Int Ophthalmol (2019) 39:1155–1161
https://doi.org/10.1007/s10792-018-0913-3

CASE REPORT

Resolution of arterial aneurysms in idiopathic retinal vasculitis, aneurysms and neuroretinitis: a case report and review of literature

Devesh Kumawat · Vinod Kumar

Received: 17 January 2018 / Accepted: 22 March 2018 / Published online: 28 March 2018

Abstract
Purpose To report a case of resolution of retinal arterial aneurysms in a patient of idiopathic retinal vasculitis, aneurysms and neuroretinitis (IRVAN) treated with oral steroids.
Methods This study contains case report and review of literature.
Results A 16-year-old girl with stage 2 IRVAN was treated with oral steroids alone. Fluorescein angiography confirmed the presence of aneurysms and absence of neovascularization in both eyes. The aneurysms resolved gradually over 4-month follow-up.
Conclusions This case demonstrates previously unreported reversibility of arterial aneurysms with steroid therapy alone in early stages of IRVAN.

Keywords Idiopathic retinal vasculitis, aneurysms and neuroretinitis · Fluorescein angiography · Steroids · Vanishing aneurysms

D. Kumawat · V. Kumar (✉)
Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi 110029, India
e-mail: drvinod_agg@yahoo.com

Introduction

The idiopathic retinal vasculitis, aneurysms and neuroretinitis (IRVAN) is an isolated retinal vascular disease. It is characterized by major features like retinal vasculitis, aneurysmal dilations at arterial bifurcations and neuroretinitis, and minor features like the presence of peripheral capillary non-perfusion, retinal neovascularization and macular exudation [1, 2]. The etiology of IRVAN is, however, not completely understood. The peculiar distribution of disease strongly suggests a migratory inflammatory process involving alternate segments of the vascular tree [3, 4]. The exact cause of inflammation is not known. Possible hypersensitivity to tubercular or fungal antigen has been reported in the literature to trigger the vasculitis [5, 6]. There is no definitive treatment for IRVAN. Depending upon the functional stage of disease, various treatment modalities like corticosteroids, laser photocoagulation, vitrectomy and immunomodulation have been described [2]. Though initially IRVAN was considered to have a benign course, more recent studies have shown worse outcomes especially in the late stages [1]. Disappearance of retinal aneurysms in IRVAN has been reported only in a handful of cases, either spontaneously or following treatment [3–8]. The retinal lesions have been believed to be unresponsive to oral steroids therapy alone in IRVAN despite having an underlying inflammatory etiology [2, 4–7]. Herein, we report

complete resolution of aneurysms in a patient of IRVAN treated with oral steroids alone.

Case report

A 16-year-old girl of Indian origin presented with gradually progressive painless diminution of vision in both eyes over 2 months. Systemic history was non-contributory. The best-corrected visual acuity (BCVA) was 20/120 in right eye and finger counting in left eye. The anterior chamber was unremarkable in both eyes apart from sluggishly reactive pupil in the left eye. A few vitreous cells (< 10/field) were noted in both eyes.

The fundus examination of both eyes revealed disk hyperemia, macular and peri-vascular hard exudates, multiple arteriolar dilatations and retinal hemorrhages

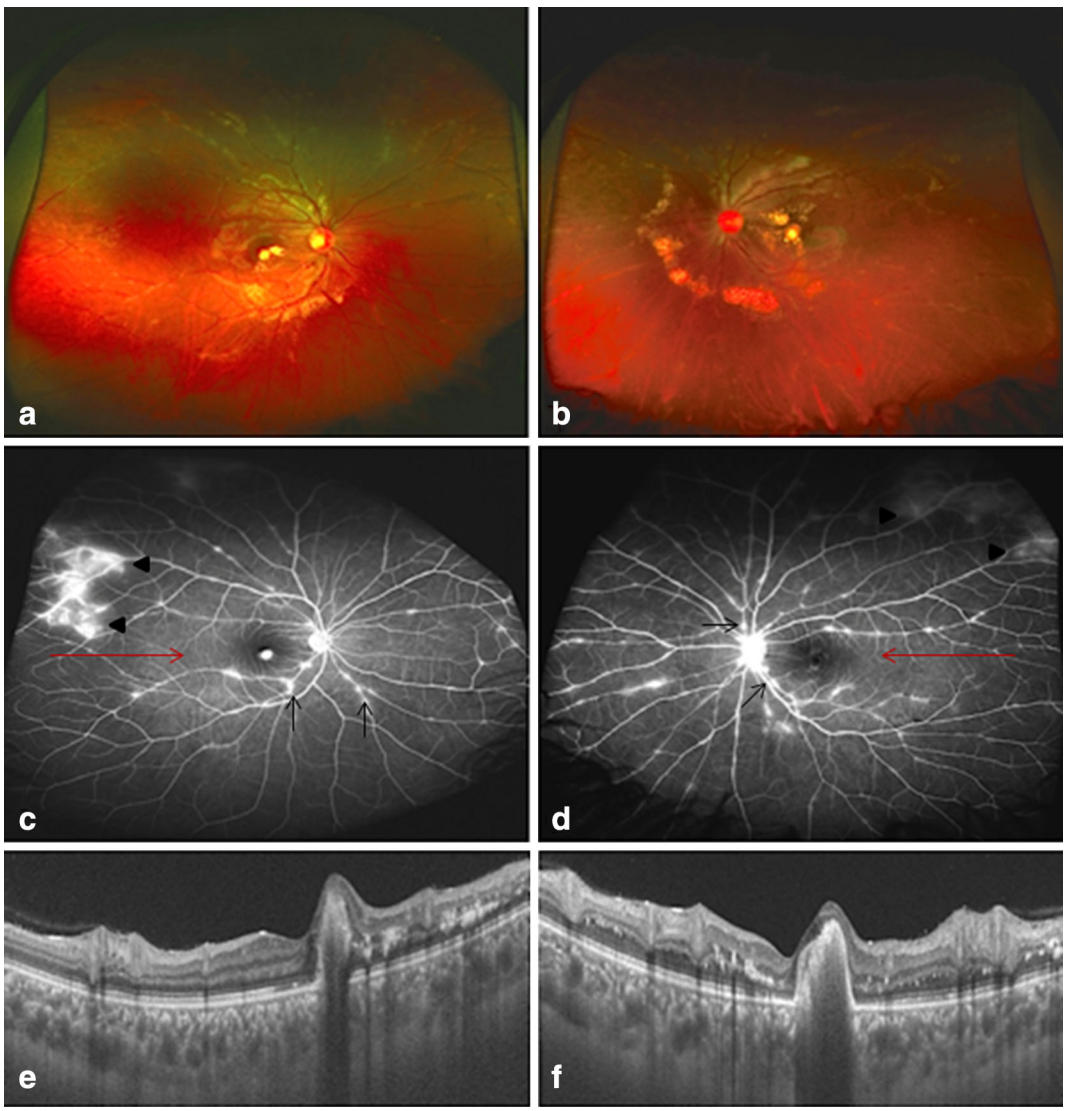

Fig. 1 Ultra-wide field fundus photographs of the right and left eye of a patient with idiopathic retinal vasculitis, aneurysms and neuroretinitis (**a**, **b**). Disk hyperemia, macular hard exudates, peri-vascular exudation and multiple arteriolar aneurysmal dilatations can be seen. Multiple leaking arterial aneurysms are seen near the vascular bifurcations (black arrows) on fundus fluorescein angiogram (**c**, **d**). Capillary non-perfusion areas are seen in the supero-temporal periphery with adjacent peri-vascular leakage (black arrowheads). OCT of the macular area (line scan as per the red arrow in fundus fluorescein angiogram) shows intraretinal exudation with loss of normal foveal architecture (**e**, **f**)

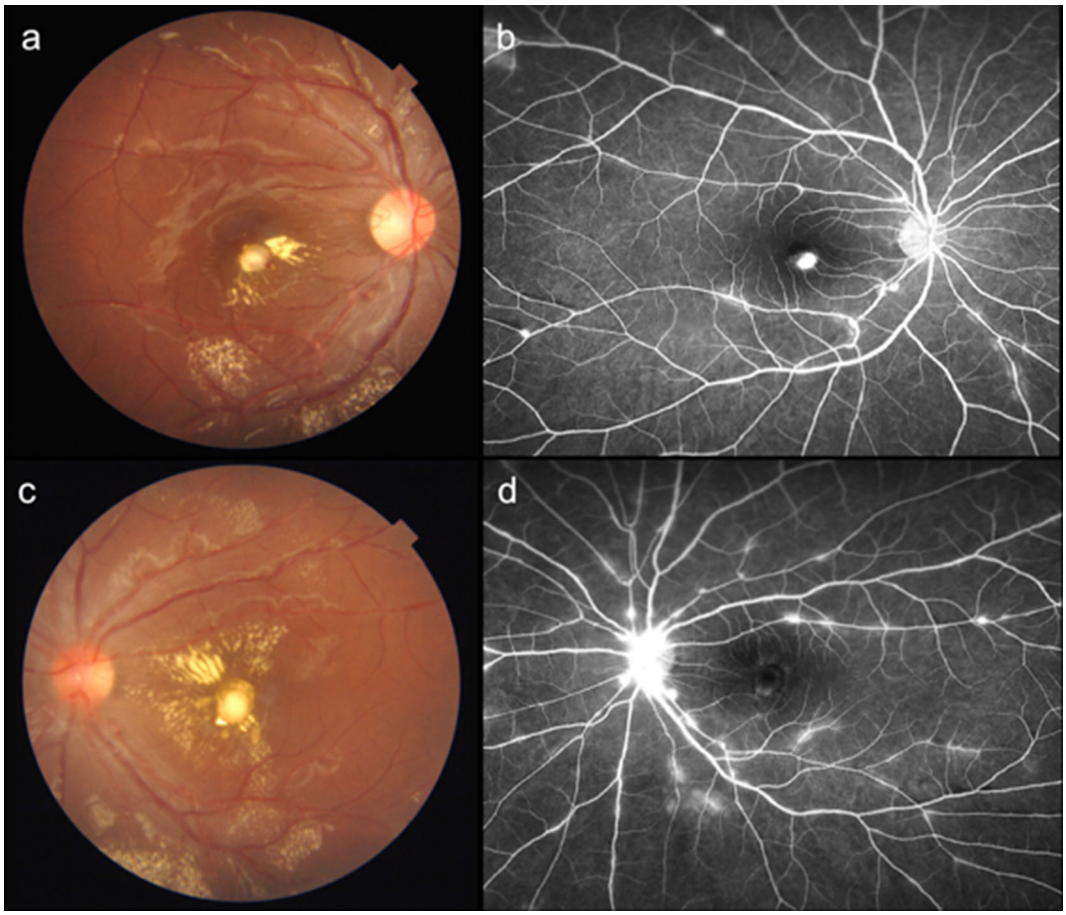

Fig. 2 Standard color fundus photograph of both eyes with prominent disk edema and macular hard exudates (**a**, **c**). Magnified view of the fundus fluorescein angiogram showing prominent arteriolar aneurysms in both eyes (**b**, **d**)

(Figs. 1a, b and 2a, c). The findings were more prominent in the left eye. Ultra-wide field fundus fluorescein angiography (UWF-FFA, Optos Inc) in both eyes was suggestive of multiple leaking arterial aneurysms at or near the vascular bifurcations, capillary non-perfusion (CNP) areas in supero-temporal periphery and adjacent vascular leakage in the absence of neovascularization (Figs. 1c, d, and 2b, d). Swept source optical coherence tomography (OCT) of the macular area in both eyes confirmed severe intraretinal exudation with loss of normal foveal architecture (Fig. 1e, f). The personal and family history was non-contributory.

An extensive systemic evaluation and biochemical workup were performed to determine the etiology. Investigations like complete blood counts, erythrocyte sedimentation rate, serum electrolytes, serum angiotensin converting enzyme levels, tuberculin skin test, contrast-enhanced computed tomography of the chest, urine analysis, serum homocysteine, venereal disease research laboratory (for Treponema), HIV serology, anti-nuclear antibody, anti-double-stranded DNA antibody, anti-phospholipid antibodies and anti-neutrophil cytoplasmic antibody were all negative. Based on these findings, a diagnosis of stage 2 (angiographic evidence of CNP areas) IRVAN syndrome was made in both eyes. The patient was started on oral prednisolone (1 mg/kg body weight) in view of retinal vasculitis. Prophylactic treatment in the form of laser photocoagulation was not performed in view of limited areas of CNP and absence of neovascularization.

At 4 months, there was considerable improvement in both eyes with the decrease in macular exudates,

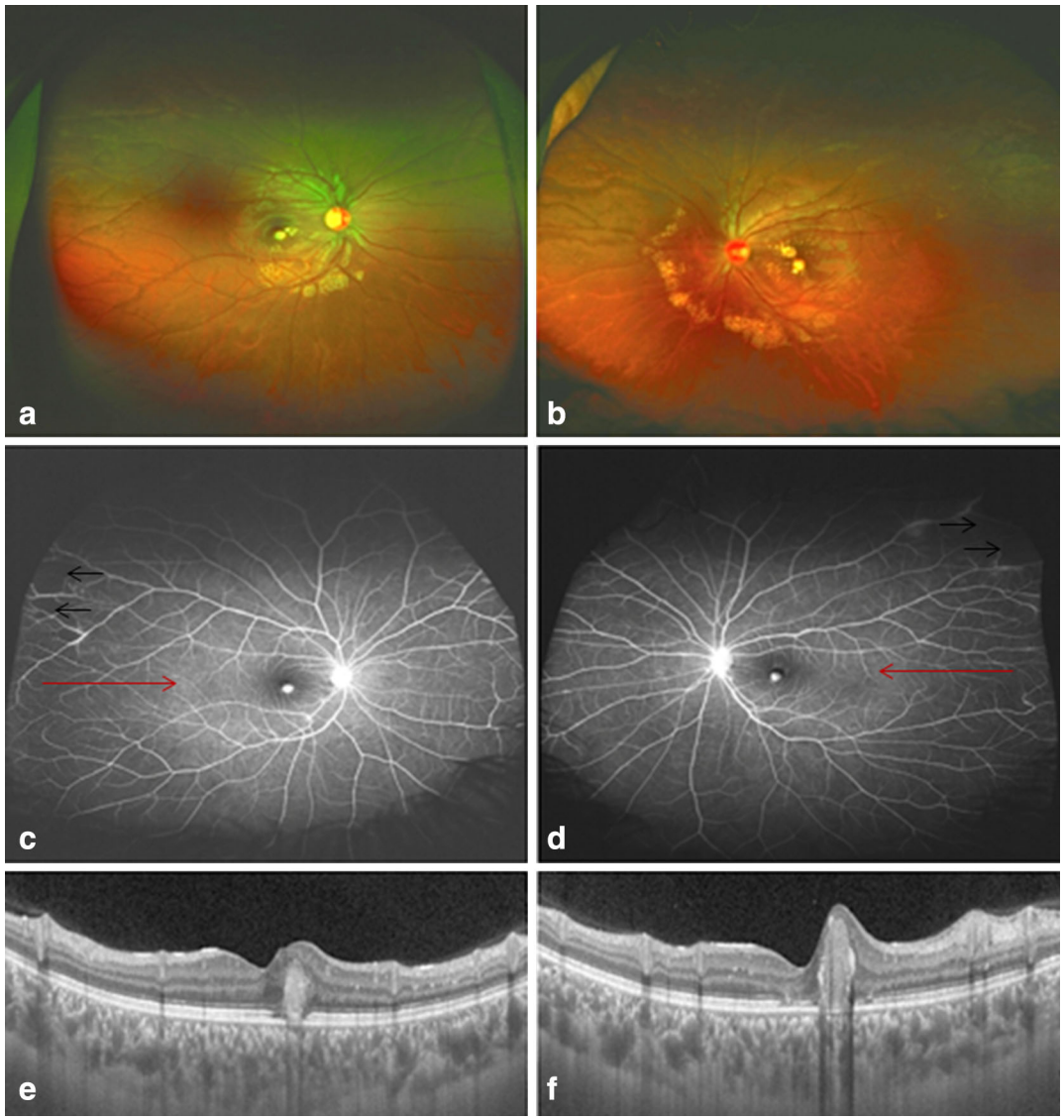

Fig. 3 Ultra-wide field fundus photographs (**a**, **b**) of the right and left eye at 4 months of starting oral steroids. Macular exudates, retinal hemorrhages and peri-vascular exudation have decreased in both eyes. Fundus fluorescein angiogram (**c**, **d**) shows resolution of retinal aneurysms and absence of disk leakage. A few capillary non-perfusion areas are noted in the temporal periphery in both eyes (black arrows). The left eye has minimal peri-vascular leakage in the supero-temporal quadrant (**d**). Macular OCT line scan as per the red arrow in fundus fluorescein angiogram shows a decrease in macular exudation in both eyes (**e**, **f**) with attainment of near normal foveal contour in the right eye (**e**)

retinal hemorrhages and peri-vascular exudation (Fig. 3a, b). The UWF-FFA confirmed the resolution of retinal aneurysms and absence of disk leakage. A few CNP areas were noted in the temporal periphery in both eyes (Fig. 3c, d). The left eye had minimal vascular leakage in the supero-temporal quadrant, while the right eye had no vascular leakage. The foveal architecture was near normal in the right eye but disturbed due to persistent hard exudates and fibrosis in left eye (Fig. 3e, f). Oral steroids were gradually tapered over a total period of 5 months. At 9 months, the BCVA was 20/40 in right eye and 20/400 in left eye. The clinical picture remained unchanged at 16-month follow-up.

Table 1 Review of literature on resolution of arterial aneurysms in idiopathic retinal vasculitis, aneurysms and neuroretinitis

Author, year	Age/sex	Symptom duration	BCVA	Fundus features	Additional features	Treatment	Final outcome	Proposed mechanism
Owens et al. 1992	18 years/F	3 years	20/120 OD, 20/20 OS	OU: multiple aneurysms, exudation, severe peripheral CNP, NVE	None	High-dose steroid and PRP did not resolve aneurysm, PPV in OD on f/u for VH	Aneurysm resolved, OD 20/200 (6 years after PPV)	Reversibility of aneurysms once disease become quiescent
Sashihara et al. 1999	14 years/M	Incidental	20/15 OD, 20/30 OS	OU: multiple aneurysms, extensive vascular occlusion peri-vascular exudation	None	Oral steroid (40 days) not beneficial, scatter laser done	Resolution of aneurysms (4 months post-laser)	Migratory inflammation involving alternate segments of retinal network
Yeshurun et al. 2002	30 years/F	4 months	FC4 months OD 20/60 OS	OU: multiple aneurysms, exudation, disk edema, no retinal ischemia	None	Oral steroids (1 month) did not resolve aneurysm	Extensive dynamics in location and size of aneurysms (6 month)	Migratory inflammation involving alternate segments along the vascular tree, spontaneous regression along the course.
Tomita et al. 2003	36 years/F	2 months	20/40 OD 20/16 OS	OU: multiple aneurysms, peripheral CNP; OD: VH, peripapillary FVP with TRD	None	Oral steroid, PRP f/b PPV OD	20/20 OD, 20/16 OS, Resolution of aneurysms (5 month)	PRP to CNP area is the most important treatment
El-Asrar et al. 2004	16 years/M	1 year	20/60 OD, 20/100 OS	OU: multiple aneurysms, peripapillary and macular exudates, extensive CNP	Asthma, allergic Aspergillus sinusitis	Endoscopic sinus debridement, oral steroid (1 year), scatter laser	Resolution of aneurysms, 20/20 OD, 20/40 OS (3 year)	Immune hypersensitivity to fungal elements trigger retinal vasculitis, surgery/steroid/laser induced resolution
Singh et al. 2016	30 years/F	1 week	20/20 OD, FCCF OS	OS: VH, peripapillary FVP, sheathed vessels—stage 3; OD: peripheral CNP—stage 2	Positive tuberculin skin test, Ghon complex, PCR vitreous positive for MTB	OS: PPV with EL f/b oral steroid (3 months) and four-drug ATT; OD: PRP	OD 20/20, OS 20/40, resolution of aneurysms (6 months)	Hypersensitivity to tubercular Ag, ATT and steroids control inflammation/hypersensitivity and resolve aneurysm
Present case	16 years/F	2 months	20/120 OD, FC1 m OS	OU: multiple aneurysms, exudation, disk edema, CNP areas, no neovascularization	None	Oral steroids (5 months)	Aneurysm resolved, OD 20/40, 20/400 OS (9 months)	Response to steroid therapy alone may be governed by the stage of disease

CNP Capillary non-perfusion, *NVE* neovascularization elsewhere, *PRP* pan-retinal photocoagulation, *PPV* pars plana vitrectomy, *VH* vitreous hemorrhage, *FVP* fibrovascular proliferation, *TRD* tractional retinal detachment, *PCR* polymerase chain reaction, *MTB* Mycobacterium tuberculosis, *EL* endolaser, *ATT* anti-tubercular treatment

Discussion

IRVAN is an uncommonly reported retinal vascular disease characterized by arterial aneurysmal dilatations occurring secondary to vessel wall inflammation and necrosis [1, 3]. This inflammatory process may be activated by immune mediated hypersensitivity reaction to tubercular or fungal antigens [5, 6]. There occurs a possible migratory inflammatory process involving alternate segments along the vascular network. In later stages of the disease, VEGF may play a major role instead of the inflammatory mediators in sustenance of vascular changes.

The treatment of IRVAN depends upon the functional stage of disease [2]. The inflammatory stages (stage 1–2) are treated with oral steroids/immunomodulation, but the treatment is often unrewarding. Stage of vascularization (stage 3) requires laser or cryotherapy to the avascular peripheral retina with or without anti-vascular endothelial growth factor. Early vitrectomy is usually needed for managing complications like vitreous hemorrhage and tractional retinal detachment.

The disappearance of retinal aneurysms in IRVAN has been reported only in a few cases, either spontaneously or following treatment. A summary of all these cases with relevant findings, outcomes and proposed hypothesis is listed in Table 1.

The existing literature does not support the role of steroids in IRVAN as retinal lesions often do not resolve with steroid therapy [2, 4–7]. However, a dramatic response to steroid therapy was seen in our case. Most of the previously reported cases had later stages of disease (stage 3 or beyond). Further steroid therapy was used in all these cases, but it was tapered over a few weeks to months. Our case had stage 2 disease with limited CNP areas which was managed well with a longer course of oral steroid.

We believe that the response to steroid therapy alone may be governed by the stage of disease. In early stages with resolution of inflammation, the strength of arterial wall may be regained which could lead to restoration of contour and resolution of aneurysms. When the disease progresses, control of inflammation with steroid alone may not help as VEGF may be playing a major role in later stages. In these scenarios, the management options left are anti-VEGF agents or laser/cryotherapy to CNP areas. When vessel walls get irreversibly damaged in the advanced stages of disease [3], both steroid and anti-VEGF-directed therapy may not reverse the aneurysmal dilatations.

To conclude, this case demonstrates previously unreported reversibility of arterial aneurysms with steroid therapy alone in early stages of IRVAN.

Authors' contribution Devesh Kumawat involved in acquisition, analysis and interpretation of data; drafting the work; final approval of the version; and agreement to be accountable for all aspects of work. Vinod Kumar gave substantial contributions to the conception/design of work and took part in acquisition, analysis and interpretation of data; drafting the work; final approval of the version; and agreement to be accountable for all aspects of work.

Compliance with ethical standards

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

Ethical approval For this type of study, formal consent is not required.

Informed consent Informed consent was obtained from the participant included in the study.

References

1. Chang TS, Aylward GW, Davis JL, Mieler WF, Oliver GL, Maberley AL et al (1995) Idiopathic retinal vasculitis, aneurysms, and neuro-retinitis. Retinal vasculitis study. Ophthalmology 102:1089–1097
2. Samuel MA, Equi RA, Chang TS, Mieler W, Jampol LM, Hay D et al (2007) Idiopathic retinitis, vasculitis, aneurysms, and neuroretinitis (IRVAN): new observations and a proposed staging system. Ophthalmology 114:1526–1529
3. Yeshurun I, Recillas-Gispert C, Navarro-Lopez P, Arellanes-Garcia L, Cervantes-Coste G (2003) Extensive dynamics in location, shape, and size of aneurysms in a patient with idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN) syndrome. Idiopathic retinal vasculitis, aneurysms, and neuroretinitis. Am J Ophthalmol 135:118–120
4. Sashihara H, Hayashi H, Oshima K (1999) Regression of retinal arterial aneurysms in a case of idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN). Retina 19:250–251
5. Abu El-Asrar AM, Jestaneiah S, Al-Serhani AM (2004) Regression of aneurysmal dilatations in a case of idiopathic retinal vasculitis, aneurysms and neuroretinitis (IRVAN) associated with allergic fungal sinusitis. Eye Lond Engl 18:197–201

6. Singh R, Sharma K, Agarwal A, Dogra M, Gupta V, Sharma A et al (2016) Vanishing retinal arterial aneurysms with antitubercular treatment in a patient presenting with idiopathic retinal vasculitis, aneurysms, and neuroretinitis. J Ophthalmic Inflamm Infect 6:8
7. Owens SL, Gregor ZJ (1992) Vanishing retinal arterial aneurysms: a case report. Br J Ophthalmol 6:637–638
8. Tomita M, Matsubara T, Yamada H, Takahashi K, Nishimura T, Sho K et al (2004) Long term follow up in a case of successfully treated idiopathic retinal vasculitis, aneurysms, and neuroretinitis (IRVAN). Br J Ophthalmol 88:302–303