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CASE REPORT

Combined photodynamic therapy and intravitreal ranibizumab as primary treatment for subretinal neovascular membrane (SRNVM) associated with type 2 idiopathic macular telangiectasia

Pukhraj Rishi · Daraius Shroff · Ekta Rishi

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Abstract
Background To report the efficacy of combination photodynamic therapy and intravitreal ranibizumab for juxtafoveal, subretinal neovascular membrane (SRNVM) associated with type 2 idiopathic macular telangiectasia (IMT).
Methods A 56-year-old woman with visual loss due to SRNVM secondary to IMT underwent primary treatment with a combination of photodynamic therapy (PDT) and intravitreal ranibizumab (0.5 mg). PDT was done as per the TAP study protocol, except that the laser spot size was same as the greatest linear diameter (GLD) of the lesion. This was followed by intravitreal ranibizumab (0.5 mg), 2 days later.
Results At the 16-week follow-up, clinical examination revealed regression of the SRNVM, with no evidence of subretinal fluid, exudates or fresh hemorrhages. Visual acuity improved by 2 Snellen lines (from 6/36 to 6/18). Clinical findings were confirmed on FFA and OCT. At the last follow-up at 9 months, the SRNVM remained quiescent and visual acuity stable. No treatment-related adverse effects were noted.
Conclusion Combination therapy with PDT and intravitreal ranibizumab appears to be efficacious in the treatment of SRNVM associated with proliferative type 2 IMT.

Keywords Subretinal neovascular membrane · Idiopathic macular telangiectasia · Photodynamic therapy · Ranibizumab

The authors have full control of all primary data and they agree to allow Graefe's Archive for Clinical and Experimental Ophthalmology to review their data upon request. There are no funding or other conflicts of interest.

P. Rishi (✉) · D. Shroff · E. Rishi
Sankara Nethralaya, Medical Research Foundation,
18, College Road,
600006 Chennai, Tamil Nadu, India
e-mail: docrishi@yahoo.co.in

D. Shroff
e-mail: daraiuss@hotmail.com

E. Rishi
e-mail: ek_and@yahoo.com

Introduction

Type 2 idiopathic macular telangiectasia (IMT), also known as perifoveal telangiectasia, manifest as bilateral lesions with mildly telangiectatic capillaries. In the proliferative stage, retinal exudation and hemorrhages from subretinal neovascularization causes visual loss [1]. Results of photocoagulation and sub-retinal surgery for subretinal neovascular membrane (SRNVM) associated with IMT have not been good [2, 3]. Photodynamic therapy (Novartis AG, Basel, Switzerland) and intravitreal bevacizumab (Genentech, Inc., South San Francisco, CA, USA) have been used, individually [4, 5] and consecutively [6], for SRNVM secondary to IMT. To the best of our knowledge, no reports exist on the use of ranibizumab (Genentech, Inc.) as monotherapy or as a part of combination therapy in the treatment of proliferative type 2 IMT.

Materials and methods

A 56-year-old woman presented with a complaint of blurring of vision in the right eye over the previous 4 weeks. Her best-corrected visual acuity was 6/36, N36 in the right eye and 6/12, N6 in the left. She had a history of diabetes

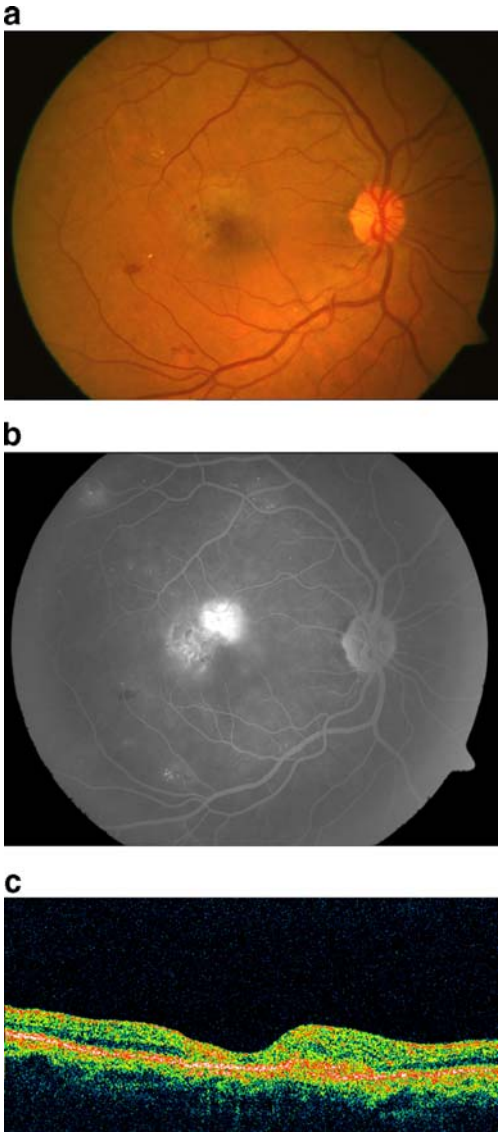

Fig. 1 **a** Color fundus photograph of the right eye reveals areas of increased opacification in the perifoveal retina, with the presence of a right-angled venule and sub-retinal hemorrhage temporal to the fovea, inferior to which is an area of hyperpigmentation. A subretinal neovascular membrane is noted superior to the fovea. **b** Fundus fluorescein angiography (FFA) confirms the presence of a right-angled venule with a classic, juxtafoveal SRNVM seen superior to the fovea. **c** Optical coherence tomography reveals the presence of a SRNVM superior to the fovea in the right eye. Both eyes show hyper-reflective echoes at the inner retinal layers suggestive of IMT

mellitus over the previous 12 years, and was under treatment for the same with a good glycemic control. Biomicroscopic evaluation of the anterior segment was unremarkable in both eyes, except for early cataractous changes. Fundus examination of the right eye revealed areas of increased opacification in the perifoveal retina, with the presence of a right angled venule and sub-retinal hemorrhage temporal to the fovea, inferior to which was an area of hyperpigmentation. A subretinal neovascular membrane (SRNVM) was noted superior to the fovea. A blot hemorrhage was noted temporal to the macula. Fundus examination of the left eye showed an area of opacification in the perifoveal retina, with circinate hard exudates and microneurysms away from the fovea. The fundus picture of both eyes was suggestive of type 2 IMT along with changes of non proliferative diabetic retinopathy (Fig. 1a). Fundus fluorescein angiography confirmed the diagnosis of proliferative Type 2 IMT (early hyperfluorescence with intense late leakage) in the right eye (Fig. 1b). A juxtafoveal SRNVM superior to the fovea with increased retinal thickness was also noted (Fig. 1c). OCT also revealed small hyper-reflective lesions at inner retinal layers with hyporeflective spaces in both eyes, suggestive of IMT. The

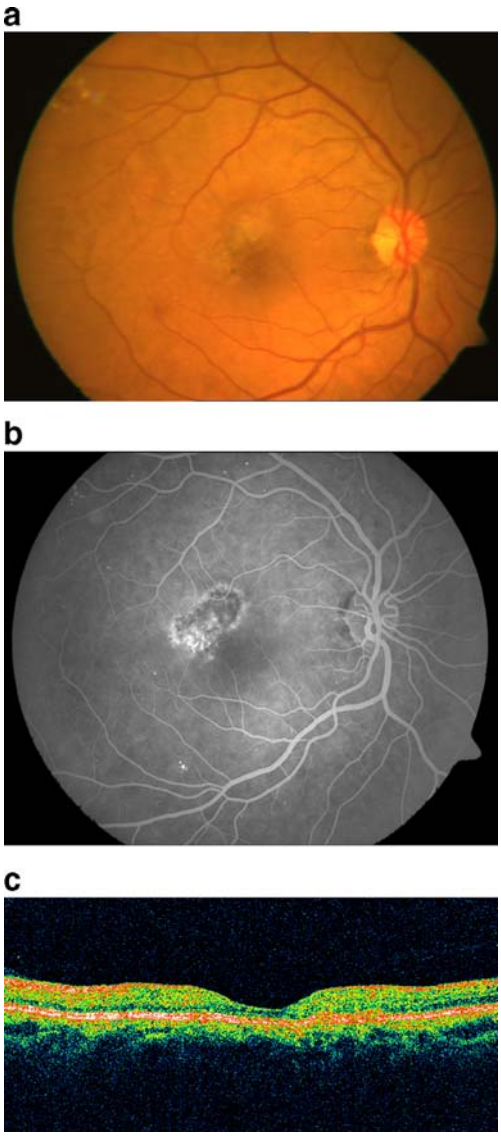

Fig. 2 **a** Color fundus photograph of the right eye at 16 weeks shows a regressed SRNVM with resolving retinal hemorrhages. **b** FFA reveals staining of the SRNVM, with no leakage. **c** Optical coherence tomography reveals the presence of a highly reflective, scarred SRNVM with no sub-retinal fluid (SRF)

patient underwent PDT (as per the TAP study protocol) [7], while keeping the laser spot size (LSS) the same as the greatest linear diameter (GLD) of the lesion. This was followed by intravitreal ranibizumab (0.5 mg), 2 days later.

Results

At the 16-week follow-up, visual acuity in the right eye improved to 6/18, N12. Clinical examination revealed regression of SRNVM, with no evidence of subretinal fluid, exudates or fresh hemorrhage. Clinical findings were confirmed on FFA and OCT (Fig. 2a,b and c). The visual acuity and fundus findings remained stable at the 9-month follow-up.

Discussion

The natural history of untreated SRNVM in IMT is generally poor, with 81% of eyes in a series of 26 eyes having a final visual acuity of 20/200 or worse [8].

Although the neovascular membranes in IMT appear to originate from the retina rather than the choroid, clinically favorable outcomes have been reported after the use of PDT for SRNV in these cases [4]. PDT has been described as resulting in the resolution of leakage from the neovascular membranes [9] and the maintenance of baseline visual acuity in patients with SRNVM secondary to IMT [4]. However, in the interventional case series reported by Potter and co-workers, an average of 2.4 PDT treatments were required for the cessation of leakage after a mean follow-up of 21 months [4]. Hence, retreatments have to be resorted to with this mode of monotherapy. The laser spot size (LSS) for PDT used in our case was kept equal to the greatest linear diameter (GLD) of the lesion, in order to prevent/reduce the risk of RPE atrophy related to PDT use in such cases [10].

Of late, intravitreal bevacizumab, a humanized monoclonal antibody targeted against proangiogenic, circulatory vascular endothelial growth factor (VEGF), has been reported to improve visual outcome and reduce leakage in these cases [5]. Ranibizumab is a FDA-approved monoclonal antibody fragment that targets all VEGF-A isoforms. Based on their respective mechanisms of action, it would seem that ranibizumab would have a better—albeit transient—regressing effect on a SRNVM in IMT than PDT, due to its location above the RPE and the presence of anastomotic retinal vascular connections that could facilitate the concentration of the drug in the SRNVM [5]. However, combined treatment using PDT and bevacizumab has been shown to be effective in improving visual acuity and decreasing retreatment rates in choroidal neovascularization (CNV) associated with AMD. The combined regime is postulated to have a beneficial synergistic effect that could reduce the need for cyclic injections [8, 11]. Even though VEGF inhibition alone could prevent neovascularization at an early developmental stage, once neovascular beds are established they are unlikely to regress with anti-VEGF therapy alone [11]. At this stage, a combined approach using a non-thermal laser has been seen to be beneficial. Since it is still unknown as to which stage a CNVM would become unresponsive to VEGF inhibition alone, combination therapy treatment using PDT and ranibizumab as the first line management in such cases could be a viable option. This approach may also help in defining an optimal treatment end-point.

However, larger studies with longer follow-up are warranted to validate this observation.

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