laser photocoagulation, maintaining normal visual acuity in one eye and preventing retinal neovascular complications.

Keywords Retinal aneurysms · Uveitis · Vasculitis · Neuroretinitis · Wide-field angiography

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Background

IRVAN is a rare disease affecting young patients characterized by bilateral retinal arteritis, peripheral retinal vascular occlusion, multiple posterior aneurysms of the retinal and optic nerve head arterioles, and uveitis [1–5]. Childhood uveitis on fluorescein angiography was first described by Karel et al. [1] in 1973. Verdaguer, in his 1978 publication, included an angiography of a case with multiple retinal aneurysms, suggesting a congenital origin [2]. Kincaid and Schatz first reported the association of macroaneurysms with retinal vasculitis and neuroretinitis [3]. In 1986, Melan et al. reported a similar case [4]. In 2007, Samuel and Chang et al. who coined the idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN) acronym described the largest series of cases and defined the five stages of the disease process. They were also successful in treating some of these cases with panretinal photocoagulation [6].

Visual loss is caused by exudative maculopathy and neovascular sequelae of retinal ischemia with exudation and vascular sheathing. IRVAN aneurysms can be found throughout the fundus but are more frequently seen at the bifurcations of the larger posterior retinal arterioles. Aneurysms tend to leak causing lipid depositions that can extend to the fovea like in the bilateral case here reported. Peripheral capillary nonperfusion may progress bringing about the development of preretinal neovascularization and secondary vasoproliferative complications [3, 5, 6], including vitreoretinal hemorrhages, neovascular glaucoma and blindness that ought to be prevented [5, 6].

Treatment of IRVAN includes simple observation [7]. Owens and Gregor observed a vanishing retinal arterial aneurysm [8]; panretinal laser photocoagulation was used by Chang, Samuel and Yhesurun [6, 9]. Others have used macular grid photocoagulation, transscleral cryotherapy, steroid therapy [10–12], intravitreal anti-VEGF [10, 13, 14] and administration of monoclonal antibodies like infliximab [15]. Samuel et al. conducted the largest IRVAN cohort study and concluded that early panretinal laser photocoagulation should be considered in the event of angiographic evidence of widespread retinal nonperfusion is present, hopefully before the development of neovascularization [3, 5, 6] and the disappearance of aneurysms. Osman Saatci et al. reported successful treatment with dexamethasone implant, laser and azathioprine, reducing serous retinal detachment and peripapillary exudates [12]. The role of immunomodulatory treatment remains uncertain [12, 15]. However, Cheema et al. reported successful reduction in optic nerve inflammation and leakage in two patients on infliximab therapy [15].

Bilateral case report and outcome

A 21-year-old woman consulted on September 1985 with exotropia and a central scotoma in her left eye. On examination, visual acuity was 20/20 in the right eye and 20/400 in the left eye. Biomicroscopy showed mild anterior uveitis, mild vitritis, and bilateral intraocular pressures within normal limits, in both eyes. Ophthalmoscopy found retinal vasculitis and neuroretinitis with macular star, bilaterally (Fig. 1). The major finding was the bilateral triangular

aneurysms 75–300 microns in size, staining on fluorescein angiography (including one in the optic papilla of the left eye), bilateral macular stars, peripheral temporal retinal ischemia in the left eye and early peripheral retinal neovascularization (Figs. 2, 3). Systemic and laboratory findings did not suggest abnormalities. However, the patient recently revealed she attempted suicide at age 13, taking several of her sister's contraceptive pills. She received hospital treatment with no apparent subsequent complications.

She was now treated with panretinal argon laser photocoagulation, two sessions in the right eye (1985, 1988) and three sessions in the left eye (1985, 1988, 1992). Laser photocoagulation was performed on and around aneurysms until cicatricial closure, without rupture or bleeding of aneurysms [16, 17]. The 1992 photocoagulation session in the left eye included an area of peripheral capillary nonperfusion and early neovascularization. Application parameters were: power = 200 mw, time = 150 ms, size = 200 microns. The optic disk aneurysm in the left eye was left untreated for fear of complications and remains active but without exudates.

In the year 2000, the patient was lost to follow-up, returning in 2012 for complete eye examination, fluorescein angiography and OCT. At that time, visual acuity was 20/20 in the right eye and had improved to 20/100 in the left. Ophthalmoscopy and fluorescein angiography showed cicatricial closure, without staining of treated arterial aneurysms and bilateral resolution of macular stars, fluid and exudates (Fig. 4). The left eye had a noniatrogenic foveal scar, causing the persistently diminished visual acuity. OCT revealed a normal macula in the right eye and a macular scar in the left eye with atrophy of the retinal neuroepithelium, foveal retinal pigment epithelium hyperplasia (Fig. 5), and a still active papillary aneurysm deemed dangerous to treat on site (Fig. 6). However, the peripheral retinal areas of ischemia and neovascularization had regressed. In 2012, the patient was once more lost to follow-up for 4 years, returning in 2016, when a wide-field fluorescein angiography was performed revealing normal vascular perfusion in the right eye (Fig. 7), an inferior and temporal peripheral vasculitis, and an area of inferonasal and peripheral temporal ischemia in the left eye (Fig. 8). In addition, the left optic disk aneurysm appeared to be in involution (Fig. 9). The patient still has a macular
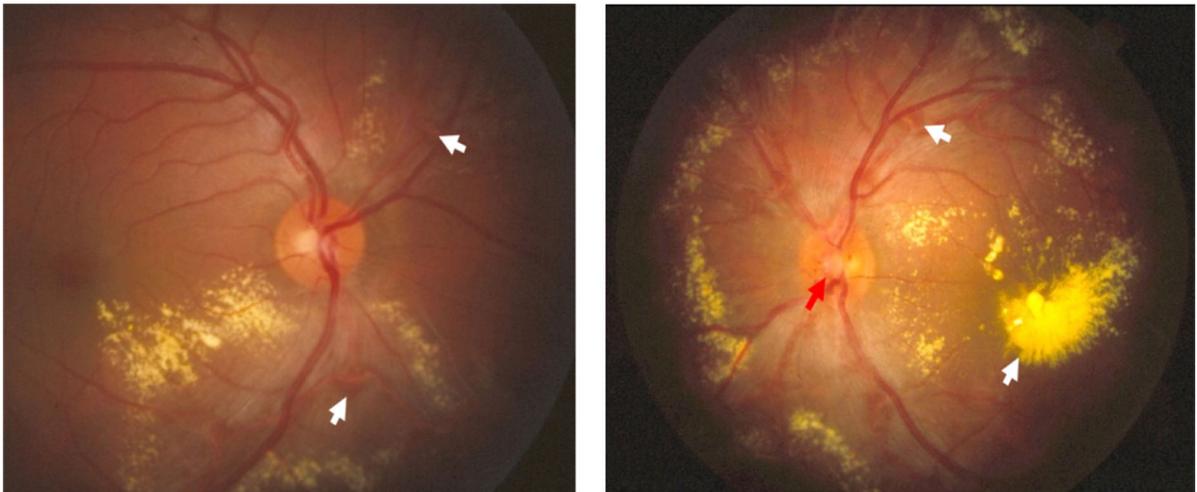
Fig. 1 Retinal aneurysms and neuroretinitis with macular star in both eyes (white arrow). Optic disk aneurysms in left eye (red arrow)
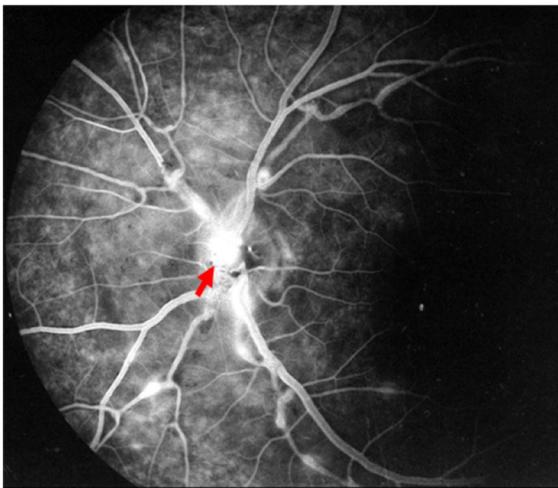

Fig. 2 Fluorescein angiography of left eye. Aneurysms in retina and left optic disk (red arrow)
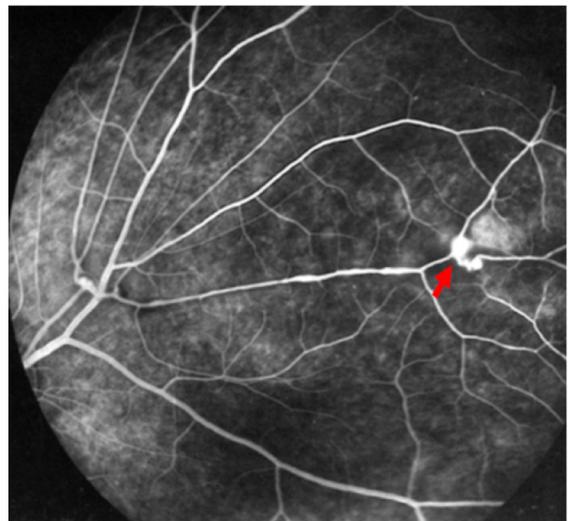

Fig. 3 Fluorescein angiography of left eye. Temporal retinal peripheral ischemia and neovascularization (red arrow)

microperimetry pending and the decision of whether the ischemic peripheral areas and the focal neovascularizations require photocoagulation and/or further observation has not yet been made.

Discussion and summary

In 1985, when the patient was first seen, our diagnosis was a modified Coats disease; then, the diagnosis was modified based on clinical features.

Three major criteria (retinal vasculitis, aneurysmal dilatation at arterial bifurcations and neuroretinitis) and three minor criteria (peripheral capillary nonperfusion, retinal neovascularization and macular exudation) are used to diagnose IRVAN [3–6]. However, the presence of an optic disk aneurysm is pathognomonic [18]. The etiology of this syndrome has not been established [19]. Few other cases have been reported worldwide [9, 16–22]. Differential diagnosis includes a range of inflammatory and infectious vascular diseases; among others, childhood uveitis, Behcet's disease, sarcoidosis, multiple sclerosis, tuberculosis, syphilis and collagen vascular disorders such as polyarteritis nodosa, Wegener granulomatosis and
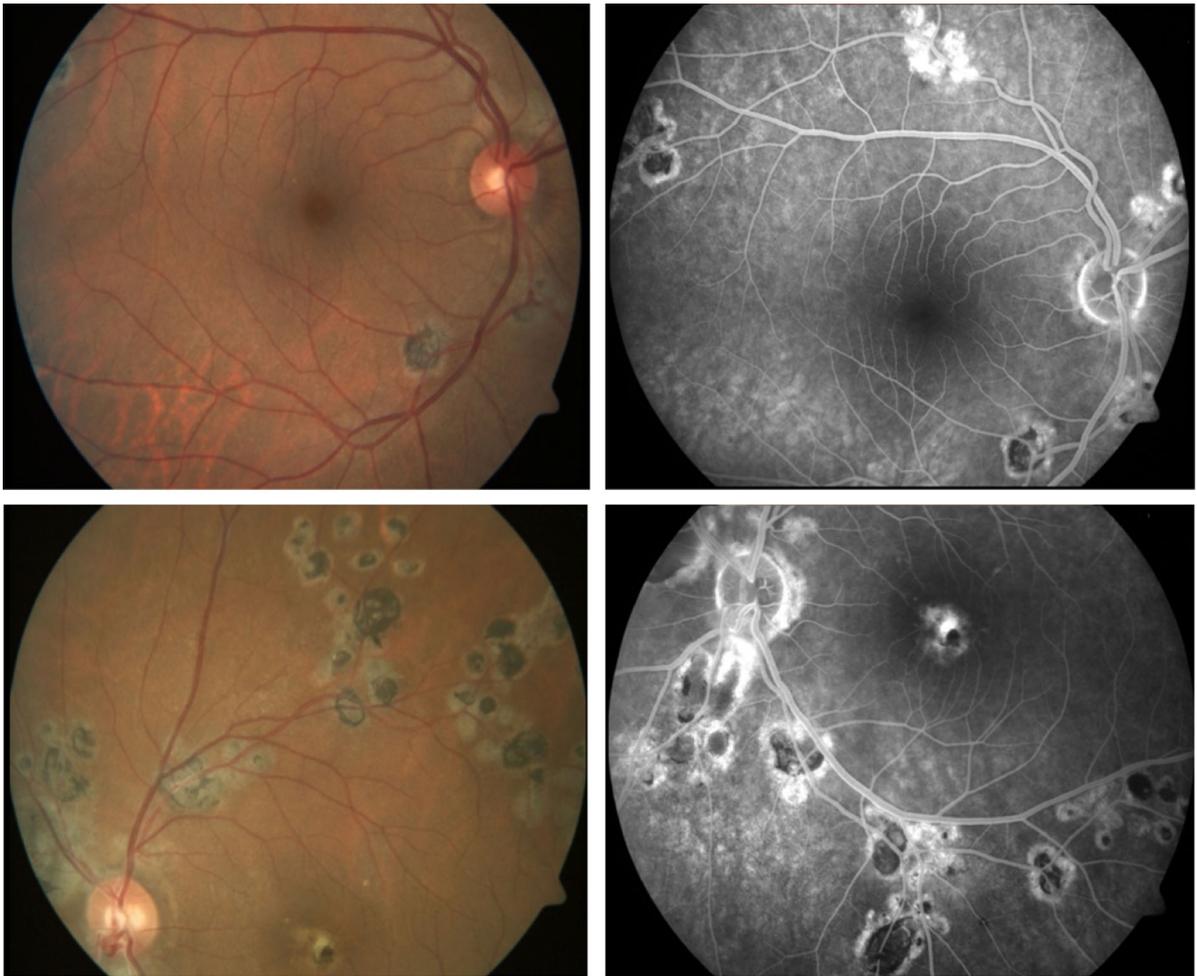
Fig. 4 Post-photocoagulation fluorescein angiography of both eyes with resolution of aneurysms, macular star and peripheral retinal neovascularization
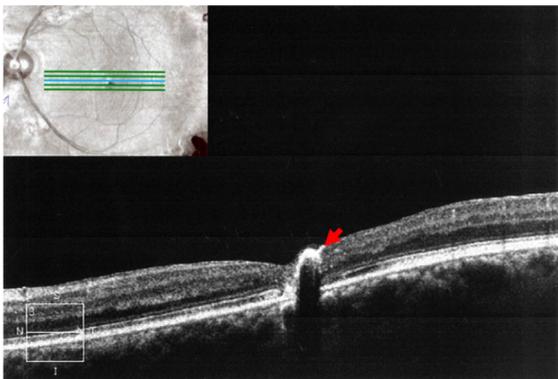

Fig. 5 Left eye: OCT image demonstrated macular scar, atrophy of neuroepithelium and secondary RPE hyperplasia in the fovea (red arrow)
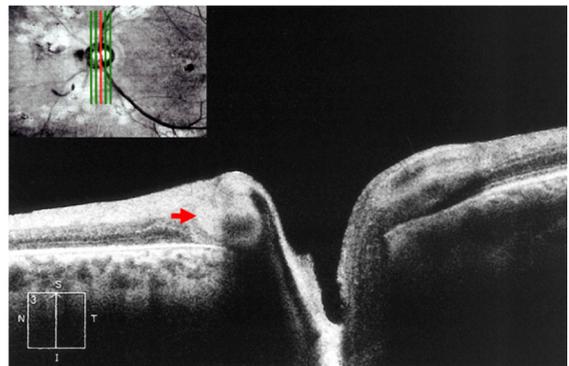

Fig. 6 Left eye. OCT image showing aneurysms in optic disk (red arrow)

systemic lupus erythematosus may also cause neuroretinitis and macroaneurysms. These diseases were not specifically investigated, and immunology testing has not been done except for syphilis and tuberculosis that were negative. The most revealing diagnosis examination is fluorescein angiography, where aneurysms and their leakage are well defined, as are the nonperfusion peripheral and neuroretinitis areas [22].

A new method for abnormalities evaluations at the retinal periphery is wide-field fluorescein

angiography, helpful in recognition, prognosis and therapy at all ages [23–25].

Visual prognosis in IRVAN depends on early diagnosis and treatment of the ischemic retinal disease. Samuel and Chang et al. [6] reported that panretinal laser photocoagulation improved visual outcome and the natural history of the disease, a fact confirmed by others [4–6] and by the bilateral case herein reported as having good anatomic and functional results. This report is a 32-year follow-up of a bilateral syndrome the evolution of which involves several periods to be considered. The first period
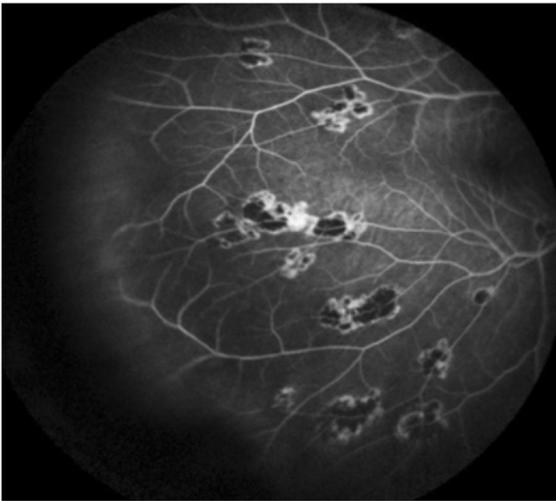

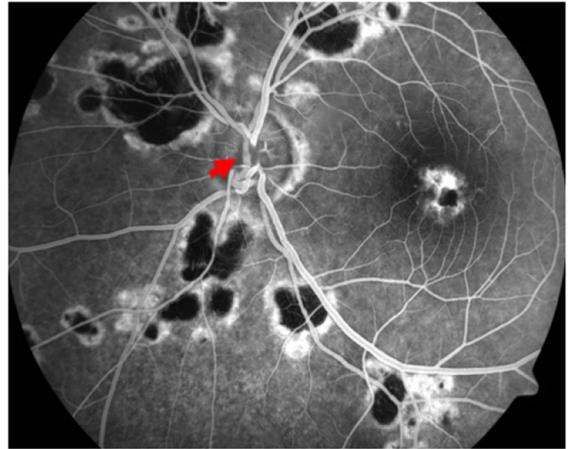Fig. 7 Wide-field angiography of right eye with normal vascular perfusion

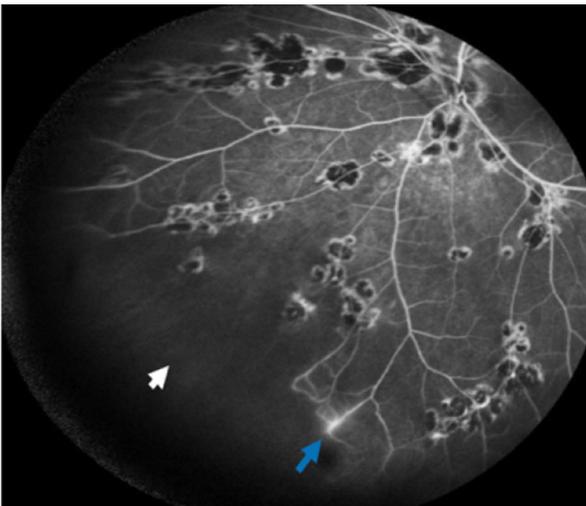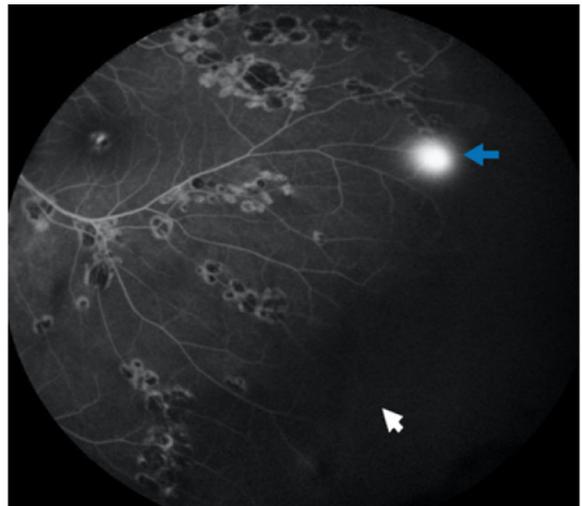Fig. 9 Left optic disk aneurysm involuted (red arrow)

Fig. 8 Post-photocoagulation wide-field angiography of left eye, 31 years later. There are nonperfusion areas (white arrow) and peripheral vasculitis (blue arrow)

(1985–2000) is the recognition, documentation and management of the syndrome with laser photocoagulations of all bilateral macroaneurysms except one located on the left optic disk. The second period comprises those periods during which the patient was lost to follow-up (2000–2011 and 2012–2016) and, upon her return, was re-examined with new current diagnostic techniques: OCT in 2012, multimodal images and wide-field fluorescein angiography in 2016 (Fig. 10) expanding the information on the natural history of the disease. IRVAN syndrome is a rare disease with few cases reported in the literature and a not fully known natural history that requires additional patients, long-term observation, and comparison of photocoagulation results with those of newer modalities of treatment used in other centers.

A review of the literature indicates that panretinal photocoagulation was first performed in IRVAN by
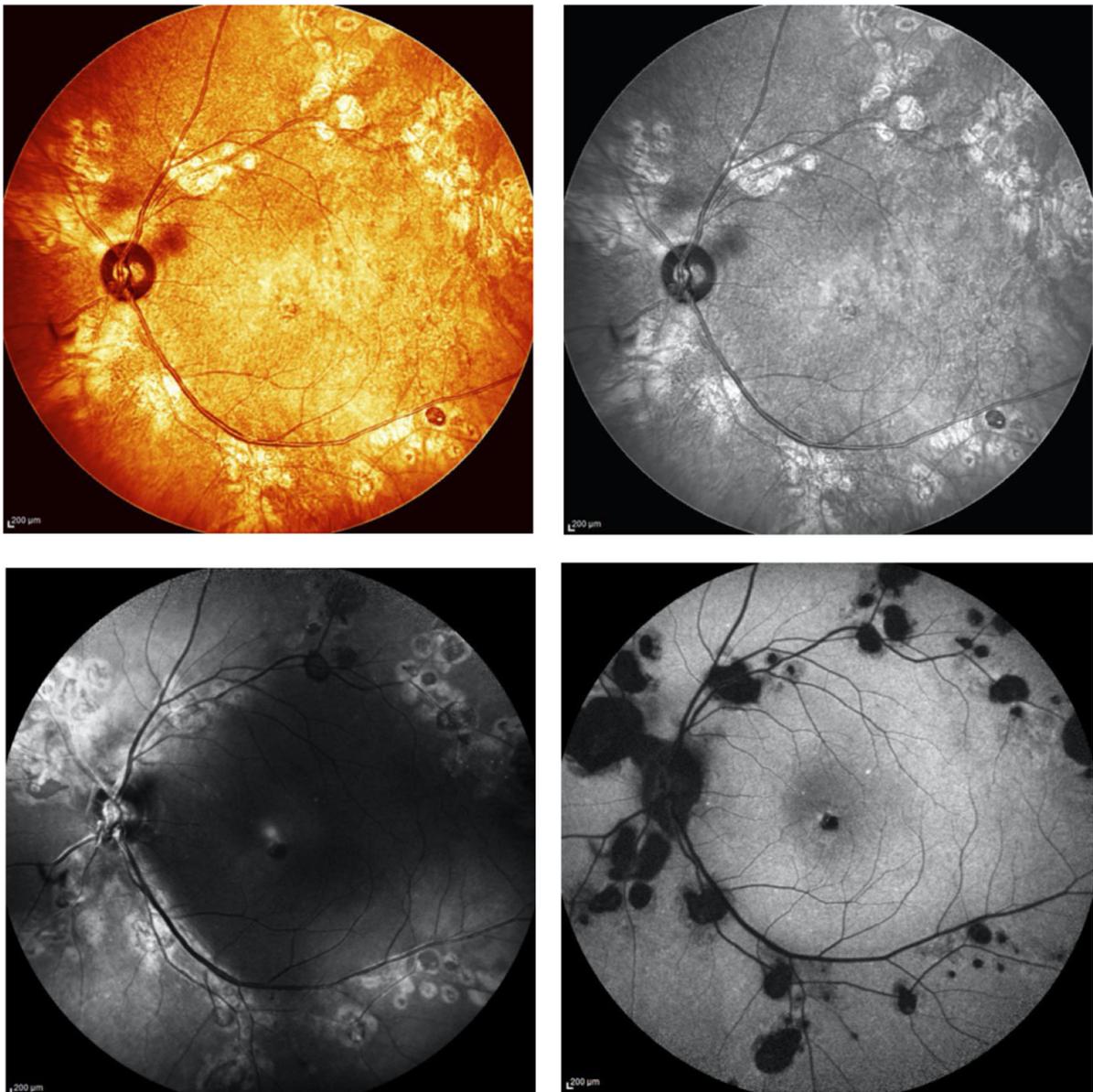

Fig. 10 Multimodal imaging: color infrared, free red infrared, blue reflectance and blue autofluorescence. No major changes are evident except for chorioretinal scarring

Melan in France in 1983. Thus, the fact of having performed, in 1985, bilateral photocoagulation of the retinal aneurysms does make this a pioneer report.

Conclusion

A bilateral case of IRVAN syndrome was recognized in a young woman presenting all characteristic clinical features and observed throughout a long-term follow-up. Treatment with argon laser photocoagulation on and around retinal aneurysms led to their closure, to involution of posterior neuroretinitis and peripheral vasculitis preventing retinal neovascularization. A recent wide-field fluorescein angiography allowed recognition of hidden peripheral pathology, expanding the knowledge of the natural history of the disease.

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Informed consent Other methods of treatment, currently available, can be used for comparison, if required. Written informed consent was obtained from the patient for publication of this bilateral case report and the accompanying images.

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